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Stress in Families of Children with Disabilities

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Abstract

Background: The institution of family is considered essential for the existence of society. Family serves as a shock absorber in times of crisis and stress. Having a child with disability in a family is not the same as having a child without a disability. This study intends to portray the characteristics of families with children with mental retardation. The various forms of stress experienced by these families and their expectations, experiences and limitation are described during the course of the study.

Materials and Method: Parents of Mentally Retarded children from 7 special schools for children with disabilities in the urban limits of Trichy District were chosen for the study. Family Interview for Stress and Coping in Disabilities (FISC-MR) was the tool used for the study.

Results: Fathers reported more stress related to their child's temperament and their relationship to their child. Mothers reported more stress from the personal consequences of parenting. Fathers were more sensitive to the effects of the family environment whereas mothers were more affected by their personal support networks.

Conclusion: The delicate balance of family relationships can be strengthened or broken by the impact of stress felt by the parents of these special children.

Keywords: *Stress, Family, Mental Retardation, Disability.*

Introduction

The institution of family is considered essential for the existence of society. Family serves as a shock absorber in times of crisis and stress. Having a child with disability in a family is not the same as having a child without a disability. Presence of a special child in a family is known to impact families in varied ways. Past research has focused much on the mother and child. We know less about fathers and their role in families with children with disabilities. Mothers are frequently the spokesperson for the family, and hence we do not truly have an individualized family opinion or feeling. Hence fathers need to be specifically included in order to obtain a holistic picture about the experiences of the family ⁽¹⁾.

Parents of children with special needs were chosen for the study. This study intends to portray the characteristics of families with children with mental retardation. The various forms of stress experienced by

these families and their expectations, experiences and limitations are described during the course of the study. Most researchers have found that having a child with a disability increases family stress⁽²⁾. A comprehensive picture of stress experienced or perceived by families caring for children with disabilities and certain key coping resources available for the family which are likely to modify the perceived stress have been studied as part of this research.

⁽³⁾In a study on predictors of distress and well-being in parents of young children with developmental delays and disabilities: the importance of parent perceptions found that moving from family-centered to child-centered models of service delivery can be stressful for parents as their young children with developmental delays and disabilities transition into school. The results of this study highlight not only the importance of including positive as well as negative outcomes in research with

parents but also the importance of including parent characteristics such as coping strategies (e.g. reframing and empowerment/self-efficacy) as potential predictors of outcome in such studies.

Poorer emotional well-being contributed to higher stress and was more frequent among mothers, single parents and those whose children had behavior problems. Having other dependents living at home and more sources of informal support improved the emotional wellbeing of parents but not their stress or family functioning.⁽⁴⁾ One research study⁽⁵⁾ identified that parenting a child with an intellectual disability is not always a negative role; it is a role that parents find both rewarding and empowering. Yet high levels of parent stress, illness, anxiety, and depression are apparent as found out by⁽⁶⁾.

⁽⁷⁾Feelings of loss in parents of children with infantile cerebral palsy was studied. These parents experience stress in the first stage of the diagnosis and when the severity of the cerebral palsy is greater. Emotional intervention on the part of health care providers is needed to aid parents in facing the various obstacles encountered throughout their child's up-bringing.

A study of this kind will enable counselors, therapists and rehabilitation professionals who work with the parents of special children understand the variety of emotional reactions experienced by parents and help in developing and strengthening innovative psychosocial models of treatment. This study will ultimately help towards a better understanding of parent's unique concerns, problems and feelings.

Materials and Method

Aim of the Study:

- 1 The general aim of this study is to assess the psychosocial implications faced by families of children with disabilities.
- 2 To describe the socio-demographic background of parents with children with disabilities.
- 3 To assess the stress experienced by such families.

Families (mothers and fathers) of children with special needs were chosen as the universe for this study. This study was conducted on all the 7 Special Schools for Children with Disabilities located within the Trichy city limits a town in the state of Tamil Nadu, South India. Due to the limited size of the sample all the families

(500), which include 500 mothers and 500 fathers, were taken for the study. Hence the census method has been adopted.

The initial data collection was done with a self-prepared Socio-Demographic Schedule. Family Interview for Stress and Coping in Disabilities (FISC -- MR): This tool is a semi-structured interview schedule developed by Dr. Sathish Chandra Girimaji et.al., 1999 at NIMAHNS, Bangalore to evaluate stress and its mediators in the families of children with Mentally Retardation. It attempts to systematically elicit and quantify (i) the stress experience (perceived) by families caring for a child with disabilities and (ii) certain key coping strategies specific to disability employed by the families that are likely to modify the perceived stress (mediators). Scoring: FISC-MR has 2 major sections: Section-I has 4 areas and a total of 11 sub-scales, whereas Section-II has 5 areas and a total of 9 sub-scales.

A consent for the purpose of study was obtained from the parents. The tool was administered to the sample of 1000 respondents (500 mothers and 500 fathers. After briefing they were administered the questionnaires. Item wise explanation was given in the vernacular. The responses to the scales were scored with the help of the standardized scoring key to obtain an overall index for all the scales. The data thus collected was analyzed using the SPSS package.

Results and Discussion

Fathers and mother's perception of stress remains almost the same with a high of 50.6% and 48%. Mothers experience more stress in family care than fathers. A Study ⁽⁸⁾ compared mother and father's perception of the effect of young children with and without disabilities and mothers reported more stress than did fathers. The burden of child care generally falls on the shoulders of the mother who happens to spend more time with the special child. ⁽⁹⁾ Fathers reported more stress related to their child's temperament and their relationship to their child. Mothers reported more stress from the personal consequences of parenting. Fathers were more sensitive to the effects of the family environment whereas mothers were more affected by their personal support networks.

There is significant difference between nuclear and joint families with regard to the various dimensions of stress like family care, social stress and overall stress. Though the size of the family does not have an impact

on stress yet it is found that nuclear families experience a slight more stress than joint families. ⁽¹⁰⁾ Results of a study on parental stress showed a higher level of stability in parental stress and a modest degree of consistency over time in family functioning in families of children with disabilities. ⁽¹¹⁾ One study has also reported that parents living in joint or extended families face greater extra demands, career adjustments, mental worries, emotional reactions and strained relationships.

Parents from urban families experience more stress and greater emotional reactions than parents from rural families. This could be because of the busier style of living and more challenges faced by parents in urban areas than rural areas. ⁽¹¹⁾ Urban parents experience more social and financial stress than rural parents. This could be because of the greater awareness of the condition of disabilities among urban parents and the social stigma attached thereof.

Whether the child is a boy or a girl, there is no significant difference in terms of stress experienced by parents. This finding is aptly supported by one more finding⁽¹²⁾ that family stress was not affected by the sex of the mentally retarded child. A study focused to examine the relationship between child characteristics and stress reported by mothers. There was no significant difference between amount of stress reported by mothers of boys and girls ⁽¹³⁾.

The degree of impact, frustration, or disappointment does not correlate directly with the degree of deficiency. There is no significance between the level of retardation and stress.⁽¹⁴⁾ A study assessed the quantity of stress in mothers of children with disabilities of different

etiologies. The degree of the children’s disabilities as well as conspicuous behavior correlated positively with maternal stress. There was a positive relation between the level of disability and the total family stress and its components ⁽¹²⁾. But in most studies, the severity and nature of the child’s intellectual as against physical impairments on behavior problems seem to be unrelated to reported levels of stress ⁽¹⁵⁾

Several researchers have compared stress in parents of children with disabilities to that reported by other parents. Studies have been fairly consistent in finding normative levels of levels of stress reported during the infancy period ⁽¹⁶⁾, followed by increasing stress levels during early childhood ⁽¹⁷⁾, and high stress levels during middle childhood ⁽¹⁸⁾. Middle childhood appears to be a particularly vulnerable time for parents of children with disabilities; stress levels are higher than at any other childhood phase ⁽¹⁹⁾. Middle childhood may be a particularly vulnerable period for parents because they expect children’s behaviors to be better regulated than in earlier years.

Table 1: clearly indicates that there is a negative correlation between income and social stress and family size and social stress for fathers. When there is more income, social stress decreases. When the size of the family increases social stress decreases. But when the age of the child increases financial stress also increases. As children grow older, the demand for caring also increases. Therefore, as the age of the child increases financial stress also increases. There is also a negative correlation between income and family care, the age of the mother and age of the child with regard to social and financial stress.

Table 1: Karl Pearson’s Correlation between Dimensions of Stress and Demographic Variables

S. No	Dimensions of Stress	Age		Income		Family Size		Age of Child	
		Father	Mother	Father	Mother	Father	Mother	Father	Mother
1	Family Care	-0.20	0.083	0.064	-0.154**	-0.029	-0.111**	0.000	-0.065
2	Family Emotional Stress	-0.016	-0.067	0.049	-0.005	0.050	-0.196**	0.003	-0.071
3	Social Stress	-0.047	-0.120**	-0.149**	-0.048	-0.101*	-0.271**	-0.024	-0.220**
4	Finance Stress	0.058	-0.161**	0.046	-0.046	-0.073	-0.190**	0.097*	-0.185**
5	Overall Stress	-0.025	0.011	0.034	-0.119**	-0.061	-0.292**	0.022	-0.184*

Hauser-Cram et al. (2001) Both mothers and fathers had increasing levels of stress related to their child with a disability from the early through middle childhood years, fathers showed greater increases in

stress than mothers during the early childhood period ⁽²⁰⁾ In addition, increasing patterns of stress were found for mothers with less helpful social support networks and for fathers with fewer problem-focused coping skills.

In a study (21) eighty- two (82) Israeli families. Results indicated that when the number of children in the family was smaller, they reported being more stressed by the child’s disability. With regard to mothers, there is a negative correlation between the family size and the various dimensions of stress. It is evident that when the family size increases the overall stress decreases.

The inter correlation (Table 2) was done to find out the relationship between the various dimensions of stress for both parents. The inter correlation matrix between

the various dimensions of stress clearly indicates a significant positive and negative correlation between the parameters and overall effect of stress. There is a significant positive correlation between social stress, and overall stress for mothers. But there is a significant negative correlation between family emotional stress and financial stress. Fathers experience a significant positive correlation between family care and family emotional stress and overall stress. It is evident that both fathers and mothers feel that when family cares increase family emotional stress and social stress, also increase.

Table 2: Inter Correlation Matrix between Various Dimensions of Stress for Both Parents

Various Dimensions of Stress		Family Care		Family Emotional Stress		Social Stress		Financial Stress		Overall	
		Mother	Father	Mother	Father	Mother	Father	Mother	Father	Mother	Father
Family Care	Mother	1.000									
	Father	0.056	1.000								
Family Emotional Stress	Mother	-0.318**	-0.005	1.000							
	Father	-0.024	0.143**	0.050	1.000						
Social Stress	Mother	0.129*	-0.018	-0.008	-0.019	1.000					
	Father	-0.003	0.068	0.032	0.238**	0.064	1.000				
Finance Stress	Mother	-0.095*	-0.001	-0.012	0.010	-0.047	-0.009	1.000			
	Father	0.046	0.004	0.025	0.112*	0.015	0.275**	-0.018	1.000		
Overall Stress	Mother	0.678**	0.036	0.290**	0.003	0.498**	0.039	0.212**	0.236**	1.000	
	Father	0.029	0.687**	0.037	0.688**	0.003	0.541**	-0.002	0.350**	0.046	1.000

There are many times when the raising of children is absolutely exasperating particularly with a special child. This research clearly points to the importance of the family system in promoting positive development of children with developmental disabilities, their mothers and fathers. The delicate balance of family relationships can be strengthened or broken by the impact of stress felt by the parents of these special children. It is therefore essential that such investigations be undertaken because families of children with developmental disabilities, like all families, deserve to be nurtured in ways that will optimize their functioning and ultimately help special children lead meaningful lives.

Ethical Clearance: This study was undertaken with the consent from the participating families. The parents of children with disabilities were the main respondents for the study. The institutional research and review body explicitly approved the conduct of this research.

Source of Funding: Self

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Reference

1. Seligman M, Darling RB. Ordinary families, special children: A systems approach to childhood disability. Guilford Publications; 1989.
2. Beckman-Bell P. Child-related stress in families of handicapped children. Topics in Early Childhood Special Education. 1981 Oct;1(3):45-53.
3. Minnes P, Perry A, Weiss JA. Predictors of distress and well-being in parents of young children with developmental delays and disabilities: the importance of parent perceptions. Journal of Intellectual Disability Research. 2015 Jun;59(6):551-60.
4. Samadi SA, McConkey R, Bunting B. Parental

- wellbeing of Iranian families with children who have developmental disabilities. *Research in developmental disabilities*. 2014 Jul 1;35(7):1639-47.
5. Willingham-Storr GL. Parental experiences of caring for a child with intellectual disabilities: A UK perspective. *Journal of Intellectual Disabilities*. 2014 Jun;18(2):146-58.
 6. Dykens EM. Family adjustment and interventions in neurodevelopmental disorders. *Current opinion in psychiatry*. 2015 Mar;28(2):121.
 7. Fernández-Alcántara M, García-Caro MP, Laynez-Rubio C, Pérez-Marfil MN, Martí-García C, Benítez-Feliponi Á, Berrocal-Castellano M, Cruz-Quintana F. Feelings of loss in parents of children with infantile cerebral palsy. *Disability and health journal*. 2015 Jan 1;8(1):93-101.
 8. Beckman PJ. Comparison of mothers' and fathers' perceptions of the effect of young children with and without disabilities. *American journal on mental retardation*. 1991 Mar 95(5) : 585 – 595
 9. Krauss MW. Child-related and parenting stress: Similarities and differences between mothers and fathers of children with disabilities. *American journal on mental retardation*. 1993 Jan 97 (4): 393-404
 10. Dyson LL. Response to the presence of a child with disabilities: parental stress and family functioning over time. *American journal on mental retardation*. 1993 Sep. 98 (2) : 207 – 218.
 11. Peshawaria R, Menon DK, Ganguly R, Roy S, Pillay RP, Gupta A. understanding Indian families having persons with mental retardation. Secunderabad NIMH. 1995.
 12. Shamugavelagutham, K. Mentally retarded children and their families – Challenges ahead. Mittal Publications, New Delhi, India (1999).
 13. Beckman PJ. Influence of selected child characteristics on stress in families of handicapped infants. *American journal of mental deficiency*. 1983 Sep 88 (2): 150 – 156
 14. Gosch A. Maternal stress among mothers of children with Williams-Beuren syndrome, Down's syndrome and mental retardation of non-syndromal etiology in comparison to mothers of non-disabled children. *Zeitschrift fur Kinder- und Jugendpsychiatrie und Psychotherapie*. 2001 Nov;29(4):285-95.
 15. Wikler L, Wasow M, Hatfield E. Chronic sorrow revisited: Parent vs. professional depiction of the adjustment of parents of mentally retarded children. *American Journal of Orthopsychiatry*. 1981 Jan;51(1):63.
 16. Shonkoff JP, Hauser-Cram P, Krauss MW, Upshur CC. Development of infants with disabilities and their families: Monographs of the Society for Research in Child Development 1992.
 17. Innocenti MS, Huh K, Boyce GC. Families of children with disabilities: Normative data and other considerations on parenting stress. *Topics in Early Childhood Special Education*. 1992 Oct; 12(3):403-27.
 18. Warfield ME, Krauss MW, Hauser-Cram P, Upshur CC, Shonkoff JP. Adaptation during early childhood among mothers of children with disabilities. *Journal of Developmental and Behavioral Pediatrics*. 1999 Feb.
 19. Orr RR, Cameron SJ, Dobson LA, Day DM. Age-related changes in stress experienced by families with a child who has developmental delays. *Mental Retardation*. 1993 Jun 1;31(3):171.
 20. Leyser Y, Dekel G. Perceived stress and adjustment in religious Jewish families with a child who is disabled. *The Journal of psychology*. 1991 Jul 1;125(4):427-38.

Physical Activity Measurement Using Accelerometer in Phase-I Cardiac Rehabilitation

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Abstract

Background: Cardiovascular disease (CVD) is the leading cause of death and disability worldwide. Cardiac rehabilitation (CR) is important in improving cardiovascular fitness. Estimating physical activity (PA) levels and Energy Expenditure (EE) in Phase-I CR using Accelerometer can help in understanding cardiovascular fitness better.

Method and materials: PA of 16 participants post Coronary Artery Bypass Graft (CABG) and Percutaneous Transluminal Coronary Angioplasty (PTCA) in Phase-I CR was measured using Actigraph accelerometer. Metabolic Equivalents (METs) and average of daily EE (in Kcals) and steps taken were calculated. Correlation of the Six minute walk distance (6MWD) on the day of discharge and PA levels measured by Actigraph accelerometer was done.

Results: PA energy expenditure averaged 283.71 Kcals/3days, step counts/day 4861.50, METs 5.79 and the EE in light and moderate intensity activities were 1.01 Kcals and 5.72 Kcals respectively. The time spent in these activities were 62.25 minutes in light intensity and 2 minutes in moderate intensity activities.

Conclusion: PA measured by Actigraph accelerometer was of low to moderate levels in Phase-I CR. There was a weak correlation between PA levels measured by Actigraph accelerometer and 6MWD achieved at the time of discharge.

Keywords: Cardiovascular disease, Phase I Cardiac rehabilitation, Physical activity, Accelerometer.

Introduction

Cardiovascular disease is the leading cause of death and disability worldwide. In 2015, out of 17.7 million CVD deaths, 7.4 million occurred due to coronary heart disease.⁽¹⁾ With increasing urbanization and sedentary lifestyles, prevalence of Coronary Artery Disease (CAD)

being doubled in rural areas (3-4%) and quadrupled in urban areas (9-11%) in the past 4 decades in India.⁽²⁾ Increased risk factor prevalence and lack of preventive approaches have been primary factors in the currently accelerating CVD epidemic in India. The magnitude of CVDs continues to accelerate world-wide, increasing the demands for increased awareness and stronger and more specific prevention and cost-effective management.

Physical inactivity is the 4th leading risk factor for mortality and is an independent risk factor for CAD. In adults, participation in 150 minutes of moderate PA each week is estimated to reduce the risk of CAD by approximately 30%.⁽¹⁾ PA increases functional capacity and reduces the risk of re-hospitalization of cardiac

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patients, and improves the prognosis and quality of life of patients with CAD.⁽³⁾ Meta-analysis of clinical trials have proved that exercise based CR reduces the mortality rates of CAD patients.⁽⁴⁾ Benefits of exercise based CR program are now largely demonstrated resulting in 30% decreased mortality.⁽⁵⁾

The World Health Organization has defined “CR as the sum of activities required to favorably influence the underlying cause of the disease, as well as the best possible physical, mental, and social conditions, so that they may, by their own efforts, preserve or resume, as normal a place as possible in the society.”⁽⁶⁾ CR mainly consists of 4 phases. The Phase-1 is the acute phase and involves the hospitalized period of the patient following acute MI, Phase-2 is the convalescent stage which is the immediate post-discharge period, Phase-3 is the training phase of supervised structured outpatient CR program and Phase-4 is the long-term maintenance program.^(7,8)

Physical fitness has been defined as “a set of attributes that people have or achieve that relates to the ability to perform PA”.⁽⁹⁾ Therefore, to detect changes in this variable it is important to accurately measure PA. The ability to measure PA behavior is useful, not only to understand the association between PA and health but also for many other reasons, such as to monitor trends in behavior and to evaluate the effectiveness of interventions and programs. Currently, the most widely used research method for measuring PA don't yield objective data.⁽¹⁰⁾

In CR, PA is routinely measured either subjectively or objectively. Subjective measurements of PA have their own limitations, therefore, measurement of PA with motion sensors such as Triaxial Actigraph accelerometer provide objective quantification. Accelerometers are electronic sensors capable of measuring and storing measurements of the intensity, frequency, pattern, and duration of activity.⁽¹¹⁾ Triaxial accelerometers show good correlation between accelerometer output and EE measured by doubly labeled water.⁽¹²⁾

Inter and Intra instrument reliability of Actigraph accelerometer has been found to be good and the use of this device has been validated in CR.⁽¹³⁾ Even though the accelerometer is gaining popularity in PA measurement, there is a dearth of studies in India regarding the use of accelerometers for estimating the PA levels and EE in Phase-I CR, therefore, the aim of this study is to identify objective data for estimating PA levels in Phase-I CR.

Materials and Method

An observational study, with convenience sampling was carried out on 16 patients, who had undergone CABG and PTCA and were referred for Phase I CR.

44 participants were screened for the inclusion and exclusion criteria, of which 16 (9 CABG and 7 PTCA) met the inclusion criteria.

Inclusion and Exclusion Criteria: Patients included were CAD subjects with low to moderate risk⁽¹⁴⁾ immediate post-PTCA and post CABG. Patients were excluded for the following reasons:

1. Patients at high risk. Patient on prolonged mechanical ventilation for more than 48 hours after the medical/surgical intervention or episode of CAD
2. Orthopedic and neurological conditions which prevent participation in exercise
3. Individuals who were not ready to wear accelerometer.

All patients underwent structured Phase-I CR program in the hospital till discharge which comprised of 5 steps. The total length of stay for CABG and PTCA on an average was 4 days and 2 days respectively.

Actigraph accelerometer was given to the patient to be worn on the wrist for 24 hours till discharge. 24 hours PA (excluding bathing and sleeping) was recorded using the accelerometer. EE in kilocalories and MET's were interpreted with the accelerometer at the end of the day.

According to the American Thoracic Society guidelines, prior to discharge, a submaximal stress test was performed by all the patients using the 6MWT, and MET's achieved in the test were recorded on the Actigraph accelerometer.⁽¹⁵⁾

Statistical Analysis: Data were analyzed using SPSS version 15. Descriptive analysis was used to estimate the patient characteristics included in the study, the median and IQR of total Energy expenditure (KCals) till the day of discharge and the median and IQR value of average MET's till the day of discharge. Pearson's correlation coefficient was used to determine the correlation between METs measured by Actigraph accelerometer during six-minute walk test (6MWT) and the distance covered during the 6MWT.

Results

The mean age of participants with the anthropometric measurements in (years) was 56.43±10.93 SD, mean weight in (kg) of the participants was 65.56±13.41 SD and the mean BMI (kg/m²) was 23.32±4.94 SD. The clinical characteristics of the included participants were, Hypertension (n=7); Diabetes mellitus (n=5); Obesity (n=1) and HTN+DM (n=3). Out of 16 participants, 10 were males and 6 were females. Descriptive statistics were used to determine the median and interquartile range values of measurement of the amount of PA and is represented in Table 1.

Table 1. Measurement of PA level using Actigraph accelerometer during Phase-I CR

Parameter	Median (IQR)
Energy expenditure (Kcals)	283.71 (167.25 - 628.87)
Step counts/day	4861.50 (3484.25 – 6933.75)
METs	5.79 (4.69 - 7.27)
Time (minutes)	148.5 (115.0 – 310.25)

The amount of PA and the time spent in light and moderate PA are presented in Table 5. The EE and the time spent in light intensity activity (PA corresponding to < 3 METs); moderate intensity activity (PA corresponding to 3-6 METs); vigorous intensity activities (PA corresponding to >6 METs) are given in table 2.

Table 2. The duration and intensity of PA measured by Actigraph accelerometer in phase I CR

Physical activity	Intensity of PA in Kcals Median (IQR)	Time spent (min) Median (IQR)
Light	1.013 (58.54 -2.011)	62.25 (30.07-1.023)
Moderate	5.727 (0.70 -16.08)	2 (0.25-5.41)

The descriptive statistics were used to determine the mean 6MWD covered by the participants at the time of discharge. It was found to be 45% of the predicted distance. (Table 3)

Table 3. Mean six-minute walk distance in phase I CR

Parameter	Mean ± SD
6MWD (meters)	252.125 ± 68.24
% predicted 6MWD	45.18 ± 14.50

Correlation between 6MWD and METs measured by Actigraph accelerometer at the time of discharge was

analyzed using Pearson’s correlation coefficient test. The mean & SD for 6MWD was 252.125 ± 68.24 and METs during 6MWD 11.06 ± 1.44 with r-value 0.347 and p-value 0.187. No correlation was found between the 6MWD and the METs measured.

Discussion

Demographic and clinical characteristics: The present study focused on measuring PA levels using Actigraph accelerometer in Phase-I CR and correlating the 6MWD with the METs measured by Actigraph accelerometer. PA levels were measured in Phase- I CR of CABG and PTCA patients in a tertiary care hospital. Participants on an average had co-morbidities such as diabetes mellitus, obesity, and hypertension. As these co-morbidities affect the functional capacity of the patients, this could have influenced their PA levels in our study.

Out of 9 participants who underwent CABG, 3 had triple vessel disease and 6 double vessel diseases respectively. However, all participants who underwent PTCA had only one vessel involved. The number of grafts harvested could have influenced the PA as well as the site of the graft taken. For example, the great saphenous vein taken from the lower limb can affect the mobility of the participants.⁽¹⁶⁾

Physical activity in CR: CAD patients have a reported benefit post-PA, however, vigorous exercises can have dangerous effects.⁽¹⁷⁾ In the present study, Actigraph accelerometer was used to quantify the PA levels of the participants in Phase-I CR. In the present study, we observed that the EE and the time spent in the light intensity activity by the participants was more as compared to the moderate intensity activity. Whereas, none of the participants were involved in vigorous intensity activities.

Studies document that benefits associated with participation in CR, include stabilization and potential regression of CAD.⁽¹⁸⁾ To halt the disease progression, it is recommended that a minimum of 1500 kcal/week of EE is required for participants undergoing CR program.⁽¹⁹⁾ The amount of EE to be achieved by the end of phase-I CR is currently not known. The objective measurement of EE using Actigraph accelerometer during Phase-I CR may help in formulating the guidelines for PA prescription.

The results presented in the study are in median and IQR values, for the betterment of understanding, the comparisons from the other studies are done in mean and SD values. In the present study the average daily EE in Kcals (142.86 ± 121.47) was more than the Kcals (128.6 ± 77.8) measured in a study by Izawa et al. ⁽¹⁵⁾ The probable reason for more EE reported in our study could be due to the use of a Triaxial accelerometer which takes into account all the three axis during any activity as compared to uniaxial accelerometer which monitors only one axis which was used in the above-mentioned study.

EE was measured in Kcals of the participants by Actigraph accelerometer at the end of each day. The mean EE on Day 1 was 139.41 ± 146.38 Kcals and that of Day 2 was found to be 175.88 ± 120.27 Kcals.

The mean daily MET's measured by Actigraph accelerometer was 3.9 ± 1.9 . It has been recommended that participants of CR should achieve 5-6 METs for completion of Phase-I and is also one of the criteria followed to start with Phase-II CR. ⁽¹⁹⁾ The participants in our study achieved the target METs. As Actigraph accelerometer gives an accurate measure of PA in free-living conditions, it can be used to objectively monitor the metabolic equivalents achieved by the person and therefore, can be used to provide a tailored program.

The average daily no. of steps (5146.43 ± 1997.14) in this study was similar to the step counts (4588.0 ± 2056.3) reported by Izawa et al, ⁽¹⁵⁾ in Phase-I CR indicating that the step counts measured might also be the appropriate target values to achieve necessary EE recommended for secondary prevention in cardiac patients. ⁽¹⁹⁾ At present, there are no guidelines for the required step counts during Phase-I CR. As the accelerometer is accurate to measure the step counts, it can be used to promote PA levels in Phase-I CR.

Six-minute walk test in CR: Walking performance is a good indicator of patient's progress and physical status, hence, the 6MWT is routinely used to assess the patient's performance. ⁽¹⁵⁾ In our study, the mean 6MWD was found to be 252.125 ± 68.24 meters (i.e. 45.18% of the predicted value) which were less as compared to a study in which the mean 6MWD of participants was 470 ± 151.76 meters. ⁽²⁰⁾ The probable reason for this decrease in 6MWD can be the difference in length of stay in hospital which, in our study was shorter due to early discharge.

Correlation between Six-MWT and METs measured by Actigraph accelerometer: 6MWT which gives a measure of functional capacity is used as a marker for prognosis in patients with CVDs undergoing CR. ⁽¹⁵⁾ Currently, there is no method of measuring PA levels other than self-reporting or diary or 6MWT at the hospital exercise clinics. Often conducted in a clinical setting, 6MWT may be contaminated by factors pertaining to the clinical environment and the clinical coordinator of the patients being tested. Regardless, 6MWT still remains as the more readily used measure of functional capacity.

Actigraph accelerometers have been looked upon as an objective means to measure the patients PA in free-living conditions, hence 6MWT by objective monitoring will overcome some of the limitations or contamination that prevail in the current method of 6MWD measurement and assessment. We hypothesized that PA levels during phase I CR may influence the functional capacity of the cardiac patient measured by 6MWT prior to discharge from the hospital. However, there was no correlation between 6MWD covered and the METs measured by the Actigraph accelerometer during 6MWT.

One important observation was noted that all patients post-surgery on an average got discharged by the fourth day (CABG) and second day (PTCA), even though the existing protocols recommend 1-7 days of Phase-I CR. The PA levels measured in our study may not be generalized for Phase-I CR due to variations in the hospital protocols.

The limitations of this study are only 3 days of monitoring due to early discharge of participants and sub-group analysis for CABG and PTCA was not done due to a small sample size. Future scope for research could focus on measurement of customized rehabilitation programs using the accelerometer.

Conclusion

In the present study, PA measured by Actigraph accelerometer was of low to moderate levels in Phase-I CR. There is a weak correlation between PA levels measured by Actigraph accelerometer and 6MWD achieved at the time of discharge.

Ethical Clearance:

Source of Funding: Nil

Conflict of Interest: Nil

References

1. World Health Organization (WHO). Cardiovascular diseases (CVDs). (2017) [online] Available at: <http://www.who.int/mediacentre/factsheets/fs317/en/> [Accessed 2 Aug. 2017].
2. Murthy PD, Prasad KT, Gopal PV, Rao KV, Rao RM. A Survey for Prevalence of Coronary Artery Disease and its Risk Factors in an Urban Population in Andhra Pradesh. *J Assoc Physicians India* 2012; 60:17–20.
3. Niebauer J, Hambrecht R, Velich T, Hauer K, Marburger C, Kälberer B. Attenuated progression of coronary artery disease after 6 years of multifactorial risk intervention: the role of physical exercise et al. *Circulation* 1997; 96:2534-41.
4. Connor GT, Buring JE, Yusuf S, Goldhaber SZ, Olmstead EM, Paffenbarger RS Jr et al. An overview of randomized trials of rehabilitation with exercise after myocardial infarction. *Circulation* 1989; 80: 234-244.
5. Taylor RS, Brown A, Ebrahim S, Jolliffe J, Noorani H, Rees K et al. Exercise-based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomized controlled trials. *Am J Med.* 2004; 116:682-92.
6. World Health Organization Committee. Rehabilitation after cardiovascular diseases, with special emphasis on developing countries. Technical report series no. 831. Geneva: WHO, 1993.
7. Pryor JA, Webber BA. Physiotherapy for respiratory and cardiac problems. 2nd ed. Edinburgh: Churchill Livingstone; 1998: 387-408.
8. Cardiac Rehabilitation, No. 57. Edinburgh: 2002. Scottish Intercollegiate Guidelines Network (SIGN): 1–2.
9. U.S. Department of Health and Human Services. Physical Activity and Health: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, 1996.
10. Ward DS, Evenson KR, Vaughn A, Rodgers AB, Troiano RP. Accelerometer Use in Physical Activity: Best Practices and Research Recommendations. *Med Sci Sports Exerc.* 2005; 37:S582-8.
11. Swartz AM, Strath SJ, Bassett DR Jr, O'Brien WL, King GA, Ainsworth BE. Estimation of energy expenditure using CSA accelerometers at hip and wrist sites. *Med Sci Sports Exerc.* 2000; 32:S450-6.
12. Westerterp KR. Physical activity assessment with accelerometers. *Int J ObesRelatMetabDisord.* 1999;23(3): S45-9.
13. Lozano AS, Marin PJ, Luque GT, Ruiz JR, Lucia A, Garatachea N. Technical variability of the GT3X accelerometer. *Med Eng & Phys* 2012; 34: 787-790
14. AACVPR Stratification Algorithm for Risk of Event. [online] Available at: https://www.aacvpr.org/Portals/0/Registry/AACVPR%20Risk%20Stratification%20Algorithm_June2012.pdf [Accessed 2 Aug. 2017].
15. Ramanathan RP, Chandrasekaran B. Reference equations for 6-min walk test in healthy Indian subjects (25–80 years). *Lung India* 2014; 31(1): 35–38
16. J. Mountney, G.A.L. Wilkinson. Saphenous neuralgia after coronary artery bypass grafting. *European Journal of Cardio-Thoracic Surgery* 1999,16(4): 440–443
17. Thompson PD, Franklin BA, Balady GJ, Blair SN, Corrado D, Estes NA 3rd, et al. Exercise and acute cardiovascular events placing the risks into perspective: A scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism and the Council on Clinical Cardiology. *Circulation* 2007; 115:2358–68.
18. Hambrecht R, Niebauer J, Marburger C, Grunze M, Kalberer B, Hauer K, et al. Various intensities of leisure time physical activity in patients with coronary artery disease: effects on cardiorespiratory fitness and progression of coronary atherosclerotic lesions. *J Am CollCardiol* 1993; 22:468-77.
19. Izawa KP, Watanabe S, Hiraki K, Morio Y, Kasahara Y, Takeichi N, et al. Determination of the effectiveness of accelerometer use in the promotion of physical activity in cardiac patients: a randomized controlled trial. *Arch Phys Med Rehabil* 2012; 93:1896-1902.
20. Babu AS, Noone MS, Haneef M, Naryanan SM. Protocol-Guided Phase-1 Cardiac Rehabilitation in Patients with ST-Elevation Myocardial Infarction in A Rural Hospital. *Heart Views.* 2010; 11:52-6.

A Study to Assess the Effect of Childbirth Education on Intrapartum Coping behaviours of Primiparous Women in a Selected Maternity Center of a Tertiary Level Hospital in Pune

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Abstract

Introduction: Child birth is a normal physiological process, yet gaining confidence by enhancing knowledge about childbirth can be considered an important factor influencing a parturient's birthing experience.

Method: A prospective quasi-experimental study conducted on 60 registered primigravidae attending the ANC OPD of a hospital at Pune. 30 included in the intervention group, received 3 sessions of CBE. The effect of this measured intranatally by a self-developed Intrapartum Behavioural Observation Checklist. The coping behaviours of the intervention group measured and compared against 30 primigravidae women who received conventional antenatal education.

Results: Primigravidae were poorly informed about childbirth preparedness and not prepared for the experience of childbirth. Majority had no concept regarding the severity of pain, duration of labour and coping measures stress of labour.

Significant reduction in episiotomy rates, use of analgesics and improvement in coping behaviours found among the experimental group. Hence the research hypothesis was accepted, level of significance = 0.001.

Discussion: Gaps identified in the knowledge and practice of childbirth preparedness among primigravidae in urban Pune. Also analyzed the positive effects of childbirth education on intrapartum coping behaviours of primiparous women. Episiotomy rates and use of intrapartum analgesics were less in the Intervention group. Intrapartum behavioural compliance and exhibition of positive self-care, intra partum coping behaviours were also significantly high.

Conclusion: The findings of this study indicate that the short term; need based childbirth educational intervention demonstrated a highly significant impact on the intrapartum coping behaviours of primiparous women.

Keywords: *Childbirth education, intrapartum coping behaviours, primigravidae women.*

Introduction

Childbirth is a normal physiological process, yet it is a life changing experience for the woman becoming pregnant for the first time. Gaining knowledge about childbirth can be considered an important factor influencing a parturient's birthing experience.^[1,2,3]

Background of the study: When the woman is well informed regarding the events that she would

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experience during the process of labour, her role in the child birthing process and the information regarding the intrapartum coping behaviour would probably make a positive physical and psychological impact on the postnatal mother. A quasi-experimental, multi-time series research study conducted by Krish J A in 2003, revealed a significant inverse relationship between maternal confidence for labor and fear of childbirth was found throughout the period of gestation.^[4]

A qualitative analysis done by Ibach F et al on knowledge and expectations among 30 African women indicated, primigravidae were inadequately prepared for the experience of childbirth^[5]. A study conducted in 2006 by Mutiso SM et al to evaluate the birth preparedness and complication readiness among 394 antenatal clients in an antenatal clinic at Nairobi, Kenya, revealed that education and counseling on different aspects of birth preparedness was not given to all respondents.^[6] A similar cross sectional descriptive study was conducted in Rewa district of MP, India, by Deoki Nandan et al to assess birth preparedness and complication readiness intervention among 2022 respondents including Pre natal and post natal mothers and health care providers. The researchers concluded that the birth preparedness index of the study population was low (47.5%).^[7] Rising cesarean sections among primigravidae is another concern.^[12,13,14] Mukherjee S N on rising cesarean section rate, it was quoted cesarean section on demand in absence of any specific risk are increasing. Inadequately informed women choose CS to avoid painful natural childbirth.^{[12][15]}

Evidences show that childbirth preparation classes have the potential not only to increase pregnant women's intrapartum coping ability with labor pain but also to reduce stress during the processes of pregnancy and childbirth^[16,17]

Midwives hold an important key to positive foeto-maternal care around the time of childbirth that will contribute to a good start for the baby and mother during the critical period of human life.^[1]

Need for the study: During the investigators experience as a midwife, in the labour room it was observed that most of the time the primigravidae parturients were anxious, took more time to understand and follow the instructions given to them and unable to cope up with the normal labour.

Statement of problem: A study to assess the effect

of child birth education on intrapartum coping behaviours of primiparous women in a selected maternity center of a tertiary level hospital in Pune.

Aim of the study: To compare the intrapartum coping behaviours of the primiparous women in intervention group who received the childbirth education developed by the investigator with the control group of primiparous women who received conventional antenatal health education.

Objectives of the study:

1. Identify the gaps in the existing knowledge of primigravidae women regarding childbirth preparedness.
2. Develop a childbirth education based on the assessed knowledge needs.
3. Assess the effect of childbirth education on intrapartum coping behaviours of primiparous women in the intervention group.
4. Assess the effect of conventional antenatal education on intrapartum coping behaviours of primiparous women in the control group.
5. Compare the intrapartum coping behaviours of primiparous women between intervention group and control group.

Material and Method

The steps taken towards achieving the data

Pilot Study

Sample Primigravidae women (n=40)

Self-developed Tool :

Semi structured interview schedule on childbirth preparedness,

Established validity & reliability

Result Analysis

Developed childbirth education

Self Developed IPBO Checklist

Feasibility study & tool tryout

Establish validity & reliability

Training Observers Establish inter rater reliability

Establish Content validity

Research Study:

1. Sample 60 term primigravidae women
2. Intervention group n=30 :Imparted childbirth education in OPD
3. Control group n=30 :Conventional antenatal education received in OPD
4. Register of attendance maintained-Coding of each participant done
5. Outcome measurement done by observer using
6. Intra Partum Behavioural Observation Checklist in labour room
7. Coding data - cross checked
8. Data compilation, Analysis and Interpretation

Findings:

Socio demographic profile of the knowledge assessment sample under study: Majority (95%) of the women were in the reproductive age group of 18-25 years and among them 25% belonged to the teenage group. Maximum respondents (80%) hailed from joint families. Majority belonged to middle class (60%) and upper middle class families(35%).

Their educational status ranged from primary level till graduation. Many of them, 60% were educated upto higher secondary level and the rest combinely had completed primary and secondary level of education and only 5% were graduates. All the participants (100%) included in the study were housewives.

Sample characteristics as per the existing knowledge of primigravidae women regarding childbirth preparedness: The information gathered indicated gross knowledge deficit regarding childbirth preparedness. The highlights of the findings are as given below.

Nobody was aware about the stages of labour and the procedure of childbirth. Majority (75%) of women reported that they were unaware about bag of waters. Maximum (80%) were unaware about the approximate duration of labour in a first time mother. Few primigravidae were aware regarding the impending signs and symptoms of labour. Passage of blood/blood mixed vaginal discharge and commencement of labour pains were the signs, which got the maximum response whereas back pain and rupture of membranes as an

impending sign of labour fetched the least of responses.

Majority (90%) of the women did not know the correct place and time of reporting for labour on or after commencement of labour process. Only a few women (20%) knew that labour pains were intermittent and progressive.

Most of the study population (55%) knew regarding examination of pregnant abdomen/uterus but very few (15%) were aware about digital vaginal examination as a kind of intrapartum assessment. Also, there were few primigravidae (20%) who were unaware about the types of intrapartum monitoring. Majority of women (75%) were unaware of the purpose of doing PV examination during labour. 10% out of 25% who knew the reason for performing a PV examination, had history of first trimester abortions.

Many (65%) women reported as having no knowledge and access to knowledge regarding birth preparedness. The sources of information from which the primigravidae women gained knowledge of childbirth were mainly through books/ magazines, friends and family members.

Though few women (35%) reported having information about birth preparation and process, only 5% among them opted for all aspects on child birth preparation and child birth process. When few of them (15%) reported their understanding of childbirth preparedness as financial preparedness for birth related expenditures, most of them (60%) understood it as physical and psychological preparation of a pregnant woman. 10% associated it with arrangement of a support person during labour whereas more than half of them(55%) linked it with preparation of a vehicle for transportation. Only few (5%) thought about arranging a blood donor and 10% related it to preparation of antenatal kit for hospital stay.

Nearly half of the assessment population had done a few preparations for childbirth, of which attendance for regular and essential antenatal checkups ranked high (75%), while a quarter of them had not done any child birth preparation.

Maximum (95%) women were unaware about certain breathing techniques that would help them to relax during labour and childbirth. Less than half of the assessment population (45%), was aware about the practice of episiotomy during childbirth.

Most of the primigravidae (95%) did not know the time of resuming first meal after childbirth, and the breast feeding practices were not popular among first time mothers.

Overall, it was found that majority of the primigravidae population (85%) had poor knowledge regarding childbirth preparation, and a few (15%) had average knowledge about childbirth preparation.

Sample characteristics according to the sociodemographic profile of the samples under study: The average education in the experimental group was more in the Intervention group (20% and 53.3% up to intermediate level and higher secondary level respectively against 56.6% from control group educated up to higher secondary level and 23.3% being graduates. Also, a few women (3.3%) from intervention group were illiterate.

Majority of the participants i.e. 96.6% of the intervention group and 86.6% of the control groups were housewives. The rest of the study population was reported to be self employed. Average income in the control group was higher than that reported in experimental the group. A minor percentage of 3.3% of the Intervention group and 13.3% of the control groups belonged lower socio economic strata.

Most of (63.3%) of the Intervention group and some (46.6%) of the control group hail from joint/ generation families while 36.6% of the Intervention group and 53.3% of the control groups belong to nuclear families.

On an average, participants in the experimental group were younger than those from the control group. 93.3% of the Intervention group and 76.6% of the control group were from the age group of 25-35 yrs. However it was seen that, 6.6% of each Intervention and the control group belonged to teenage group. Rest of the control group (16.6%) population belonged to elderly age group of beyond 35 years.

Description of Intrapartum Data: Women who underwent vaginal delivery without an episiotomy were more (30%) in intervention group than in control group (20%) whereas episiotomy rates were seen higher in control group (76.6%) than in Intervention group (60%). However incidence of vacuum extractions was same (3.3%) in both the groups.

Proportion of women who did not use any

intrapartum analgesics was more (83.4%) in Intervention group than in control group (66.7%). Use of epidural anesthesia, however, was same (3.3%) between both the study groups.

Description of the stage wise intrapartum coping behaviours

1. Intrapartum coping behaviours in first stage of labour were better in the intervention group (mean- 69.06) than in control group (mean- 56.56).
2. The coping behaviours of the intervention group (mean- 20.33) in second stage was highly significant compared to control group (mean- 16.26)
3. The mean scores of the intervention group (mean- 9.16) in their third stage was also found more than that of control group (mean- 7.20 with a highly significant p value of less than 0.001.

Description of compliance to selected intrapartum coping behaviours: At the base-line, the compliance to intra partum instructions of the Intervention group (M = 9.5667, SD = 1.2228) was higher than that of the control group (M = 8.6333, SD = 2.2664), however, the difference was not statistically significant, (Mann-Whitney Z = 1.621, p = 0.105.)

The compliance to intrapartum communication of the first time mothers with the labour room staff for the Intervention and control group was analyzed to be higher in the intervention group with a significant p value of 0.005.

The statistical analysis show a highly significant difference in the self care behaviours of the intervention group (Mean scores of Intervention group = 26.7, SD = 4.457 and mean scores of control group = 21.2, SD = 3.942, Z = 4.297)

The compliance to breathing relaxation was seen significantly high in intervention group than in control group (Intervention group mean scores = 32.3667, SD = 4.8386. Control group mean scores = 24.1667, SD = 5.91365, Z = 4.607)

A significant difference existed in Intervention group's compliance to Physical preparation and self reporting (mean scores of intervention group = 42, mean scores of control group = 34.33, SD (intervention) = 6.280, SD (control) = 8.809, Z = 3.002)

Significant behavioural modification in women who were taught self care activities during labour. Mean scores for cooperation during per-vaginal examinations, periodically emptying bladder, having no bad breath, performing abdominal massage, and absence of dehydration were higher in intervention group than in control group with a significant p values for each.

Scores of intrapartum coping behaviours of primiparous women who received childbirth education:

Primiparous women (40%) reported to have excellent intrapartum coping while (53%) had good coping. A few (7%) had averagely coping. No participant in the intervention group had poor coping.

Scores of intrapartum coping behaviours of primiparous women who received conventional antenatal education:

No Participant from the control group had excellent intrapartum coping. Most of them (60%) had average coping and some of them (37%) were reported to have fairly good coping. Only 3% had poor intrapartum coping.

Comparison of the intrapartum coping behaviours of primiparous women between the study groups:

There was highly significant difference in the intervention group's compliance to intra partum coping during periodic and single observation of intrapartum coping behaviours. (Total scores mean scores (trial) = 162.57 (control) = 130.77 SD (trial) =17.60 SD (control) =23.06 Z=4.734 P=<0.001).

Maximum women in the control group(25) reported good intrapartum coping scores in contrast to 11 women from control group. Similarly 5 women in the control group reported to low intrapartum coping scores against the 19 women from control group. There were neither any scores representing poor coping among women in trial group nor an excellent coping reported in control group. The difference is highly significant with a p value of <0.001.

Conclusions

There exists a gross knowledge deficit among primigravida regarding childbirth preparedness. The findings of this study indicated that the short term; need based childbirth educational intervention demonstrated a highly significant impact on the intrapartum coping behaviours of primiparous women.

Discussion of the Findings: Primiparae- 30 in the control group and 30 in the intervention group in were included. Most of the women were housewives with family income of above Rs.5000/per month. Many in the study groups had lower education levels and were younger i.e. below 25 yrs.

The intrapartum coping behaviours of the mothers of the intervention group who received CBE were significantly better than the control group. This result has rejected the null hypothesis H0 that there was a highly significant difference in the intrapartum coping behaviours among the intervention group and control group with a level of significance of 0.001.

Conclusion

The findings of this study indicate that the short term, need based childbirth educational intervention have highly significant impact on the intrapartum coping behaviours of primiparous women. The findings from this study contribute to the deep understanding of the effect of childbirth education classes that will be useful for the development of prenatal midwifery services.

Conflict of Interest: There is no conflict of interest that exist in the present study.

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References

1. Fraser M D, Cooper A M. Myles textbook for midwives. 15th ed. London: Elsevier Churchill Livingstone publishers; 2009
2. Simpson K R, Creehan P A. Perinatal nursing. 3rd ed. USA: Wolters Kluwer/ LWW; 2008;473-500.
3. Wong HW, Perry L. Maternal child nursing care. 3rd ed. USA: Mosby/Elsevier; 2006;437-500.
4. Kish J A. The development of maternal Confidence for labor among nulliparous pregnant women. College Park: Dissertation submitted to the Faculty of the Graduate School of the University of Maryland; 2003; Unpublished.
Available from URL: <http://drum.lib.umd.edu/bitstream/1903/275/1/dissertation.pdf>
5. Ibach F, Dyer R A, Fawces S, Dyer S J. Knowledge and expectations of labour among primigravid

- women in the public health sector. SAMJ. 2007 June; 97(6): 461-464.
6. Mustiso SM, Qureshi Z, Kinnthia J. Birth preparedness among antenatal clients. EAMJ 2008 June; 85 (6): 275-83.
 7. Nandan Deoki, Kushwah SS, Dubey DK. A study for assessing birth preparedness and complication readiness intervention in Rewa district of MP. NIHFV, unpublished. Available from URL: <http://nihfw.org/pdf/RAHI-II%20Reports/REWA.pdf>
 8. International Institute for Population Sciences (IIPS) and Macro International. 2007. National Family Health Survey (NFHS-3), 2005–06: India: Volume I. Mumbai: IIPS. Available from URL:<http://www.measuredhs.com/pubs/pdf/SR128/SR128.pdf>
 9. International Institute for Population Sciences (IIPS) and ORC Macro. 2000. National Family Health Survey (NFHS-2), 1998–99: India. Mumbai: IIPS. Available from URL:<http://www.measuredhs.com/pubs/pdf/SR128/SR128.pdf>
 10. International Institute for Population Sciences (IIPS) and Macro International. 1995. National Family Health Survey (NFHS-3), 1992–93: India: Volume I. Mumbai: IIPS. Available from URL:<http://www.measuredhs.com/pubs/pdf/SR128/SR128.pdf>

Physicochemical Characteristics, Heavy Metal Analysis and Antioxidant Potential of Jamun Honey (*Syzygium Cumini* L.) from Western Ghats, India

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Abstract

Context: This study is aimed to analyse heavy metal content and antioxidant potential of three types of Jamun honey samples from Western Ghats of India. Ash, pH, and colour intensity were analysed. Heavy metal analysis for Arsenic (As), Lead (Pb), chromium (Cr) and Mercury (Hg) were carried out using inductively coupled plasma - optical emission spectrometry (ICP-OES). Total polyphenol (TPC), total flavonoid content (TFC) and antioxidant assays such as 2, 2-diphenyl-1-picrylhydrazyl (DPPH), ferric reducing antioxidant power (FRAP) were performed. Comparative studies of Jamun honeys revealed strong correlation between TPC and TFC as significant radical scavenging activities. Colour values represented strong correlation with TPC and TFC at ($r=0.9$) and FRAP at ($r=0.8$) whereas a negative correlation with IC 50 values of DPPH at ($r=-0.6$) was observed.

Keywords: Honey, Unifloral, Antioxidant, Heavy Metals.

Introduction

Honey is a natural high energy source, carbohydrate food processed by honey bees¹. In human history, honey is not only used as nutrient but also used as a drug delivery system in medicine. In recent years, industries utilize

honey for cosmetic and drug production. Commercial advertisements have created the awareness of honey consumption amongst the human population². Honey has enticed flavour, colour, aroma and texture largely due to the presence of volatile oils, aromatic acids, carotenoids, flavonoids and polyphenols. Because of this unique and complex nature, it exhibits some biological potentials such as antibacterial, anti-inflammatory, antiviral, antioxidant, and anticancer activities³. Studies have shown that physicochemical characteristics of honey depend predominantly on the quality, source of nectar, geographical region, and processing of honey⁴. The unifloral honey has majority of nectar from flower of a specific plant species and when compared with multifloral honey it exhibits a similar range of biological properties containing identical constituents in varying concentrations⁵.

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Honey does contain elements as minor constituent. Presence of metal in honey is largely based on elemental composition of the nectar with regards to its botanical origin, soil and geography of source plants. Honey can also be contaminated with heavy metals during packaging and processing or due to industrial and agriculture pollution. Due to recent increase in consumption of honey as nutraceuticals, it may set a base for heavy metal toxicity in population. India being a large consumer of honey there is still lack of information regarding heavy metal content of Indian honeys.^{6, 7}

Unifloral Jamun honey samples were collected from mountain ranges of Western Ghats. Jamun is fruit from Jamun tree (*Syzygium cumini*) and so honey called as Jamun honey. The plant parts, i.e. bark, leaves, seeds and fruits are extensively studied for their antioxidant properties and used for the treatment of medicinal ailments such as constipation, diabetes, ringworm infection, pharyngitis, dermatopathy⁸. Thus the nectar collected by bees to produce honey from this plant gives us the perspective to explore the physicochemical, heavy metal analysis and antioxidant potential of Jamun honey from Western Ghats India.

Materials and Method

Reagents and Instruments: Gallic acid, Quercetin, FeSO₄·7H₂O, F-C reagent (Folin Ciocalteu), DPPH, 2,4,6-Tris (2-pyridyl)-1,3,5-triazine (TPTZ) were purchased from Hi-Media Laboratories Pvt. Ltd. Methanol, Sodium carbonate, Ferric chloride, acetate buffer and dilute HCl, aluminium chloride, sodium nitrite and sodium hydroxide all chemicals are of analytical grade. UV spectrophotometer (SHIMADZU spectrophotometer UV-1800).

Honey samples: Collection and Preparation: Honey samples were collected during the year 2015-16 from honey hunters and apiaries of Ponda area (Goa state)(J-1), Pune (J-2) and Mahabaleshwar (Maharashtra state) (J-3) of Western Ghats of India. Collected samples were filtered and stored in air tight containers at room temperature under hygienic conditions until analysis.

Melissopalynological Analysis: In the present study, based on the recommendations of International Commission for Bee – Botany⁹ honey samples which had pollen count of similar plant species (*Syzygium cumini*) with more than 45% was considered as unifloral Jamun honeys.

Physical Analysis: Ash content and pH analysis was performed according to official reported analysis method: AOAC 1990 guidelines¹⁰. Colour intensity was estimated with previously mentioned method of Beretta Get al.¹¹

Phytochemical estimation:

Total polyphenol content: Total polyphenol content was determined by F-C reagent method in 96 well plate each well had 150 µL solution containing standard or 10% honey solution, freshly prepared F-C reagent and 7.5% of sodium carbonate. The plate was incubated in dark for 30 min and absorbance was measured at 630 nm¹². Gallic acid (5 -160 µg/ml) was used as standard and results were expressed as mg Gallic acid equivalents (GAE) per 100 gm of honey.

Total flavonoid content: Total flavonoid content was estimated using aluminium chloride method¹³. The Quercetin (12.5-800 µg/ml) was used as standard and results were expressed as mg of Quercetin equivalents (QE) per 100 gm of honey.

Antioxidant activity:

2, 2-diphenyl-1-picrylhydrazyl (DPPH) assay

The free radical scavenging ability of honey samples was determined according to the method of Brand-Williams et al.,¹⁴ with required modifications. Honey samples of 100 µL were allowed to react with 1900 µL of the DPPH solution for 1 h. The reaction mixture was read at 517 nm and the standard Gallic acid concentration was ranging from (200-6.25 µg/ml). The results were taken in triplicates and % of radical scavenging activity was expressed by using the formula:

$$\% \text{ of Radical Scavenging Activity} = \left[\frac{\text{Abs}_{(\text{blank})} - \text{Abs}_{(\text{sample Honey})}}{\text{Abs}_{(\text{blank})}} \right] \times 100$$

Ferric reducing antioxidant power (FRAP) assay: The assay was performed with FRAP reagent based with minor modifications¹⁵. Briefly, reaction solution contained 200 µl of 10% honey sample, 1800 µl of FRAP reagent. The solution was incubated in dark condition for 10 min at room temperature and absorbance was measured at 593 nm. FeSO₄·7H₂O (100-1000 µM) was used as assay standard for calibration per 100 gm of honey and results were expressed in triplicates as micromoles of ferrous equivalents (µM Fe (II)) of per gram honey solution.

Heavy metal analysis: Honey sample digestion was carried out in a microwave assisted extraction system Milestone START D (MilistoneSrl., Italy). The digested samples were quantitatively analyzed for heavy metals such as Arsenic, Lead, chromium and Mercury in an Inductivity Coupled Plasma–Optical Emission Spectrometer (iCAP 6300 Duo, Thermo fisher Scientific, Cambridge, England) with dual configuration (axial and radial) and iTEVA (version 2.8.0.97) operational software. ICP multi-element standard solution (CertiPUR, Merck) was used for preparation of calibration solutions. Yttrium was used as internal standard¹⁶.

Statistical Analysis: Analyses were made in triplicate and data obtained are expressed as the mean ± standard deviations. Comparison of inter sample concentrations for study parameters were tested using Kruskal Wallis ANOVA. While, correlations were established using Pearson’s correlation coefficient (r) in bivariate linear correlations ($p < 0.01$). These correlations were analysed using Graph pad prism version 7 and SPSS software with statistical significance set at $p < 0.05$.

Findings and Discussion

To our knowledge, it’s the first study reporting physicochemical, heavy metal analysis and antioxidant potential of Indian Jamun honey from Western Ghats of India. The Melissopalynological analysis depicts maximum percentage of pollen grains from the Jamun tree (*Syzygium cumini*) in all three honey samples [J-1(94.6%), J-2(67%), and J-3(92.4%)] collected from the Western Ghats of India. The findings for ash content, pH and colour intensity are presented in Table 1. The ash content of Jamun honey samples varies from (0.14% -0.42%) which is according to the reference range of <0.6%¹⁷. The ash content mainly depends on the floral origin, which represents the mineral and trace elements content. The pH range of the Jamun honey in the present study was found to be acidic i.e., (4.17 to 4.48) and are comparable with ranges of the Tualang and Manuka honey¹⁸. Colour of honey samples indicates that Jamun honey (J-3) with dark brown in colour has highest colour intensity along with higher level of polyphenol and flavonoid content than the (J-2), (J-1) honey. Therefore, the higher colour intensity specifies the maximum presence of MRPs, phenolic and flavonoid compounds which are previously established to contribute for antioxidant properties¹⁹.

Table 1: Physical characters, Colour intensity of Jamun honey samples from Western Ghats of India.

Sample	pH	Ash (%)	Colour intensity(450nm)
J-1	4.17	0.42	0.530±0.24
J-2	4.29	0.27	0.339±0.03
J-3	4.48	0.14	0.836±0.43

Phytochemical estimation: The total polyphenol content in the tested Jamun honey sample ranges between 31.67±0.00 mg to 77.90±18.73GAE/100gm. J-3 honey sample was observed with a significant difference ($p < 0.05$) in terms of polyphenol and flavonoid content as compared to other two honey samples (Fig. 1). Supporting this study observations, several earlier studies have been reported for polyphenol content in different honey samples such as Tualang (251.7 ± 7.9 mg GAE/Kg)²⁰. On the other hand, total flavonoid content ranges between 25.84±7.83 to 51.20±16.35 mg of QE/100 gm which is comparable to Algerian honey (54.23 ± 0.62 mg catechin/kg)²¹. Previous research have presented that polyphenol and flavonoid content depends on floral source and their geographical origin²². Honey sample from Mahabaleshwar region (J-3) has higher polyphenol and flavonoids which is directly accountable for higher antioxidant potential.

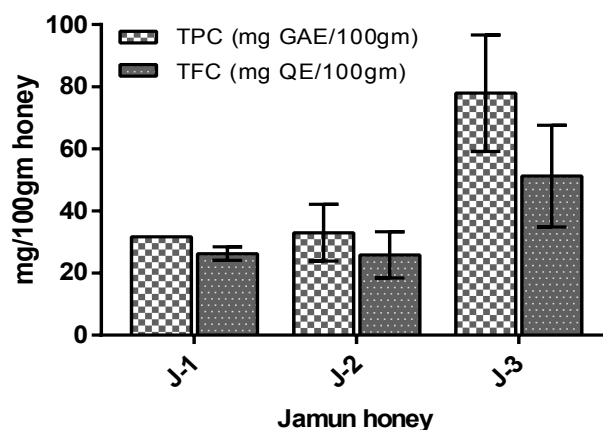


Figure 1. Phytochemical estimation of Jamun honey samples

Antioxidant Assays: DPPH investigates the hydrogen /electron donating capacity of samples and is reduced in presence of an antioxidant molecule. The current study represents DPPH IC 50 values ranging from 27.69±0.61 to 46.95±2.74 mg/ml (Fig 2). The J-3 honey displayed the significant ($p < 0.05$) highest level antioxidant potential at lower concentration when

compared to other honey samples and is comparable to DPPH activity for Tualang honey (41.30%)²⁰, Algerian honey (44.55%)²¹, Indian honey samples (>50%)²³.

different regions are: Malaysian Tualang honey (576.91 ± 0.64 µMFe (II)/100 g)²⁰, Sudanese honey (567.8±0.6-1340.2±8.6Mm)²⁴.

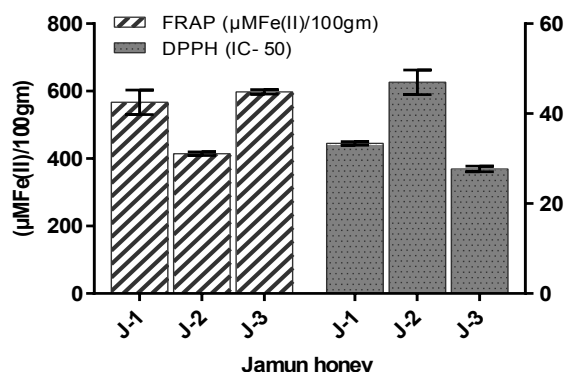


Figure 2. Antioxidant assay of Jamun honey samples

Ferric reducing antioxidant power FRAP assay is based on the ability of analyte towards reducing the ferric to a ferrous couple (Fe⁺³/Fe⁺²). The mean value of the Jamun honey for the assay was in the range of 410±0.01 to 600±0.01 µMFe (II)/100gm. As assumed, J-3 exhibited the significantly (*p*<0.05) quantity of antioxidant activity when compared with J-1 and J-2 (Fig 2). The previous documented FRAP value of other honey samples from

Heavy metal analysis: Heavy metals such as Mercury, Chromium and Lead were below the detection limit in all honey samples only Arsenic was detected in Mahabaleshwar (J-3) honey with 0.55±0.42 ppm. Results are comparable to other studies^{6, 7} and indicate consumption of these Jamun honey may have no toxic effects.

Correlation: Colour, Phytochemical, and Antioxidant Properties: The correlation has been summarized in Table 2. A very high positive correlation was detected between polyphenols and flavonoid content (*r* = 0.9) and high negative correlation with DPPH at (*r* = -0.7) indicating high radical scavenging activity by both phytochemicals in the sample. A moderate positive correlation between FRAP assay and polyphenols and flavonoid content at (*r*= 0.6). Correlation observed in the present study revealed an overview that Jamun honey with dark colour possesses high amount of TPC and TFC, which aids in free radical scavenging activity.

Table 2: Pearson Correlation amongst Total Polyphenol content (TPC), Total flavonoid content (TFC), antiradical power (DPPH), FRAP values, honey colour, pH.

	TPC	TFC	DPPH	FRAP	COLOUR	pH
TPC	1					
TFC	0.999**					
DPPH	-0.710	-0.7373				
FRAP	0.610*	0.641*	-0.991			
COLOUR	0.910**	0.926**	-0.937	0.883**		
pH	0.999**	0.997**	-0.687	0.585*	0.896**	1

**Correlation is significant at the 0.01 level; *correlation is significant at the 0.05 level.

Conclusion

Since, the Western Ghats of India is rich in flora and fauna, the honey obtained from this geographical distribution show a good antioxidant potential with below detection limit of heavy metals. Present study signifies that unifloral Jamun honey has higher antioxidant with medicinal and biological properties associated with high grade of nutritional value for health benefits of the population. Herbal chemist is

recommended to specifically use Jamun honey for their drug preparations and observe the effects which help in promoting local honey consumption by consumers. Study with large sample size and other biological aspects of this indigenous honey are to be explored.

Conflict of Interest: Nil

Source of Funding: Self-funding

Ethical Clearance: Not applicable

References

- Bogdanov S, Jurendic T, Sieber R. Honey for Nutrition and Health: a Review. *American Journal of the College of Nutrition*. 2008;27(6):677–89.
- Ajibola A, Chamunorwa JP, Erlwanger KH. Nutraceutical values of natural honey and its contribution to human health and wealth. *Nutr Metab*. 2012;9:1–12.
- Alvarez-Suarez, J., Gasparrini, M., Forbes-Hernández, T., Mazzoni, L., & Giampieri, F. The Composition and Biological Activity of Honey: A Focus on Manuka Honey. *Foods*. 2014; 3(3): 420–432.
- El Sohaimy, S. A., Masry, S. H. D., & Shehata, M. G. Physicochemical characteristics of honey from different origins. *Annals of Agricultural Sciences*. 2015; 60(2): 279–287.
- Soares, S., Amaral, J. S., Oliveira, M. B. P. P., & Mafra, I. A Comprehensive Review on the Main Honey Authentication Issues: Production and Origin. *Comprehensive Reviews in Food Science and Food Safety*. 2017; 16(5):1072–1100.
- Aghamirlou, H. M., Khadem, M., Rahmani, A., Sadeghian, M., Mahvi, A. H., Akbarzadeh, A., & Nazmara, S. Heavy metals determination in honey samples using inductively coupled plasma-optical emission spectrometry. *Journal of Environmental Health Science and Engineering*. 2015; 13(1).
- Ru QM, Feng Q, He JZ. Risk assessment of heavy metals in honey consumed in Zhejiang province, southeastern China. *Food Chem Toxicol*. 2013; 53:256–62.
- Arya SS, Pegu K, Sadawarte PD. Bioactive Compounds and Health Benefits of Jamun (*Syzygium cumini*). *Bioact Mol Food*. 2017; 1–20.
- Louveaux J, Maurizio A, Vorwohl G. Method of Melissopalynology. *Bee World*. 1978;59(4): 139-57.
- Helrich K. AOAC: Official Method of Analysis, 1990;1(1): 552.
- Beretta G, Granata P, Ferrero M, Orioli M, Facino RM. Standardization of antioxidant properties of honey by a combination of spectrophotometric/fluorimetric assays and chemometrics. *Anal Chim Acta*. 2005;533(2):185–91.
- Serem, J. C., & Bester, M. J. Physicochemical properties, antioxidant activity and cellular protective effects of honeys from southern Africa. *Food Chemistry*. 2012; 133(4):1544–1550.
- Ukom AN, Ojmelukwe PC, Ezeama CF, Ortiz DO, Aragon IJ. Phenolic content and antioxidant activity of some under-utilized Nigerian yam (*Dioscorea spp.*) and cocoyam (*Xanthosomamaffa (scoth))* tubers. *IOSR J Environ Sci Toxicol Food Technol*. 2014;8(7): 104–11.
- Brand-Williams W, Cuvelier ME, Berset C. Use of a free radical method to evaluate antioxidant activity. *LWT - Food Sci Technol*. 1995;28(1): 25–30.
- Gorjanović SŽ, Alvarez-Suarez JM, Novaković MM, Pastor FT, Pezo L, Battino M, et al. Comparative analysis of antioxidant activity of honey of different floral sources using recently developed polarographic and various spectrophotometric assays. *J Food Compos Anal*. 2013;30(1):13–8.
- Binsi PK, Viji P, Panda SK, Mathew S, Zynudheen AA, Ravishankar CN. Characterisation of hydrolysates prepared from engraved catfish (*Nemapteryx caelata*) roe by serial hydrolysis. *J Food Sci Technol*. 2016;53(1):158–70.
- Codex Alimentarius Commission (2001): Codex Standard for Honey. Alinorm 01/25: 19–26. FAO, Rome
- Ahmed S, Othman NH. Review of the medicinal effects of tualang honey and a comparison with manuka honey. *Malays J Med Sci*. 2013;20(3):6–13.
- Brudzynski K, Miotto D. The relationship between the content of Maillard reaction-like products and bioactivity of Canadian honeys. *Food Chem*. 2011;124(3): 869–74.
- Mohamed M, Sirajudeen KNS, Swamy M, Yaacob NS, Sulaiman SA. Studies on the antioxidant properties of tualang honey of Malaysia. *African J Tradit Complement Altern Med*. 2010;7(1):59–63.
- Khalil MI, Moniruzzaman M, Boukraâ L, Benhanifia M, Islam MA, Islam MN, et al. Physicochemical and antioxidant properties of algerian honey. *Molecules*. 2012;17(9):11199–215.
- Gheldof, N., Wang, X.-H., & Engeseth, N. J. Identification and Quantification of Antioxidant Components of Honeys from Various Floral Sources. *Journal of Agricultural and Food Chemistry*. 2002; 50(21): 5870–5877.

23. Saxena S, Gautam S, Sharma A. Physical, biochemical and antioxidant properties of some Indian honeys. *Food Chem.* 2010;118(2):391–7.
24. Tahir HE, Xiaobo Z, Zhihua L, Yaodi Z. Comprehensive evaluation of antioxidant properties and volatile compounds of sudanese honeys. *J Food Biochem.* 2015;39(4):349–59.

Short Term Effect of Isolytic Contraction on Hamstring Flexibility in Asymptomatic Subjects with Hamstring Tightness: A Randomised Controlled Trial

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Abstract

Aim: To Study short term effect of Isolytic contraction on Hamstring flexibility in asymptomatic subjects with hamstring tightness with respect to active knee extension test, Straight Leg Raise test and Lumbar Lordosis Index.

Objectives: The Objectives of the study are as follows:(1) To find effect of Isolytic contraction on hamstring flexibility. (2) To find effect of Isolytic contraction on static and dynamic hamstring flexibility.

Method: This study was conducted for the duration of 6 months. 300 subjects of age 20 to 40 years were screened out of which 276 subjects were selected for the study depending on the inclusive and exclusive criteria. Asymptomatic subjects with AKT <20 degree in the age group of 20 to 40 years were included in the study. These subjects were then divided into 2 groups Pre-treatment assessment and Post-treatment assessment were recorded.

Results: Statistically significant differences in the AKT, SLR, and LI were seen between the two groups. AKT (Right) It indicated that it was extremely significant ($p < 0.0001$) and ($p = 0.0079$) in the interventional group subjects. AKT (Left) It indicated that it was extremely significant ($p < 0.0001$) and ($p = 0.6384$) in the interventional group subjects. SLR (Right) It indicated that it was extremely significant ($p < 0.0001$) and ($p = 0.1199$) in the interventional group subjects. SLR (Right) It indicated that it was extremely significant ($p < 0.0001$) and ($p = 0.2819$) in the interventional group subjects. Intra group analysis of these values within the group was done using Wilcoxon test and the Inter group analysis between the groups was done by Mann-Whitney test.

Conclusion: The study results concluded that there was a significant result using isolytic contraction on hamstring flexibility in asymptomatic subjects having hamstring tightness with respect to Active knee extension test, Straight leg raise test and Lumbar lordosis index.

Keywords: *Isolytic Contraction, Hamstring Flexibility, Hamstring Tightness, Asymptomatic, Straight Leg Raise, Lumbar Lordosis Index, Active Knee Extension, Flexi-e-Curve*

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Introduction

Hamstring tightness is one of the most common musculoskeletal problem faced by individuals. Many studies had found out that maximum 70% of adult population was suffering with hamstring tightness and mostly it causes with the age group 20-40 years.

[1]Tightness in hamstring muscles leads to hamstring injuries and hamstring injuries are the most common type of injury among individuals. These injuries are slow to recover, make high health expenditure and decrease the performance level of the individual. [1]

Many of the etiologies have found that hamstring tightness gives rises to numerous numbers of musculoskeletal problem. "Inability to extend the knee completely when the hip is flexed accompanied by discomfort or pain along the posterior thigh and/or knee is usually attributed to hamstring muscle tightness". Clinically, hamstring muscle length is not measured directly but instead, it is represented indirectly by angular measurements of unilateral hip flexion with the knee extended. Hamstring muscle tightness is defined as Knee Extension Angle (KEA) greater than 20 degrees where KEA is the degree of knee flexion from terminal knee extension. [1],[3]

Hamstring Tightness: Muscle tightness is caused by a decrease in the ability of the muscle to deform, resulting in a decrease in the range of motion at the joint on which it acts. Inability to achieve greater than 160° of knee extension with hip at 90° of flexion is considered as hamstring tightness. Hamstring tightness leads to hamstring injuries and hamstring injuries are the most common type of injury. These injuries are slow to recover, make high health expenditure and decrease the performance level of the individual.[3]

Method

1. **Type of Study:** Experimental Study
2. **Design of Study:** Randomized Control Trial
3. **Sampling Method:** Simple Random Sampling
4. **Study Duration:** 6 months
5. **Place of study:** Krishna Hospital, Physiotherapy Department
6. **Sample Size:** 276
7. **Target Population:** Both Male and Female With Positive Active Knee Extension Less Than 20 Degree

Criterion of the Study: Inclusion Criteria

1. Asymptomatic subjects
2. AKT<20 degree

3. Age: 20 to 40 years

Exclusion Criteria:

1. Previous Hamstring injury
2. History of low back ache
3. Open Wound on posterior aspect of thigh
4. Osteoporosis of lumbar spine, hip and knee joint
5. Soft tissue injury relating to hamstring and low back region
6. Hamstring Strain both acute and chronic
7. Fractures around lumbar spine, hip and knee

Procedure: An approval for the study was obtained from the Protocol committee and institutional Ethical Committee of KIMSUDU. This study was conducted for the duration of 6 months. 300 subjects of age 20 to 40 years were screened out of which 276 subjects were selected for the study depending on the inclusive and exclusive criteria. Asymptomatic subjects with AKT <20 degree in the age group of 20 to 40 years were included in the study. The study was undertaken after obtaining the approval of Protocol committee and the Institutional Ethical committee of KIMSUDU. These subjects were then divided into 2 groups by where the Type of Study was Experimental study, Design of Study was Randomized Control Trial and Sampling Method was Simple random sampling Pre-treatment assessment and Post-treatment assessment were recorded. Subjects in Group A were given Isolytic contraction + HMP+ Passive manual stretching intervention while subjects in Group B were given conventional treatment. i.e. HMP+ Passive Manual stretching. Where isolytic contraction was performed with a rapid movement with 3 sets of 15 repetition. And Passive manual stretching, 3 sets were given with a hold time of 15 sec. Pre-treatment and Post treatment Assessment with the help of outcome measure of SLR, AKT and lumbar lordosis index were taken and statistics was done. consent of all the participants was taken.

Results

A. Active knee extension test: Active knee extension test Comparison of pre-intervention and post-intervention within the group (Right and Left Side).

Table No. 1

	Side	Pre	Post	P value	Inference
Group A	Right	31.768±6.858	44.70±11.254	<0.0001	Extremely significant
Group B	Right	31.299±5.455	35.86±5.294	<0.0001	Extremely significant
Group A	Left	33.78±6.470	51.036±20.020	<0.0001	Extremely significant
Group B	Left	33.45±4.774	38.47±4.892	<0.0001	Extremely significant

Table No. 2: Active knee extension test Comparison of pre and post AKT Between the group (Right and Left Side)

	Side	Pre	Post
Group A	Right	31.768±6.858	44.702±11.254
Group B	Right	31.29±5.455	35.868±5.294
P value	Right	0.0079	<0.0001
Inference	Right	Not significant	Extremely significant
Group A	Left	33.783±6.470	51.036±20.020
Group B	Left	33.45±4.774	38.474±4.892
P value	Left	0.6384	<0.0001
Inference	Left	Not significant	Extremely significant

Table No. 3: B. Straight Leg Raise: Comparison of Pre-Interventional and Post Interventional SLR within the group (Right and Left Side)

	Side	Pre	Post	P value	Inference
Group A	Right	51.1231±11.191	71.28±12.477	<0.0001	Extremely significant
Group B	Right	53.014±8.755	58.48±8.736	<0.0001	Extremely significant
Group A	Left	53.52±13.945	73.405±13.320	<0.0001	Extremely significant
Group B	Left	55.189±11.711	60.810±11.457	<0.0001	Extremely significant

Table No. 4: Comparison of Pre-Pre and Post-Post SLR between the group (Right and Left Side)

	Side	Pre	Post
Group A	Right	51.123±11.191	71.282±12.477
Group B	Right	53.014±8.755	58.481±8.735
P value	Right	0.1199	<0.0001
Inference	Right	Not significant	Extremely significant
Group A	Left	53.521±13.945	73.405±13.320
Group B	Left	55.189±11.711	60.810±11.457
P value	Left	0.2819	<0.0001
Inference	Left	Not significant	Extremely significant

Table No. 5: C.Lumbar Lordosis Index Comparison of Pre and post LI within the group

	Lumbar Lordosis index		P value	inference
Group A	Pre	Post		
	56.90±14.568	44.22±13.408	<0.0001	Extremely significant
Group B	51.97±10.987	48.41±11.042	<0.0001	Extremely Significant

Table No. 6: Comparison of Pre-Pre and Post-Post of LI in between the group.

	Pre	Post
Group A	56.90±14.568	44.22±13.408
Group B	51.97±10.987	48.41±11.042
P value	0.0017	0.0050
Inference	Very significant	Very significant

Discussion

The current study is aimed to find short term effect of isolytic contraction on hamstring flexibility in asymptomatic subjects with hamstring tightness using a randomized control trial. 276 subjects were selected based on the inclusion and exclusion criteria and were allotted in 2 groups. Objectives of this study were to find whether there is any effect of isolytic contraction on hamstring flexibility, because in general the subjects with hamstring tightness can lead to Low back Pain, Limited hamstring flexibility, Risk of Hamstring strain, Poor core stability, Increased lordosis, Increased Fatigue, Tight hip flexors and many more musculoskeletal problems which may lead to limitation in daily activity may it be athlete or old individual. [5]

Prevalence of Hamstring tightness was taken into consideration, according to previous studies conducted, concluded that the age of 20 to 30 has been the most population having tight hamstring. According to study 40.17% were the male population affected. [1] So considering the population a total of 300 sample were screened and depending on the inclusive and exclusive criteria of the study 276 sample were included in the study.

According to previous studies of Ballantyne F, Fryer G, McLaughlin P; 2003. The Effect of Muscle Energy Technique on Hamstring Extensibility. The study concluded that 'There is significant increase in hamstring extensibility following MET, where Muscle energy technique produced an immediate increase in passive knee extension. This observed change in range of motion is possibly due to an increased tolerance to stretch as there was no evidence of visco-elastic change. Results showed A significant increase in range of motion at the knee ($p < 0.019$) following a single application of MET to the experimental group. No change was observed in the control group. [11] When an identical torque was applied to the hamstring both before and after the MET, no significant difference in range of motion of the knee was found in the experimental group.

Where as compared to isolytic contraction is proven to be more effective than then the controlled group with the results showing extremely significance because the physiological evidence shows increased in tone, stretching and repetitive work on antagonist muscle increases the flexibility with no injury. [11]

Similarly, Sonal et al; 2016. Comparison between Post Isometric Relaxation and Reciprocal Inhibition maneuvers on hamstring flexibility in young healthy adults. The study concluded that both PIR and RI are effective techniques to improve hamstring flexibility is better and effective technique as compared to RI. As per the present study isolytic contraction is proven to be more effective than then the controlled group with the results showing extremely. [21]

Gayle Silveira, Mark Sayers, Gordon Waddington – Department of Health, Design and Science, University of Canberra, Effect of dynamic versus static stretching in the warm-up on hamstring flexibility, March 3, 2011, the intervention study comparing the effects of static and dynamic stretching routines in the warm-up on hamstring flexibility demonstrated that dynamic stretching enhanced static as well as dynamic flexibility. Static stretching on the other hand did not have an impact on dynamic flexibility. This has implications for the use of static stretching in the warm-up for dynamic sport. The role of static stretching for injury prevention in dynamic sport is also being questioned. [14]

¹Dr. Shweta P. Pachpute ²Nancy Patel ³Dr. Seema Saini, EFFECT OF STATIC STRETCHING ON STRENGTH OF HAMSTRING MUSCLE, Static stretching showed significant change in pre and post RM of hamstring muscle and active knee extension test. There was significant improvement of hamstring muscles flexibility and strength after giving static stretching in female population. So, it is possible that females who are unable to participate in traditional strength training activities may be able to experience gains through static stretching. As mentioned in the above study. [22]

Considering the above 2 literatures of Dr Shweta she concluded that static stretching is more effective whereas Gayle Silveira concluded that Dynamic stretching shows a great difference of impact that can increase hamstring flexibility than static, But in the present study where in the group B it shows passive stretching is less effective than the control group because, where comparing it with isolytic contraction, it is more effective than dynamic

as well as static stretching. According to the outcome measure.

The present study presents the subject of 276 sample were divided into 2 groups Group A and Group B. subjects were given explanation what subject is going to receive and what benefits and its effects are, the subjects were asked to sign a consent form, Treatment for both the groups was started 2 months prior Group A was given HMP, Passive Static Stretching and Isolytic contraction and Group B was given HMP and Passive Static Stretching. Range of Motion, Straight Leg Raise test and Lumbar Lordosis Index was assessed after the treatment and before the treatment. Pre-Treatment and Post Treatment Assessments was done for the comparative study between these 2 groups. Reposes will be recorded and results were seen to be extremely significant. As the mechanism responsible for increasing the hamstring flexibility is proven to be effective after hot moist pack the isolytic contraction on the antagonist muscle helps in lengthening the muscle as well as allows the muscle to tone. Bidirectionally support the tighten hamstring which gives a flexible movement to the muscle and increases flexibility. [3]. [8]

Conclusion

The present study provided evidence to support the use isolytic contraction on hamstring flexibility in asymptomatic subjects having hamstring tightness. Statistically there was extremely significant difference in both the values showing significantly more improvement in subjects of Group A when compared to subjects in Group B, hence it can be stated Short term effect of isolytic contraction in hamstring flexibility in asymptomatic subjects with hamstring tightness has proven to be effective extremely significant. The authors do not have any conflict of interests.

Conflict of Interest: The author declares that there are no conflicts of interest concerning the content of the present study.

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Ethical Clearance: The study was approved by Institutional Ethics Committee, KIMSUDU.

References

- 1 Shakya N R, Manandhar S, Prevalence of Hamstring muscle tightness among undergraduate physiotherapy students of Nepal using Passive Knee Extension Angle Test IJSRP, Volume 8, Issue 1, January 2018 Edition [ISSN 2250-3153].
- 2 Back of thigh In Krishna Garg editor text book of Human Anatomy B.D Chaurasai 6th edition, New Delhi 2013, p 83-86
- 3 Frankel, M.N.V.H., Basic Biomechanics of the Musculoskeletal System. Third ed. 2001, New York, New York: Lippincott Williams & Wilkins
- 4 Srbinoska, H., et al., Correlation between back shape and spinal loads. Journal of Biomechanics, JBiomech. 2013 July 26;46(11):1972-75. doi: 10.1016/j.jbiomech.2013.04.024.Epub 2013 May 29. 2013. 46: p. 1972-1975.
- 5 Fellingham G.W., Measom.G.W. The effect of duration of stretching of the hamstring muscle group for increasing range of motion in people aged 65 years or older, physical therapy, May 2001,81(5),1110-1117.
- 6 Abdela/ AA, Soliman ES, Abdelraouf OR. Isokinetic peak torque and flexibility changes of the hamstring muscles after eccentric training: Trained versus untrained subjects. Acta Orthop Traumatol Turc. 2018 Jul;52(4):308-314. doi: 10.1016/j.aott.2018.05.003.
- 7 Shepherd E, Winter S, Gordon S (2017) Comparing Hamstring Muscle Length Measurements of the Traditional Active Knee Extension Test and a Functional Hamstring Flexibility Test. Physiotherapy Rehabil 2:125. doi:10.4172/2573-0312.1000125
- 8 Day, J., G. Smidt, and T. Lehmann, Effect of Pelvic Tilt on Standing Posture. Physical Therapy, 1984. 64(4).
- 9 DariuszC, Leszczewska J, Aleksandra K, Paulina P, Agnieszka K, Piotr J, and Kotwicki T Harty J, Soffe K. The Comparison of the Effects of Three Physiotherapy Techniques on Hamstring Flexibility in Children: A Prospective, Randomized, Single-Blind Study. The role of hamstring tightness in Plantar Fasciitis. Foot and Ankle International December 2005;26:1089-092
- 10 Gribble PA, Guskiewicz KM, Prentice WE, Shields EW. Effects of static and hold-relax stretching on hamstring range of motion using the Flexibility LE1000. Journal of Sport Rehabilitation. 2015 Feb; Volume 27(2) Page: 535–538.
- 11 Ballantyne F, Fryer G, McLaughlin P. The

- effect of muscle energy technique on hamstring extensibility: the mechanism of altered flexibility. *Journal of Osteopathic Medicine*. 2003; Volume 6(2) page :59-63.
- 12 Prem P. Gogia James H. Braatz Steven J. Rose Barbara J. Norton; Reliability and Validity of Goniometric Measurements at the Knee. *Physical therapy* February 1987, Volume 67 / Number 2,
- 13 Hsieh, C. Y., Walker, J. M., & Gillis, K. (1983). Straight-leg-raising test. Comparison of three instruments. *Physical Therapy*, Vol 63(9), p 1429-1433.
- 14 Silveira G, Sayers M, Waddington G – Department of Health, Design and Science, University of Canberra, Effect of dynamic versus static stretching in the warm-up on hamstring flexibility, *The sports journal* March 3, 2011,
- 15 Bandy WD, Irion JM. The effect of time on static stretch on the flexibility of the hamstring muscles. *Physical Therapy*. 1994 September; Vol 74(9) P: 845-50.
- 16 Gajdosik R, Lusin G. Hamstring muscle tightness: Reliability of an active-knee-extension test. *Physical Ther*. 1983;63 Vol (7) P:1085-1088
- 17 Gajdosik and Lusin G. Reliability of an active knee extension test, *Physical therapy*. July 1983. Vol 63(7), P1085-1088.
- 18 Gopi et al., Correlation of hamstrings flexibility with age and gender with subjects having Chronic Low Back pain, *International Journal of Therapies and Rehabilitation research* 2014; Vol 3(4) P: 31-38.
- 19 Knight C A, Rutledge C R, Cox M E, Acosta M, Hall S J. Effect of Superficial Heat, Deep Heat, and Active Exercise Warm-up on the Extensibility of the Plantar Flexors. *Physical Therapy* June 2001; Vol 81:1206-1214
- 20 Boissière L, Bourghli A. The lumbar lordosis index: a new ratio to detect spinal malalignment with a therapeutic impact for sagittal balance correction decisions in adult scoliosis surgery, *Eur Spine J*. 2013 Jun; Vol 22(6) p: 1339–1345.
- 21 Sonal et al; 2016. Comparison between Post Isometric Relaxation and Reciprocal Inhibition manoeuvres on hamstring flexibility in young healthy adults, *International Journal of Medical Research & Health Sciences (IJMRHS)* 2016; Vol 5(1) p: 33-37
- 22 Dr. Pachpute S P, Patel N, Dr. Saini S, EFFECT OF STATIC STRETCHING ON STRENGTH OF HAMSTRING MUSCLE, *Int J Physiotherapy* 2016; vol 3(2), p 218-221, April 2016

Analysis and Comparison of Salivary L-Fucose and HSP 70 in Oral Potentially Malignant Disorders and Oral Cancer

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Abstract

The aim of this study was to assess the level of salivary L-Fucose and Heat Shock Protein 70 in subjects in subjects with Oral Potentially Malignant Disorders and Oral Cancer.

Method & Results: The study was done among 90 subjects - 30 healthy subjects, 30 subjects with Oral Potentially Malignant Disorders and 30 subjects with Oral Cancer. Saliva samples were collected and the levels of L-Fucose and HSP-70 were determined. Data obtained was analyzed using ANOVA test for the comparison between the groups. Post hoc tukey's analysis was used for comparing the study groups to the control group. The levels of L-Fucose and HSP-70 in saliva were increased significantly in subjects with Oral potentially malignant disorders and Oral Cancer in comparison to the healthy subjects.

Conclusion: Elevated levels of HSP 70 and L-fucose in saliva in oral potentially malignant disorders and oral cancer indicate their usefulness as biomarkers for early prediction.

Keywords: Saliva, Oral Cancer, HSP 70, L fucose

Introduction

On a global scale, cancers of the lip, oral cavity and the pharyngeal regions were estimated to be accountable for 529,500 incident cases and 292,300 deaths in 2012, thus making it responsible for approximately 3.8% of all cancers and 3.6% of deaths.¹ According to global reports, cancers of the oral cavity region are grouped and

together represent the 6th most common form of cancer in the world.² Oral cancer is generally detected in the advanced stages, regardless of the accessibility to the oral cavity during clinical examination, the commonest reason being initial misdiagnosis and negligence of the patient or the treating professional, apparently reducing the survival in spite of therapeutic measures.³ Squamous Cell Carcinoma's account to nearly 90% of tumors in the oral cavity, with adenocarcinoma/minor salivary tumors make up 5%, and 2% each with verrucous carcinoma and lymphoma 2% . The rest are unusual sarcomas or odontogenic tumours.⁴

Heat shock protein-70(HSP70) is present in the body and body fluids like blood, lymph, spinal fluid and saliva. They are categorized as intracellular HSP70

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(iHSP70) and extraellular HSP70 (eHSP70). eHSP70 activates the production of pro-inflammatory cytokines via binding with toll-like receptors (TLR)-2 and TLR-4, causing inflammation.^{5,6}In the oral cavity, eHSP70 plays the part of mucosal defense which includes entrapping, agglutinating, opsonization of bacteria, and inhibition of pathogenic adhesion to the mucosal surface.⁷ HSP70 prevent apoptosis due to direct physical interaction with apoptotic molecules, which are also overexpressed in many tumor cells.⁸

Fucose is a monosaccharide which is a usual constituent of many N and O-linked glycans and glycolipids elaborated by the mammalian cells.⁹The existing literatures about the levels of L-Fucose activity and HSP 70 in saliva is scarce. Thus, the information obtained from the study could be useful in determining L - Fucose as a salivary biomarker in the diagnosis of oral potentially malignant disorders and oral cancer. It would also be useful in determining the association of salivary HSP70 with oral potentially malignant disorders and oral cancer.

Material and Method

The present study is an observational study. After obtaining ethical clearance (Cert. No: ABSM/EC13/2016) by the institution, the participants were provided with a written informed consent before data collection. The study sample comprised of 90 subjects in the age group of 20–60 years who were divided into 3 groups of 30 each.

Control Group : 30 healthy subjects without any oral lesions

Study Group 1: 30 subjects with oral potentially malignant disorders

Study Group 2: 30 subjects with oral cancer.

Method of Collection of Data: The study was conducted for a period of 2 years from 2016-2018. Informed consent was obtained from the patients included in the study along with recording of detailed case history and thorough examination of the oral cavity.

Saliva Collection: The subjects were asked not to consume any food 2 hours prior to the collection of saliva.¹⁰ Following a mouth rinse, they were asked to sit with their head tilted forward and asked not to speak or swallow any saliva. They were then asked to spit into a sterile container every minute for 8-10 minutes. The

collection of saliva was limited to the hours between 9:00 A.M and 11:00 A.M to minimize diurnal variation.

Heat Shock Protein 70 (Hsp70) Estimation: The estimation of HSP 70 in Saliva was done using ELISA kit method, procured from Hysel India Pvt Ltd. This kit (Bioassay Technology Laboratory Cat.No-E1813Hu) utilized enzyme-linked immune sorbent assay (ELISA) based on the Biotin double antibody sandwich technology for the purpose of assaying the Human Heat shock protein 70 (HSP70). Heat shock protein 70 (HSP70) was added to the wells, which are pre-coated with Heat shock protein 70(HSP70) monoclonal antibody and then incubated. After this step, anti HSP70 antibodies labelled with biotin were added to unite with streptavidin-HRP, which formed an immune complex. Unbound enzymes were removed after incubation and washing. Substrate A and B were added. Then the solution turned blue and changed into yellow with the effect of acid. The shades of solution and the concentration of Human Heat shock protein 70 (HSP70) were positively correlated.

Estimation of L Fucose: The estimation of L-Fucose was done based on the method of Winzler.¹¹Fucose is a methyl pentose which is present in the glycoproteins. The assay can be done by dissolving ethanol precipitated proteins of the serum in alkali, heating with sulphuric acid and then determining the colour by adding cysteine. The colour production by hexoses under the above conditions is rectified by determination of absorbance at two wavelengths.

Findings: The present study was done to evaluate the levels of HSP-70 and L-fucose in saliva of oral potentially malignant disorders and oral cancer. The data collected was entered into Microsoft Excel spreadsheet and analyzed SPSS 20.0 from IBM incorporated.

The mean salivary HSP-70 levels in the control group was 2.87ng/ml, while the mean salivary HSP-70 levels in Study group 1 was 4.48ng/ml and 5.23ng/ml in Study group 2. (TABLE 1). On comparing salivary HSP-70 levels of Control Group (2.87ng/ml) and Study Group I (4.48ng/ml), difference was statistically significant ($p < 0.001$). Similarly, when salivary HSP-70 levels of control group were compared with levels of study Group II (5.23 ng/ml), significant differences were obtained ($p < 0.001$). When a statistical comparison between salivary levels of HSP-70 levels of study group I and study group II was done, significant differences were obtained ($p < 0.001$). (TABLE NO.2 & 3)

The mean salivary L-Fucose levels in the control group was 18.27 mg/dl, while the mean salivary HSP-70 levels in Study group 1 was 23.26mg/dl and 27.61 mg/dl in Study group 2. (TABLE 1). On comparing salivary L-Fucose levels of Control Group (18.27mg/dl) and Study Group I (23.26mg/dl), difference was statistically significant (p<0.001). Similarly when salivary L-fucose levels of control group were compared with levels of study Group II (27.61 mg/dl), significant differences were obtained (p<0.001). When a statistical comparison

between salivary levels of L-fucose levels of study group I and study group II was done, significant differences were obtained (p<0.001). (Table No. 2 & 3).

Table No. 1: Mean HSP-70 and L-Fucose Levels

Group	HSP 70 (ng/ml)	L Fucose (mg/dl)
Control group	2.87±.68	18.27±4.90
Study group 1	4.48±.57	23.26±6.15
Study group 2	5.23±.89	27.61±4.33

Table No. 2: One Way Anova:

	Groups	N	Mean	Std. Deviation	Welch Statistics (*)/F (ANOVA)	P Value
AGE	CONTROL	30	34	12.646	19.087	<0.001
	GROUP S1	30	40.5	11.953		
	GROUP S2	30	52.77	11.199		
	Total	90	42.42	14.169		
HSP 70 (ng/ml)	CONTROL	30	2.878532	0.684249	77.432*	<0.001
	GROUP S1	30	4.483919	0.575274		
	GROUP S2	30	5.230884	0.896457		
	Total	90	4.197778	1.223222		
L-FUCOSE (mg/dl)	CONTROL	30	18.272	4.908986	24.358	<0.001
	GROUP S1	30	23.268	6.156379		
	GROUP S2	30	27.616	4.333575		
	Total	90	23.052	6.407813		

Table No. 3: Post Hoc Tukey`S Test

Dependent Variable	(I) group	(J) group	Mean Difference (I-J)	Std. Error	P VALUE
AGE	CONTROL	GROUP S1	-6.5	3.085	0.094
		GROUP S2	-18.767*	3.085	<0.001
	GROUP S1	GROUP S2	-12.267*	3.085	<0.001
HSP 70 (ng/ml)	CONTROL	GROUP S1	-1.6053874*	0.188725	<0.001
		GROUP S2	-2.3523523*	0.188725	<0.001
	GROUP S1	GROUP S2	-.7469649*	0.188725	<0.001
L-FUCOSE (mg/dl)	CONTROL	GROUP S1	-4.9960000*	1.339809	0.001
		GROUP S2	-9.3440000*	1.339809	<0.001
	GROUP S1	GROUP S2	-4.3480000*	1.339809	0.005

Discussion

Human saliva is a clear, slightly acidic (pH=6.0-7.0) biological fluid comprising of a mixture of secretions from parotid, submandibular, sublingual glands, the minor glands beneath the oral mucosa and gingival crevicular fluid.¹²From a Salivary specimen, multiple

samples can be collected from the same individual at the optimum time for the purpose of diagnostic data.¹³It is now gained recognition as having a chief role in various biomedical basic and clinical areas.¹⁴Saliva contains an array of analytes like protein, mRNA and DNA, and can be used as a biological marker for translation and clinical applications.¹⁵

The total amount of protein in whole saliva ranges between 0.5 to 3 mg/ml.¹⁶Saliva contains Heat Shock Proteins like HSP 60, 70 and 90.¹⁷ HSP 70 has crucial extracellular actions as noticeable from experiments involving exogenous HSP 70 administration to human promonocyte cells prior to tumor necrosis factor-alpha (TNF- α) exposure where the numbers of apoptotic and necrotic cells were reduced significantly. HSP 70 which is present in saliva involves passive transport from blood serum.¹⁸

In the present study, the salivary HSP 70 levels in Oral potentially malignant disorders had increased significantly on comparison with controls. Though the literature on saliva pertaining to HSP 70 is scarce, studies have been conducted in serum and in tissues, which have been subjected to immunohistochemistry. NJ Mary et al conducted that HSP 70 levels in serum increased significantly in oral leukoplakia on comparison with the controls.¹⁹Heat shock proteins are the primitive defense system in all living organisms. They are a class of functionally related proteins which increase expression in cells when exposed to increased temperature or stresses like infection, irradiation, ethanol, oxidants and heavy metals.^{19,20,21}

Patil et al, in their study which examined tissues of leukoplakia subjected immunofluorescence along with controls, proved that there was an increase in the expression of HSP 70 in leukoplakia.²²As the grade of dysplasia increased, the intensity of staining also increased thus indicating that over expression of HSP 70 occurred during oral carcinogenesis, concluding that an overexpression of HSP 70 could be a marker of epithelial dysplasia.²² Similar results were seen in our study, where saliva was analyzed for HSP 70 levels. HSP 70 is secreted in saliva, the major route being the passive transport from blood serum or salivary gland cells.¹⁸

In the present study, there was significant increase in the levels of HSP 70 in oral cancer when compared to controls. This was similar to the study done by Hegde et al, where an increased level of salivary HSP 70 was found in patients who were undergoing radiotherapy for head and neck cancer.²³ Heat shock factor 1, a transcription factor is responsible for maintaining the expression of HSP 70. HSP 70 imparts thermo tolerance and protein folding during post translation import into the mitochondria. It also prevents proteins which are denatured partially from aggregation, allowing unfolding during stress and thermal stress.²⁴

In the present study, the salivary L-fucose levels were increased in oral potentially malignant conditions and oral cancer on comparison with the controls. This has been in accordance to the study conducted by Pradeep et al.²⁵Fucose is a monosaccharide.²⁶The universal characteristic of cancer is the unusual glycosylation. The addition of L-fucose at the terminal end of the oligosaccharide, called fucosylation mediates several biological functions. By modulating their surface to increase fucosylation, tumor cells cause several abnormal characteristics like decreased adhesion and uncontrolled tumor growth.²⁶

Saliva is a biological fluid which is clinically informative and is useful for novel approaches to clinical and laboratory diagnosis, management, monitoring and prognosis of patients with oral and systemic diseases.¹⁴ Hence our study highlights the significance of saliva as a non-invasive diagnostic tool measuring the levels of salivary HSP 70 and L-fucose in oral potentially malignant disorders and oral cancer.

Conclusion

Elevated levels of HSP 70 and L-fucose in saliva in oral potentially malignant disorders and oral cancer indicate their usefulness as biomarkers in the early prediction. This study also establishes the significance of saliva as a non-invasive diagnostic tool, where even the presence of small quantities of such biomarkers can be detected. More such salivary studies should be undertaken on a larger scale to establish the efficiency of both HSP 70 and L fucose as biomarkers.

Conflict of Interest: None

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Ethical Clearance: Ethical Clearance was obtained by the Ethical Committee of the University(Cert. No: ABSM/EC13/2016)

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References

1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M et al. Cancer incidence and mortality worldwide: sources, method and major patterns in GLOBOCAN 2012. *Int J Cancer*. 2015; 136(5):E359-86.
2. Warnakulasuriya S. Global epidemiology of oral and oropharyngeal cancer. *Oral Oncol*. 2009;45:309–316
3. Markopoulos AK. Current aspects on oral squamous cell carcinoma. *Open Dent J*. 2012;6:126–130.
4. Agar NJM, Patel RS. Early Detection, Causes and Screening of Oral Cancer. *JSM Dent*. 2014;2(3): 1039.
5. Asea A, Rehli M, Kabingu E, Boch JA, Bare O, Auron PE et al. Novel signal transduction pathway utilized by extracellular HSP70: role of toll-like receptor (TLR) 2 and TLR4. *J Biol Chem*. 2002;277(17):15028–15034.
6. Asea A, Kraeft SK, Kurt-Jones EA, Stevenson MA, Chen LB, Finberg RW, Koo GC, Calderwood SK. *Nat Med*. 2000 Apr; 6(4):435-42.
7. Fabian TK, Hermann P, Beck A, Fejerdy P, Fabian G. Salivary defense proteins: their network and role in innate and acquired oral immunity. *Int J Mol Sci*. 2012;13(4):4295–4320.
8. Dudeja V, Mujumdar N, Phillips P, Chugh R, Borja-Cacho D, Dawra RK et al. Heat shock protein 70 inhibits apoptosis in cancer cells through simultaneous and independent mechanisms. *Gastroenterology*. 2009;136:1772–1782.
9. Becker JD, Lowe JB. Fucose: Biosynthesis and biological function in mammals. *Glycobiology*. 2003;13(7):41R-53R.
10. Navazesh M. Method for collecting saliva. *Ann NY Acad Sci*. 1993;694(1):72-77.
11. Winzler RJ. In: *Method of biochemical analysis*. Glick D, editor. New York: Interscience Publishers Inc; 1955.
12. Spielmann N, Wong DT. Saliva: diagnostics and therapeutic perspectives. *Oral Dis*. 2011;17(4):345–354.
13. Lindsay FH. Human Saliva as a Diagnostic Specimen: *Dent Clin North Am*. 2011;55(1): 159–178. *J Nutr*. 2001;131(5):1621S-5S.
14. Malamud D, Rodriguez-Chavez IR. Saliva as a Diagnostic Fluid. *Dent Clin North Am*. 2011;55(1):159-178.
15. Jiang J, Park NJ, Hu S, Wong DT. A universal pre-analytic for concurrent stabilization of salivary proteins, RNA and DNA at ambient temperature. *Arch Oral Biol*. 2009;54:268–273.
16. Fabian TK, Fejerdy P, Csermely P. Salivary genomics, transcriptomics and proteomics: The emerging concept of the oral ecosystem and their use in the early diagnosis of cancer and other diseases. *Curr. Genomics*. 2008;9(1): 11–21.
17. Chatterjee S, Damle SG, Sharma AK. Salivary heat shock proteins and their interactions with oral microenvironment. *Inflamm Cell Signal*. 2014;1:e101.
18. Fabian TK, Gaspar J, Fejerdy L, Kaan B, Balint M, Csermely P et al. Hsp70 is present in human saliva. *Med Sci Monit* 2003;9(1):BR62-65.
19. Mary NJ, Prashanth K, Jaysheel AS. Estimation of Serum Levels of Heat Shock Proteins (HSP) – 70 in Patients with Oral Dysplastic Lesions of Leukoplakia. *J Cont Med A Dent*. 2016;4(2):70-73.
20. Garcia GV, Martinez AB, Kass AG, Clay CPM, Kuffer R, Fernandez EA et al. Analysis of the expression of heat-shock protein 27 in patients with Oral Lichen Planus. *Oral Dis*. 2013; 19 (1): 65- 72.
21. Tekkesin MS, Aksakalli N, Olgac V. Expression of heat shock proteins 27, 60 and 70 in oral carcinogenesis. An immunohistochemical study. *TürkOnkolojiDergisi*. 2011;26(3):115-120.
22. Patil P, Nandimath K, Prabhu S, Naikmasur VG. Heat shock protein (HSP70) as a marker of epithelial dysplasia in oral dysplastic lesions: A clinicopathological study. *J Oral Maxillofac Pathol*. 2015;19(1):53-57.
23. Hegde MN, Shetty N, Kumari SN. Saliva as Biomarker of Heat Shock Protein 70 in Radiotherapy. *RRJDS*. 2019;7(2):1-5.
24. Schlesinger MJ. Heat shock proteins. *J Biol Chem*. 1990;265(21):12111–12114.
25. MR Pradeep, K Deepa, Kumar S, Kumar DV, R Sujith. Serum and Salivary Sialic Acid and L-Fucose as prognostic markers in Potentially Malignant Disorders and Oral Cancer. *Unique J Med Dent Sci*. 2014;2(4):76-83.
26. Shamberger RJ. Serum sialic acid in normals and in cancer patients. *J Clin Chem Clin Biochem*. 1984;22(10): 647-651.

Knowledge Attitude and Practices of Biomedical Waste Management among Dental Practitioners in Karad City Maharashtra, India

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Abstract

Introduction: Biomedical waste is generated routinely in high amounts in the dental office, the correct disposal of which bears importance to the dentist, staff and healthcare workers. This is the first of its kind study in the city of Karad which will provide an important insight into the proper method and knowledge of disposal of health care waste by the dental practitioners. The application of this study will be in accessing the legal necessity and social responsibility of the healthcare personnel's in the effective management of biomedical waste.

Materials and Method: The study population included 100 private practitioners in Karad City, Maharashtra. A self-administered questionnaire was distributed to assess the knowledge, attitude and practices regarding dental waste management. Descriptive statistics was used to summarize the results.

Results: Out of 100 study participants, 73 (73%) were males and 27 (27%) were females. The maximum number of participants belonged to the age group of 34-38 years (29%). Undergraduate qualification was more (80%) and 43% participants had an experience of 0-5 years. Chi-square analysis showed a highly significant association between participant who attended continuing dental education (CDE) program and their practice of dental waste management.

Conclusion: Lack of knowledge and professional training in disposal of biomedical waste becomes a direct threat to the humans as well as the environment. CDE programs would help bring about a change in the management of healthcare waste.

Keywords: Biomedical waste, dentist, hospital waste.

Introduction

The health care sector produces a huge amount of biomedical waste in the course of curing health

problems. The management of hospital waste or biomedical waste is considered as an important aspect to avoid various hazards to the humans and environment. Since this waste keeps generating continuously, it is the legal necessity and social responsibility of every healthcare professional to meticulously segregate and dispose the waste.¹ Biomedical waste means any waste, which is generated during the diagnosis, treatment and immunization of human beings or in research activities pertaining thereto or in the production or testing of biological, and including categories mentioned in Schedule 1 of the Government of India's Biomedical Waste (Management and Handling) Rules 1998.²

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On an average per day per bed, 0.5-2 kg waste is generated in India. Annually 0.33 million tons of hospital waste is generated in India. Biomedical waste not only poses great threat to the environment and the general population, but also to the ones who handle it and carry out the disposal.³ 15% of the total waste generated is infectious and hazardous. This waste pertains to be a threat to the living as well as the non living thing.⁴

This waste plays a significant role in the spread of pathogens like HIV, Hepatitis B & C. Dental offices generate a large amount of biomedical waste daily. This waste is of equal harm to the environment and atmosphere as to the humans.⁵ Lack of knowledge persists regardless of the professional training and thus, necessary measures to deliver awareness is the need of the hour.^{6,7} Hence this study has been undertaken to assess the knowledge of dental practitioners in Karad city, understand the practices of waste disposal, train the healthcare workers and to take measures in establishing a protocol.

Materials and Method

A cross-sectional study was conducted among the dental practitioners in Karad city, Maharashtra, India from December 2018 to February 2019.

A pre-tested, self-administered, closed-ended questionnaire was designed for recording all the relevant data pertaining to general information of the study participants and knowledge and practices regarding dental waste management in a private clinic. Ethical approval was obtained from the Institutional Ethics Committee of KIMS Deemed to be University, Karad. Questionnaires were adopted from previous studies and modified.^{1,8} A few new questions were formulated, some questions were modified while some were considered unnecessary and removed since this did not hamper with the fluidity of the questions.

The questionnaire consisted of 18 questions to assess the knowledge and the practice of biomedical waste management. The questions were grouped under Knowledge/Cognizance, Attitude and Practices/ Execution of biomedical waste and its management.

Questions to access knowledge were of a multiple choice type, only one response being the correct one. Questions to access attitude were presented in positive or negative response format (Yes/No/Don't Know). Questions regarding practice were of multiple choice type, including the various method which may

be implemented in routine practice. Each correct and incorrect response in the knowledge section and each yes and no or don't know for the attitude and practice question are to be given 1 and 0 mark, respectively.

The study sample was collected. The study population comprised of 112 private dental practitioners, of which 100 dental Practitioners gave consent to participate in the study. The study participants were given sufficient time to answer the questionnaire and the questionnaire was collected back on the same day or the next day. Questions about KAP were assessed for scores individually. Descriptive summary using frequencies, proportions and cross tabs were used to present study results. The collected data was entered in Microsoft excel sheet and subjected to statistical analysis. Statistical significance was analyzed using Chi-square test. The level of significance was set at 5%. The Statistical Package for Social Sciences (SPSS) version 21.0 was used for the statistical analysis.

Results

Table 1: Demographic distribution of Practicing Dentists in Karad according to age gender, qualification and experience

Sociodemographic variables	n (%)
Age in years	
23-28	8(8)
29-33	24(24)
34-38	35(35)
39-43	19(19)
44-48	5(5)
49-53	4(4)
54 & Above	5(5)
Gender	
Male	73(73)
Female	27(27)
Qualification	
BDS	80(80)
MDS	20(20)
Experience (in Years)	
0-5	43(43)
6-10	35(35)
>10	22(22)

A total of 100 participants were recruited for this study, with a 100% response rate. As shown in Table

1, 73(73%) participants were males and 27 (27%) were females. The maximum number of respondents belonged to the age group of 34-38 years (35%). Respondents with undergraduate qualification were more (80%) compared to postgraduate qualification (20%). 43 (43%) participants had an experience of 0-5 years.

Table 2: Association between CDE program and knowledge scores of dental waste management

CDE Program	Knowledge Scores					Chi-Square Value	Df	P value
	Very poor	Poor	Average	Good	Total			
CDE								
Attended	1	12	19	15	47	53.95	3	0.628 (NS)
Not Attended	1	11	29	12	53			
Total	2	23	48	27	100			

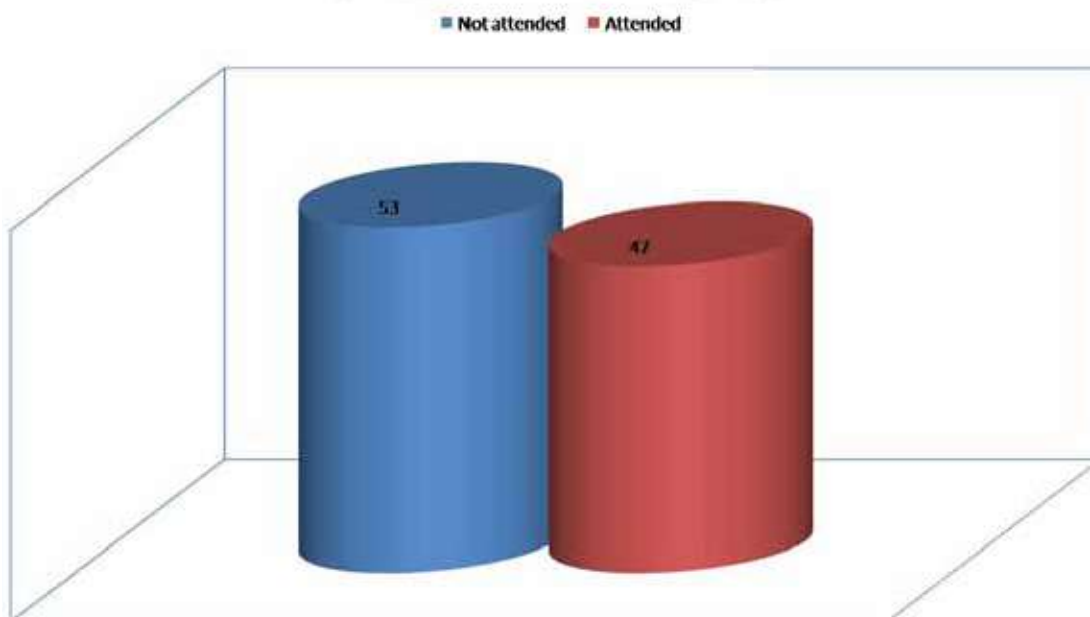
P<0.05 Significant (S); p>0.05 Not significant(NS)

Table 3: Association between CDE program and Practice scores of dental waste management

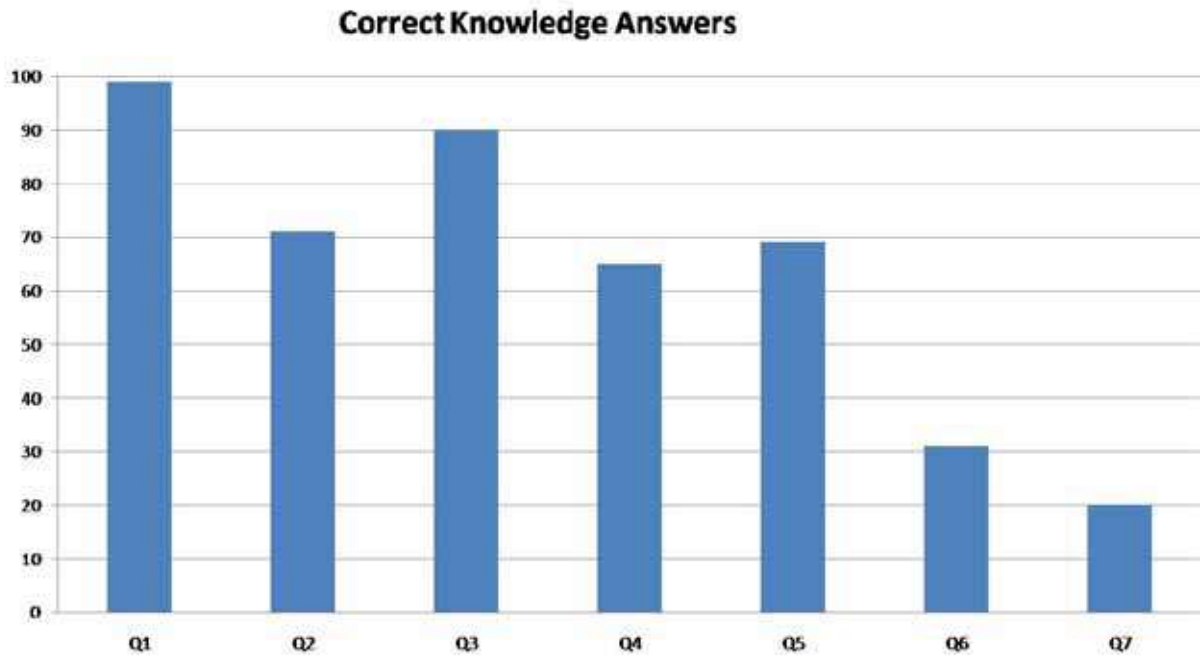
CDE Program	Practice Scores					Chi-square Value	Df	P value
	Very poor	Poor	Average	Good	Total			
CDE								
Attended	0	9	21	17	47	9.83	3	0.0152 (S)
Not Attended	0	12	25	16	53			
Total	0	21	46	33	100			

P<0.05 Significant (S); p>0.05 Not significant(NS)

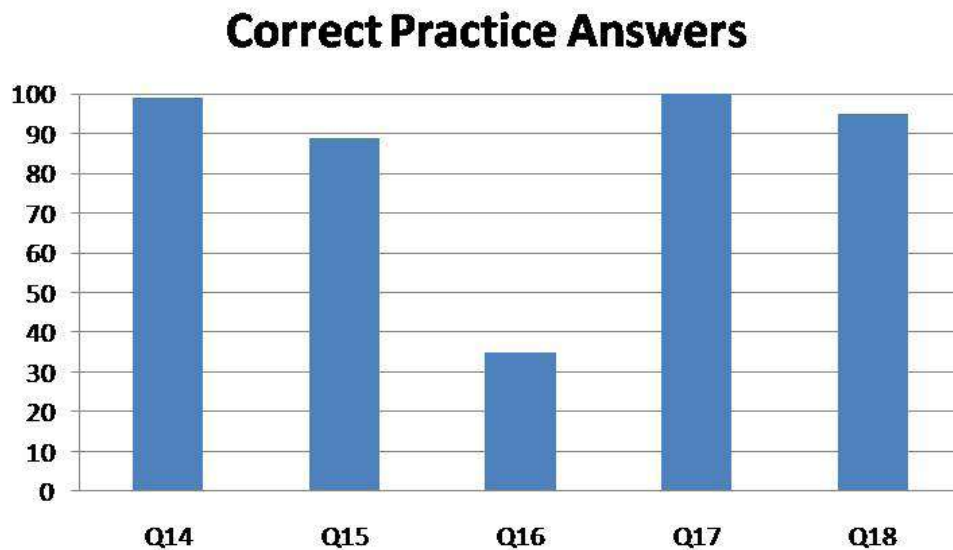
Study subjects attended CDE programs



Graph 1: Distribution of Study subjects as per CDE programs attended



Graph:2 Distribution of Respondents by correct Knowledge answers



Graph : 3 Distribution of Respondents by correct practice answers

Graph 1 shows that 47 participants have attended CDE programs on dental waste management.

Graphs 2 and 3 show that the distribution of respondents by correct knowledge and practice answers.

Table 2 shows the association between CDE program and knowledge scores of dental waste management. Knowledge score was good among 31.91% subjects who attended CDE programs.

Table 3 it is evident that good waste management practice was observed in those who attended CDE programs 36.17% compared to those who did not attend CDE programs. Association between CDE program and practice scores of dental waste management was statistically significant (<0.05)

Discussion

Hospital waste generation is a continuous process.

This waste needs to be disposed in place or, it may serve to be a potential carrier for various diseases and pollution. A major contribution to this waste is from dental clinics. Dental waste consists of a wide range of materials from amalgam, cements and files to bloody cotton swabs, needles and human anatomical waste.

Although the dental profession is a team effort, management of biomedical waste is done at an individual level. The dental waste travels through the hands of numerous individuals and thus, monitoring of proper disposal is one of the many tasks the dental professional needs to observe. In order to assess the present situation and to gain insight on the efforts that need to be undertaken to help with the cultural needs, a learning instrument (questionnaire) based on the knowledge, attitude and practices of the dentist has been arranged.^{1,5} 100 subjects involved in this study, including 80 graduate and 20 post-graduate qualification. 99% subjects reported to be aware of the different categories of biomedical waste and that efficient segregation of this waste was carried out in their practice. While, only 71% of these subjects had knowledge of the color coding given by the biomedical waste management in India. 65% individuals showed knowledge of the use of yellow bag/containers to dispose human anatomical waste.

96% subjects reported to be registered with a certified waste carrier service to recycle or dispose the biomedical waste generated in the clinic. 34% dental clinics were registered with a private biomedical wastage service. Most of the private dental clinics did not show much use of dental amalgam. 69% private dental professionals were aware of mercury spill kit being the most effective way to remove accidental spill of mercury. This result is similar to a study conducted at dental clinics in Karnataka, India.¹ 89% subjects informed that they used needle burn to dispose infected needles.

In the present study, 47% of the participants have attended CDE program based on biomedical waste management, the results of which showed increased awareness and better practice of waste disposal. 78% subjects are willing to attend training on biomedical waste management or think they need more knowledge regarding the issue. Although specialized waste carrier services are available in India, dental professionals and students need to be made accustomed to the availability of these services.

Conclusion

Insufficient professional training regarding this topic becomes a major contributor to the neglect of biomedical waste management. Lack of awareness and interest fails one to register their clinic under certified waste management services. Dentists should be focused not only in delivering healthcare needs up to the mark but also, taking responsibility of the effects of waste generated routinely.

Limitation of Study: As this study was confined to the only single city but this topic is relevant to large regional area so more extensive studies with larger and broader population cohort are required for better assessment and implementation of biomedical waste guidelines.

Conflict of Interest: Nil

Source of Funding: Self

Ethical Clearance: Obtained (KIMSDU/IEC/08/2018 dated 17/11/2018).

Referneces

1. Abhishek KN, Suryavanshi HN, Sam G, Chaithanya KH, Punde P, Singh SS. Management of biomedical waste: An exploratory study. *J Int Oral Health* 2015;7:70-74.
2. Patnaik S, Sharma N. Assessment of cognizance and execution of biomedical waste management among health care personnel of a dental institution in Bhubaneswar. *J Indian Assoc Public Health Dent* 2018; 16:213-9.
3. Gupta NK et al. Knowledge, attitude and practices of biomedical waste management among health care personnel in selected primary health care centres in Lucknow. *Int J Community Med Public Health*. 2016;3: 309-13.
4. Anand P, Jain R, Dhyani A. Knowledge, attitude and practice of biomedical waste management among health care personnel in a teaching institution in Haryana, India. *Int J Res Med Sci* 2016;4: 4246-50.
5. Shilpa Gupta Saini, Sukhdeep Singh Kahlon, Dr Parvinder Singh, Dr Gulpreet, Navneet, Gurpreet Singh Aujla. To study biomedical waste (BMW) awareness among private practitioners in Amritsar region. *Indian Journal of Comprehensive Dental Care* 2015;5: 542-5.

6. Malini A and Bala Eshwar. Knowledge, Attitude and Practice of Biomedical waste management among health care personnel in a tertiary care hospital in Puducherry. *International Journal of Biomedical Research* 2015; 6: 172-176.
7. Bangennavar BF, Gupta A, Khullar S, Sukla N, Das A, Atram P. Biomedical waste disposal: Practice, knowledge, and awareness among dentists in India. *J Int Oral Health* 2015;7:53-56.
8. Pawan A Pawar¹, Tejashri S. Patil. Knowledge, practice and attitude of dental care waste management among private dental practitioners in Latur city *International Dental Journal of Student's Research* 2017;5:80-4.
9. Bansal M, Vashisth S, Gupta N. Knowledge, awareness and practices of dental care waste management among private dental practitioners in Tricity (Chandigarh, Panchkula and Mohali). *J Int Soc Prevent Communit Dent* 2013;3:72-6.
10. Treasure ET, Treasure P. An investigation of the disposal of hazardous wastes from New Zealand dental practices. *Community Dent Oral Epidemiol* 1997;25:328-31.

Gynaecological Manifestations of Systemic Malignancies

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Abstract

Context: Round cell tumours and haematolymphoid malignancies presenting with gynaecological symptoms are not infrequent. Often, those are a component of a symptom complex which has a clue towards the aetiology. Round cell tumours or haematolymphoid malignancies presenting solely as structural lesions of the female genital tract are really uncommon. A series of 10 such cases are depicted here.

Aims:

1. To study the epidemiological pattern among these patients
2. To assess the prognosis of such cases

Settings and Design: Single institutional observational study

Method and Material: Cases were selected from the case record files and data collected. CT scan of (Thorax +Abdomen + Pelvis)was done in all cases. The diagnosis was established by histopathology and immunohistochemistry in each case.

Statistical Analysis Used: Descriptive statistics used for analysis

Results: Median age of presentation was 25 years. Median duration of symptoms was 3 months, most commonly pain abdomen. Fallopian tubes and ovaries were involved in 90% cases, with pelvic and retroperitoneal lymphadenopathy in 80% cases. Majority of the underlying malignancies were haematolymphoid malignancies.

Conclusions: Clue to suspicion of underlying round cell tumours or haematolymphoid malignancies are younger age, mass lesion of uterus and adnexa, regional lymphadenopathy and absence of ascites. Earlydiagnosis is necessary since the above group of diseases represent curable malignancies even at advanced stages so we need to treat before their performance score deteriorates.

Keywords: *Haematolymphoid malignancies, gynaecological manifestations.*

Introduction

Haematolymphoid malignancies and round cell tumours presenting with gynaecological symptoms

are not infrequent. Often these manifestations are components of a symptom complex, having a clue towards the aetiology. However, round cell tumours or haematolymphoid malignancies presenting solely as structural lesions of the female genital tract are really uncommon. The most common worldwide type of Non-Hodgkin Lymphoma (NHL) is Diffuse Large B-Cell Lymphomas (DLBCL)^[1]. Majority of the DLBCLs originate in the lymph nodes, but $\leq 40\%$ initially have extranodal presentation^[2]. Differences in molecular pathogenesis, clinical presentation and natural history

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indicate that extra nodal DLBCLs are distinct entities [2]. The World Health Organization (WHO) Classification describes three clinical variants of Burkitt lymphoma – endemic, sporadic and immune-deficiency-associated types. Endemic Burkitt lymphoma usually occurs in African children, 4–7 years old, with a male:female ratio of 2:1, involving the jaw and other facial bones, kidneys, gastrointestinal tract, ovaries, breast and other extranodal sites [3]. Sporadic Burkitt Lymphoma occurs worldwide – Most common site of involvement being the abdomen, specially the ileocaecal area. Other sites such as ovaries, kidneys, omentum, Waldeyer’s ring may be involved [4]. Lymph node involvement is more common among young adults than children [5]. Patients may have malignant pleural effusion or ascites [3,5]. Ewing’s Sarcoma is the second most common malignant bone tumour in children and young adults, though, rarely, it may be of extraskeletal origin [6]. Patients with extra osseous Ewing’s sarcoma (EES) are usually of higher mean age and less likely to be male or White, compared to patients with skeletal tumours [7]. Commonly affected extraskeletal sites are - paravertebral spaces, lower extremities, head and neck and pelvis [8]. Other rare locations of EES include the retroperitoneum, omentum, orbit, skin and chest wall [9]. Extraskeletal tumours are more likely to arise from axial locations and less likely to arise from the pelvis [9]. Here we have depicted a series

of 10 cases of systemic malignancies with an aim to study the epidemiological pattern and assess the prognosis.

Materials and Method

A single institutional observational study was carried out at a tertiary care cancer hospital. Cases were selected from the outpatient, indoor and day-care records. CT scan of (Thorax + Abdomen + Pelvis) was done in all cases. The diagnosis was established by histopathology (image guided biopsy or laparotomy) and immunohistochemistry in each case. Epidemiological data with respect to age, type of malignancy, sites of involvement, method of diagnosis, chemotherapy drugs used, duration of therapy, grade III/IV adverse effects, outcome were recorded and analysed using descriptive statistics. The median follow up duration was 3.5 years.

Results

Total 10 cases were selected and studied. The age at presentation varied from 5 years to 45 years, the median age at presentation being 25 years. Median duration of symptoms was observed to be 3 months.

The common presenting symptoms and their frequency are shown in Fig 1.

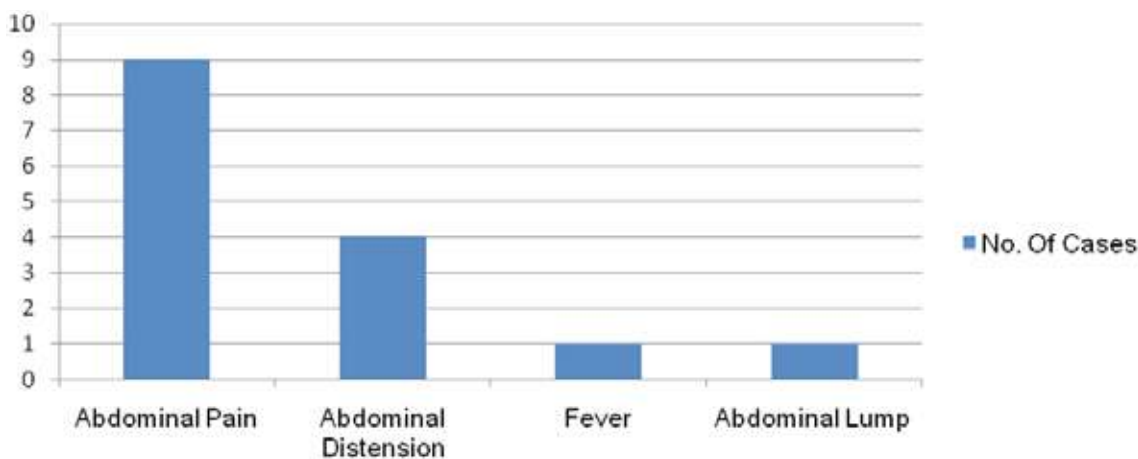


Fig 1: Presenting Symptoms

The diagnoses were established by the following method:

1. CT guided core biopsy from adnexal mass in 1 case
2. CT guided core biopsy from retroperitoneal lymph node in 1 case
3. Immunophenotyping of ascitic fluid in 1 case
4. Immunophenotyping of bone marrow in 1 case
5. Rest by laparotomy

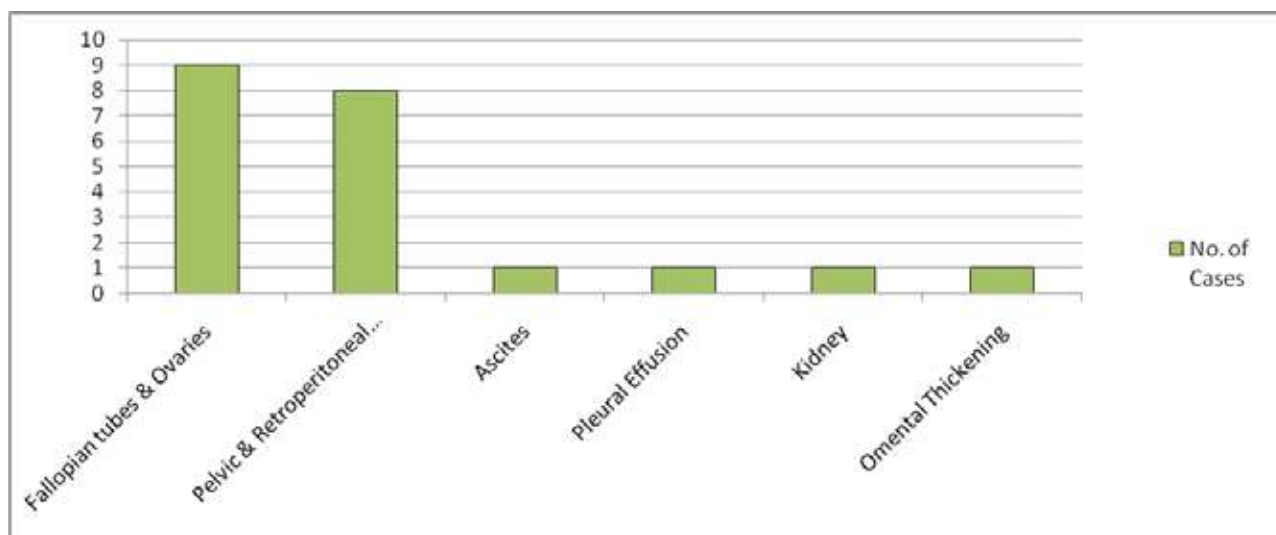


Fig 2: Sites of Involvement

The common sites of involvement along with their frequencies are shown in Fig 2.

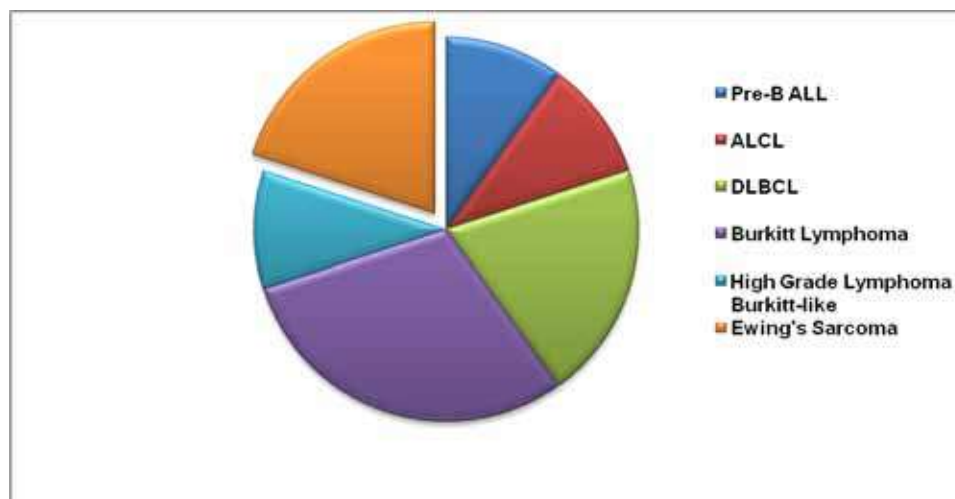


Fig 3: Underlying Malignancy

Fig 3 shows the distribution of underlying malignancies found in the 10 cases.

Of the 2 cases of Ewing’s Sarcoma, 1 was paracervical and the other was ovarian.

The median latency from symptom onset to the start of treatment was 1.5 months.

The patients were treated with multi-agent noncrossresistant chemotherapy according to the existing guidelines.

1 case of Burkitt Lymphoma and 1 case of DLBCL suffered toxic death on treatment.

Discussion

It is quite clear that haematolymphoid malignancies outnumber others. Clue to the suspicion of round cell tumours or haematolymphoid malignancies are younger age, mass lesion of uterus and/or adnexa, regional lymphadenopathy and absence of ascites. Early diagnosis is necessary since the above group of diseases represent curable malignancies even at advanced stages so we need to treat before their performance score deteriorates.

Conflict of Interest: None

Source of Funding: Self

Ethical Clearance: The study was conducted in accordance with the ethical standards of IEC.

References

1. De Paepe P, De Wolf-Peeters C. Diffuse large B-cell lymphoma: a heterogeneous group of non-Hodgkin lymphomas comprising several distinct clinicopathological entities. *Leukemia* 2007;21:37-43.
2. Moller MB, Pedersen NT, Christensen BE. Diffuse large B-cell lymphoma: clinical implications of extranodal versus nodal presentation—a population-based study of 1575 cases. *Br J Haematol* 2004; 124:151–159.
3. Diebold J, Jaffe ES, Raphael M, et al. Burkitt lymphoma. In: Jaffe ES, Harris NL, Stein H et al.(Eds.). *World Health Organization classification of tumours. Pathology and Genetics of Tumours of Haematopoietic and Lymphoid Tissues*. Lyon, France: IARC Press, 2001:181–184.
4. Blum KA, Lozanski G, Byrd JC. Adult Burkitt leukemia and lymphoma. *Blood* 2004;104:3009–3020.
5. Boerma EG, van Imhoff GW, Appel IM et al. Gender and age-related differences in Burkitt lymphoma—epidemiological and clinical data from The Netherlands. *Eur J Cancer* 2004;40:2781–2787.
6. Paoletti H, Colineau X, Acalet L, Tourette JH, Civatte M, Fesselet J, Dussaut JP, Pujol A, Muiyard B, Aubspin D, Nun P, Dufour M, Curvale G, Solacroup JC. *J Radiol*. 1999 May; 80(5):477-82.
7. Ahmad R, Mayol BR, Davis M, Rougraff BT. *Cancer*. 1999 Feb 1; 85(3):725-31.
8. Cheung CC, Kandel RA, Bell RS, Mathews RE, Ghazarian DM. *Arch Pathol Lab Med*. 2001 Oct; 125(10):1358-60.
9. Geens L, Robays JV, Geert V, der Speeten KV. *Case Rep Oncol*. 2013 May; 6(2):293-302.

A Study to Assess the Effectiveness of Structured Teaching Programme on Knowledge Regarding Substance Abuse and its Impact on Health among Higher Secondary Students among Atulya Healthcare Pune

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Abstract

Context: Healthcare professionals are crucial in the identification and accessibility to treatment for people with substance abuse. The objective of the study was to assess students' knowledge towards substance use disorders and examine the consequences of these on health.¹ Substance abuse is a social problem, not in India alone, but the entire world. The use of drugs has its own culture and history, which varies from country to country. The problem of substance abuse is growing at an explosive rate and in just little over a decade it has spread its malevolent tentacles to almost every part of the globe surmounting almost all barriers of race, caste, creed, religion, sex educational status, economic strata etc. As the first experience of substance abuse often starts in adolescence, and studies have shown that drug use is mainly related to cigarette and alcohol consumption, an initial exploration of substance abuse prevalence, including cigarette and alcohol, seems to be the first step in preventing and controlling drug consumption.³

Keywords: Knowledge, substance abuse, impact on health.

Introduction

Alcohol is only drug whose self-induced intoxication is socially acceptable.[1] Worldwide alcohol accounts for 3.3 million deaths yearly which represent 5.9% of all deaths.[2] Use of alcohol depends upon many environmental factors such as economical development, culture, ease of availability and alcohol policies of the area. This phenomenon is palpable in India, as its on road of rapid transition economically and socially. This transition can easily be noted by surge in figures of per capital alcohol use, as it has increased from 3.6 liters in 2003 – 05 to 4.3 liters in 2008 – 10 of which almost half of alcohol comes from unregulated market.

If their experimentation could be prevented by making them aware about the abuse and its consequences, the prevalence of the substance abuse can be reduced² Substance abuse has become a global phenomenon. It has affected almost every country, although its extent and characteristics differ from region to region. It is said, that at least 40 million people throughout the world are regular substance or drug abusers. The problems of drug abuse are seen in semi-urban and along the border areas of India. The period of adolescence is a vulnerable period in the life of an individual. The increased vulnerability in this period related to psychological factors like curiosity, poor impulse control, run away from reality, psychological distress and so forth. The social factors like peer influence, lack of clear identity, and self or intra-familial conflict also expose the adolescent to substance abuse.⁴

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Statement of the Problem: “A study to assess the effectiveness of structured teaching programme on knowledge regarding substance abuse and its impact

on health among higher secondary students at Atulya Health Care Pune.”

Objectives of the Study:

1. To assess the pre- test knowledge regarding substance abuse and its impact on health among adolescent students.
2. To evaluate the effectiveness of structured teaching on knowledge regarding post-test score.
3. To find out association between selected demographic variables and study findings.

Operational Definitions:

1. **Knowledge:** In this study knowledge refers to the correct response and understanding of the knowledge regarding substance abuse and its impact on health as measured by structure knowledge questionnaire.
2. **Substance Abuse:** Substance abuse refers to the harmful or hazardous use of psychoactive substances, including alcohol and illicit drugs.

Population: The study population for this study is higher secondary students.

Sampling and Sampling Technique:

Sample: The samples for the study were the higher secondary students studying Atulya healthcare, Pune.

Sample Technique: Sampling is the process of obtaining information about on entire population by examining only a part of it.

A purposive sampling technique was used to select the sample for the present study, which will meet the purpose of the study.

Inclusive Criteria: Students who are,

1. Studying in Atulya healthcare, Pune, willing to participate in this study.
2. Present at the time of data collection.
3. Will be able to read and write Marathi and English.

Exclusive Criteria:

1. Students who are not present at the time of data collection.
2. Not willing to participate in the study.
3. Not able to read and write Marathi and English.

Tool: The instrument used by data collection was self-administered closed-ended questionnaire which consist of two sessions.

Content Validity and Reliability: The content validity of the instrument was assessed by obtaining opinion from 8 experts. The experts suggested simplification of language, reorganization and addition of certain items. Appropriate modifications were made accordingly and the tool was finalized.

Reliability was assessed using Pearson’s coefficient correlation and found reliable.

Data Collection:

Section I

Demographic Data: It consists of demographic variables like sex, religion, family type, occupation of parents and socioeconomic status.

Section II

Structured Self Administered Questionnaire: It consists of 25 closed ended questions to assess the knowledge regarding “substance abuse and its impact on health”. This includes introduction, definition, prevalence, etiological factors of substance abuse, commonly used psychotropic substances and its impact on health.

Reliability: The reliability of the tool was established by test method using a correlation coefficient method. The reliability was found to be significant ($r=1$).

Table 1: Depicts the demographic variables in terms of numbers and percentage

Sr. No.	Demographic Variables	Number	Percentage
1)	Sex		
	a)Male	13	43.33%
	b)Female	17	56.67%
2)	Religion		
	a)Hindu	30	100%
	b)Muslim	-	-
	c)Christen	-	-
	d)Other	-	-
3)	Family Type		
	a)Single	9	30%
	b)Joint	13	43.33%
	c)Nuclear	8	24.67%
	d)Other	-	-
4)	Occupation of Parents		
	a)Labor	3	10%
	b)Government employee	10	33.33%
	c)Farmer	15	50%
	d)Private employees	2	6.67%
5)	Socioeconomic Status		
	a)Less than 10,000	-	-
	b)20,000-30,000	8	26.67%
	c)30,000-50,000	9	30%
	d)More than 50,000	13	43.33%

Section: II Assessment of level of knowledge regarding substance abuse and its impact on health among higher secondary before the implementing of structure teaching program Area, wise comparison of mean, SD, and mean percentage of pretest knowledge scores about substance abuse and its impact on health among higher secondary college students.

Table No: 2. Depicts comparison of mean, SD, and mean percentage of pretest knowledge scores

Area	Max Obtainable Score	Pre-test		
		Mean	SD	Mean (%)
Introduction	3	1.9	0.64	63.33
Definition	1	0.17	0.70	17
Prevalence	2	1.1	0.64	55
Causes	5	3.33	1.3	66.6
Commonly used Psychotropic Substance Abuse	9	4.8	1.5	53.33
Impact on Health	5	2.6	1.14	52
Overall	25	13.9	5.92	55.6

Table no. 2 Shows that the highest mean score [4.8+ 1.5(SD)] which is 53.33% of the total score obtained in the area of “knowledge oncommonly used psychotropic substance abuse” whereas lowest mean score [0.17+ 0.70(SD)] which is 17% of the total score was in the area of “knowledge on definition of substance abuse”

It reveals that the students had average knowledge in the area “knowledge on commonly used psychotropic

substance abuse” and below average knowledge in the area “knowledge on definition of substance abuse”.

Further the overall mean was 13.9 +5.29(SD) which is 55.6% of the total mean score, which reveals that the students had poor knowledge in the area “introduction, prevalence, etiological factors and impact on health of substance abuse”.

Comparison of pre-test and post-test level of knowledge on substance abuse and its impact on health among higher secondary students.

Table No: 3. DepictsComparison of pre-test and post-test level of knowledge scores.

Sr. No	Level of Knowledge	Pre-test Score		Post-test Score	
		Number	Percentage	Number	Percentage
1	Adequate (17-25)	9	30	29	96.67
2	Moderate (9-16)	20	66.67	1	3.33
3	Inadequate (0-8)	1	3.33	-	-

Table No.3: Shows that during pre-test 66.67% of higher secondarystudents had moderately adequate knowledge, 30% of higher secondary students had adequate knowledge and 3.33% of higher secondary student had inadequate knowledge whereas, during post-test 99.67% of student had adequate knowledge and 3.33% of student had moderate adequate knowledge.

Regarding substance abuse and its impact on health among higher secondary before the implementing of structure teaching program Area, wise comparison of mean, SD, and mean percentage of pretest knowledge scores about substance abuse and its impact on health among higher secondary college students.

Conclusion

The present study access the knowledge level of higher secondary students at Atulya healthcare, Pune. Regarding the, “substance abuse and its impact on health” and found that the students having 29 (96.67%) had adequate knowledge, and 01(3.33%) of students had moderate knowledge regarding “substance abuse and its impact on health”.

Conflict of Interest: Nil

Source of Funding: The present study is self-funded.

Ethical Clearance: Ethical Clearances obtained from the college committee and informed consentwas taken.

References

1. Van Boekel LC, Brouwers EP, Van Weeghel J, Garretsen HF. Stigma among health professionals towards patients with substance use disorders and its consequences for healthcare delivery: systematic review. Drug and alcohol dependence. 2013 Jul 1;131(1-2):23-35.
2. Anderson P, Baumberg B. alcohol in Europe. London: Institute of alcohol studies. 2006 Jun;2:73-5.
3. S F Billalli, Paramesh G M,Prasannakumar D R. A Study To Assess the Knowledge Regarding Drug Abuse and its Ill Effects among First Year Degree Students at D.R.M Science College in Davangere. Int. J. Adv. Nur. Management. 2017; 5(1): 70-72.
4. Lazarus RS, Folkman S. Stress, appraisal, and coping. Springer publishing company; 1984 Mar 15.

Selective Proprioceptive Neuromuscular Facilitation on Pelvic Mal-Alignment in Acute Post-Stroke Hemiparesis: A Case Report

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Abstract

Context: Stroke is one of the common upper motor neurological disorders with the overall worldwide prevalence of 3% . Majority of post-stroke individuals develop abnormal pelvic muscles function and pelvic tilt which can affect the trunk and lower limb functions. Proprioceptive neuromuscular facilitation less commonly used to treat the acute stroke population. Thus, we conducted this case study to evaluate the clinical usefulness of selective PNF on the pelvic pattern in two subjects with acute post-stroke hemiparesis. Both cases were treated with routine and selective PNF techniques such as rhythmic initiation, the dynamic and stabilizing reversal in anterior elevation and posterior depression pattern for 30 minutes, daily for 4 consecutive weeks. Trunk impairment scale and PALM device were used to assess the trunk balance and pelvic tilt respectively before and after 4 weeks of treatment. Both cases were improved with a clinically meaningful difference. Therefore we also precede this treatment protocol in our randomized clinical trial further.

Keywords: Hemiplegia, Pelvic Symmetry, Neuromuscular Facilitation, Diagonal Movement Pattern, Trunk Control.

Introduction

Stroke is one of the common upper motor neurological disorders which affect 3% of overall worldwide population¹. Post-stroke individuals develop the abnormal function of sensory, motor, cognitive and other higher cortical neurons;² ultimately hemiparesis alter the neuromuscular control of muscles in the various body segments such as limbs, neck, trunk, and girdles.

Further altered neuromuscular functions cause difficulty to balance while performing static and dynamic activities³.

Poor sensory-motor integration in the trunk and pelvis produces pelvic mal-alignment which can affects the trunk and lower limb functions^{3,4}. Altered pelvic alignment due to poor trunk-pelvis dissociation and reduced hip muscular control acting around pelvis may account for asymmetric weight distribution onto a most affected lower limb during walking⁴. The most of stroke patients have poor trunk control and forward lean posture with anteriorly tilted pelvis which causes poor postural stability of the lower trunk^{4,5}.

Zakaria et al. have shown a correlation between pelvic tilt and trunk control in post stroke⁵. And Suruliraj et al. state that more lateral pelvic tilt towards the affected side and an anterior pelvic tilt in bilaterally are commonly seen in patients with hemiparesis⁴. So,

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the management of pelvic mal-alignment is an essential step to improve the functional recovery in patients with acute stroke. Dubey et al. reported that the management of pelvic mal-alignment is beneficial in improving the trunk and lower extremity movement⁶. Therefore, pelvic bridging, and trunk stabilization, postural correction, balance and coordination exercises were used to manage the pelvic mal-alignment^{7,8,9}.

Even though various individual exercise protocols were used to manage the pelvic asymmetry, it is evident that there is a lack of training which can activate synergistic muscles in relation to functional pattern movements of the pelvis^{10,11,12}. Apart from the weakness of the pelvis and trunk muscles, the impaired proprioception has been considered for the poor trunk control and pelvic mal-alignment after stroke^{4,11}. Therefore, various techniques of proprioceptive neuromuscular facilitation (PNF) are also used to treat pelvic mal-alignment among patients with stroke^{10,11,12}.

PNF is a dynamic evaluation and treatment tool to improve the dynamic strength, flexibility, coordination, and specific muscle recruitment^{12,13,14}. Some studies documented the various types of PNF techniques on trunk, pelvis and lower limb pattern to improve the respective regional functions^{13,14}. But previous studies have used generalized techniques rather than selective PNF techniques in hemiparesis or hemiplegic cases¹²⁻¹⁴. So we have decided to treat the hemiparesis subjects using selective PNF techniques in order to effectively manage the mal-alignment of the pelvis and improve the trunk control.

Case Report: There were 2 patients with post-stroke hemiparesis referred to physiotherapy treatment by the general physicians. According to the medical records, both patients were medically stable to undergo physical therapy program; therefore they were referred to PT interventions. Each patient was further assessed by a neurological physiotherapist in order to plan and apply for the individualized treatment program on each patient.

As per the medical record and reference letter of physician, a 40 years old male patient was suffering from left-sided hemiparesis over a period of 30 days since from the onset of stroke. On the day of PT assessment his systolic and diastolic BP were recorded as 130 and 90 respectively, BMI 22.65 and MMSE score of 30. He communicated verbally to the people around him and he

also followed the instruction of assessing clinician which suggested us there is no cognitive impairment in him. Gait observation revealed that there is a circumduction gait with moderate pelvic hike and increased lumbar lordosis. And he was able to walk independently with mild support of stick and importantly he faced difficulty while turning and staircase walking. The pelvic alignment was measured with the help of PALM device¹⁵ which showed that 15 degree of pelvic malalignment and trunk impairment scale (TIS)¹⁶ score was 17.

61 years old female patient with right-sided hemiparesis over the period of 13 days was assessed by PT assistant and her systolic and diastolic BP were recorded as 140 and 90 respectively; BMI 24.83 and MMSE score of 29. She was experiencing mild oromotor dysfunction with lower quadrant facial paralysis and however, she was able to follow the instruction of assessing clinician. Gait observation revealed that there is a circumduction gait with moderate pelvic hike and increased lumbar lordosis. Her static standing balance was good enough to stand for 1 minute without any major sway. But dynamic standing balance and balance reaction while turning were poor. The pelvic alignment was measured with the help of PALM device¹⁵ which showed that 20 degree of pelvic malalignment and trunk impairment scale¹⁶ score was 13.

Based on the pelvic malalignment and reduction in the pelvic movement in both cases we decided to apply the PNF technique. We hypothesized that application of selective PNF on the hip may stimulate both deep and superficial sensory receptors and may improve the movement quality by increasing the ROM, muscle strength, and stabilization of pelvis corresponding to the lower trunk and proximal lower hip. Prior to the selection of specific PNF techniques in the anterior elevation and posterior depression pattern, the movement quality was assessed through this pattern passively and actively¹³⁻¹⁴.

After positioning the patient in side-lying comfortably, one hand of the therapist was placed over the ischial tuberosity and another hand over the ASIS using lumbrical grip. Then the anterior elevation and posterior depression pattern was produced passively and repeated several times to provide the information regarding the movements to the patients. Later the patients were asked to imitate the same movement pattern; at the same, we observed the movement quality throughout the pattern¹³⁻¹⁴.

Active rhythmic initiation was performed repeatedly for five minutes (2 minutes session of two sets, 1-minute rest between them). Once the patients were well aware of the movement pattern, then repeated stretches were applied wherever required to the muscles in order to facilitate the effective movements. First 3 days of intervention only rhythmic initiation was applied on both patients to adequately activate the muscles and achieve the full range of motion. Later half of the week, dynamic reversal and stabilizing reversal techniques were applied alternatively for the total duration of 20-30 minutes with adequate rest between the sets of treatment. From the second weeks onwards all three techniques were applied for the total duration of 30 minutes, two sessions in a week. Both patients were treated for 4 weeks with pelvic PNF and routine care⁷⁻¹⁰.

After the four weeks of intervention, pelvic symmetry and trunk control ability was assessed using PALM device and trunk impairment scale respectively. In case 1 post-treatment pelvic asymmetry was reduced to 7 degrees with the difference of 8 degrees, and trunk impairment score was improved to 20 from pre-treatment score of 17. Similarly in case 2 also palm device score was reduced to 12 and improvement in trunk impairment with TIS score of 19. These outcomes from the two cases show significant improvement in the pelvic asymmetry and trunk impairment after the 4 weeks of PNF application along with routine care.

Discussion

Based on the clinical usefulness of PNF in peripheral muscles weakness caused by peripheral and central nervous system dysfunction we have decided to treat the abnormal pelvic positioning in post-stroke hemiparesis individuals⁷⁻¹⁰. Importantly we treated 2 different age individuals in this experiment to know the effectiveness of PNF in the post-stroke population and its clinical usefulness. Abnormal pelvic tilt and changes in the trunk balance among these two patients support the findings of Suruliraj et al^{4,11} where they found excessive anterior and lateral pelvic tilt among the post-stroke subjects.

The change scores of pelvic malalignment and trunk impairment scale from baseline to post-intervention assessment (4 weeks) among the two subjects suggest that there is a reduction in the pelvic malalignment and improvement in the trunk balance. These outcomes indicate the clinically meaningful improvement in the pelvic symmetry and trunk balance post application

of selective PNF technique among the post-stroke individuals.

As per our understanding about the PNF use in the pelvis, the selection of appropriate PNF technique which gives specific importance to increase the ROM, coordination, and strength is important to achieve the meaningful difference in the respective clinical outcomes⁷⁻⁹. So, we have selected rhythmic initiation, dynamic and static reversal PNF techniques in these two post-stroke hemiparetic individuals. Rhythmic initiation was implemented to facilitate muscle work and improve the range of pelvic motion in the pattern of anterior elevation and posterior depression. Dynamic reversal and stabilizing reversal were used to improve the dynamic and static muscle work respectively in order to achieve good muscle strength, intra and intermuscular coordination¹³⁻¹⁴.

Wang et al on 15 post-stroke subjects with abnormal lower limb muscle tone was treated with rhythmic initiation and combination of isotonic and achieved the immediate reduction of spasticity and muscle tightness in the lower limb muscles¹⁰. Joshi et al experimented trunk PNF techniques (45 minutes) using the pattern of movement to improve the trunk control and achieved improvement in trunk control¹³. But they have not applied the pelvic PNF techniques and specialized PNF techniques were also not used in their study.

Shinde et al used the PNF to improve the trunk lateral flexion, Kumar et al used 30 minutes of PNF to improve the mobility function, and Kim et al applied 10 minutes of PNF for 6 weeks (thrice a week) to improve the functions of hemiplegic side¹⁷. Overall these studies have used rhythmic initiation, dynamic and stabilizing reversal, and rhythmic stabilization PNF techniques. But the frequency and duration of intervention have differed among these studies.

Conclusion

Based on the outcomes from these two subjects in the pelvic symmetry and trunk control suggest that there are indications for the effectiveness of selective PNF techniques among the subjects with post-stroke hemiparesis. Furthermore, we also are conducting a randomized control trial to evaluate the definite use of selective PNF in post-stroke hemiparetic subjects.

Conflict of Interests: We declare that there is no conflict of interests in term of finance, concepts and

method and publications among the authors participated in this study

Source of Funding: Financial assistance related to material purchase, laboratory investigations and other expenses was provided by NITTE (Deemed to be University), Mangaluru, India.

Ethical Approval: Prior to the study ethical approval was obtained from institutional ethics committee of Nitte Institute of Physiotherapy, Mangaluru, India.

References

- Pandian J. Stroke prevention: a global perspective. *Lancet Neurol* 2018;392:1268-1278.
- Kamalakaran S, Gudlavalleti A, Gudlavalleti V, Goenka S, Kuper H. Incidence and prevalence of stroke in India: A systematic review. *Indian J Med Res* 2017;146(2):175-185.
- Verheyden G, Ruesen C, Gorissen M, Brumby V, Moran R, Burnett M, et al. Postural alignment is altered in people with chronic stroke and related to motor and functional performance. *J NeurolPhysTher* 2014;38(4):239-245.
- Karthikbabu S, Chakrapani M, Ganesan S, Ellajosyula R. Pelvic alignment in standing, and its relationship with trunk control and motor recovery of lower limb after stroke. *NeurolClinNeurosci* 2016;5(1):22-28.
- Zakaria Y, Rashad U, Mohammed R. Assessment of malalignment of trunk and pelvis in stroke patients. *Egypt J NeurolPsychiatNeurosurg* 2010;47(4):599-604.
- Dubey L, Karthikbabu S, Mohan D. Effects of pelvic stability training on movement control, hip muscles strength, walking speed and daily activities after stroke: a randomized controlled trial. *Ann Neurosci* 2018;25(2):80-89
- Sharma V, Kaur J. Effect of core strengthening with pelvic proprioceptive neuromuscular facilitation on trunk, balance, gait, and function in chronic stroke. *J ExercRehabil* 2017;13(2):200-205.
- Yu S, Park S. The effects of core stability strength exercise on muscle activity and trunk impairment scale in stroke patients. *J ExercRehabil* 2013;9(3):362-367.
- Trueblood P, Walker J, Perry J, Gronley J. Pelvic exercise and gait in hemiplegia. *PhysTher* 1989;69(1):18-26.
- Wang R. Effect of proprioceptive neuromuscular facilitation on the gait of patients with hemiplegia of long and short duration. *PhysTher* 1994;74(12):1108-1115.
- Karthikbabu S, Chakrapani M, Ganesan S, Ellajosyula R. Relationship between pelvic alignment and weight-bearing asymmetry in community-dwelling chronic stroke survivors. *J Neurosci Rural Pract* 2016;7:37-40.
- Kim K, Chun S, Kang T, Kim G. Effects of core stability training on postural control ability and respiratory function in chronic stroke patients. *Int J BiosciBiotechnol* 2015; 7(3): 83-93.
- Joshi D, Chitra J. The effect of proprioceptive neuromuscular facilitation techniques on trunk control in hemiplegic subjects: A pre post design. *J Indian AssocPhysiother* 2017;11(2):40-44.
- Hindle K, Whitcomb T, Briggs W, Hong J. Proprioceptive neuromuscular facilitation (PNF): its mechanisms and effects on range of motion and muscular function. *J Hum Kinet* 2012;31(1):105-113.
- Petrone M, Guinn J, Reddin A, Sutlive T, Flynn T, Garber M. The accuracy of the palpation meter (PALM) for measuring pelvic crest height difference and leg length discrepancy. *J Orthop Sports PhysTher* 2003;33(6):319-325.
- Verheyden G, Nieuwboer A, Mertin J, Preger R, Kiekens C, De Weerd W. The Trunk Impairment Scale: a new tool to measure motor impairment of the trunk after stroke. *ClinRehabil* 2004;18(3):326-334.
- Shinde K, Ganvir S. effectiveness of trunk PNF techniques after stroke: a meta analysis. *NJMS* 2014;3:29-34
- Shin Y, Choi E, Choe Y, Peng C, Kim M. Immediate effects of posterior pelvic tilting taping on gait ability of chronic stroke patients: a randomized controlled trial. *J Exp Stroke Transl Med* 2017;10(1):1-10.

Original Article Effect of Scapular Position: Motion Maintenance Exercise Programme During Post Traumatic Shoulder Immobilization

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Abstract

Background: The scapula plays a key role in nearly every aspect of normal shoulder function. Alteration in scapular position and motion is found in association with most shoulder injuries. This alteration is term as scapular dyskinesis. Prevalence of scapular dyskinesis is about 67 to 100% . But many literature focus on treatment after occurrence but very few aim at prevention during immobilization phase. This made indeed to study the effect of scapular position – motion maintenance programme during shoulder immobilization phase.

Objectives: To determine the effect of scapular position -motion maintenance exercise programme during post traumatic shoulder immobilization phase, To compare the effect of scapular position -motion maintenance exercise programme and conventional physiotherapy during post traumatic shoulder immobilization phase.

Method: A Total of 40 subjects were selected aged between 20 to 50 years. They were divided into two groups. Group A (experimental) and group B (conventional). Both groups received treatment for 6 weeks for a duration of 30 minutes. The outcome measure used were VAS, Posture assessment, pectoralis minor muscle length, Linnies test and scapular assistance test.

Result: The study concludes that experimental group (scapular position- motion programme) proved more efficacious in reducing risk of scapular dyskinesis in patients with humerus fracture during immobilization phase as compared with conventional treatment.

Keywords: *scapular dyskinesis, Immobilization phase, proximal humerus fracture, exercise therapy*

Introduction

Effective shoulder position, motion, stability, muscle performance and motor control are largely dependent on the scapular performance. Mechanically, the coordinated coupled motions between the scapula and humerus, is called scapula humeral rhythm.¹ Scapular Dyskinesis is

found in association with various shoulder pathologies, although exact relationship between dyskinesis and clinical pathology is doubted. In case of nerve injury, fracture, Ac separation, muscle detachment, the injury results in dyskinesis, affecting shoulder function. In some cases like labral tear, rotator cuff disease, dyskinesis may be causative, creating pathomechanics that predispose the arm to such injuries.² Humeral fractures accounts for approximately 7 to 8% of all adult fractures, further incidence has been reported to increase with age. Proximal humerus fractures being most common (50%) of all humerus fractures.³ According to a study “Prevalence of scapular dyskinesis in patients with

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Distal radius fracture with or without shoulder pain” by Hector it was found that almost 80% of all patients with distal radius fracture showed scapular dyskinesia, with an increase in value 90.9% in group of patients with shoulder pain.⁴ Scapular Motions provide optimal muscle length – tension ratios for accurate movement pattern, and promotes muscular energy conservation during arm motion. The most common causative mechanisms of scapular dyskinesia is soft tissue alterations i.e inflexibility or tightness of pectoralis minor creating anterior tilt and protraction, glenohumeral internal rotational deficits, which creates a wind up of scapula on thorax leading to horizontal abduction.⁵

One of the most important abnormalities in abnormal scapular biomechanics is the loss of linking function in kinetic chain.⁶ The scapula and shoulder are dependent links in kinetic chain. It helps transferring the forces from the large segments, the legs and trunk, to the smaller, rapidly moving small segments of the arm. If scapula becomes deficient in motion or position, transmission of the large generated forces from the lower extremity to upper extremity is impaired. This creates a situation of catch up in which more distal segments work at a higher level of activity for compensation of the loss of proximally generated forces. Calculations depicts that 20% decrease in kinetic energy delivered from hip and trunk to the arm necessitates an 80% increase in mass and 34% increase in rotational velocity at shoulder to deliver the same amount of resultant forces to hand .The kinetic chain is the most efficient system for developing energy and force.⁷⁻⁸

Scapular dyskinesia causes weakness, tightness and muscle imbalance. most of the scapular motion and position can be treated by means of physical therapy relieving the symptom associated with in flexibility or trigger points, re-establishing muscle strength and activation patterns.⁹ But many literature focus on treatment after occurrence but very few aim at prevention during immobilization phase. This made indeed to study the effect of scapular position – motion maintenance programme during shoulder immobilization phase which primarily focuses on linking function of kinetic chain.

Materials and Methodology

This experimental study was carried out with 40

subjects in Krishna Hospital Karad. A total of 40 subjects was divided equally into two groups by Simple random Sampling (Group A and Group B). Subjects were in immobilization phase with proximal humerus fracture. Both males and females between the age group of 20-50 years were included.

The Inclusion criteria in this study was Age group of 20 – 50 age, Both the genders and Patients with Proximal Humerus post reduction or post operative immobilization phase and Exclusion criteria was Neurological condition, Non cooperative patients, Patients with Fracture of scapula, Patients with External fixators, Patients with distal neurovascular deficit and Patients with rib and spinal fractures.

The Outcome measures was Pain assessment – VAS scale, Posture assessment, pectoralis minor muscle length and special test for Linnies test and scapular assistance test.

The materials used in the study was Plinth, Towel, Inch-tape, Swiss ball, Pressure biofeedback, Data collection sheet, Consent form.

Procedure: An approval for the Study was obtained from the Protocol committee and institutional Ethical committee of KIMSDU scapular dyskinesia. Subjects who fulfilled the inclusion and Exclusion Criteria was divided into two groups. Informed consent was taken from each of the subject prior to Participation. Instructions were given to the subjects about techniques performed. A total of 40 subjects were divided equally into two groups by Simple random Sampling (Group A and Group B). The subjects were divided into two groups according random allocation.

Pre-test: Visual Analogue Scale (VAS) and Posture assessment, pectoralis minor muscle length and special test for Linnies test and scapular assistance test was used to assess the Subjects.

Group A:

The treatment program was include: First 3 week scapular stabilization exercise and next 3 week spinal stabilization exercise will be added with scapular stabilization exercise.

Group A (Experimental)¹⁰⁻¹²

Week 1

1. Posture training
 - Scapular retraction exercise
2. Isometric exercise for scapular muscle
 - .Shoulder Depression
 - Shoulder Protraction
 - Shoulder retraction

Week 2

Scapular stabilization exercise

1. Scapular clock exercise on a wall
2. T to Y to W exercise on swiss ball

Week 3

Scapular motion exercise (closed chain stabilization)

- Static close chain exercise (weight bearing)

Week 4

Spinal stabilization exercise was added with scapular stabilization

- **Pressure biofeedback in supine**
 - Lumbar flexion
1. Multifidus facilitation
 2. Alternate single leg heel touch
 - Lumbar extension
 1. Oblique abdominal facilitation
 2. Alternate single leg heel touch
 - **Lumbar multifidus activation**
 - **Transv. erse abdominis activation**

- Abdominal hollowing: activation of transverses abdominis in crook-lying position.
- Abdominal hollowing: activation of transverses abdominis in sitting.
- Abdominal hollowing: activation of transverses abdominis in four point kneeling.
- Activation of multifidus from sitting to lumbar neutral position

Week 5

Swiss ball exercise

- Sitting knee raise on swissball
- Abdominal slide
- Lying trunk curl with leg lift
- Wall slides

Week 6

1. Pelvic floor exercise
 - Pelvic bridging
2. Diaphragmatic strengthening exercise
3. Single leg standing on foam

Group B (Control group)

- Rest
- Isometric exercise for scapular muscle (Shoulder Depression, Shoulder Protraction, Shoulder retraction), active exercise (daily for 6 weeks)

Post-test: Visual Analogue Scale (VAS) and Posture assessment, pectoralis minor muscle length and special test for Linnies test and scapular assistance test was used to assess the Subjects.

Data Analysis: Between the group comparison

Table No 1: Baseline parameters comparison between both the groups (visual analog scale, Linnies test, pectoralis minor muscle length)

Group A & B						
Parameters			Post A	Post B	T Value	P Value
Visual analog scale			4.8±1.32	3.90±1.16	2.28	0.028
Linnies test	T2	RIGHT	8.32±0.94	8.42±1.61	0.23	0.81
		LEFT	9.1±1.93	10.22±2.67	1.25	0.21
	T4	RIGHT	9.22±0.52	9.27±0.75	0.79	0.8
		LEFT	9.21±0.80	9.82±1.51	0.24	0.12
	T7	RIGHT	10.8±1.24	9.57±2.57	1.95	0.05
		LEFT	10.52±1.77	9.42±2.64	1.54	0.13
Pectoralis minor muscle length		RIGHT	2.54±0.16	2.64±0.10	1.11	0.27
		LEFT	2.58±0.15	2.64±0.10	1.38	0.17

Table No 2: Baseline parameters comparison between both the groups (scapular abnormalities, scapular motion)

Group A & B			POST A	POST B
Scapular Abnormalities	TILT	Present	6	13
		Absent	14	7
	WING	Present	2	6
		Absent	18	14
Scapular Motion	Type 1		4	7
	Type 2		0	0
	Type 3		0	0
	Type 4		14	7
	Type 1,2		0	0
	Type 1,2,3		2	6
Scapular Assistance Test	Positive		14	7
	Negative		6	13

Discussion

The present study “Effect of scapular position - motion maintenance exercise programme during post traumatic shoulder immobilization phase” was conducted to see the effect of scapular stabilization and spinal stabilization exercise during immobilization phase in post traumatic shoulder. The scapula is anatomically and mechanically linked with shoulder function. Alteration in scapular position and motion is found in association with most shoulder injuries, termed as scapular dyskinesis. In a previous study “Prevalence of Scapular

dyskinesis in patients with distal radius fractures with or without shoulder pain” by Hector states that prevalence of Scapular Dyskinesis is shown in 80% of all patients with Distal Radius Fracture, with an increasing value of 90.9% in patients with shoulder pain. The ratio was found to be 10 times greater in patients with Distal Radius Fracture accompanying with shoulder pain.¹³

A group of adult population with proximal humerus fracture treated conservatively with plaster cast or closed reduction were evaluated. In a similar study by Ayhan Et. Al .stated following findings: Distal Radius Fracture had

influence on scapular motion, exhibit altered scapular kinematics, increased posterior tilt, internal and upward rotation.¹⁴⁻¹⁶ Further the study added to find the quality of motions at scapula if more proximal structures were affected. Another study by Edward Shields, "Scapular dyskinesis following displaced fractures of the middle clavicle" similar results were noted, Scapular Dyskinesis is common after displaced middle third clavicle fractures.¹⁷ In the present study we found a significant relation of scapular dyskinesis with proximal humerus fracture. Though there is no enough literature to support this evidence, but may studies approve findings of Scapular Dyskinesis occurrence after or with shoulder injuries. In a previous study by Mathew B. "Prevalence of scapular dyskinesis in overhead and non overhead athletes" reported that Scapular Dyskinesis in overhead athletes (61%) was more compared to those with non overhead athletes (33%).⁶ In a previous study by Poonam SS, "effect of desensitization method during the early mobilization phase in post fracture conditions of upper extremity" reported that combination of desensitization along with the conventional physiotherapy was effective in decreasing pain, improving ROM and muscle strength than the conventional therapy alone.¹⁸ Another study by Diksha U, "Effect of movement with mobilization in supraspinatus tendinitis" had noted that movement with mobilization, ultrasound, TENS and exercises are effective in management of supraspinatus tendinitis.¹⁹

The majority of studies included utilized visual observation of abnormal scapular rhythm to identify scapular dyskinesis. Two major abnormalities noted were scapular winging and scapular tilting. Scapular tilting was found in almost all subjects in Group A and Group B. Scapular winging was present in 8 subjects in Group A and 6 subjects in Group B. This interprets the fact not all patient with scapular tilting present with scapular winging. The mean pain values recorded using VAS showed a significant level of pain in both groups with pre values of 7 in Group A and 6.65 in Group B. There was a significant reduction in pain levels post treatment with 4.8 and 3.9 mean values respectively. The two main components scapular motion and scapular position were assessed using Kiblers classification and Linnes test respectively. According to Kiblers classification it was found that majority of subjects belonged to Type I dyskinesis with 12 subjects (60%) in group A and 14 subjects (70%) in group B. This interprets that inferior angle positioning was severely affected. Group A was found to be more effective in correction of this fault

by reduction of number from 12(60%) to 4(20%) as compared to Group B in which only 7 subjects (35%) showed corrections. Also subtype 3 and 4 that is medial border prominence and excessive superior border elevation was found to be noted though there rates were relatively less as compared to Type 1. Post treatment it was found that Group A had 14 Subjects (70%) showing T4 subtype that is symmetric and normal scapulae and group B had 7 subjects (35%) which showed that correction of scapular motion rate was almost double in Group A proving efficacy of scapular positioning program. The second component that is linnies test added to the results of Kiblers classification by providing objective findings. The results of Linnies test showed significant results in group A. However group B showed not significant results. This measure although a subjective approach doesn't much count on the therapist findings rather the results are patient based. From the above gained results we can state that scapular position and motion programme is more effective in prevention of scapular dyskinesis.

Dyskinesis may be caused by multi factors such as bony causes, joint causes, neurological causes and soft tissues causes of alteration. Bony causes include thoracic kyphosis or clavicle fracture non-union or shortened mal-union. Joint causes include high grade acromioclavicular instability, glenohumeral joint internal derangement. Neurological causes include cervical radiculopathy, long thoracic or spinal accessory nerve palsy. Soft tissue mechanisms for scapular dyskinesis involve inflexibility or intrinsic muscle problems. The upper and lower trapezius force couple may be altered, with delayed onset of activation in the lower trapezius, which alters scapular upward rotation and posterior tilt. Altered scapular motion or position both decrease linear measures of the subacromial space, increase impingement symptoms, decrease rotator cuff strength, increase strain on the anterior glenohumeral ligaments and increase the risk of internal impingement.¹ The Mechanism contributing to scapular dyskinesis primarily include the following factors like Inadequate serratus anterior activation, excess upper trapezius activation, pectoralis minor tightness, posterior glenohumeral joint soft tissue tightness, thoracic kyphosis or flexed posture. This associated effects leads to lesser scapular upward rotation and posterior tilt, greater clavicular elevation, greater scapular medial rotation and anterior tilt, greater scapular anterior tilt, greater scapular medial rotation and anterior tilt, lesser scapular upward rotation.¹³

This study had some limitations but were majorly due to the small sample size. Further studies can be done on a larger sample size including more age groups. Also similar studies can be done taking into account some other fractures like distal humerus fractures, radius fractures, wrist fractures, elbow dislocation.

Conclusion

The study concludes that experimental group (scapular position- motion programme) proved more Efficacious in reducing risk of scapular dyskinesis patients with humerus fracture during immobilization phase as compared with conventional treatment.

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Referances

1. Kibler BW, Ludewig PM, McClure PW, Michener LA, Bak K, Sciascia AD. Clinical implications of scapular dyskinesis in shoulder injuries: the 2013 consensus statement from the ‘Scapular Summit’. *Br J Sports Med.* 2013 Sep 1;47(14):877-85.
2. Kibler BW, Sciascia A, Wilkes T. Scapular dyskinesis and its relation to shoulder injury. *JAAOS-journal of the American academy of orthopaedic surgeons.* 2012 Jun 1;20(6):364-72.
3. Kim SH, Szabo RM, Marder RA. Epidemiology of humerus fractures in the united states: nationwide emergency department sample, 2008. *Arthritis care & research.* 2012 Mar;64(3):407-14.
4. Gutierrez-Espinoza H, Olguin-Huerta C, Zavala-Gonzalez J, Rubio-Ozarun D, Araya-Quintanilla F. prevalence of scapular dyskinesis in patients with distal radius fracture with or without shoulder pain. *Physiother Rehabil.* 2017;2(140):2.
5. Ben Kibler W. The role of the scapula in athletic shoulder function. *The American Journal of sports medicine.* 1998 Mar;26(2):325-37.
6. Burn MB, McCulloch PC, Lintner DM, Liberman SR, Harris JD. Prevalence of scapular dyskinesis in overhead and non overhead athletes: a systematic review. *Orthopaedic journal of sports medicine.* 2016 Feb 17; 4(2):2325967115627608.
7. Kibler BW, McMullen J. Scapular dyskinesis and its relation to shoulder pain. *JAAOS – Journal of the American academy of Orthopaedic Surgeons.* 2003 Mar 1;11(2):142-51.
8. Moezy A, Sepehrifar S, Dodaran MS. The effects of scapular stabilization based exercise therapy on pain, posture, flexibility and shoulder mobility in patients with shoulder impingement syndrome: a controlled randomized clinical trial, *medical journal of the Islamic Republic of Iran,* 2014;28:87.
9. Akhtar MW, Karimi H, Gilani SA, Effectiveness of core stabilization exercises and routine exercise therapy in management of pain in chronic nonspecific low back pain: A randomized controlled clinical trial, *Pakistan journal of medical sciences,* 2017 Jul;33(4):1002.
10. C Kisner, L.A Colby, therapeutic exercise: foundation and techniques, 6th edition, Jaypee brothers medical publishers (P) Ltd, 2013.
11. Luque-Suarez A, Diaz-Mohedo E, Medina-Porqueres I, et al, stabilization exercise for the management of low back pain, In *low back pain, 2012,* In Tech. A randomized controlled clinical trial, *Pakistan journal of medical sciences,* 2017 Jul;33(4):1002.
12. S. B. Brotzman and K. E. Wilk, clinical orthopedic rehabilitation, second edition Mosby, 1996.
13. David J Magee. Orthopaedic physical assessment .sixth edition. Reed Elsevier India Private Limited. 2014
14. McQuade KJ, Dawson J, Smidt GL. Scapulothoracic muscle fatigue associated with alterations in scapulohumeral rhythm kinematics during maximum resistive shoulder elevation. *Journal Orthopaedic and Sports Physical Therapy.* 1998 Aug;28(2):74-80.
15. Gould D . Visual analogue scale (VAS) .*J Clin Nurs* 2001; 10 :697 – 706 .
16. Struyf F, Nijs J, Mottram S, et al, clinical assessment of the scapula: a review of the literature, *Br J Sports Med.* 2014 Jun 1;48(11):883-90.
17. Shields E, Behrend C, Beiswenger T, Strong B, English C, Maloney M, Voloshin I. scapular dyskinesis following displaced fractures of the middle clavicle. *Journal of shoulder and elbow surgery.* 2015 Dec 1;24(12):e331-6
18. Poonam SS, Sandeep BS. Effect of desensitization method during the early mobilization phase in

- post fracture conditions of upper extremity. Asian journal of pharmaceutical and clinical research. 2018 Feb 15;11(7):93-96
19. Diksha U, Sandeep BS. Effect of movement with mobilization in supraspinatus tendinitis. International journal of science and research. 2017 Feb;6(2):673-676

Hand Hygiene Practices and Training Gap in a Neonatal Intensive Care Unit at Coastal Karnataka India

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Abstract

Background: Non-adherence to hand hygiene practices is a well-known factor contributing to healthcare-associated infections in any healthcare setting. Mere knowledge of such practices doesn't guarantee the compliance to the practices by healthcare personnel. In this study we explored the quantum of adherence to hand hygiene practices, the opportunity missed, the steps and the duration to be followed for hand hygiene practices and the training gap among the healthcare providers.

Methodology: A six-month cross-sectional study using a mixed-method approach of observations, interview and feedback mechanism is used to find the effectiveness of hand hygiene practices and any training gap to prevent healthcare-associated infections. Observations for two thousand opportunities for hand washing and written interview of 40 healthcare workers is carried out on hand hygiene practices at a neonatal intensive care unit of coastal Karnataka, India.

Results: The hand hygiene practices were as low as 0% observed while performing a non-invasive activity like clearing an alarm at the bedside. There is a gap found in the duration of hand-washing practices, hand hygiene before and after any care activity is performed on the neonate. This gap resulted in the spread of healthcare-associated infections.

Conclusion: During the infections control training emphasis should also be given on the opportunities and hands on practices of hand hygiene.

Keywords: Hand hygiene; Infection control; healthcare-associated infections; Neonate; India.

Introduction

Handwashing is the foundation for infection control practices¹. Healthcare providers are trained and empowered to practice hand hygiene during their formal training. There can be a high rate of healthcare-associated infections if the perception and practice of hand hygiene are mismatched². Performing hand hygiene and compliant to complete hand hygiene practices are two different avenues. When all the five steps of hand hygiene are not performed in timely manner is considered

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ineffective and when all steps are completed with appropriate time duration hand hygiene is considered to be effective¹. There can be instances when one may presume completing optimum hand hygiene but it is not. We are exploring the gaps in training adherence to the steps needed to be followed, the opportunity missed for hand hygiene practice and maintaining stipulated time for each step by healthcare provider.

Materials and Method

In a neonatal intensive care unit (NICU) of a tertiary care teaching hospital situated at coastal Karnataka, India, a cross-sectional study was carried out for six months duration July 2017-Jan 2018. Hand washing and hand hygiene practices of all the healthcare workers were recorded for all the five moments and steps of hand washing as suggested by the world health organization. The questionnaire on five moments of hand hygiene was prepared; content and face validation were done. A sample size of 40 healthcare workers considering a 95% confidence level for a definite population N=44 with 5% confidence limit were selected for written interview based on their availability and consent for participation. The healthcare workers working in NICU responded on these questionnaires that include five physicians, 23 nurses, six paramedic trainee and six pediatric postgraduate trainees. Eighty observations at each opportunity for a total two thousand chances of performing hand hygiene were observed for these healthcare providers randomly on different time interval, preferably at non-peak hours using a checklist. The observations and questionnaire were related to WHO five moments of hand hygiene¹. In each observation, if any step or opportunity was missed or partially completed, it was considered as non-

compliance. Completion of activity as per the standard was considered as compliance with the practices. The data obtained was entered in Microsoft excel was analyzed further using R software version 3.1.1. The qualitative variables were summarized as number and percentage. The difference between the reported and observed practices is considered as a gap that needs to be focused on further training on hand-hygiene practices. Institutional ethic committee approval was taken with IEC approval number “MUEC/014/2016-17”. Informed written consent for participation was obtained from all the participants before interviewing them.

Findings: Two thousand observations and forty interviews on twenty-five variables were carried out for healthcare workers at NICU. There was a mismatch in the practices observed and knowledge of hand hygiene reported among healthcare workers. We categorized observations and responses under three subheadings; time duration, hand hygiene before an activity and hand-hygiene after an activity performed.

Time Duration: Nearly 65% of healthcare workers reported that the ideal duration for hand washing with soap and water is <20 sec. However, only 12.5% healthcare workers practice handwashing with soap and water for >40 sec. 75% opportunities to carry out hand-washing practices were of less than 20-sec duration with soap and water. None of the healthcare workers reported the durations of hand hygiene using hand rub solution as 21 to 40 sec and we also observed the similar findings. Only one opportunity was recorded complying to 21-40 sec duration of hand hygiene using hand rub solution (Table 1).

Table 1: Showing time duration for hand hygiene practices by healthcare workers

Variables	Observations n=80	Reported n =40	The gap in reported vs observed*
	n (%)	n (%)	(%)
Duration of hand washing with soap and water			
05-20 sec	60 (75.0)	26 (65)	-10
21->40 Sec	20 (25)	14 (35)	-10
Duration of hand disinfection with hand rub solution (Min)			
05 - 10 Sec	62 (77.5%)	4 (10%)	-67.5
11- 20 Sec	17 (21.2%)	36(90%)	+68.8
21 - 40 Sec	1 (1.2%)	0 (0)	+1.2

* The gap is the percentage difference between reported and observation practices. A positive or negative gap of more than 20% is considered a significant gap in practice.

Table 2: Hand hygiene practice before any activity

Variables	Observations n=80	Reported n =40	The gap in reported vs observed*
	n (%)	n (%)	(%)
Compliance for practice hand hygiene before having contact with neonate	53 (66.2)	23 (57.5)	-8.7
Clean hands before providing personal care activities: handling, moving, bath/sponge, feeding, changing linen, etc.	33 (41.2)	23 (57.5)	+16.3
Clean hands before delivering care and other non-invasive treatment: applying oxygen mask, giving a massage.	67 (83.8)	23 (57.5)	-26.3
Clean hands before Performing a physical non-invasive examination: Taking pulse, blood pressure, chest auscultation, recording ECG.	30 (37.5)	22 (55)	+17.5
Clean hands before Instilling eye drops, examining mouth, nose, ear with or without an instrument, inserting a suppository, suctioning mucous.	34 (42.5)	27 (67.5)	+25
Clean hands before Dressing a wound with or without an instrument, applying ointment On vesicle, making a percutaneous injection/puncture.	76 (95)	32 (82.5)	-12.5
Clean hands before Inserting an invasive medical device	68 (85)	35 (87.5)	+2.5
Clean hands before Preparing food, medications, pharmaceutical products, sterile material.	80 (100)	25 (62.5)	-37.5

* The gap is the percentage difference between reported and observation practices. A positive or negative gap of more than 20% is considered a significant gap in practice.

Hand hygiene before an activity: Reported compliance for hand hygiene before contacting neonate, handling or moving baby or applying a mask or giving massage was 57.5%, but observations showed more compliance than reported 83.8% and 57.5% respectively. While performing non- invasive procedures or examination reported hand hygiene was always more

than the observed. Considering any opportunity to perform hand hygiene during non-invasive procedure reported and observed was as low as 37.5% and 0% respectively. In case of performing hand hygiene before invasive procedure, reported and observed was always >80% (Table 2).

Table 3: Hand hygiene practices after an activity

Variables	Observations n=80	Reported n =40	The gap in reported s observed*
	n (%)	n (%)	(%)
Clean hands after the contact with a mucous membrane and with non-intact skin end.	78 (97.5)	28 (70)	-27.5
Clean hands after A percutaneous injection or puncture; after inserting an invasive medical device	80 (100)	34 (85)	-15
Clean hands after Removing an invasive medical device.	18 (22.5)	33(82.5)	+60
Clean hands after Removing any form of material offering protection (napkin, dressing, gauze, sanitary towel, etc.).	22 (27.5)	29 (72.5)	+45
Clean hands after handling a sample containing organic matter, after clearing excreta and any other body fluid, after cleaning any contaminated surface and soiled material (soiled bed linen, diaper etc.).	63 (78.8)	34 (85)	+6.2
Clean hands after providing personal care activities: handling, moving, bath/sponge, feeding, changing linen, etc.	44 (55)	20 (50)	-5
Clean hands after Delivering care and other non-invasive treatment: applying oxygen mask, giving a massage.	26 (32.5)	20 (50)	+17.5
Clean hands after Performing a physical non-invasive examination: Taking pulse, blood pressure, chest auscultation, recording ECG.	67 (83.8)	18 (45)	-38.8

Variables	Observations n=80	Reported n =40	The gap in reported s observed*
	n (%)	n (%)	(%)
Clean hands after an activity involving physical contact with the patients' immediate environment: changing linen, holding a side of the cradle, clearing sides of cradle.	2 (2.5)	20 (50)	+47.5
Clean hands after A care activity: adjusting perfusion speed, clearing a monitoring alarm.	0 (0)	11 (27.8)	+27.8
Clean hands after Other contacts with surfaces or inanimate objects: leaning against the cradle, leaning against a side table /ventilator.	0 (0)	14 (35)	+35
Practice hand hygiene after having contact with neonate?	53 (66)	24 (60)	-6
Practice hand hygiene after removing gloves?	26 (32.5)	29 (72.5)	+40
Wear gloves when hands may be contaminated with bodily fluid (e.g. Suctioning)	65 (81.2)	33 (82.5)	+1.3

* The gap is the percentage difference between reported and observation practices. A positive or negative gap of more than 20% is considered a significant gap in practice.

Hand hygiene practices after an activity:

Reported compliance towards hand hygiene practices post non-invasive procedure was nearly 50% whereas observed was as low as 2.5%. Hand hygiene compliance was reported less than 35% post touching any part of the neonatal environment and observed was nearly 0%. Compliance for hand hygiene was recorded better, >60% in post invasive procedure/ touching any mucosal part of neonate & the noted observations showed >95% compliance (Table 3).

Discussion

No healthcare worker want any patient especially neonate to suffer from healthcare-associated infection because of any preventable cause. Maintaining good hand hygiene is vital for infection control practices, but mere awareness on how to perform handwashing is an incomplete effort to achieve a goal. The healthcare worker may be aware of the hand hygiene practices required to follow hence they reported at various instances the hand hygiene practices is required. However due to various reasons the practice is not followed and that can be captured through observations³. There are reports supporting our findings that there is a gap in the awareness and practices among healthcare workers for handwashing practices⁴⁻⁶. The very fact that even the healthcare providers were not aware of performing hand hygiene post touching the neonatal environment or clearing the alarm provides scope to work further and improve on training programs. Any invasive procedure requires thorough handwashing using soap and water, whereas for non-invasive activities like clearing an

alarm or changing linen etc., a handrub disinfectant solution should be used⁷. Invasive activities do include any contact with bodily fluid during the procedure. Many training programs are carried for healthcare workers to optimize hand hygiene practice. There are limited training opportunities to learn when to perform hand hygiene practices⁸. Routinely in healthcare organizations professionals are also not made aware of the quantity of liquid soap solution or hand-rub solution required for appropriate hand hygiene. The study not only highlights the importance for the healthcare workers to learn and plan for training program on how to perform hand-washing but also when to perform which type of hand hygiene is equally important to prevent healthcare-associated infection. Studies have reported that a single classroom training approach may not work alone, rather a multimodal approach including role-play, video and game activities may show better results^{9,10}. Whenever we are planning for handwashing campaign or training program, we need to prepare holistically to get optimum desired outcome. The healthcare workers also need to be clarified on the quantity of hand hygiene substance either soap or disinfectant solution along with clear demarcation on which practice to follow in which circumstances. As it was observed the healthcare workers were not clear whether to use hand rub solution or do handwashing or do both the practices. The significant importance of making the hand dry after any hand hygiene practice was missing that was captured during observations. The difference in reporting and observation practices gives insight to the training team about the focus area. If the gap is considerably high, as we considered a gap >20%

as high, such instances need immediate special attention and training.

Conclusion

Training on hand washing must include sessions on when to perform hand hygiene how to perform, and the minimum duration required for optimum hand hygiene. Various identified opportunities should be enlisted in healthcare settings to minimize any mis-opportunity.

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References

1. WHO. WHO Guidelines on Hand Hygiene in Health Care First Global Patient Safety Challenge Clean Care Is Safer Care.; 2009.
2. Whitby M, Pessoa-Silva CL, McLaws M-L, et al. Behavioural considerations for hand hygiene practices: the basic building blocks. *J Hosp Infect.* 2007;65(1):1-8. doi:10.1016/j.jhin.2006.09.026
3. Legeay C, Bourigault C, Lepelletier D, Zahar JR. Prevention of healthcare-associated infections in neonates: room for improvement. *J Hosp Infect.* 2015;89(4):319-323. doi:10.1016/j.jhin.2015.02.003
4. Hwang JH, Choi CW, Chang YS, et al. The efficacy of clinical strategies to reduce nosocomial sepsis in extremely low birth weight infants. *J Korean Med Sci.* 2005;20(2):177-181. doi:10.3346/jkms.2005.20.2.177
5. Asare A, Enweronu-Laryea CC, Newman MJ. Hand hygiene practices in a neonatal intensive care unit in Ghana. *J Infect Dev Ctries.* 2009;3(5):352-356.
6. Won S-P, Chou H-C, Hsieh W-S, et al. Handwashing program for the prevention of nosocomial infections in a neonatal intensive care unit. *Infect Control Hosp Epidemiol.* 2004;25(9):742-746. doi:10.1086/502470
7. Halder AK, Molyneaux JW, Luby SP, et al. Impact of duration of structured observations on measurement of handwashing behavior at critical times. *BMC Public Health.* 2013;13(1):705. doi:10.1186/1471-2458-13-705
8. Chou DTS, Achan P, Ramachandran M. The World Health Organization "5 Moments of Hand Hygiene" The Scientific Foundation. *J Bone Jt Surg Br.* 2012;94(4):441-446. doi:10.1302/0301-620X.94B4
9. Lam BCC, Lee J, Lau YL. Hand hygiene practices in a neonatal intensive care unit: a multimodal intervention and impact on nosocomial infection. *Pediatrics.* 2004;114(5):e565-71. doi:10.1542/peds.2004-1107
10. Moghnieh R, Soboh R, Abdallah D, et al. Health care workers' compliance to the My 5 Moments for Hand Hygiene: Comparison of 2 interventional method. *Am J Infect Control.* 2017;45(1):89-91. doi:10.1016/j.ajic.2016.08.012

A Study to Assess the Effectiveness of Protocol on Care of Newborn in Phototherapy on Knowledge and Practice among Nurses at Selected Hospitals in South India

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Abstract

Background: The present study assess the Effectiveness of Protocol on Care of Newborn in Phototherapy on Knowledge and Practice among Nurses at Selected Hospitals in South India

Method and Material: A pre - experimental one group pre and post test study design was used to collect all the necessary and relevant data from nurses. The study was conducted in the maternity ward and phototherapy unit of two hospitals. Based on inclusion criteria 50 nurses were selected and non probability convenient sampling techniques were used.

Results: In pre test level of knowledge of nurses regarding care of newborn in phototherapy, 17 (34%) had inadequate knowledge, 19 (38%) had moderately adequate knowledge and 14 (28%) had adequate knowledge. In post test majority of 44(88%) had adequate knowledge, 6 (12%) had moderately adequate knowledge and no one had inadequate knowledge. The improved mean value for knowledge was 10.43 with “t” value of 13.47 and improved mean value for practice was 6.78 with “t” value of 17.26. This results shows the high statistical significance at $p < 0.001$.

Conclusion: The study concludes that there was a significantly improvement of knowledge and practicable in post test after administration of protocol. Thus protocol was observed to an effective tool to improve the knowledge and practice on care of newborn in phototherapy and it may be useful to implement future reference.

Keywords: Protocol, Nurses, Newborn, Knowledge, Practice, Hospital and south India.

Introduction

Newborns are considered to be tiny and powerless beings, completely dependent on others for their adaptation in the external environment. Within one

minute of birth the normal newborn adapts from the dependent fetal existence to an independent being capable of carrying on the physiological processes. This transition, in many babies takes place in a smooth, uneventful way.

In controversy to the above, a few newborns face some minor disorders. During the process of physiological adaptation for its survival, the neonate has to face many life threatening problems, such as asphyxia, hypothermia, hyper bilirubinemia, infections etc.

One of the most important minor disorder that occur in the newborn during the transition phase is

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hyperbilirubinemia. It is the yellow discoloration seen in the skin and sclera due to an increase in the serum bilirubin level. Excess amount of bilirubin in the blood that causes hyperbilirubinemia. (Halliday, H. L. 1989)

Globally, 65% of the newborns develop hyperbilirubinemia making it one of the most common problems in the majority of the newborn. (William, W. Hay., 2009). In India approximately 4 million babies are born every year. Of them, 60 to 70% of the newborns develop hyperbilirubinemia. These statistics indicate that hyperbilirubinemia is a very common condition.

Stokowski, L. A.³ (2006) said that proper nursing care enhances the effectiveness of phototherapy and minimizes complications. Nursing responsibilities include ensuring effective irradiance delivery, minimizing skin exposure, providing eye protection and eye care, carefully monitoring thermoregulation, maintaining adequate hydration, promoting elimination and supporting parent-new born interaction.

Nurses play a vital role in providing comprehensive care for neonates on phototherapy based on their needs. Meticulous and appropriate nursing care during phototherapy is the best way to prevent the complications.

Newman & Esterling⁴ (2000) stated that according to the British Columbia Reproductive Care Program of Neonates, hyperbilirubinemia is a common neonatal problem especially during the 1st week of life when approximately 50 percent of all newborns have visible jaundice, of them 8-20 percent of term neonates exceed the total serum bilirubin values of 13 mg/dl, and need phototherapy.

All the above studies tell about the various complications that occur due to phototherapy, and stress that prevention can be possible with good care of the newborn. Neonates need close monitoring and careful nursing measures to improve their health status and to prevent complication.

During this time nurses play a very vital role in preventing complications and maintaining the well being of the newborn. With growing technology in the health sciences and increasing specialization of the Nursing profession, more rigorous control is required to ensure that nurses should possess sound scientific knowledge and skills to deliver safe and quality care.

Asha P. Shetty⁵ (2003) conducted an experimental

study, to assess the effect of photo therapy among full term newborn with a view to develop a nursing care protocol. The study concluded that, most often newborns with hyperbilirubinemia are treated with phototherapy which was effective. It was noted that development of a valid protocol for care of newborns in phototherapy would help practicing nurses to act promptly and independently.

Many studies in this area have been conducted in the western countries and protocols have been developed. But in India the investigator has observed that there is no specific protocol used by nurses while caring for babies in phototherapy. Hence the care provided was observed to be inadequate and many complications arose for the newborns. Having this in mind the investigator took up the responsibility of preparing a protocol to be followed while providing care for babies in phototherapy and also decided to test the effectiveness of the protocol through a pre- experimental study. The investigator tries to focus the effectiveness of the protocol which is cheap and resourceful intervention to care for the newborn during phototherapy and to assess the knowledge and practice among nurses for the same.

Method and Material

The study was designed to assess the the effectiveness of protocol on care of newborn in phototherapy on knowledge and practice among nurses at selected hospitals, Madurai. Investigator obtained formal permission from the administrative officer of Kasthuriba hospital and from the medical director of Leonard hospital, Madurai prior to the initiation of the study

Study Design: A quantitative research approach includes the research design in this study was pre experimental one group Pretest – Post test study design was considered to be the most appropriate to achieve the set of objectives in this study. The objectives were to assess the pre & post test level of knowledge and practice of nurses regarding care of newborn in photo therapy. To compare the pre and post test level of knowledge and practice of nurses regarding care of newborn in photo therapy. To correlate the mean improvement level of knowledge and practice among nurses regarding care of newborn in phototherapy. To associate the mean improvement knowledge and practice scores on care of newborn in phototherapy with selected demographic variables. The study was conducted in maternity

ward and photo therapy units of two hospitals viz... Kasthuriba hospital and Leonard hospital, Madurai. Kasthuriba hospital is a 200 bedded hospital which has well established maternity ward and photo therapy unit. Totally 35 - 40 newborns were admitted per month for the treatment of hyperbilirubinemia. Leonard hospital is a 250 bedded hospital. The phototherapy unit has 15 phototherapy machines in which 25-30 newborns were admitted per month for the treatment of hyperbilirubinemia. Totally 25 nurses are employed, all of them are posted in the maternity ward and phototherapy unit in a rotation.

Study Population: Fifty nurses who are qualified and working in maternity ward and phototherapy unit were included in this study

Inclusion Criteria: The nurses were working in photo therapy units and maternity wards and nurses were qualified as Diploma, B.Sc (N) Postbasic and B.Sc Basic (N).

Description of the Tool: A non probability convenience sampling technique was used in this study. The tool of the study has three section.

Section A: The demographic variables which includes age, gender, professional education, year of experience in service, total year of experience in phototherapy unit and source of information.

Section B: A structured knowledge questionnaire, it's consists of 30 multiple choice questions with 4 options and a single correct answer. Correct answer carries 1 mark and wrong answer carries-0 mark. The Questions covered the following aspects -Knowledge about hyperbilirubinemia-13, Knowledge about phototherapy - 7 and Care of newborn in phototherapy - 10.

The knowledge and practices score range as follows

Range	Score
> 75%	Adequate knowledge
50 – 75%	Moderately Adequate knowledge
< 50%	Inadequate knowledge

Section C : The observation check list has 25 items. The items were in the 'Yes' or 'No' form. The score for yes is 'one' and No 'Zero'.

Content Validity And Reliability Of The Tool: Content validity of the tool and protocol was got from three nursing experts in the field of obstetrics and gynecological nursing and two medical (DGO) experts. The reliability of the tool was established by using test-retest method to assess the reliability for knowledge with the same samples at different timings. The reliability score $r = 0.9$. To assess the reliability for the observational check-list, inter -rater method was used. The r value was 0.87. It indicated highly positive correlation.

Data Collection Procedure: The formal permission was obtained from the administrative officer and from the medical director of hospital, Madurai. The data for the study was collected with in the period of 4 weeks. During data collection period the investigator worked from 8 am to 4 pm for 5 days a week. The investigator covered 3-4 nurses per day. After getting their oral consent the investigator collected the pre test data using structured questionnaire to assess the knowledge and observational check list for assessing the practice. Each nurse took 30 – 40 minutes to answer all the questions. The investigator spent 25-30 minutes for assessing the nurses' practice on care of newborn in phototherapy. After the completion of the pre test data collection, the protocol on care of newborn in phototherapy was administered to the nurses. After 7 days post test was conducted by using the same structured questionnaire and observational check list for the same samples. The data obtained were analyzed using both descriptive and inferential statistics.

Findings: The findings from the study are tabulated, analyzed and interpreted below. In relation to demographic variables, the majority of 14 (28%) were in the age group of more than 31 years, 40 (80%) were females, 28 (56%) had completed GNM.

Table 1 : Frequency and percentage distribution of the Pre test & Post test level of knowledge of nurses regarding care of newborn in phototherapy. N=50

VARIABLES	Pre Test						Post Test					
	Inadequate (< 50%)		Moderately Adequate (50 – 75%)		Adequate (> 75%)		Inadequate (< 50%)		Moderately Adequate (50 – 75%)		Adequate (> 75%)	
	NO	%	NO	%	No	%	NO	%	NO	%	NO	%
Knowledge About Hyperbilirubinemia	16	32	25	50	9	18	-	-	-	-	50	100
Knowledge About Phototherapy.	19	38	26	52	5	10	-	-	6	12	44	88
Care of Newborn in Phototherapy	13	26	19	38	18	36	-	-	-	-	50	100

Table 1 :

PRACTICE VARIABLES	Inadequate (< 50%)		Moderately Adequate (50 – 75%)		Adequate (> 75%)	
	NO	%	NO	%	NO	%
Pre test	2	4	38	76	10	20
Post test	-	-	6	12	44	88

Table 2: Frequency and percentage distribution of the Pre & Post test level of practice of nurses regarding care of newborn in phototherapy. N-50

Variables	Knowledge			Practice		
	Mean	SD	't' value	Mean	SD	't' value
Pre test	17.78	6.67	13.47 ***	16.24	2.55	17.26 ***
Post test	28.12	2.88		23.02	2.48	

*** P < 0.001

Table 3 : Comparison of pre test and post test level of Knowledge and practice among nurses regarding care of newborn in phototherapy. N= 50

VARIABLES	POST TEST		
	Mean	S.D	' r' Value
Knowledge	28.12	2.88	0.813 ***
Practice	23.02	2.48	

*** P < 0.001

Table 4 : Correlation between the overall mean improvement level of knowledge and practice of nurses regarding care of newborn in phototherapy. N = 50

With regard to level of knowledge the post test mean score was 28.12 and S.D was 2.88. With regard to level of practice, the mean was 23.02 and S.D. was 2.48 .The calculated 'r' value was 0.813 which show that there was a positive correlation between the overall mean improvement level of knowledge and practice at a

statistically significant level of p < 0.001.

The present study supported by Milly **Mathew (2003)** on the topic can the self instructional module improves the nurse's knowledge on neonatal hyperbilirubinemia. The findings revealed that the self instructional module was effective in increasing the knowledge level of nursing personal with a t value of t=15.68 at p<0.5 level. The correlation r value between the knowledge and practice was r=0.93 which showed a good positive correlation.

Discussion

The present study was done to assess the effectiveness of protocol on care of newborn in phototherapy on knowledge and practice among nurses at selected hospitals, Madurai. The implementation of protocol was effective intervention during phototherapy

on the nurses and the overall health profession. Data were analyzed from 50 nurses. The overall pre test mean score was 16.24 with S.D was 2.55 and the post test mean was 23.02 with S.D was 2.48 and the calculated 't' value was 17.26 which had statistically high significance at $P < 0.001$ level. The protocol was found to be effective in improving the practice of nurses regarding phototherapy

Regarding association of mean improvement level of knowledge of nurses regarding care of newborn in phototherapy with selected demographic variables of source of information at $p < 0.05$. The other demographic variables have no significant association with the knowledge of nurses. Regarding practice the results revealed that there was no statistically significant association of the mean improvement level of practice with the selected demographic variables.

Conclusion

The present study was conducted to assess the effectiveness of protocol on knowledge and practice regarding care of newborn in photo therapy among nurses in maternity ward and photo therapy unit of Kasthuriba and Leonard hospitals at Madurai, 2009. From the results of the study it was concluded that protocol on care of newborn is an effective method to improve the knowledge and practice level of nurses. The findings revealed that the nurses, who had good knowledge about care of newborn in photo therapy, will have good practice too.

Ethical Clearance: Taken from institutional ethical committee faculty members

Source of Funding: Self funding

Conflict of Interest: Nil

Implications:

Nursing Practice: Nurses working in maternity ward and photo therapy unit should have adequate knowledge and practice about care of newborn in photo therapy. The nurses should update their knowledge by in service education and continue nursing education programs. Nurses who have good knowledge and practice regarding care of newborn in photo therapy will be able to promote the newborns health and thereby reduce the neonatal morbidity and mortality.

Nursing Administration: The administrator has important role in creating awareness to increase the

knowledge about care of newborn in photo therapy. In order to develop professional knowledge she has to make arrangements to conduct regular in-service education and continue nursing education programs on care of newborn in photo therapy.

Nursing Education: The nursing curriculum should be strengthened to enable nurses to excel in knowledge and practice of care of newborn in photo therapy. Students should be encouraged to have hands on experience in photo therapy units. Monitoring and assessing the newborn condition during photo therapy should be included as a clinical procedure.

Nursing Research: The findings of study can be disseminated to clinical nurses and student nurses through web site, literature, journals etc. The findings of the study will help the professional nurses and nursing students to improve their knowledge and practice

Recommendations:

1. The protocol can be placed in the maternity and phototherapy units for the nurses to read and follow.
2. A similar study can be conducted by increasing the samples size in different setting for better generalization.
3. A comparative study can be done at various setting.
4. A comparative study can be done on knowledge and practice between diploma nurses and B.Sc nurses.

Limitation:

1. The investigator faced difficulty in seeking permission in selected hospitals.
2. The investigator faced ample difficulty in collecting related literature as there was an only limited study on knowledge and practice among nurses.

References

1. Halliday H L, McClure B G, Reid M. Neonatal intensive care. In: Glenys Connolly, editor. Hand book of Neonatal intensive care. 4 ed. London: Bailliere Tindall; 1989:111
2. William,W.Hay, Neonatal Emergencies. In Georg Hansmann, editor. Textbook of Neonatal Emergencies. 1 ed. St Louis : Missouri Saunders publication;2009:84
3. Stokowski .L.A,. Fundamentals of phototherapy for neonatal hyperbilirubinemia. Advanced Neonatal

- Care. 2006; 6(6):303-312.
4. Newman et al. Jaundiced noted in first 24hours after birth in managed care. *Journal of Pediatrics*. 2001; 12(6):1388-1393.
 5. Asha .P. Shetty. Effect of phototherapy among newborn with a view to develop a nursing care protocol. *Nursing Journal of India*. 2003; 114(7):149-150.
 6. Milly Mathew. The topic can the self instructional module improve the nurses knowledge on neonatal hyperbilirubinemia. *Manipal Academy of Higher Education, Manipal University*. 2003; 15 (6): 205-210
 7. Abrol .P. Effect of phototherapy on behavior of jaundiced Neonates. *The Journal of Indian Pediatrics*. 2008June; 38(3):278-280.
 8. Agarwal. Deorari R T. Hyperbilirubinemia in newborn. *Indian Journal of Pediatrics*. 2001; 68(10):977-980.
 9. Agarwal Ramesh. Phototheapy units. *Journal of Neonatology*. 2001; 12 (1):61-68.
 10. Amirshaghghi et. al. Knowledge and practice of nurses on neonatal hyperbilirubinemia. *Journal of Biological Science*.2008; 15(6):942-945.
 11. Atkinson et.al. Phototherapy use in jaundiced newborns. *Journal of Perinatology*. 2003;14(8):126-128.
 12. Augustiion T. Common Clinical problems in newborn. *Journal of Neonatology*. 2000; 46(10):464-466.
 13. Berg and Lindelf. Phototherapy of newborns skin risk factor for malignant melanoma. *Journal of Indian Pediatrics*. 2001; 39(10):915-917.
 14. Bertini .G. et. al. Bronze baby syndrome and the risk of kernicterus. *Journal of Pediatrics*. 2005; 94(7):968-971.
 15. Boo G, Lee.M. Effectiveness of Oral versus IV fluid supplementation during phototherapy. *Journal of Indian Pediatrics*. 2002; 35(1):52-56.
 16. Boyd .S. Treatment of physiological Neonatal jaundice. *Nursing Times*. 2004; 100(33):40-43.

Health Coverage Across the Globe: A Contemporary Scenario

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Abstract

Context: Health was declared as fundamental human right by WHO constitution of 1948. The major key role playing factor in HAQ rankings is the universal health care programme and health schemes which are initiated and ran by the government. Health care provision is incredibly complex and many nations around the world spend considerable resources trying to provide it. Developed countries have their own insurance scheme which benefits its population and meets their health care needs. No uniform one-size-fits-all operational model exists when it comes to the successful implementation of a scheme. For instance, multinational insurers who are successful in one country have met failure in other countries. Developing country like India must try to improve their health care system by following certain initiatives incorporated by other countries. Low income countries like Africa and Nepal need to take extra measure to improve health insurance program and to provide quality care to their people. It is evident that there are an enormous number of ways that health care insurance programs vary around the world. There is a need to identify the characteristics of the most effective systems and the most equitable ones which could serve as a framework by all countries.

Keywords: *Health for all, Health coverage across the globe.*

Introduction

Health is a state of complete physical, mental and social well-being, and not merely the absence of disease or infirmity.¹ Health was declared as fundamental human right by WHO constitution of 1948.² The major key role playing factor in HAQ rankings is the universal health care programme and health schemes which are initiated and ran by the government.² Universal health coverage (UHC) ensures that all people have access to needed health services (including prevention, promotion,

treatment, rehabilitation and palliation) of sufficient quality to be effective while also ensuring that the use of these services does not expose the user to financial hardship.³ To achieve UHC, a country must address legal coverage and rights, health workers shortages, extension of health care shortages and quality of care.⁴ Health care provision is incredibly complex and many nations around the world spend considerable resources trying to provide it.⁵ The strength of the case for investing in health varies among countries.⁶ The return on investment is likely to be highest for emerging economies: They can obtain significant improvements in health outcomes (eg life expectancy) through modest increases in health expenditures.⁶ The basic idea of this review is to provide an insight on health coverages across various countries and there path towards universal health coverage.

Health coverage in various countries: Many countries have their own insurance scheme which benefits its population and meets their health care needs. No uniform one-size-fits-all operational model exists when it comes to the successful implementation of a

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scheme. It is not just standard processes or manuals or actuarial formula or stabilised systems that can work seamlessly across geographies such that the success is assured.⁷

High income countries: High income countries according to World Bank are United States, Germany and Singapore, Canada, Japan and Gulf countries. Important principle of The affordable care act of 2010 or OBAMA care in United states is to improve quality of care which is achieved by establishing new agencies, boards, commissions and other Government entities⁸; The 2010 Affordable Care Act (ACA) dramatically changed many features of the US health care system and should greatly reduce the number of Americans who are uninsured.

The German government sponsors mandatory universal insurance coverage for everyone, including temporary workers residing in Germany.⁹ The German system uses a unique point-based global budgeting system to control annual health care expenditures whereby the targeted expenditures are achieved by ensuring that total payments to all providers of a given specialty are equal to the total budget for that specialty in a year.¹⁰ If salary of German residents is less than 59400 euros per year or 4950 euros per month then membership is made mandatory. It covers inpatient hospitalisation, OP services as well as dental care.

Singapore has a unique-to-the-world health care system where the dominant form of insurance is mandatory self-insurance supported by sponsored saving, although complementary and special insurance programs are also central to their system.¹¹ It provides UHC through a combination of government subsidies, multi-layered healthcare financing schemes and private individual savings all at national level. It provides Government subsidy 80% of total cost in public hospitals and primary care polyclinics. It is supported by 3M's system namely Medisave, Medishield and Medifund.

Japan has a mandatory insurance system which is comprised of an employment-based insurance for salaried employees, and a national health insurance for the uninsured, self-insured and low income, as well as a separate insurance program for the elderly.¹⁰ Health insurance benefits designed to provide basic medical care to everyone are similar. They include ambulatory and hospital care, extended care, most dental care and prescription drugs.

Canada has a universal single-payer, sponsored health insurance system called Medicare which is administered independently by the thirteen provinces and territories. Every citizen and permanent resident is automatically covered. As of 2012, Canada spends about 11% of GDP on healthcare expenditures covering about 70% of healthcare expenditure.²

In Gulf countries major healthcare challenges has hampered the efforts towards ensuring UHC across the region. Mandatory health insurance is one of the measures adopted to achieve UHC. Qatar has initiated the upgradation of health care services by launching an e-health program. Saudi Arabia is digitalizing its hospitals and PHC patient medical records through healthcare information and management systems society (HIMSS). UAE in 2011 had launched integrated electronic medical record system to link public hospitals and clinics across Dubai and the Northern emirates through health information system- Wareed¹²

Middle income countries: China, India and Mexico are middle income countries. Chinese government has established a multilevel medical security system including universal health care system, commercial medical insurance and a medical charity aid. Over 90% of the population has basic insurance coverage in China. Three insurance schemes available in China as of 2011 is Urban employee basic medical insurance, Urban resident basic medical insurance and new rural cooperative medical system. Chinese government health care covers both sectors of population groups equally in order to work on urban rural disparity.¹³ In Mexico the government run system operates Clinics and hospital throughout the country in Mexico to provide health at low price.¹⁴ Whereas in India according to model based estimate by WHO through public and private sector is estimated to be INR 1,713 / Capita / Year between 2014–2015. Average medical expenditure for hospitalization in urban patient has increased to 126% and rural patient to 160% and same year GDP / Capita grew by 121% .¹⁵

Need for health insurance: India is presently in a state of health transition facing a shift from infectious diseases to non-communicable diseases that are now emerging as the leading cause of mortality. According to National Health Accounts (2014-15) 62.6% of total health expenditure in India (2.4% of GDP, Rs. 2394 per capita) by households Out of pocket expenditure¹⁵ which is defined as expenses that patient or family pays directly to health care provider without

a third party (Insurer, State) is limited with appropriate health insurance.¹⁶ People having no access to any form of health insurance scheme are being forced to make OOPE pushing 60 million Indians to poverty each year.¹⁷

Although India has been witnessing a staggering growth in the health insurance sector, still only 15% of the population is protected by medical care insurance coverage and 5% of the population buy a plan voluntarily of their own accord which suggests that Indian insurance industry has still a long way to go. The reason behind such a low acceptability is not the affordability factor, but the lack of awareness and unwillingness on the part of the potential buyers. The likelihood of utilising health care services increases with genuine health insurance scheme in place. Such schemes should be focused on achieving a two-way objective, to tell people how imperative is it to get a health care insurance and to build the trust and credibility of insurers among them.¹⁸ Global disease burden in India 2016 report suggests that deaths due to communicable, maternal, neonatal and nutritional diseases is 27.5% and Non communicable diseases is 62% in men and 52% in women; if each citizen is insured nearly 89.5% of disease burden could be averted.¹⁹ A recent data suggest that 80% of hospitals are in urban area though it comprises of only 31% of country's population and availability of qualified physician in urban area is 11.3 per 10000 population when compared to 1.9 per 10000 population in rural area. 65% of rural population have no access to essential medicines and cannot afford to medical expenditure.²⁰ Health insurance scheme are designed to provide employment to rural poor besides creating rural infrastructure so that urban-rural disparity in the country could be reduced.²¹

State based health insurance schemes (2007-2017): Some states have its own health insurance scheme for its people and they are explained in detail. Aarogyasri scheme was launched in 2007 (continued as Dr NTR Vaidya Seva (2015) AarogyaRaksha scheme (2017)). It is a unique community health insurance scheme being implemented in Andhra Pradesh. It provides financial protection upto 2 lakhs to BPL families in a year for treatment of serious ailments requiring hospitalisation and surgery.²² Chief Minister comprehensive health insurance scheme was launched in 2012 in Tamil Nadu. It provided cover for all major ailments and ensured advanced healthcare for low income and unorganised group. Its aim was to benefit 1.34 crore families with annual income of 72000 or less. The sum assured under the scheme is 1 lakh every year for a period of

4 years with total value of 4 lakh, in case of certain procedures it will be raised 1.5 lakh per annum.²³ In 2013 Sanjeevani Swasthya Bima Yojana was launched as a comprehensive health insurance scheme for citizen of Dadra Nagar Haveli and Daman and Diu. Under this scheme premium for BPL families will be borne by the UT Administration and for those families with income of 1 lakh- 2 lakh 50% will be by UT administration and 50% by their own.²⁴ Mukhyamantri Swasthya Bima Yojana was launched in 2016 in Uttarakhand for all BPL and APL families (except those on govt. salary or govt. pension or in tax payer category). It provided a cover of Rs. 50000 per eligible families and in same wake second phase with a base cover of Rs. 50000 covering 1206 diseases and critical cover package of Rs. 125000 covering 458 diseases.²⁵

Nationwide health insurance (2003-2018): At National level, health insurance schemes were implemented between 2003 -2018. Universal health insurance scheme was launched in 2003 and available for individuals as well as in a group. Age criteria 5 to 70 years and children between 3 months to 5 years are eligible if one of the parent is covered. It gives hospitalisation benefit of INR 30000 per family per policy inclusive of maternal benefit. Total expenses for any one illness is limit to INR 15000 excluding maternal benefits and also covers accident and disability.²⁶ Rashtriya Swasthya Bima Yojana in 2013 was different from the previous policy with regards to target group which included BPL families and defined categories of unorganised workers. RSBY has been the only scheme in India launched on a Pan India basis, which aimed at universal health coverage.²⁷⁻²⁹ Beneficiaries are entitled to hospitalisation coverage of Rs 30000 per annum for most of diseases that require hospitalisation. Additional transport expenses are also provided to the beneficiary.²⁸

Under RSBY health protection mission/ Pradhan Mantri Rashtriya Swasthya Suraksha Mission later renamed as Pradhan Mantri Jan Arogya Yojana was launched in 2018 at Ranchi Jharkhand. It provides coverage of 5 lakh/family/yr and benefits 10.74 crore families; 8.03 in rural and 2.33 in urban areas through a network of empanelled health care providers. Key feature of the scheme is that the beneficiaries can avail of services anywhere in India and there is no compromise on family size and age.²⁸ Budget allocation is approximately 12000 crores and 60:40 is the ratio for fund transfer from central and state government. Target group is poor, deprived rural families and identified

occupational category of urban workers' families as per Socio economic caste census 2011. All enrolled families under Rashtriya Swasthya BimaYojana (RSBY) not featured in the targeted groups as per SECC data has also been included.³⁰

Low Income Countries: Most of the African countries and Nepal belong to low income group. In Nepal to provide affordable care, quality health services, easy access and health security coverage Social health security development committee was established. It works by raising funds from healthy people and spending the same for needy.³¹In Ghana rapidly expanding National program is run by the government. In Nigeria most of the schemes are run by private investors and shareholders. In Tanzania and Uganda some programs are functioning through their own hospitals and clinic by employing their own staff on regular basis. Government must take extra measures in these low income countries to improve health insurance program and to provide quality health care to their people.³²

Conclusion

It is evident that there are an enormous number of ways that health care insurance programs vary around the world. There is a need to identify the characteristics of the most effective systems and the most equitable ones which could serve as a framework by all countries. In accordance to health for all agenda set by Alma Ata declaration in 1978¹ every country is struggling to provide an efficient health care system to its people. Health has become a basic need with emerging health care challenges. Health care delivery system in each country aims to reach the ultimate goal of universal health coverage, with effective utilisation of resources and by strategic planning this goal can be achieved in all countries across the globe.

Conflict of Interest: Nil

Source of Funding: Self

Ethical Clearance: It is a Review article, Human subjects were not interviewed and examined. Ethical Clearance is not available

Reference

1. WHO (1978). Primary health care: report of the International Conference on Primary Health Care, Alma-Ata, USSR Health for all, Sr.No.1.
2. Fullman N, Yearwood J, Abay SM, Abbafati C, Abd-Allah F, Abdela J, et al. Measuring performance on the healthcare access and quality index for 195 countries and territories and selected subnational locations: A systematic analysis from the global burden of disease study 2016. *Lancet* 2018;391:2236-2271.
3. World Health Organization [homepage on the Internet]. Health financing for universal coverage>What is universal coverage; [updated 2018 December 12; cited 2018 December 15]. Available from: https://www.who.int/universal_health_coverage/en/
4. The Lancet. Rural health inequities: data and decisions. *The Lancet*. 2015;385(9980):1803.
5. Health care around the world [Homepage on Internet]. [cited 2018 April 13]. Available from: www.globalissues.org
6. Delivering universal health coverage- A guide for policymakers [Homepage on Internet]. [cited 2018 April 13]. Available from: <https://www.imperial.ac.uk>
7. How Ayushman Bharat could be different details– [Internet] [cited 2019 January 5] Available from: <https://www.livemint.com>
8. Manchikanti L, Helm I S, Benyamin RM, Hirsch JA. A critical analysis of Obamacare; affordable care or Insurance for many and coverage for few. *Pain Physician*. 2017 Mar; 20:111-138
9. Health insurance options in Germany. [Homepage on Internet]. [cited 15 December 2018]. Available from: <https://www.howtogermany.com>
10. Forthcoming in Culyer, Anthony (ed.) *Encyclopedia of Health Economics*, Elsevier Press., Inc. 2014.8
11. Singapore: International health care system profiles. [Homepage on Internet]. [cited 2018 December 5]. Available from: <https://international.commonwealth.fund.org>
12. Tawfiqhoja, Salman Rawaf et al. Health care in Gulf cooperation council countries: A review of challenges and oppurtunities. *Cureus*.2017 Aug;9(8)
13. Yu H. Universal health insurance coverage for 1.3 billion people: what accounts for China's success? *Health Policy*. 2015;119(9):1145–1152.
14. Four countries with the best health care in the world. *International living*. [Homepage on Internet]. [cited 2018 December 5]. Available from: <https://www.cnn.com/>

15. Nandi S, Schneider H, Dixit P. Hospital utilization and out of pocket expenditure in public and private sectors under the universal government health insurance scheme in Chhattisgarh State, India: Lessons for universal health coverage. PLOS ONE. 2017;12(11):e0187904.
16. www.arthrapedia.in. 2018 [Homepage on Internet]. Out-of-pocket expense; [cited 2018 December 5]. Available from: <https://en.wikipedia.org/>
17. Balarajan Y, Selvaraj S, Subramanian S. Health care and equity in India. The Lancet. 2011;377(9764):505-515.
18. Health Insurance in India – The Need for Public Awareness. [Homepage on Internet]. [cited 2019 January 5]. Available from: <https://www.policybazaar.com/>
19. National Health Accounts (NHA) – Ministry of Health and Family Welfare. NHA – Estimate for India 2014-2016 [Homepage on Internet]. [cited 2018 December 15]. Available from: <https://mohfw.gov.in>
20. Urban rural conditions concept disparity. [Homepage on Internet]. [cited 2018 December 15]. Available from: <http://dspace.vpmthane.org>
21. Press Information Bureau [Homepage on Internet]. Pib.nic.in.2018; [cited 2018 December 15]. Available from: <http://pib.nic.in/>
22. Aarogyasri Health Care Trust [Homepage on Internet]. [cited 2018 December 15]. Available from: <http://aarogyasri.telangana.gov.in/>
23. Chief Minister’s Comprehensive Health Insurance Scheme [Homepage on Internet]. [cited 2018 December 15]. Available from: <http://www.tnhsp.org.2005-2012>
24. Directorate of Medical & Health Service [Homepage on Internet]. Easycounter.com. 2018 [cited 2018 December 15]. Available from: <https://www.easycounter.com/report/vbch.dnh.nic.in>
25. Mukhyamantri Swasthya Bima Yojana (MSBY) Uttarakhand [Homepage on Internet]. [cited 2018 December 15]. Available from: <https://mukhyamantri-swasthya-bima-yojana-msby/>
26. Universal Health Insurance Scheme: Features, Reviews & Charges [Homepage on Internet]. [cited 2018 December 15]. Available from: <https://www.coverfox.com/health-insurance/universal-health-insurance-scheme/>
27. Health insurance in India – The need for public awareness. [Homepage on Internet]. [cited 2018 January 5]. Available from: <https://www.policybazaar.com/health-insurance>
28. Pareek M. Ayushman Bharat-National Health Protection Mission a way towards Universal Health Cover by reaching the bottom of the pyramid to be a game changer or non-starter. Int J Adv and Innovative Res. 2018; 7(7):2278-7844
29. RSBY govt plans and scheme update. [Homepage on Internet]. [cited 2018 December 5]. Available from: http://www.rsby.gov.in/about_rsby.aspx <https://sarkariyojana.com;>
30. Dhaka R, Verma R, Agrawal G, Kumar G. Ayushman Bharat Yojana: a memorable health initiative for Indians. Int J Community Med Public Health 2018;5:3152-3.
31. Nepal. Government of Nepal health insurance board. [Homepage on Internet]. [cited 2018 December 5]. Available from: <https://shs.gov.nic>
32. Carapinha JL, Ross-Degnan D, Desta AT, Wagner AK. Health insurance system in five sub-Saharan African countries: Medicine benefits and data for decision making. Health policy. 2011; 99(3): 193-202

Unmet Need of Objective Monitor to Evaluate Performance Status in Lung Cancer Patients

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Abstract

Context: Quality of life (QOL) of lung cancer patients can be improved by using modern technical tools. There is a necessity to develop a system which incorporates all the functions to evaluate severity of the disease and critical condition of the patients. There exists a need of an objective monitor for monitoring performance of lung cancer patients with parameters of HRV, SPO₂ and Peak Expiratory Flow Rate (PEFR). A questionnaire-based survey was carried out in cancer physicians, surgeons and radiotherapists. Total 100 clinicians participated in this questionnaire, 35 medical oncologists, 35 oncosurgeons and 40 radiation oncologists. The analysis of this survey showed that presently ECOG (Eastern Cooperative Oncology Group) scale was preferred to KPS (Karnofsky Performance Status) scale (70% versus 30%) because of simplicity to remember. The popular parameters preferred among clinicians were SPO₂ (45%), 2D Echocardiography (30%), chest X-ray (42%). But for HRV test, all the clinicians (100%) rejected the availability of test facilities. SPO₂ and PEFR were also rated as mobile tools for assessing the performance. ECOG Scale was easier to utilize than KPS for understanding the performance Status in cancer patients. It is suggested that HRV, SPO₂ and PEFR could be an added value to improve the QOL in cancer patients.

Keywords: KPS, ECOG, monitor, questionnaire, PEFR, SPO₂.

Introduction

Karnofsky performance status (KPS) scale scoring was initiated by Dr. David A. Karnofsky and Dr. Joseph H. Burchenal in 1949¹. It was designed to evaluate the degree of cancer patient activity and medical care necessities. Eastern Cooperative Oncology Group (ECOG) score or Zubrod score was initiated by C. Gordon Zubrod, rated as 0 with perfect health to 5 with

death. It is simpler than KPS. The ECOG is used to decide the treatment and prognosis for the patient and assess the progress of the disease². The degree of patient activity and medical care requisites can be measured by the KPS³. KPS scaling factor is explained in detail in Table 1⁴. ECOG scaling factor is explained in detail in Table 2⁵.

Langley recognized the different components of the autonomic nervous system (ANS), with the term “sympathetic” limited to the thoracic outflow of the autonomic system; he suggested the term “parasympathetic” to assign its cranial and sacral outflows⁶. Brain haemodynamics can be studied in response to sensory stimulations by measuring haemoglobin oxygen saturation (SPO₂). It can be used to evaluate the effects of chemotherapy and radiotherapy on tumors⁷. Heart rate variability (HRV) along with pulmonary function test (PFT) can be an aid for early

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prognosis of cardiac disease⁸. It is hypothesized that quality of cancer patients can be improved by knowing the performance status (PS) through various media. The ECOG scale is preferable over KPS because of its simplicity of interpretation. HRV would help us understand the severity of the disease and the ANS dysfunction. SPO₂ and PFT would add an aid to the quality evaluation process. Therefore, a single multiparameter monitor exhibiting HRV, SPO₂, PFT would make the clinician's task simple to evaluate the PS using ECOG Scale.

Method: The questionnaire for clinicians in order to assess the patients' performance.

Duration: The questionnaire-based survey was conducted by clinicians for advanced cancer patients from 01/03/2015 to 01/02/2016.

Results

All the clinicians were familiar with both KPS and ECOG scores. However, in practice there was a high preference to ECOG score than KPS score (70% versus 30%). The only reason for this was simplicity and ability to remember the score.

Eighty four percent doctors agreed that there is interclinician variation in labeling the patient PS. This difference was rated as "considerable" by 35% doctors and as "gross" by 65% doctors. All the doctors agreed that there is a scope of improvement in the evaluation of PS. Sixty two percent doctors agreed that there will be alteration in management of the patient with respect to change in performance and it may prevent unnecessary hospitalizations and investigations, while 38% doctors opined that they give importance to clinical examination and investigations than patients' performance.

Fatigue (56%) was the most common symptom with deterioration of performance of cancer patients followed by dyspnea (32%) and vague complaints (23%). Regarding the preferences of different systems for clinical evaluation of deteriorating performance, 37% doctors gave foremost importance to cardiac, 33% doctor to pulmonary system while 21% doctors gave importance to metabolic parameters, i.e., blood investigations. Neurological and gastrointestinal systems were evaluated only when there were localizing symptoms rather than in general deterioration of performance.

Table 1. Karnofsky Performance Status Scale (KPS) (Adapted from^[4])

Percentage	Work carried out
100	No health issues
90	Meagrely symptomatic
80	Can carry out activity with exertion
70	Self caring but cannot perform ones activity
60	Can carry out activity of ones needs but help is necessary
50	Needs help often and medical assistance too
40	Needs personal attention and on bed more than 50%
30	Almost bedridden, badly disabled and hospitalization required
20	Totally bedridden, person attention by family and medical personnels
10	Bedridden, deadly, critical condition
0	Dead

Table 2. Eastern Co-operative Oncology Group (ECOG) scale of Performance Status (PS) (Adapted from^[5])

ECOG	MEANING
0	Normal Activity
1	Exhibits symptoms and ambulatory
2	Less than 50% on bed but difficulty in carrying out day to day activities
3	More than 50% on bed
4	Bedridden

In general, there was consensus (73%) that objective tool for monitoring performance is necessary. The parameters preferred were SPO₂ 45%, 2D Echocardiography 30%, chest X-ray 42%. However, for HRV test, all the clinicians (100%) rejected the availability of test facilities. However, 74% of clinicians underlined its need as one of the test to evaluate ANS dysfunction and probable deterioration in cancer associated performance. SPO₂ and peak expiratory flow rate (PEFR), a parameter of PFT test were also rated as mobile tools for assessing performance, i.e., home based monitoring. Correlation of various parameters plotted against time in days/ months was a need for 58% clinicians. Moreover, 66% clinicians also wanted some parameter to evaluate the recent short term performance (For example. Hemoglobin A 1C predicts blood glucose control in recent past 2 months).

Thus, detection of subclinical deterioration of performance was a felt need by most (77%) of the clinicians. Sixty five percent doctors pointed to the ANS evaluation for this subclinical progression.

Discussion

Performance status (PS) using ECOG scale of performance stated in Table 2, clinical stage and surgical treatment provided to the lung cancer patients can determine their survival rate⁹. HRV parameters importantly had a correlation with the ECOG PS grade although are not the only parameters¹⁰. Fatigue is observed on a wider scale as a side effect in NSCLC patients¹¹. KPS was less capable than ECOG PS to distinguish patients with varied prognosis. ECOG can predict the functional status better and therefore is preferred to KPS¹². HRV is derived from ECG (Electrocardiogram) signal and can be utilized to know the status of the ANS. HRV analysis can evaluate overall cardiac health and the ANS activity controlling the cardiac activity¹³. HRV conveys know-how on the sympathetic-parasympathetic autonomic balance and thus about the hazard for sudden cardiac death (SCD) in these patients¹⁴. There was no change in PFT values after Stereotactic Body Radiotherapy (SBRT) was given in Stage I lung cancer patient¹⁵. Also, it was found that there was no change in SPO₂ as well as PFT value in Non Small Cell Lung cancer (NSCLC) patients followed by SBRT¹⁶. But the pulmonary function may deteriorate more in few lung cancer patients after radiotherapy is given and the level of deterioration is more in chronic obstructive pulmonary syndrome (COPD) NSCLC

patients which affects their quality of life (QOL)¹⁷. Invasive haemodynamic monitoring is essential in lung cancer patients from admission to discharge or death¹⁸. The study of cognitive dysfunction is essential in small cell lung cancer (SCLC) before prophylactic cranial irradiation because more than 80% of subjects are susceptible to get brain metastasis¹⁹. Any gastrointestinal malignancy ceases to develop in NSCLC patients unless there is lung metastases²⁰.

Conclusion

The present subjective performance scales in lung cancer patients are vague and subjected to interpersonal difference of opinions. Clinicians need a better objective monitor of performance score. Further, noninvasive monitors are preferred over invasive monitors. Cardiac and pulmonary systems are more focused for evaluation whenever deterioration of performance is complained by patient and relatives. Moreover, ECOG scale is preferred over KPS scale to determine the performance status. HRV analysis may be helpful for studying autonomic system dysfunction. The SPO₂ and PEFR parameters can further add to scope of improving the QOL of patients.

Conflict of Interest: Not Any

Ethical Clearance: Not Applicable

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References

1. Karnofsky DA, Burchenal JH: The Clinical Evaluation of Chemotherapeutic Agents in Cancer. In MacLeod CM (Ed), Evaluation of Chemotherapeutic Agents. New York: Columbia Univ Press. 196, 1979.
2. Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, Mcfadden ET, Carbone PP. Toxicity and response criteria of the Eastern Cooperative Oncology Group. American journal of clinical oncology. 1982 Dec 1;5(6):649-56.
3. Yates JW, Chalmer B, McKegney FP. Evaluation of patients with advanced cancer using the Karnofsky performance status. Cancer. 1980 Apr 15;45(8):2220-4.
4. Péus D, Newcomb N, Hofer S. Appraisal of the Karnofsky Performance Status and proposal of a simple algorithmic system for its evaluation. BMC medical informatics and decision making. 2013 Dec;13(1):72.

5. Blagden SP, Charman SC, Sharples LD, Magee LR, Gilligan D. Performance status score: do patients and their oncologists agree? *British journal of cancer*. 2003 Sep; 89(6):1022.
6. Langley JN. On inhibitory fibres in the vagus for the end of the oesophagus and the stomach. *The Journal of physiology*. 1898 Dec 30;23(5):407-14.
7. Zhang HF, Maslov K, Sivaramakrishnan M, Stoica G, Wang LV. Imaging of hemoglobin oxygen saturation variations in single vessels in vivo using photoacoustic microscopy. *Applied physics letters*. 2007 Jan 29;90(5):053901.
8. Behera JK, Sood S, Kumar N, Sharma K, Mishra R, Roy PS. Heart rate variability and its correlation with pulmonary function test of smokers. *Heart views: the official journal of the Gulf Heart Association*. 2013 Jan;14(1):22.
9. Lilenbaum RC, Cashy J, Hensing TA, Young S, Cella D. Prevalence of poor performance status in lung cancer patients: implications for research. *Journal of Thoracic Oncology*. 2008 Feb 1;3(2):125-9.
10. Kim K, Chae J, Lee S. The role of heart rate variability in advanced non-small-cell lung cancer patients. *Journal of palliative care*. 2015 Jun;31(2):103-8.
11. Spathis A, Dhillan R, Booden D, Forbes K, Vrotsou K, Fife K. Modafinil for the treatment of fatigue in lung cancer: a pilot study. *Palliative medicine*. 2009 Jun;23(4):325-31.
12. Buccheri G, Ferrigno D, Tamburini M. Karnofsky and ECOG performance status scoring in lung cancer: a prospective, longitudinal study of 536 patients from a single institution. *European Journal of Cancer*. 1996 Jun 1;32(7):1135-41.
13. Thakur ND, Sankhe MS, Desai KD. Implementation of HRV system for understanding behaviour of Autonomic nervous system. *International Journal of Electronics and Computer Science Engineering (IJECS)*, ISSN: 2277-1956. 2012;1(03):1197-207.
14. Cysarz D, Bettermann H, Van Leeuwen P. Entropies of short binary sequences in heart period dynamics. *American Journal of Physiology-Heart and Circulatory Physiology*. 2000 Jun 1; 278(6):H2163-72.
15. Stephans KL, Djemil T, Reddy CA, Gajdos SM, Kolar M, Machuzak M, Mazzone P, Videtic GM. Comprehensive analysis of pulmonary function test (PFT) changes after stereotactic body radiotherapy (SBRT) for stage I lung cancer in medically inoperable patients. *Journal of Thoracic Oncology*. 2009 Jul 1;4(7):838-44.
16. Stanic S, Paulus R, Timmerman RD, Michalski JM, Barriger RB, Bezjak A, Videtic GM, Bradley J. No clinically significant changes in pulmonary function following stereotactic body radiation therapy for early-stage peripheral non-small cell lung cancer: an analysis of RTOG 0236. *International Journal of Radiation Oncology* Biology* Physics*. 2014 Apr 1;88(5):1092-9.
17. Borst GR, De Jaeger K, Belderbos JS, Burgers SA, Lebesque JV. Pulmonary function changes after radiotherapy in non-small-cell lung cancer patients with long-term disease-free survival. *International Journal of Radiation Oncology* Biology* Physics*. 2005 Jul 1;62(3):639-44.
18. Birkmeyer JD, Sun Y, Goldfaden A, Birkmeyer NJ, Stukel TA. Volume and process of care in high-risk cancer surgery. *Cancer*. 2006 Jun 1; 106(11):2476-81.
19. Komaki R, Meyers CA, Shin DM, Garden AS, Byrne K, Nickens JA, Cox JD. Evaluation of cognitive function in patients with limited small cell lung cancer prior to and shortly following prophylactic cranial irradiation. *International Journal of Radiation Oncology • Biology • Physics*. 1995 Aug 30;33(1):179-82.
20. Marchetti A, Martella C, Felicioni L, Barassi F, Salvatore S, Chella A, Campese PP, Iarussi T, Mucilli F, Mezzetti A, Cuccurullo F. EGFR mutations in non-small-cell lung cancer: analysis of a large series of cases and development of a rapid and sensitive method for diagnostic screening with potential implications on pharmacologic treatment. *Journal of clinical oncology*. 2005 Feb 1; 23(4):857-65.

Treatment Seeking Behaviour among TB Patients Registered Under RNTCP in District Bareilly

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Abstract

Background: Tuberculosis (TB) is a major global health problem and ranks the second leading cause of death from an infectious disease worldwide. India is the highest TB burden country accounting for more than one fifth of the global burden of tuberculosis. The objectives were **(1)** To assess the treatment seeking behaviour of TB patients registered under RNTCP in a select district and **(2)** to determine the default rate in patients having history of treatment interruptions.

Method: A cross-sectional study was conducted among the TB patients registered during 1st April 2014 to 31st March 2016 under RNTCP for DOTS in Bareilly. Purposive sampling was carried out, 10 DMCs were selected in district Bareilly of which a total of 2010 TB patients were interviewed.

Results and Conclusions: In the present study majority of the patients were in the age group of 20 - 39 years (35.0%), male (55.7%) and were sputum positive (69.5%) Cases with a history of treatment interruption had a very high default rate of 23.3% while cases that didn't interrupt their treatment had a low default rate of 3.93%. This association was found to be statistically significant. People who had a positive history for treatment interruption had seven times more risk of becoming a defaulter.

Keywords: Tuberculosis, Default, Treatment seeking behaviour, Treatment interruption.

Introduction

TB has coevolved with humans for many thousands of years and perhaps for several million years. It is caused by Mycobacterium tuberculosis. It primarily affects lungs and causes Pulmonary TB (PTB). It can also affect intestine, meninges, bones and joints, lymph glands, skin and other tissues.¹ TB is transmitted mainly by droplet nuclei generated by sputum-positive patients with PTB.²

In India under RNTCP, TB prevalence per lakh population was 195 in 2013. TB incidence per lakh population was 167 in 2014. TB mortality per lakh population was 17 in 2012.³ Despite these achievements still one-third cases of TB remain undetected in India and poor treatment adherence.

The objective of the present study was to know the treatment seeking behaviour of TB patients registered under RNTCP in district Bareilly and find the default rate in patients having history of treatment interruptions.

Method

A cross sectional study was conducted in district Bareilly over a period of 1 year from August 2015 to July 2016 to determine the treatment seeking behaviour and default rate among TB patients registered under RNTCP by using a pre designed, pretested semi-structured questionnaire. TB patients registered under

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RNTCP for DOTS in Bareilly district for treatment from 1st April 2014 to 31st March 2016. There are 45 DMCs in district Bareilly. Out of these DMCs, 10 DMCs were selected randomly by using lottery method. Interview of the TB patients registered in the DMCs was taken at the health facility or by making home visits for the selected patients. A total of 2010 TB patients were interviewed during the study period.

The study protocol was approved by the Institutional Ethics Committee. Informed consent was collected from the participants and confidentiality was assured. Patients who were not willing to give consent or moved out of the geographical area or were not available for interview on two subsequent visits were excluded from the study.

A TB patient who did not start treatment or whose treatment was interrupted for 2 consecutive months or more was defined as Defaulter.

Results

Table 1: shows the socio-demographic characteristics of 2010 subjects who participated in the study in which the age distribution revealed that maximum subjects (35.0%) were in the age group of 20 - 39 years, followed by 28.1% belonging to 40 - 59 years, 24.3% belonging to <20 years and 12.6% belonging to > 60 years. Male cases contributed 55.7% of the study population.

Table 2: reveals that majority of the cases that is 69.5% were sputum smear positive while 15% were sputum smear negative and in 15.5% cases sputum examination was not done as they were extra pulmonary cases.

More than two third (83.1%) of the cases were taking treatment in the category I while the rest (16.9%) were undergoing treatment of category II.

Table 3: shows the distribution of cases according to their first contact to the health system by the cases on the onset of their symptoms which revealed that 765 (38.1%) study subjects took their first symptomatic treatment from private practitioner followed by 32.6% individuals who went to hospitals, 11.4% cases took treatment from local quacks, 10.6% cases took treatment from chemist while only 7.2% cases went to the DOTS center for their treatment.

Table 1: Socio-demographic characteristics of the study participants

Characteristics	Frequency (N=2010)	Percentage
Age		
<20 Years	489	24.3
20 - 39 Years	703	35.0
40 - 59 Years	565	28.1
> 60 Years	253	12.6
Gender		
Male	1119	55.7
Female	891	44.3
Locality		
Urban	1050	52.2
Rural	960	47.8
Religion		
Hindu	1123	55.9
Muslim	887	44.1
Family Type		
Nuclear Family	777	38.7
Joint Family	748	37.2
Three Generation Family	485	24.1

Table 2: Distribution of TB cases according to their type and category

	Frequency (N=2010)	Percentage
Smear Status		
Smear Positive	1398	69.5
Smear Negative	301	15
Extra Pulmonary TB Cases	311	15.5
Category of Treatment		
Category I	1670	83.1
Category II	340	16.9

The biggest source of suspicion of tuberculosis in study subjects was suggested by a doctor (72.9%), followed by self-perception (13.9%), suggestion by health worker (9.3%), an effect of the awareness campaign (1.4%) and only 0.8% cases had an effect of media.

Maximum number of cases that is 40.2% were diagnosed tuberculosis at DOTS centre while 33.9% and 25.9% were diagnosed at other government hospitals and private clinics respectively.

Table 3: Distribution of TB cases according to their treatment seeking behaviour

	Frequency (N=2010)	Percentage
First symptomatic treatment was taken from		
Private Practitioner	765	38.1
Hospital	656	32.6
Local Quacks	230	11.4
Chemist	214	10.6
DOTS Centre	145	7.2
Suspicion of TB aroused by		
Suggested by Doctor	1465	72.9
Self-Perception	279	13.9
Suggested by Health Worker	187	9.3
Suggested by Peer Group	34	1.7
Effect of Awareness Campaign	29	1.4
Effect of Media	16	0.8
Place of Diagnosis		
DOTS Centre	808	40.2
Government Health Centre	681	33.9
Private Clinic	521	25.9
Time Taken for treatment to start after the diagnosing TB		
< 2 Weeks	1890	94.0
> 2 Weeks	120	6.0
History of treatment interruption		
Yes	562	28
No	1448	72

Table 4: Default rate according to the history of treatment interruption

History of treatment interruption	Total TB Patients	Defaulters	Default Rate
Yes	562	131	23.3
No	1448	57	3.93
Chi-Square value = 179.233; df = 1; p-Value = < .001			

p-Value<.05 is considered as significant

Almost all the cases (94%) started their DOTS treatment within the 2 weeks of the time period while only 6% of the cases showed delay in treatment more than 2 weeks.

Approximately one fourth of the cases (28%) showed an interruption and break in their continuity of the treatment.

It is evident from table - 4 that cases who had history of treatment interruption had a very high default rate that is 23.3% while cases who didn't interrupted their treatment had a low default rate of 3.93%. The association came out to be statistically significant. (p value< 0.001)

Logistic regression was applied on the history of treatment interruption, by keeping patients who didn't have any treatment interruption history in reference category; it was observed that people who had a positive history for treatment interruption had 7 times more risk of becoming a defaulter.(p value =0.001) (Table 5)

Table 5: Risk of defaulting from treatment according to the history of treatment interruption by applying logistic regression

History of treatment interruption	Defaulter	Non Defaulter	Odds Ratio	Confidence Interval (95%)		p-value
				Lower limit	Upper limit	
Yes	131	431	7.417	5.336	10.309	.001
No	57	1391	Reference	-	-	-

p-Value<.05 is considered as significant

Discussion

There were total 2010 TB cases interviewed in the present study. Nearly one third of the TB cases, i.e. 703 (35.0%) were from the age group 20 - 39 years of age.

The findings of this study are similar to the findings of **Sumer C et al (2012)**⁴ where most of the TB patients were in the age group of 16 - 24 years (26.95%). Whereas study done by **Roy N et al (2011)**⁵ the 27.84% of the study population was in the age group of 25 - 35 years.

In the present study out of 2010 TB patients, 1119 (55.7%) of the study participants were male, 1050 (52.2%) from urban area and 1123 (55.9%) were Hindu by religion.

The above finding is similar to **Verma AK et al (2007)**⁶ where out of 130 participants 55.8% were male. And in the study conducted by **Gupta S et al (2007)**⁷ 45.77% of patients were residents of Urban area. Whereas study done by **Varshney AM et al (2010)**⁸ 74% of the study participants were Hindu by religion.

In 2010 TB cases, 765 (38.1%) cases took their first symptomatic treatment from private practitioner; Suspicion of TB was aroused by Doctor in 1465 (72.9%) cases; most of the cases i.e. was diagnosed TB in DOTS centre and almost all the TB patients i.e. 1890 (94%) started their treatment within two weeks after getting diagnosed for TB while only 562 (28%) gave a history of treatment of interruption.

The findings of this study is similar to the findings of **Varshney AM et al (2010)**⁸ in which 52% of the study participants had first time consulted private practitioner for their illness and 48% from Government physician.

Sudha G et al⁹ in their study highlighted that private health care facilities were the first and preferred point of contact for 57% of urban and 48% of rural participants. Chest symptomatic opted for self-medication in urban and rural 33% and 21% respectively.

Suganthi P et al¹⁰ in their study in Bangalore slums found that 72% first approached private health facilities. The choice of first health facility depended primarily on distance from a residence and faith in the health care services. Predominant reasons for subsequent visits to other health facilities were persistence of symptoms and referral.

In the study by **Rajeshwari R et al**¹¹ patients first

consulted private practitioners more frequently than government providers (54% vs. 27%; $p < 0.001$). Most patients resorted to self-medication (61%) or pharmacies (7%). Only 20% were diagnosed at the health facility where they first sought care; the others shopped around for care at various health facilities before a diagnosis of tuberculosis was made. Nearly half of all the patients had to visit three or more health facility before a diagnosis of tuberculosis was made.

Conclusion

Default is one of the unfavourable outcomes for patients on DOTS and represents an important challenge for the control program. Poor treatment adherence increases the risk of drug resistance, treatment failures, relapses, deaths and prolonged infectiousness, which is a hurdle to the success of TB programs.

Declarations

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Conflict of Interest: Nil

Ethical Approval: The study was started after obtaining approval from ethical committee of SRMS Institute of Medical Sciences, Bareilly.

References

1. Park K. Park's Textbook of Preventive and Social Medicine. 23rd edition. Jabalpur (India): BanarsidasBhanot; 2015. P. 176.
2. Park K. Park's Textbook of Preventive and Social Medicine. 23rd edition. Jabalpur (India): BanarsidasBhanot; 2015. P. 181.
3. TB INDIA 2106, RNTCP Annual Status Report. Chapter 2; Page 9 – 10.
4. Sumer C, Tayade B, Keshwani P. Efficacy and treatment outcome of DOTS in RNTCP. *PJMS* 2012;2(1):32-36
5. Roy N, Basu M, Das S, Mandal A, Dutt D, Dasgupta S. Risk factors associated with default among tuberculosis patients in Darjeeling district of West Bengal, India. *Journal of Family Medicine and Primary Care* July 2015: Volume 4: Issue3
6. Verma AK, Mishra M, Singh A, Chaudhri S, Pandey S. Outcome of cases under Revised National Tuberculosis Control Programme at designated microscopy centre of a tertiary level hospital and

- medical college at Kanpur, U.P. *J ClinSci Res* 2013;2:126-31.
7. Gupta S, Gupta S and Behera D. Reasons for interruption of anti-tubercular treatment as reported by patients with tuberculosis admitted in a tertiary care institute. *Indian J Tuberc* 2011; 58: 11-17
 8. Varshney AM, Singh US, Kumar D. Source of previous Anti-tubercular drugs exposure for patients registered in RNTCP as retreatment cases in District Anand, Gujrat. *Indian Journal of Community Health*, Vol 25, No 2, April 2013 - June 2013
 9. Sudha. G, Nirupa.C, Rajasakthivel.M, Sivasubramanian.S, Sundaram.V, Bhatt.S, et.al. Factors influencing the care-seeking behavior of chest symptomatics: a community -based study involving rural and urban population in Tamil Nadu, South India. *Tropical medicine and International Health* 2003; 8(4):336-341.
 10. Sanganthi P, Chadha VK, Ahmed J, Umadevi G, Kumar P, Srivastava.R et al. Health seeking and knowledge about tuberculosis among person with pulmonary symptoms and tuberculosis cases in Bangalore slums. *Int J Tuberc lung Dis* 2008; 12(11):1268-1273.
 11. Rajeshwari.R, Chandrashekar V, Suhadev M, Sivasubramaniam S, Sudha G., Renu G. Factors associated with patient and health system delays in the diagnosis of tuberculosis in South India. *Int J Tuberc lung Dis* 2002; 6(9):789-795.

Invitro Evaluation of Shear Bond Strength of Orthodontic Brackets Cemented to Natural Teeth Treated with Various Soft Drinks

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Abstract

Introduction: The common problem during the orthodontic treatment is debonding of brackets which leads to failure of orthodontic treatment. The purpose of this study was to determine the effects of four soft drinks (Coca-Cola, 7Up, Tropicana orange, minute maid apple juice) on the shear bond strength of orthodontic brackets.

Aim: To evaluate the shear bond strength of orthodontic brackets cemented to natural teeth treated with various soft drinks

Materials and Method: A total of 50 extracted human premolars were collected and stored in normal saline solution. They were cleaned and cemented with edge wise stainless steel brackets using composite. Then they were cycled in the said four soft drinks for 2 hours up to 7 days. The samples were tested for their shear bond strength using Universal testing machine (INSTRON) with a cross head speed of 0.5mm/min. The values were tabulated and analyzed statistically using ANOVA.

Results: The lowest mean resistance to shearing forces was shown by the control group (18.74 ± 5.15 Mpa) followed by 7Up group (20.17 ± 6.76 Mpa), orange juice group (21.79 ± 5.15 Mpa), Coca Cola group (24.58 ± 11.68 Mpa) and highest resistance to shearing forces by apple juice group (26.04 ± 1.31 Mpa). There was no statistically significant difference among the groups.

Conclusion: No significant differences were observed in bond strength of the teeth among the different groups suggesting that consumption of soft drinks after cementation of orthodontic brackets do not significantly affect in de-bonding the brackets.

Keywords: Microleakage, shear bond strength, soft drinks

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Introduction

In developing countries, there is an increasing trend in consumption of soft drink, especially among young people.^{1,2} This habit often continues into adulthood. Soft drinks contain high sugar content and a pH of < 5.5 which is below the critical level that will cause enamel demineralization leading to dental erosion and

also microleakage beneath the orthodontic brackets in patients undergoing orthodontic treatment.^{3,4,5} This is a matter of concern among dental practitioners.

Debonding of brackets during orthodontic treatment is commonly seen.⁶ Hence, patients receiving orthodontic care need proper attention.

The causative factor for bond failure is due to acidic foods and drinks with the low pH in the diet of the patient which increases treatment time.^{6,7} This might also have an erosive influence on the hydroxyapatite component of teeth.^{8,9} Coca-cola is categorized as the most carbonated drink (50%) which contains high levels of citric acid and phosphoric acid that should be seen as a true hazard for patients with orthodontic appliances.^{1,3} Very few studies have been conducted in the past to evaluate the effect of soft drinks on the bond strength. Coca-cola, 7-Up, Orange juice and Apple juice are widely available in the market and is very popular among adolescents undergoing orthodontic treatment. The purpose of this study was to determine the effects of these four soft drinks (Coca-cola, 7-Up, orange juice and apple juice) on the shear bond strength of orthodontic brackets in vitro.

Materials and Methodology: This in vitro study was conducted at the department of conservative dentistry and prosthodontics, Melaka Manipal Medical College, Manipal. Ethical Clearance was obtained from the Institutional Ethical committee.

1) Sample Selection: The software G*Power 3.0.10 was used to estimate the required sample size for the study. A total of 50 extracted human premolars were collected and stored in normal saline solution. The teeth selected for the study were free from enamel cracks, caries, and fillings. These teeth were fixed in self-cure acrylic blocks using aluminium tubes (Figure 1). Fifty 0.022" stainless-steel edgewise orthodontic brackets (Centrino Standard MBT®) with a base surface of 12.2 square mm were used in this study. (Figure 2)

2) Bonding of Brackets: All 50 teeth were cleaned and polished thoroughly using pumice slurry before the bonding procedure. The teeth were etched using 37% phosphoric acid gel (DETREY Conditioner 36, Dentsply, UK) for 30 seconds as per the manufacturer's instructions. The teeth were rinsed with water spray and air dried until a frosty white appearance was seen on the etched buccal surface.

A thin uniform layer of Spectrum® bond- Nano-

Technology Dental Adhesive (DENTSPLY, UK) was applied using a brush on the buccal surfaces of each tooth and also onto the base of the orthodontic brackets following manufacturer's instruction and the bonding agent was cured. A flat-ended composite filling instrument was used to apply the required amount of Spectrum® dental composite (DENTSPLY, UK) onto the buccal tooth surface as well as the base of orthodontic brackets.

The bracket was then pressed firmly into the centre of the crown of the tooth mesiodistally and along the long axis of the tooth immediately (Figure 3). Excess (composite) was removed from the bracket using a sharp scaler.

The composite was light-cured using Dentsply LED light curing unit on all four sides of the bracket edge, 10 seconds per side at a distance of 1-2mm.

3) Immersion and Storage: The samples were then immersed in 5 different groups of beverages once daily for 2 hours. This process continued for seven days. Then they were washed with water and stored in distilled water at a temperature of 37 degree Celsius until the testing.

4) De-bonding Testing: The samples were tested for their shear bond strength using the Universal testing machine (INSTRON) with a cross head speed of 0.5mm/min. The values were obtained in Newton. The values which were obtained in Newton were converted to Mega pascals by dividing the total area with 12.2 square mm which is the area of the single bracket. (Figure 4)

Statistical Analysis: Anticipating an effect size of 0.6 and to test the null hypothesis at 5% level of significance with 80% power the required sample size was 40. It was increased to 50 (10 per group), anticipating 20% failure during testing. Mean of the debond testing was compared applying Welch ANOVA followed by Post Hoc Games-Howell test using software SPSS version 15. P<0.05 was considered statistically significant.

Results

Table 2 shows the group-wise summary (mean and SD) and the result of group mean comparison. Considering unequal variance (Levene test of homogeneity of variance (P<0.001)) group means were compared applying Welch Anova (Robust test of equality

of means). Welch ANOVA indicated a significant difference in the group means ($F(4,11.37)=3.61, P=0.038$). Post Hoc Games-Howell test for pair-wise comparison did not show any significant difference in the group means. Mean resistance was maximum for Distilled water (mean=26.04) and was least for Apple juice (mean=18.74). The difference in mean of these two groups was not significant ($P=0.08$).

Among the selected values, the lowest mean resistance to shearing forces was shown by apple juice group (18.74 ± 5.15 Mpa) followed by 7Up group (20.17 ± 6.76 Mpa), orange juice group (21.79 ± 5.15 Mpa), Coca-Cola group (24.58 ± 11.68 Mpa) and highest resistance to shearing forces by control group (26.04 ± 1.31 Mpa).

A considerable amount of intergroup variation was seen in the coca-cola group. All the other groups showed lesser inter group variation.

Table 1: Beverages were divided into five groups in this study : (Table 1)

Groups	Beverages Used
Group 1	Control – Distilled water
Group 2	Tropicana Orange Juice (PepsiCo.)
Group 3	7 – UP (PepsiCo India)
Group 4	Tropicana Apple Juice (PepsiCo.)
Group 5	Coca-Cola (Coca-Cola India Pvt. Limited)

Table 2: Mean resistance to shearing forces.

Soft drinks	n	Mean	Standard. Deviation	Welch Anova F (4,11.37)	P-value
Apple Juice	7	18.74	5.15	3.61	0.038
Orange Juice	7	21.79	5.15		
7 UP	7	20.17	6.76		
Distilled Water	7	26.04	1.30		
COCA COLA	7	24.58	11.68		

Legends:

Figure 1: Extracted premolars mounted in aluminium rings using acrylic resin

Figure 2: Stainless steel Edgewise Orthodontic brackets

Figure 3: Debonding testing procedure by INSTRON universal testing machine

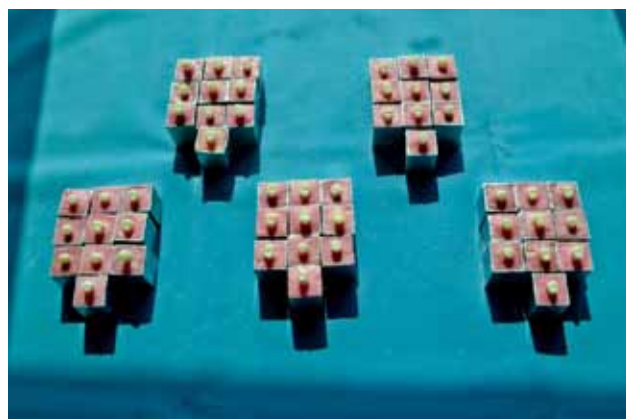


Figure 1: Extracted premolars mounted in aluminium rings using acrylic resin



Figure 2: Stainless steel Edgewise Orthodontic brackets

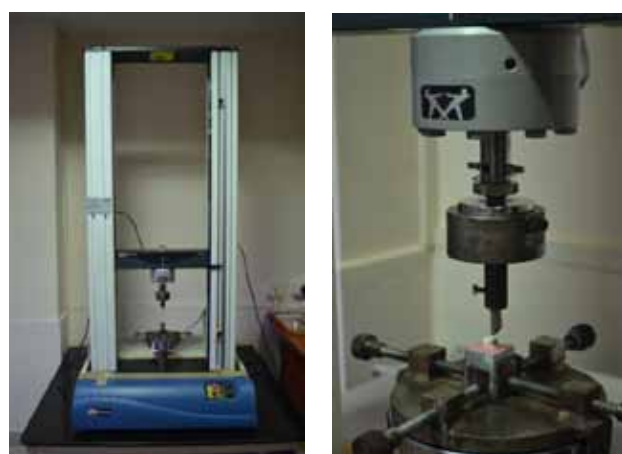


Figure 3: Debonding testing procedure by INSTRON universal testing machine.

Discussion

Several studies have reported that consumption of acidic beverages like cold drinks leads to debonding of orthodontic brackets due to decrease retention.¹⁻⁶

This is an in vitro study, designed to reproduce in vivo situation. In the experiment, different drinks that are commonly consumed by target groups which are Coca-Cola, 7Up, Orange Juice, Apple Juice, and also distilled water (control) are used as manipulative variables.

The immersion times and schedules used in the many past studies varied widely. In our study, 50 specimens divided equally were kept for 2 hours, in respective drink groups daily for seven days. The remaining time it was kept in distilled water to mimic the normal oral environment. In this way, we can assume that these drinks were consumed 3 – 4 times a day considering 45 minutes to consume one drink.⁵

Coca-Cola was the most acidic drink followed by 7 UP. The apple and orange juices were also acidic. Both Coca-Cola and 7 UP contains citric acid which gives the acidity to the drink. The apple and orange juices contain calcium citrate and ascorbic acid. All these soft drinks have demineralizing effects on the teeth surface.

The cementing of brackets under one operator minimizes the error and standardize the cementing force. During debond testing using the Instron machine with a shear head speed of 0.5 mm/min.

Also, it is noteworthy to note that the inter group variations obtained in the Coca-Cola group were higher compared to the other groups.

The results obtained are similar to the results of Navaro's et al⁵ study who reported that bond strength values for teeth treated in Coca-Cola and Schweppes Limon were not significantly different from those in their control group. Also, our results were in consistent with a study done by Suparssaraet al¹⁰

This result contradicts with some of the studies conducted^{11,12} that found Coca-Cola showing a reduction in shear bond strength of orthodontic brackets. Based on the study, the teeth were immersed in Coca-Cola thrice a day, while our study only immersed the teeth once daily in respective drink groups. Hence, the study might have a better imitation of soft drink consumption by target groups. Coca-Cola is an acidic media, and it can decalcify tooth (Borjan a Ferrari). Calcium may leach out from the teeth, thus soften and erodes the dental hard tissues. This will then facilitates abrasion. Furthermore, the structure of bisphenol A glycidyl methacrylate-based composite resins which is the main composition of the adhesive used in the study will be degraded with acid

and acidic drink consumption as mentioned as Suparssara et al.¹² The matrix of the adhesive will soften which leads to filler leaching out, thus lowering the bond strength of the brackets (Hobson RS).

The limitation of this study was an unexpected increase in the failure rate of teeth (lesser sample size) could be one of the reasons for the insignificant difference in the group means. Hence further study may be required by increasing the sample size.

There are many factors that may affect the results. For example, the experiment done is an in vitro study, which the teeth used are extracted from different patients, at different times, of different age. Hence, the mineralization level of each tooth differs as it is affected by their lifestyles, oral hygiene and age factor. Also, the biggest disadvantage in these studies is that the data of beverages consumed by the individual before the bonding is often unknown, which could be a major factor while comparing the results.

Furthermore, the teeth used are premolars, which have a convex surface. The bonding position of the brackets is not always consistent between different teeth. Thereby, affecting the force applied during the debonding process might vary. Therefore studies are required.

Conclusion

No significant differences were observed in bond strength of the teeth after debonding among the different groups suggesting that consumption of soft drinks after cementation of orthodontic brackets do not significantly affect debonding of orthodontic brackets.

Conflict of Interests: The authors declare no conflict of interests.

Ethics Approval: Obtained from the Institutional Ethical Committee.

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References

1. Chitra P, Pulgoankar R. The Effect of Three Commonly Consumed Soft Drinks on Bracket

- Bond Strength, Microleakage And Adhesive Remnant Index: An In-Vitro Study. *Papaver Indian Journal of Research*. 2014;3(10).
2. OmidKhoda M, Heravi F, Shafae H, Mollahassani H. The Effect of Different Soft Drinks on the Shear Bond Strength of Orthodontic Brackets. *Journal of Dentistry (Tehran, Iran)*. 2012;9(2): 145-149.
 3. Sajadi SS, EslamiAmirabadi G, Sajadi S. Effects of Two Soft Drinks on Shear Bond Strength and Adhesive Remnant Index of Orthodontic Metal Brackets. *Journal of Dentistry (Tehran, Iran)*. 2014;11(4): 389-397.
 4. Dincer B, Hazar S, Sen BH. Scanning electron microscopic study of the Effects of Soft Drinks on Etched and Sealed Enamel. *Am J OrthodDentofacialOrthop*. 2002 Aug;122(2): 135-41.
 5. Navarro R, Vicente A, Ortiz AJ, Bravo LA. The effects of Two Soft Drinks on Bond Strength, Bracket Microleakage, and Adhesive Remnant on Intact and Sealed Enamel. *Eur J Orthod*. 2011 Feb;33(1): 60-5.
 6. Nahidh M. The Effects of Various Beverages on The Shear Bond Strength of Light-cured Orthodontic Composite (An In-Vitro Comparative Study). *J Bagh College Dentistry*. 2014;26(3): 144-148.
 7. Akova T, Ozkomur A, Aytutuldu N, Toroglu MS. The Effect of Food Simulants on Porcelain-Composite Bonding. *Dent Mater*. 2007;23(11): 1369-72.
 8. Oncag G, Tuncer AV, Tosun YS. Acidic Soft Drinks Effects on the Shear Bond Strength of Orthodontic Brackets and a Scanning Electron Microscopy Evaluation of the Enamel. *Angle Orthodontist*. 2005 Mar;75(2): 247-53.
 9. Rugg-Gunn AJ, Maguire A, Gordon PH, McCabe JF, Stephenson G. Comparison of Erosion of Dental Enamel by four Drinks using An Intra-Oral Appliance. *Caries Res*. 1998;32(5): 337-343.
 10. Sirabanchongkran S, Wattanapanich S. Effects of Acidic Green Tea Soft Drinks on The Shear Bond Strength of Metal Orthodontic Brackets. *J Dent Assoc Thai*. 2015;65(1): 43-51.
 11. Pasha A, Sindhu D, Nayak RS, Mamatha J, Chaitra KR, Vishwakarma S. The Effect of Two Soft Drinks on Bracket Bond Strength and on Intact and Sealed Enamel: An In Vitro Study. *Journal of International Oral Health : JIOH*. 2015;7(Suppl 2): 26-33.
 12. Abdelbassetblqasim al-taibslimani ,Abd Rahman, Normastura, Ayat Khan, Rafeeah. Effect of carbonated beverage and fluoride mouth rinses on enamel surface and shear bond strength of conventional resin based orthodontic adhesive composite. *Malays J Med Sci*. 2012 Jul-Sep; 19(3): 124–125.

Understanding the Basics of Research as a Beginner: A Highlighter

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Abstract

Context: Research has grown beyond leaps and bounds; scientific progress solely depends on inquisitiveness and tireless coordination of teamwork. The word research is so attractive for a beginner, the student fraternity is overwhelmed about this process. Irrespective of any field, now the research is becoming an indispensable part of the educational system. This article is intended to create basic awareness about research and its components, especially for the research-oriented students in the field of medical, paramedical, allied health sciences, etc.

Keywords: Research, bioethics, clinical trials, good clinical practice

Introduction

Biomedical research is based on fundamental biological scientific principles, which will focus on personal healthcare and public health. Basic research is also called as bench side research; it deals with in-vitro and in vivo experimental models involving the organisms or animals to obtain a valid outcome to further try on the humans. When the basic research results are tried on clinical patients it is called translational research, which is solely intended to trial the results of basic research from bench side to bedside, clinically by using patients virtually¹.

Research is practiced by humans since the time of evolution on earth. In history, the ancient practice of folklore medicine stands as the best example for the oldest model for clinical research; with the time it has gradually evolved through trial and error method.

India is at the forefront of contributing to the field of clinical research; medical science like Ayurveda, Siddha, Unani; their medical literature has mentioned the use of medications for several human ailments for thousands of years. Based on its principles, Ayurveda has mentioned therapeutic interventions, and a number of herbs and mineral formulations applied directly to the human subjects with the sole purpose of alleviating human sufferings^{2,3}.

Classification of type of study:

Basic Research: The basic medical research deals with understanding the functional, cellular or molecular mechanisms in primates through in vivo or invitro studies.

Preclinical Research: Preclinical research deals with the study on humans, which further supports the clinical trials on patients.

Clinical Research: It is conducted on patients in the hospital or on the selected population; it is supervised by physicians.

What is the Research Question.?: It is the main inquiry of the issue which needs to be addressed through research. The research question should be clear, targeted and simple.

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What is a Pilot Study.?: It is the study performed on a small scale by using a minimum number of participants/subjects. This study gives every opportunity to the researcher/investigator to understand all aspects of the main study including its feasibility, sample size, time duration, troubleshooters, etc.

What are the Study Parameters.?: Parameters are study exponents in the research; which are later subjected to analysis.

Bioethics: Bioethics deals with the study of ethical dimensions of medicine and biological sciences. Important principles of bioethics are including Autonomy (respect to self-governing), Beneficence (best interest of the subject), Non-maleficence (causing no harm) and Justice (fair treatment)⁴

Basic research in Non-Human Primates: Research on non-human primates is a prerequisite for conducting trials on subsequent levels. Animal experiments mean, the use of animals preferably mammals in the experiments for education and research. The basic experiments use nonhuman primates like rats, mice, rabbits, hamsters, guinea pig, monkey, chimpanzee, dog. It can also be done by using fruit flies, cell lines, fish, etc. There are millions of animals that will be sacrificed worldwide for the sake of research every year. Experiments performed by using both vertebrates and non-vertebrates, but using the vertebrates will be taken into account as they are under more strict ethical vigilance. For research, all these animals should be procured from the authorized breeders who are registered under CPCSEA (committee for control and supervision of experiments on the animal) guidelines or from the recognized higher research centres.

Importance of animal testing in biomedical research: In the field of biomedical research, the use of the animal model experiments stands as “**Hall Mark**” of an interventional research study. The great scientists like Aristotle, Erasistratus Galen, etc. have tried their initial experiments on the animals for scientific purposes⁵. Age back, the use of animals got much attention, particularly to test the surgical procedures or use of drugs or devices before applying them clinically to humans. In spite of heavy criticism by the public and the animal protection activists there is a rise in several basic research experiments on animals; because in history, we have learned about the adverse effects of drugs that were used directly on patients. Causing harm to the animals

can't justify the human benefit. But still, animal-based research outcome retains its importance in several aspects including, toxicological studies, where the animal experiment model stands as an inevitable tool in supporting the increasing hierarchy of evidence. In the present situation to justify the rationality and inevitability of the use of animals in the experiments we need to follow principles of 4R.

Replacement: Use of alternate to animal model Ex: in silico i.e. use of computer modeling, in vitro cell line studies, etc.

Reduction: Method which minimizes the number of animals in experiments

Refinement: It deals with the reduced invasiveness, by adopting improved, non-invasive, non-painful procedures by using the most appropriate method⁶.

Rehabilitation: As a 4th component, the rehabilitation of animals will be done after its justified usage⁶.

Toxicity Study: It is a branch of science deals with the toxins and poisons and their effect and treatment. As per US food and drug administration (FDA), for the development of a new drug entity, it is essential to conduct toxicity tests in the biological subjects⁷.

Trials Before Regulations: In the olden days, before formulating guidelines for clinical research activities, any individual or group of people would be a part of the research event; it was tried on the helpless community like war prisoners or people who convicted under crime, children, patients, aged people, etc. The direct use of drugs like thalidomide and Elixir Sulfanilamide on humans has resulted in the death of the study participants. Based on such consequences of unethical trials on humans, the present era has formulated a code that is mainly focused on obtaining voluntary consent. By considering the above discrimination in the clinical research, a judgment formulated with a code known as “Nuremberg code” which has streamlined the research at all levels with the sole intention to protect the safety and dignity of the participants to achieve more precise and valid outcome⁸.

History of Clinical Trials: The credit of clinical research goes to a Scottish physician Dr. James Lind, M.D. (1716–1794) has treated the disorder called scurvy in sailors, where patients were presented with the sign

of bleeding through their gums. He has noticed that the administration of the orange and lemon has shown drastic improvement in their condition⁹.

Regulations of Clinical Trials:

Good Clinical Practice (GCP): It is an international ethical and scientific standard protocol for conducting biomedical and behavioral research involving human participants; which protects participants' safety, rights and confidentiality at all levels¹⁰.

International Conference on Harmonization (ICH): It is an international council that brings together the regulatory authorities and pharmaceutical industry to discuss the technical aspects of drug registration. ICH's regulations are intended to achieve greater harmony worldwide to ensure safety, effectiveness, and quality of medicines; which are developed and registered in a hassle-free manner¹¹.

Institutional Ethics Committee (IEC): It plays a role in appointing members; it will review the protocol and informed consent forms (ICF), and periodic progress of the study¹².

World Medical Declaration of Helsinki: It is developed by the World Medical Association (WMA) in the year 1964; it is including ethical guidance for physicians and all other participants in the research team involving in clinical trials on human subjects. This rule binds all the research participants to the applicable law under its declaration¹³.

Role of the Investigator: All trial investigations are conducted by qualified and trained persons who are personally supervising the work.

Sponsor for Trials: The sponsor for a clinical trial may include an individual, an industry, an institution, etc. which takes the responsibility of initiation, management, financing, and auditing. They are also taking the responsibility of subjecting the study participants under sufficient insurance coverage, and compensating the subjects in any untoward incidence or reactions¹⁴.

Role of Statistics in Research: Since the time of conception of the research protocol, the statistics play an important role to format different components of research like study design, conduct, sample size, data analysis, reporting, etc. they are essential to derive a valid and precise conclusion.

What is the Placebo Effect.?: Placebo is an inert substance without any therapeutic value; it is used to compare with standard control groups. The psychosomatic profile is an important factor to be considered in assessing the placebo drug response. The placebo effect can be better appreciated in the alleviation of symptoms of the pain rather than any other condition¹⁵.

Clinical Trials: Clinical trials are research study on human subjects, which is intended to evaluate the effect of biomedical interventions like vaccines, drugs, treatments, devices, new ways of using known drugs or to study drug interactions, etc. The study may also include the evaluation of behavioral interventions¹⁶.

The ultimate goal of CT is to ascertain the drug safety of the subject, risk and benefit ratio before its final approval for marketing. There are many factors involved in research, out of which some are can be controlled, and some others are beyond one's control. Randomization means being nonselective to any application or intervention. Randomization in clinical trials is considered as the basis for the "Evidence-based Medicine"¹⁷.

Blind Experiments: Bias is the main concern of the clinical trials where blinding becomes essential to reduce the bias and increase the validity of the outcome. Blinding is a process where one or the other participants in the study were deliberately kept unaware of intervention. Blinding is an important factor to ensure objectivity in the clinical trial by avoiding or preventing the conscious and unconscious bias in the study¹⁸.

Types of Blind Trials: Open clinical trials: it is the trial where all the level of study participants in the research group will be knowing the intervention.

Single-blind study: where the subject alone in the research study is unaware of intervention.

Double-Blind Study: where the subject, as well as the researcher both, are unaware of the intervention

Triple-Blind Study: where the subject, researcher, and analyser are unaware of intervention. At the end of the study result analysis, all masked or blinded interventions will be disclosed.

Protection of Subjects: The protection of the clinical trial participants at all levels is an important issue. Concerned authorities should take care of all necessary precautions to address personal, social and

legal issues during and after completion of trials. Any relevant issues should be addressed, and it should be properly compensated for the loss. It is essential to ensure proper compensation for all the study participants who are involved in the clinical trials.

Importance of Informed Consent (IC): Clinical trial participants are strictly volunteer in its true sense without coercing them for any benefit. Informed consent is an important prerequisite before allocating any human subject to the clinical trials. Privacy and confidentiality of IC should be maintained in all the circumstances. It is very much essential to know whether the subject is a literate or illiterate, or whether he is fit to give valid consent. The investigator should explain and clarify all the doubts of participants regarding the research protocol before taking consent¹⁹.

Types of Clinical Trials:

Screening Trial: screening for the possibility of occurrence of diseases in a healthy population

Prevention Trail: it deals with the prevention of disease by using supplements, vaccines, devices, lifestyle modifications, etc.

Diagnostic Trail: it deals with the accuracy of the disease

Treatment Trail: it deals with the effectiveness of treatment in diseased

Conventionally the CT is Having the Following Phases:

Phase 0: It is an Exploratory Investigational New Drug (IND) Study. It will be conducted first on humans; it is also known as human micro-dosing studies by using the sub-therapeutic dose. It is conducted by using 10-15 numbers of limited volunteer healthy human subjects to understand the pharmacokinetics, pharmacodynamic activity, and safety of a new drug or a molecule.

Phase I or Clinical Pharmacology Trial: It is also called "First in Man", done in small groups with 20-100 in number in healthy volunteers. It is to assess safety through pharmacovigilance and the details of the pharmacokinetic and pharmacodynamic effects of a drug. Dose escalation trial can give an idea about the appropriate maximum tolerable dose which can be used under subsequent trials.

Phase II or Exploratory Trial: The third phase of the clinical trial can be done in 200-300 number of larger healthy human volunteers. It is done in Phase I A is to assess the clinical efficacy or biological activity, and Phase II B is to assess and match the optimum dose, benefit with minimum side effects

Phase III trial or Confirmatory Trial: It is a randomized control multicentric trials in a large number of volunteer patients in a group of 300-3000 or more. Such trials are more expensive, time-consuming and difficult to handle, especially while dealing with chronic disease conditions or disease with a long latency/incubation period.

Phase IV or Post-marketing Surveillance: Called post-marketing surveillance trial. It involves a pharmacovigilance study after receiving permission to market an approved drug. If the drug/treatment is found satisfactory in three phases, then it will be approved under the country's national regulatory authority for its use in the general population. Phase IV trials are invariably always under the research radar.^{20,21}

Multicentric Clinical Trials: It includes a large number of participants from different parts of the world, including a wide range of populations; which will compare the results of different centers.

Accessibility of Clinical Trial Reports: Accessing clinical trial data or information is an important prerequisite to tackle the challenges before considering them under policymaking. Archiving the clinical trial documents is a must, which helps to analyze the data retrospectively in a systematic manner. Now online updates are available on the registered websites which are developed at the national institute of health under the national library of medicine. CT information is always accessible to any common man, through website clinical trials govand also through Cochrane Library, it is a collection of databases in medicine and other healthcare specialities^{22,23}. The ultimate goal of accessing the clinical trial results is to introduce newer government policies and regulations to provide improvised health care facilities for the benefit of the population at large.

Conclusion

For a beginner, the present review will highlight the components of basic research, preclinical and clinical research. It has created basic awareness about the ethical factors involved in the research at different levels.

Ethical Clearance: Obtained from Institution ethical committee

Conflict of Interest: Nil

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References

1. Translational science spectrum. Available from: <https://ncats.nih.gov/files/translation-factsheet>
2. Prasad LV. In: Indian System of Medicine and Homoeopathy Traditional Medicine in Asia. Roy C R, Muchatar R U, Editors. New Delhi: WHO-Regional Office for south-east Asia; 2002:283–286.
3. Ravishankar, Bplaysand Shukla, V.J.Indian systems of medicine: A brief profile. Afr J Tradit Complement Altern Med. 2007 Feb16;4(3):319-37
4. Beauchamp TL, Childress JF. Principles of Biomedical Ethics. 5th ed. Oxford: Oxford University; 2001.
5. Rachel Hajar MD . Animal testing in medicine. Heart Views. 2011; 12(1): 42.
6. Mandal J , Parij S C. Ethics of involving animals in research. Trop Parasitol. 2013; 3(1): 4–6.
7. The Drug Development Process. Available from:<https://www.fda.gov/ForPatients/Approvals/Drugs/ucm405382>.
8. Moreno J D, Schmidt U, Joffe S, MD, The Nuremberg Code 70 Years Later.JAMA. 2017;318(9):795- 796.
9. Trohler U,James Lind and scurvy. JLL Bulletin: Commentaries on the history of treatment evaluation Available from <https://www.jameslindlibrary.org/articles/james-lind-and-scurvy-1747-to-1795/>.
10. Guideline for Good Clinical Practice–ICH Available from URL:https://www.ich.org/fileadmin/Guidelines/Efficacy/E6_R1_Guideline.
11. Guideline for Good Clinical Practice – ICHhttps://www.ich.org/Guidelines/Efficacy/E6/E6_R1_Guideline.
12. Central Drugs Standard Control Organization, Directorate General of Health Services, India. Good Clinical Practices for Clinical Research in India. Available from: <http://cdsco.nic.in/html/gcp1>.
13. Declaration ofHelsinki - World Health Organization Available from: <https://www.who.int/bulletin/archives> by WorldMedical Association.
14. Indian GCP Guidelines. 2004. Available from: <http://www.cdsco.nic.in/html/GCP1.html>
15. Colloca L, Benedetti F. Placebos and painkillers: Is mind as real as matter? Nature Reviews. Neuroscience. 2005;6(7):545–552.
16. “Clinical Trials”. Bill and Melinda Gates Foundation. Available from:https://docs.gatesfoundation.org/documents/clinical_trials
17. DH Au, Castro M and Krishnan J A.Selection of Controls in Clinical Trials:Introduction and Conference Summary.Proc Am Thorac Soc Vol 4. 2007; 567–569.
18. Kao LS, Aaron BC, Dellinger EP. Trials and tribulations: Current challenges in conducting clinical trials.Arch Surg. 2003 Jan; 138(1):59-62.
19. ICMR Ethical Guidelines for Biomedical Research. Available from:www.cns.iisc.ac.in/wordpress/wp-content/uploads/2017/01/ethical.
20. Kumar S, Rubinstein L, Kinders R, Parchment RE, Gutierrez ME, Murgu AJ, et al.Phase 0 clinical trials: conceptions and misconceptions. Cancer J. 2008;14(3):133-7.
21. Thorat S B, Banarjee S K, Gaikwad D D, Jadhav S L, Thorat R M. Clinical trial: a review. International Journal of Pharmaceutical Sciences Review and Research. 2010; 1 (2):101-106.
22. Clinical Trials.gov - National Library of Medicine – NIH. Available from: https://www.nlm.nih.gov/archive/news/press_releases/clntrlpr00.
23. Deborah H. Charbonneau. The Cochrane Library.J Med Libr Assoc. 2005; 93(3): 409–410.

Food Insecurity Standard of Living and Nutritional Status of People Living with HIV/AIDS (PLHAs) on ART: Rural–Urban Differences

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Abstract

Background: Synergistic effect of malnutrition, food insecurity and poor standard of living pour significant changes and poor outcome in already compromised PLHAs due to increased financial burden as well as emotional breakdown.

Objective: To assess the nutritional status, food insecurity and standard of living (SLI) with rural urban differences and their association if any among the PLHAs who have been established with one year of treatment

Methodology: A facility based cross-sectional study on PLHAs was carried out in tertiary care centre of western Maharashtra with a sample size of 246. Data was collected by means of pretested semi structured questionnaire after taking Institutional clearance. Strict confidentiality was maintained throughout the study.

Results: The mean age of the study participants was 43.37 years with majority (50.9% rural, 39% Urban) were secondary class educated. Only 20% of urban and 8.5% of rural had income above 10,000 per month. Maximum (48.2 %) of rural were doing heavy works (construction/agricultural) while majority of urban were unemployed (30.5%) followed by business (21%) work. 36.9% (Rural) and 28.6 % (Urban) had spouse positive for HIV status. Even after one year of treatment, only 36.9% rural and 41% urban PLHAs were having CD4 count above 500. 49.6% (Rural) and 46.7% (Urban) were food insecure while 27.7% (Rural) and 14.3% (Urban) had low standard of living. 36.2% (Rural) and 30.5% (Urban) were undernutrition with 51.8% (Rural) and 54.3% (Urban) having abnormal waist circumference. BMI Category had statistically significant association with SLI and food insecurity in urban participants while it was not statistically associated with rural participants

Conclusions: In spite of freely delivered ART for one year and majority having good adherence rate, there were actionable changes in nutritional changes among PLHAs of both rural and urban areas. Neglected factors like food insecurity and standard of living needs to given special focus to affectively curb the high incidence of undernutrition among them. Immediate long term measures need to be taken to provide them adequate food and basic amenities of life with secure Job status.

Keywords: HIV, nutritional status, food insecurity, standard of living

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Introduction

HIV/AIDS is modern day epidemic with estimated total of 36.7 million people living with HIV/AIDS (PLHAs) globally¹ and 21.17 lakhs Nationally². With sustained international focus and recent scientific

advancement, measures are been taken to curtail the epidemic. In this view, Global strategy has been adopted to end the AIDS epidemic by 2030 with zero new HIV infections, HIV related deaths and discrimination and making people live longer healthier life³.

With the latest WHO and NACO policy of starting the Anti-Retroviral treatment (ART) at the diagnosis level, will go a long run in making PLHAs lead a happy comfortable life similar to any lifestyle disorders like diabetes and hypertension. However there are various other factors which would determine how well PLHAs lead their life and maintain their clinical stability. Important among them are socio-economic conditions and nutritional status which form the pillars for ART accessibility, adherence, action and disease stability per se.

Nutritional status depends on various factors such as food insecurity, standard of living, income status, awareness level, diet-drug interaction, loss of weight due to opportunistic infections and disease per se⁴.

Synergistic effect of malnutrition, food insecurity and poor standard of living pour significant changes and poor outcome in already compromised household conditions due to increased financial burden as well as emotional breakdown. With this even a minor amount of weight loss would result in significant morbidity and decreased survival rate among PLHAs⁵. It is also hypothesized that rural people maybe incurring higher impact due to these as compared to urban PLHAs due to lack of resources, income generation and facilities hinting the need for a study these differences. Undernutrition is thus one the significant factor for increased morbidity and mortality among PLHAs inspite of ART and highlight the importance of measures to be taken to improve nutrition including food security and standard of living in addition of free ART availability⁶.

In view of above, this study was carried out among the PLHAs who have been established with one year of treatment with the objective to assess the nutritional status, food insecurity and standard of living (SLI) with rural urban differences and their association if any

Methodology: A facility based cross-sectional study on people living with HIV/AIDS was carried out in tertiary care centre of western Maharashtra. Considering the prevalence of food insecurity, undernutrition and Standard of living (SLI) as per previous studies^{7,8,9}, the

sample size was calculated as 246. Adult PLHAs who came for collecting the medicines, after completion of one year of treatment and consented to be part of the study were included in the study based on systematic random selection. PLHAs with permanent residence were taken for the study while migratory PLHAs with opportunistic infections, HIV wasting syndrome and those who didn't consent for the study were excluded. Institutional clearance was obtained, Informed consent was taken from all study participants as per format and strict confidentiality was maintained throughout the study

Data Collection: Data was collected by means of pretested semi structured questionnaire which included basic demographic profile along with anthropometric measurements, clinical parameters, food insecurity scale¹⁰ and parameters assessing household status using standard of living scale¹¹. Urban/rural status, Standard of living, food insecurity and nutritional status were the main variables in the study. Data was entered in excel sheet and was analyzed using stata version 10 and rural urban differences among various variables was studied.

Standard of living (SLI) index was defined in terms of ownership of household goods (as per the NFHS-2 survey principals¹¹) by adding the nine components (Table 1). Out of total score of 9, household with 1-3 marks were labelled as low SLI, 4 to 6 scores as medium SLI and 7 to 9 scores were labelled as high SLI. All households were categorized into food secure and Food insecure by means of WHO Household food insecurity access scale (HFIAS) Measurement Tool¹⁰. Nutritional status was categorized into underweight, Normal and overweight based on WHO BMI (Body mass Index) classification for Asians

Results

The mean age of the study participants was 43.37 years with majority (50.9% rural, 39% Urban) were secondary class educated. 22.9% of urban and 8.5% of rural were college and above educated. 20% of urban and only 8.5% of rural had income above 10,000 per month. Maximum (48.2 %) of rural were doing heavy works (construction/agricultural) while majority of urban were unemployed (30.5%) followed by business (21%) work. 36.9% (Rural) and 28.6 % (Urban) had spouse positive for HIV status. 51.1% (rural) and 41% (urban) were female

Table 1 : Household Characteristics of study participants

	RURAL		URBAN	
	Frequency	Percent	Frequency	Percent
Accommodation				
Own	93	66.0%	66	62.9%
Rent	48	34.0%	39	37.1%
Fuel	Frequency	Percent	Frequency	Percent
Charcoal	5	3.5%	0	0.0%
Gas	134	95.0%	99	94.3%
Kerosene	1	0.7%	6	5.7%
Nil	1	0.7%	0	0.0%
House type	Frequency	Percent	Frequency	Percent
Kuchha	15	10.6%	7	6.7%
Pucca	107	75.9%	77	73.3%
Semi-Pucca	19	13.5%	21	20.0%
Latrine	Frequency	Percent	Frequency	Percent
Open	6	4.3%	3	2.9%
Own	91	64.5%	72	68.6%
Public	44	31.2%	30	28.6%
Light	Frequency	Percent	Frequency	Percent
Electricity	141	100.0%	105	100.0%
Persons per room	Frequency	Percent	Frequency	Percent
<=2 persons	18	12.8%	23	21.9%
3 – 5 persons	79	56.0%	57	54.3%
> 5 persons	44	31.2%	25	23.8%
Property (Land)	Frequency	Percent	Frequency	Percent
No	106	75.2%	72	68.6%
Yes	35	24.8%	33	31.4%
Source of drinking water	Frequency	Percent	Frequency	Percent
Pipe	102	72.3%	94	89.5%
Public	9	6.4%	8	7.6%
Pump	13	9.2%	3	2.9%
Tanker	1	0.7%	0	0.0%
Well	16	11.3%	0	0.0%
Water processing	Frequency	Percent	Frequency	Percent
Aquaguard	0	0.0%	1	1.0%
Boil	8	5.7%	4	3.8%
Filter	26	18.4%	17	16.2%
Nil	107	75.9%	83	79.0%
Total	141	100.0%	105	100.0%

Table 2 : ART and CD4 Characteristics of study participants

	RURAL		URBAN	
Adherence	Frequency	Percent	Frequency	Percent
< 90%	3	2.1%	4	3.8%
> 90%	138	97.9%	101	96.2%
Total	141	100.0%	105	100.0%
ART initiation	Frequency	Percent	Frequency	Percent
At the time of detection	126	89.4%	97	92.4%
< 2 years of detection	2	1.4%	1	1.0%
2- 5 years of detection	8	5.7%	3	2.9%
> 5 years of detection	5	3.5%	4	3.8%
Total	141	100.0%	105	100.0%
CD4 Counts	Frequency	Percent	Frequency	Percent
<=500	89	63.1%	62	59.0%
> 500	52	36.9%	43	41.0%
Total	141	100.0%	105	100.0%

Table 3 : Association of Nutritional status and standard of living of study participants

	SLI - RURAL					SLI - URBAN				
BMI Category	Low	Mid	High	Total	P-value	1	2	3	Total	P-value
Undernutrition Row % Col %	18 35.3 46.2	28 54.9 32.9	5 9.8 29.4	51 100.0 36.2	0.422	10 31.3 66.7	20 62.5 27.0	2 6.3 12.5	32 100.0 30.5	0.010
Normal Row % Col %	12 25.0 30.8	28 58.3 32.9	8 16.7 47.1	48 100.0 34.0		2 5.1 13.3	28 71.8 37.8	9 23.1 56.3	39 100.0 37.1	
Overweight/Obese Row % Col %	9 21.4 23.1	29 69.0 34.1	4 9.5 23.5	42 100.0 29.8		3 8.8 20.0	26 76.5 35.1	5 14.7 31.3	34 100.0 32.4	
TOTAL Row % Col %	39 27.7 100.0	85 60.3 100.0	17 12.1 100.0	141 100.0 100.0		15 14.3 100.0	74 70.5 100.0	16 15.2 100.0	105 100.0 100.0	

Table 4 : Association of Nutritional status and food insecurity of study participants

	FOOD INSECURITY - RURAL			FOOD INSECURITY - URBAN				
BMI Category	Insecure	Secure	Total	P-value	Insecure	Secure	Total	P-value
Undernutrition Row % Col %	21 41.2 30.0	30 58.8 42.3	51 100.0 36.2	0.0836	10 31.3 20.4	22 68.8 39.3	32 100.0 30.5	0.0026
Normal Row % Col %	30 62.5 42.9	18 37.5 25.4	48 100.0 34.0		15 38.5 30.6	24 61.5 42.9	39 100.0 37.1	
Overweight/Obese Row % Col %	19 45.2 27.1	23 54.8 32.4	42 100.0 29.8		24 70.6 49.0	10 29.4 17.9	34 100.0 32.4	
TOTAL Row % Col %	70 49.6 100.0	71 50.4 100.0	141 100.0 100.0		49 46.7 100.0	56 53.3 100.0	105 100.0 100.0	

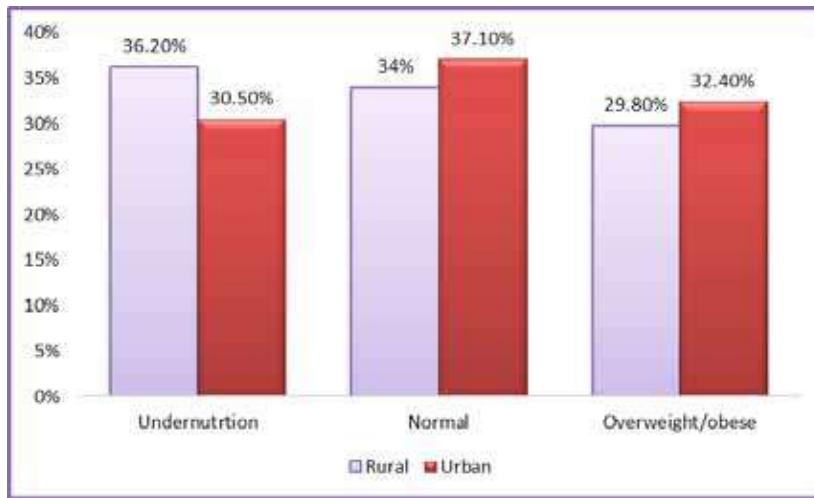


Fig 1 : Nutritional status of PLHAs of study participants



Fig 2: Food insecurity status of study participants

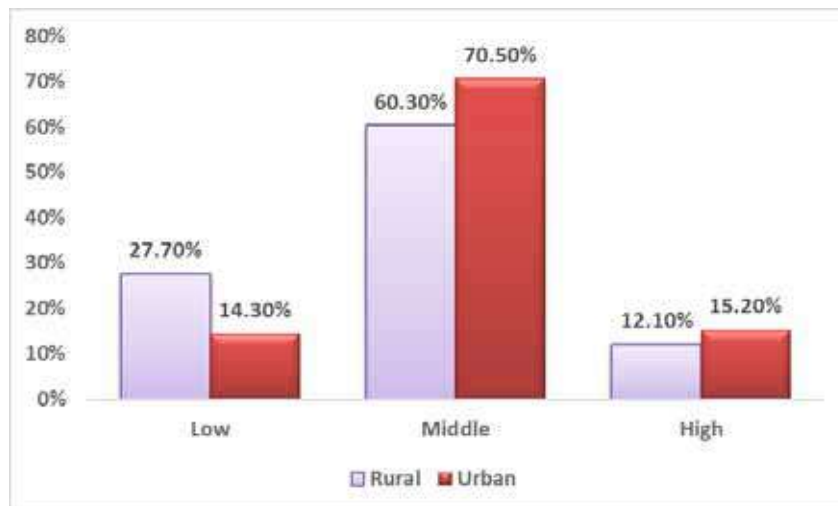


Fig 3: Standard of living status of study participants

ART adherence was above 90% (as per pill count) among 89.9% rural and 96.2% urban. Majority (92.4% urban, 89.4% rural) had started their ART at the time of detection. Even after one year of treatment, only 36.9% rural and 41% urban PLHAs were having CD4 count above 500. 49.6% (Rural) and 46.7% (Urban) were food insecure (Fig 2) while 27.7% (Rural) and 14.3% (Urban) had low standard of living (Fig 3). 36.2% (Rural) and 30.5% (Urban) were undernutrition with 51.8% (Rural) and 54.3% (Urban) having abnormal waist circumference. BMI Category had statistically significant association with SLI and food insecurity in urban participants while it was not statistically associated with rural participants

Discussion

Nutritional status has multidimensional effect on HIV disease progression. It hampers immune system, thereby increase the frequency, severity, duration and complications of infections, the symptoms of which lead to increase weight loss and thereby starts the vicious cycle. In our study, in rural areas, majority (36.2%) were undernutrition while in urban areas majority (37.1 %) had normal BMI followed by 32.4% obese/overweight and 30.5% being undernutrition. The higher number of undernutrition in rural areas may be due to most PLHAs in rural areas had income less than 5000 (77.3%) than urban areas (42.8%) and majority were doing Heavy (construction/agriculture) job getting less pay and more energy expenditure. To co-relate undernutrition, majority (63.1%) of rural had CD4 count less than 500, even after ART of one year.

In a study carried out in Iran by Hamzeh B et al¹², mean BMI of PLHAs men and women was 22.12 and 25.54 KG/m². Although the malnutrition was seen in 42.2 % but undernutrition was seen only in 11.08% and rest were obese/overweight. Majority of undernutrition was seen in men and married PLHAs and main reason was low consumption of diet as compared to standard recommendations. In the contrary, in our study, the under nutrition was quite high (36.2% Rural and 30.5% Urban) with low CD4 counts (less than 500) inspite majority of them had 90% ART adherence for one year,

While another study carried out by Anand D et al⁷ in India showed mean BMI of PLHAs was 19.73 KG/m² with 40 % under nutrition among PLHAs which was much higher as compared to our study among both rural and urban PLHAs and major reason was poor consumption of diet (both quantity and quality).

Food insecurity being an important marker for malnutrition even in PLHAs. In our study only 50.4% of rural and 53.3% of urban were food secure. The higher percentage of under nutrition in rural (36.2%) and urban (30.5%) areas in spite of one year of free ART probably hints at higher level of food insecurity (Urban – 49.6%, Urban-46.7%) among them. In our study, BMI had statistically significant association with food insecurity among Urban PLHAs only but not the rural ones

Dasgupta P et al¹³ in a study in Darjeeling, India showed that 50.9% of the PLHAs were food insecure. Higher education, higher standard of living and males has statistically significantly associated with high food security while poor morbidity status, more people with HIV positive status in family were associated with high food insecurity. PLHAs used to take loans, borrow money from family, friends and banks to cope up with financial hardship.

Gebremichael DY et al⁵ conducted a study in Central Ethiopia showed that 23.6% of PLHAs were malnutrition, 35.2% were food insecure. Important factors which led to malnutrition were no job, clinical morbidity, low CD4 counts and opportunistic infections and importantly the food insecurity similar to our study. Similar findings were also seen in a study carried out by Thapa R et al¹⁴ in Nepal where in one out of five PLHAs were undernourished and important contributing factors being low literacy, low CD4 counts, home care, clinical morbidity and opportunistic infections. The study also assessed the Quality of life domains among the PLHAs and found to be statistically significant association with Body mass Index.

Water sources, water processing technique, sanitary facilities, overcrowding and house type which determine the standard of living have an important influence on the health of

household members, especially PLHAs. In our study, only 12.1% rural and 15.2% urban were having high standard of living while majority (Rural – 60.3%, Urban -70.5%) were having middle SLI. As per NHFS 2 survey¹¹, Standard of living index was low in 24.1 % of Urban and 61.7% rural households with Bihar (57%) being highest in low SLI where as in our study on PLHAs households - 27.7% rural and 14.3% urban had low SLI which had influence on nutritional status. We couldn't find any other studies comparing the standard of living among rural and urban PLHAs

Conclusions

In spite of freely delivered ART for one year and majority having good adherence rate, there were actionable changes in nutritional changes among PLHAs of both rural and urban areas. With freely available ART, the neglected factors like food insecurity and standard of living needs to given special focus among both Urban and rural areas to affectively curb the high incidence of undernutrition among them. Immediate longterm measures need to be taken to provide them adequate food and basic amenities of life with secure Job status.

Conflict of Interest: Nil

Source of Funding: Self

Ethical Clearance: Taken

References

- (1). Global HIV & AIDS statistics - 2019 fact sheet. Available at <https://www.unaids.org/en/resources/fact-sheet>. Accessed on 15 Aug 2019
- (2). NACO report 2016-17. Available at <http://naco.gov.in/sites/default/files/NACO%20ANNUAL%20REPORT%202016-17.pdf>. Accessed on 15 Aug 2019
- (3). WHO. Global health sector strategy on HIV 2016–2021 towards ending AIDS. Available at <https://apps.who.int/iris/bitstream/handle/10665/246178/WHO-HIV-2016.05-eng.pdf;jsessionid=2F2E0E21C7530786BFF1C098725BA05E?sequence=1>. Accessed on 15 Aug 2019
- (4). Thuppall SV, Jun S, Cowan A, Bailey RL. The Nutritional Status of HIV-Infected US Adults. *Curr Dev Nutr*. 2017;1(10)
- (5). Gebremichael DY, Hadush KT, Kebede EM, Zegeye RT. Food Insecurity, Nutritional Status, and Factors Associated with Malnutrition among People Living with HIV/AIDS Attending Antiretroviral Therapy at Public Health Facilities in West Shewa Zone, Central Ethiopia. *BioMed Research International*. 2018.
- (6). Hiremath RN, Patil SS, Yadav AK. Nutritional status of people living with HIV/Acquired immunodeficiency syndrome - A cross-sectional study. *Asian Journal of Pharmaceutical and Clinical Research*. 2018; 11(7); 456-9,
- (7). Anand D, Puri S. Anthropometric and nutritional profile of people living with HIV and AIDS in India: an assessment. *Indian J Community Med* 2014;39:161-8
- (8). Osei-Yeboah J, Owiredu WKBA, Norgbe GK et al. Quality of Life of People Living with HIV/AIDS in the Ho Municipality, Ghana: A Cross-Sectional Study. *AIDS Research and Treatment*. 2017.
- (9). Tesfaye M, Kaestel P, Olsen MF et al. Food insecurity, mental health and quality of life among people living with HIV commencing antiretroviral treatment in Ethiopia: a cross-sectional study. *Health and Quality of Life Outcomes*. 2016; 14
- (10). Coates J, Swindale A, Bilinsky P. Household Food Insecurity Access Scale (HFIAS) for Measurement of Food Access: 2007. Available at http://www.fao.org/fileadmin/user_upload/eufao-fsi4dm/doc-training/hfiass.pdf. Accessed on 15 Aug 2019
- (11). National Family Health Survey (NFHS-3) 2005–06 INDIA. 2007. Available at http://rchiips.org/NFHS/NFHS-3%20Data/VOL-1/India_volume_I_corrected_17oct08.pdf. Accessed on 15 Aug 2019
- (12). Hamzeh B, Pasdar Y, Darbandi M, Majd SP, Reza Mohajeri SA. Malnutrition among patients suffering from HIV/AIDS in Kermanshah, Iran. *Ann Trop Med Public Health* 2017;10:1210-4
- (13). Dasgupta P, Bhattacharjee S, Das DK. Food Security in Households of People Living With Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome: A Cross-sectional Study in a Subdivision of Darjeeling District, West Bengal. *J Prev Med Public Health*. 2016;49(4):240–248.
- (14). Thapa R, Amatya A, Pahari DP, Bam K, Newman MS. Nutritional status and its association with quality of life among people living with HIV attending public anti-retroviral therapy sites of Kathmandu Valley, Nepal. *AIDS Research and Therapy*. 2015;12

Reading Skill of Deaf Students from Ludhiana Punjab

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Abstract

Context: Learning to read is a complex cognitive perspective, it's a child ability to decode, analyze and construct linguistic meaning from a the written print; reading include identification of alphabets, bond of spellings and assessing them in memory i.e. word reading, phonic awareness and knowledge of alphabets are the base of learning to read^[15]; Total 60 students were enrolled in the study, 30 deaf and 30 age-matched hearing, all the students were from age group of 8.5 to 11.5 years (50% male and 50% female in each group); extensive eye examination was performed prior to the study, all the participants were free from Ocular and systemic pathology. Two different tests were performed for reading skill; Reading comprehension was evaluated with ADR I Net Dynamic reader, and English reading tool was used, the tool was developed and used by Pratham-ASER Centre to evaluate reading speed; both the test showed statistically significant difference; (P-Value of <0.001) were deaf students had scored less marks in reading comprehension test and they were slow in reading speed also; deaf were taking more time to read in comparison of hearing students (P-Value of <0.001).

Keywords: Reading Speed, Reading Comprehension.

Introduction

Auditory impairment is the sensory deficiency which is commonly seen among human population, which is affecting a huge amount of population approximately 250 million people are suffering from auditory impairment in the world^[1]. In India, 63 million people that is (6.3%) suffering from significant hearing impairment ^[2]. Children who are born with deafness with bilateral hearing loss less than 70–89 dB are called severe loss and children who are >90 dB hearing losses are referred to as deaf ^[3]. The psychosocial difficulty is seen among hearing impaired children's which is ranging from 20 to 50 % which eventually reflected in

their behavior and social wellbeing^[4]. The consequences of the hearing impairment leads to the inability to understand the communicate which eventually delay in their language development, which can affect their educational achievement's, which eventually lead to social isolation and stigmatization^[5].

Effect of Deafness on Reading: Phonological awareness and knowledge of sound is building block for reading, educational and psychological research suggest and support this evidence; profoundly deaf students are visually depended while reading; visual senses play major role in formation of sentences for them^[16]. Deaf students do not have phonological awareness facility; they have limited or zero access to spoken language; which affect their reading skill ^[17]. Reading is always a challenge to deaf students; hearing students learn to read by using phonic sound; which is absent in deaf readers; deaf students can't describe the difficulties in reading ^[6]. Deaf students always perform lower than the hearing group in reading skill; although deaf readers are visually depended for understanding or learning to read; visual

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way of communication in deaf infants by their parents can be establishing the base of visual communication [7]. The Reading is one of the most complex behavior that is composed of many skills at a time, thus no single reading test assesses all aspects of reading completely. The Reading assessment should link directly to a widely accepted definition of reading, by Understanding the principles & relationships of assessment and instruction should enable teachers to select procedures that will assist in identifying and describing students' achievements and progress in reading [8].

Material and Methodology

60 students were enrolled in the study, 30 deaf students (congenital deaf; deafness equal or more than 90%) from, The Deaf Children School Humbera Road, Kitchlu Nagar, Ludhiana – 141001 and 30 Hearing students from Peace public school Ferozepur Road, V.P.O. Bhanohar, Ludhiana. (Both group had 50% Male and 50% Female participants); Informed consent was taken from all students, who participated in the study, including the consent explained to the hearing-impaired children by relevant instructors. Students participants in this study needed to satisfy the following criteria to be included in the study: Best corrected visual acuity of 6/6 and a near visual acuity N6, using the relevant Snellen acuity chart for distance and the standardized reading chart for near. Ocular abnormalities were ruled out using standard anterior and posterior eye examination. The Reading comprehension was evaluated with ADR I Net Dynamic reader. [9]. And English reading tool was used developed and used by Pratham-ASER Centre to evaluate reading speed; this reading tool is having five level Levels being: first is Beginner second is Letter; third is Word and fourth Paragraph and last one is fifth i.e. Story [10]. The students were divided in two groups; Deaf and age-matched hearing group; two different test type was used, first was ADR I Net Dynamic reader for reading comprehension and second one is English reading tool by Pratham-ASER Centre to evaluate reading speed (Hard copy). In dynamic reader student is seating 16 inches away from the screen and 12 font size prints is moving 60 word per minute speed in front of the screen, were student need to read that story and once the story is completed there are 10 questions were asked based on the story and student need to tick the correct answer; whereas in Reading speed tool 5 different levels are there; first level is graded as '0' if students is not identifying any alphabet; second level is few alphabet if student identify them correctly he/she moves to next

level where 3rd level where student need to read small spelling and in 4th level small paragraph and last 5th level story. For deaf students special educators help was taken were students were using ASL (American Sign Language) evaluation and documentation was done by special educator from the respective deaf school.

Result

Total 60 subjects were enrolled in the study, 30 Deaf and 30 hearing; the data was analyzed with the help of STATA 11.2 (College station TX USA) and Wilk test for normality. The reading comprehension by Test ADR I Net Dynamic Reader showed significant difference hearing group was better than the deaf group with mean difference of 8.28 and p-value of 0.001 (Deaf Mean \pm SD 0.36 \pm 1.06 and Hearing Mean \pm SD 8.64 \pm 1.06) deaf students had scored very less in reading comprehension in comparison of hearing students; deaf students were unable to answer most of the questions related to story. The reading speed test by Pratham-ASER Centre the reading speed was evaluated and (time was noted in seconds) compare with age matched hearing students, The Statistical analysis was performed by student T-Test and 2nd level (identification of alphabet) deaf group took more time than hearing group (Deaf Mean \pm SD 15.49 \pm 5.56 & Hearing mean \pm SD 10.40 \pm 1.22 ; P-Value of <0.001); for 3rd level (small spelling) (Deaf Mean \pm SD 27.99 \pm 8.26 & Hearing mean \pm SD 5.36 \pm 1.55 ; P-Value of <0.001) deaf were slower than hearing; for 4th level (small paragraph) (Deaf Mean \pm SD 51.75 \pm 12.20 & Hearing mean \pm SD 8.34 \pm 1.44 ; P-Value of <0.001) deaf took more time to read; and the last level (story) (Deaf Mean \pm SD 104.81 \pm 39.57 & Hearing mean \pm SD 19.17 \pm 2.84 ; P-Value of <0.001) deaf were taking more time to read than hearing; in all level deaf students were taking more time to read, as they were joining the alphabets and making all spellings, on the other hand the observation indicates that the deaf students do have letter identification knowledge although they take more time to read.

Discussion

Our result shows that deaf students do have reading comprehension problem and the reading speed is decreasing as the levels are getting complicated which is correlating with Reading comprehension research was done by Lisa M. Bickham were the respective author had found that deaf students do struggle in reading comprehension in comparison with hearings

students^[11]. Fiona and Kate had done research on deaf students reading skill; they have done comparison of deaf and hearing children's reading comprehension were the respective author had found deaf children's were weaker in reading skill when compared with the age matched hearing children's which eventually affect their achievement's^[12] our study do support the findings of Fiona and Kate. Rachel I. Mayberry had done research on cognitive development of deaf children; the respective author study indicates the deafness delay in the language, the cognitive development is directly propositional to language which in general leads to cognitive changes^[3]Cognitive Development in Deaf Children by Dr. Sharmista in 2013, the respective author had taken 28 deaf and 31 hearing students; Raven's colour metrics and cognitive development status test was used; Visual perception did not show much difference; 4% difference between hearing and deaf group but there is a significant difference in achievement and as deafness in increasing reading ability decreases^[13].Hearing subjects read by converting print material into phonological code that impact their auditory language system; but deaf subject use visual information for reading according to Duncan in 1984; whereas author has taken 43 subjects (age between 18-40 years); on computer screen various stimulus is shown to all subjects^[14].Academic activity especially reading has been affected in hearing impaired subjects ; deaf students normally show below average in reading skill and vocabulary when they are compare with age matched hearing subjects the research done by Fagan et al in 2007 ^[18]. Learning how to read is one of the critical developmental task which is based on developmental social and vocational development; which is a challenge for deaf subjects according to Musselman in 2000 ^[19].

Conclusion

Our goal of the study is to find out the reading skill of deaf children's of deaf school and compare with age matched hearing students hence Our study like to conclude that reading comprehension difficulties are seen in deaf students when they are compare with age matched hearing students and deaf students had shown lower reading speed as compared with age matched hearing students in all level from identification to reading story; although deaf students were slow in identification but none of the deaf student have not made any mistake in identification that indicate there is an awareness of letter and they could read by joining the alphabet's and making spelling; but very few understood the meaning of story

whereas they have scored less in reading comprehension also; we like to conclude with our study that yes deaf students do have reading problem but at the same time they have awareness of letter also which is statistically significant low in comparison of hearing students; this study can be useful for all special educators teaching deaf students to enhance their teaching strategies taking in evidence that deaf students do have awareness of letter and they do read by joining the alphabet's.

Ethical Clearance: The evaluation was noninvasive hence the clearance was not required. (applied in Chitkara university for ethical clearance in case it is necessary)

Source of Funding: Self

Conflict of Interest: No

Reference

- [1] Colin D. Mathers, Claudia Stein, Doris Ma Fat, Chalapati Rao, Mie Inoue, NielsTomijima, Christina Bernard Alan D Lopez, Christopher J.L. Murray Global burden of hearing loss in the year 2000. *Global Burden of Disease*. 2000; (4):1–30.
- [2] SuneelaGarg, Shelly Chanda, Sumit Malhotra, A.K.Agarwal. Deafness: Burden, prevention and control in India. *The National Medical Journal of India*. 2009; 22(2):79-81.
- [3] Rachel I. Mayberry. Cognitive development in deaf children : The interface of language and perception in neuropsychology. *Hand book of Neuropsychology*. 2002; 2(8): 71-107.
- [4] JesperDammeyer. Psychosocial Development in a Danish Population of Children with Cochlear Implants and Deaf and. *Journal of Deaf Studies and Deaf Education*, 2009; 15(1):50–58. <http://doi.org/10.1093/deafed/enp024>
- [5] Vishwambhar Singh. Hearing in India: All aspects. *Otolaryngology Online Journal*, 2015; 5(1).
- [6] Dr Rosalind Herman, Professor Penny Roy, Dr Fiona Kyle. *Reading and Dyslexia in Deaf Children*, City University of London, Nuffield Foundation, 2017
- [7] Gerrit Loots and Isabel Devise' Wolfgang Jacquet. The Impact of Visual Communication on the Intersubjective Development of Early Parent–Child Interaction with 18- to 24-Month-Old Deaf Toddlers. *Journal of Deaf Studies and Deaf Education* 2005; 10(4)358-374.
- [8] McAnally, P., Rose, S., & Quigley S. Reading

- practices with Deaf Learners, 2nd ed. Austin, TX: PRO-ED. Educational Psychology ,Research output: Book/Report 2007.
- [9] LTC Jose' E. Capo'-Aponte, MS USA; LTC Thomas G. Urosevich, MS USAR; Leonard A. Temme, PhD; Aaron K. Tarbett, OD; Navjit K. Sanghera, OD. Visual Dysfunctions and Symptoms During the Subacute Stage of Blast-Induced Mild Traumatic Brain Injury. *Military Medicine*. 2012; 177(7):804-812.
- [10] Rukmini Banerji and MadhavChavan, Improving literacy and math instruction at scale in India's primary schools: The case of Pratham's Read India program, *Journal of Educational Change*. 2016; 17(4) 453-475.
- [11] Lisa M. Bickham, Reading Comprehension in Deaf Education: Comprehension Strategies to Support Students Who are Deaf or Hard of Hearing, *Education Masters*. 2015;314.
- [12] Fiona E. Kyle and Kate Cain, A Comparison of Deaf and Hearing Children's Reading Comprehension Profiles, *TOPICS IN LANGUAGE DISORDERS/ APRIL-JUNE 2015*;35(2):144-156.
- [13] Sharmista. Cognitive Development in Deaf Children. *International Journal of Education and Psychological Research*. 2013; 2(2): 92-94.
- [14] John Duncan. Selective Attention and the Organization of Visual Information. *Journal of Experimental Psychology: General* .1984;113(4): 501-517.
- [15] Linnea C. Ehri Learning to Read Words: Theory, Findings, and Issues, *Scientific Studies of Reading Volume 9*, 2005 167-188.
- [16] Margaret Harris and Constanza Moreno. Speech Reading and Learning to Read: A Comparison of 8-Year-Old Profoundly Deaf Children With Good and Poor Reading Ability; *journal of Deaf Studies and Deaf Education*. 2006;11(2):190-200.
- [17] Perfetti, C. A., & Sandak, R. Reading optimally builds on spoken language: Implications for deaf readers. *Journal of Deaf Studies and Deaf Education*, 2000; 5:32-50.
- [18] Mary K. Fagan, David B. Pisoni, David L. Horn, Caitlin M. Dillon. Neuropsychological Correlates of Vocabulary, Reading, and Working Memory in Deaf Children with Cochlear Implants. *Journal of Deaf Studies and Deaf Education*. 2007;12(4):461-471.
- [19] Carol Musselman. How Do Children Who Can't Hear Learn to Read an Alphabetic Script ? A Review of the Literature on Reading and Deafness. *Journal of Deaf Studies and Deaf Education*.2000;5(1):9-31.

A Twin Inside a Twin/Fetus-in-Fetu-Review Article

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Abstract

Context: The case was described in a British medical journal in 1808 and is thought to occur in about one in every 500,000 births¹. In recent years, similar births have occurred in India, Indonesia and in Singapore³. It is the process in which baby carries a twin inside them is called fetus in fetu. This is a rare condition characterized by abnormal embryogenesis in a diamniotic, monochorionic pregnancy⁴. Covering is made up of a fibrous membrane that contains some fluids (equivalent to the amniotic fluid) and a fetus attached by a cord or pedicle. In the uterus, the growth of an FIF initially similar to its twin, but stops suddenly because of either the vascular dominance of the host twin or any defect in the parasitic twin [2]. Parasitic twin mostly seen anencephalic, but in almost all cases its vertebral column and limbs are present (91% and 82.5%, respectively).

Keywords: *Twin; Fetus in fetu; Abdomen masses; Embryogenesis; diamniotic; Monochorionic; Fibrous membrane; pedicle.*

Introduction

The condition is defined as a monozygotic twin gets assimilated into the abdomen of its sibling during developmental phase. Often Feuts in fetu is seen with differential diagnosis of any abdominal mass⁷. Unlike teratomas, it is a benign disorder. It is commonly present in the retroperitoneum(80%) but cases have been also reported in other sites in body like cranial cavity(8%), oral cavity, neck, mediastinum, back, sacrococcygeal region(8%) and scrotum⁸. In most of the cases, single parasitic fetus is present however number can range from 2 to 5.

Path Physiology: According to parasitic twin theory Fetus inside fetu is a parasitic fetus developing within its host twin. It is observed that very early in a monozygotic

twin pregnancy both fetuses share a common placenta, one fetus wraps around and envelops the other. The enveloped twin develops as a parasite, in which its survival depends on the survival of the host twin. The parasitic twin is anencephalic and without some organs is not able to survive on its own. As the host twin has to provide nourishment to the enveloped twin from the nutrients received over a single umbilical cord resulting in death before birth.

Case Presentation: March 20, 2019

A Colombian woman has given birth to a baby whose abdomen contained the tiny, half-formed — but still growing — body of her own twin sister³.

This type of birth, an example of “fetus-in-fetu,” is very rare but not unprecedented³.

The latest case was even more unusual, because doctors clearly identified the fetus-in-fetu during the pregnancy, said Dr. Miguel Parra-Saavedra, a high-risk pregnancy specialist in Baranquilla, Colombia, who oversaw the birth³.

He first saw the mother, Monica Vega, when she was in her 35th week of pregnancy, five weeks short of

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a full-term birth. Her obstetrician believed her fetus had a liver cyst.

But, using color Doppler and 3D/4D ultrasound imaging, Dr. Parra-Saavedra was able to see that the fluid-filled space actually contained a minuscule infant, supported by a separate umbilical cord drawing blood where it connected to the larger twin's intestine³.

"I told the mother, and she said, 'What? No, doctor, this is impossible,'" Dr. Parra-Saavedra said. "But I explained step by step, and she understood³."

He alerted a local television news network, which followed Mrs. Vega, who is now 33, through the birth of her daughter, Itzamara, and the surgery to remove Itzamara's partially formed twin.

(Dr. Parra-Saavedra had developed relationships with several journalists during Colombia's Zika outbreak in 2016, because he treated mothers whose babies had microcephaly, or small heads, caused by the virus³.)

On Feb. 22, when Itzamara was at 37 weeks and weighed about seven pounds, doctors decided to deliver her by cesarean section, because they feared the internal twin would crush her abdominal organs.

The next day, they removed the fetal twin by laparoscopic surgery. It was about two inches long and had a rudimentary head and limbs, but lacked a brain and heart, Dr. Parra-Saavedra said³.

fetus-in-fetu is sometimes misdiagnosed as a teratoma, a tumor that may contain bones, muscle tissue and hair. A DNA comparison is being done, but Dr. Parra-Saavedra has no doubt that the fetuses started out as identical twins from the same ovum.

Because the smaller fetus took nourishment from its sibling, it is called a heteropagus or parasitic twin³.

Some heteropagus twins are born conjoined to their healthy siblings, while some grow partially inside and partially outside their twin's body.

The fetus-in-fetu condition is believed to arise soon after the 17th day of gestation, when the embryo flattens out like a disc and then folds in on itself to form the elongated fetus³.

Doctors believe that in exceedingly rare cases, the twin embryos only partially divide, and the larger one

wraps around the smaller.

The condition may go undetected for many years. In 2015, a 45-year-old Englishwoman living in Cyprus underwent surgery for what appeared to be a four-inch tumor on her ovary³.

On dissection, the growth turned out to have a partially formed face with an eye, a tooth and black hair. Doctors concluded that it was a twin she had absorbed while in her mother's womb.

Itzamara is doing well, Dr. Parra-Saavedra said. "She has a little scar on her abdomen, but she is a normal baby now except that the whole world is talking about her³."

Case Presentation: 2. A 15-year-old boy presented to hospital with history of abdominal swelling since birth which progressively enlarged recently. He also complains of abdominal pain and was unable to tolerate orally for 1 week prior to admission. On examination, there was tender, hard mass over central part of abdomen⁹.

Investigations: CT abdomen and pelvis revealed a big intra-abdominal mass 14×18.5×23.8 cm that extends up to the sub hepatic region with inferior extension into anterior pelvis. Components in favour of a fetus that were observed within the mass include deformed skull, vertebral body and long bones. CT angiography was done to find out the feeding vessels involved. CT angiography shows multiple small arteries supplying the wall of the mass. No tumour markers were seen preoperatively⁹.

Differential Diagnosis: The differential diagnosis of this condition can be organised teratoma⁷.

Treatment: Laparotomy was done through a midline laparotomy incision with detection of a 15×10 cm intraperitoneal mass with multiple big feeding vessels attached to small bowel mesentery. The mass was perforated over pelvic region with 1000 cc pus aspirated. A gestational sac weighing 2.5 kg was taken out, and when opened, a 1.6 kg non-viable baby seen with shortened and malformed upper and lower limbs, hypoplastic trunk, long hair, developed male genitalia with pubic hair, imperforated anus, fused malformed eyes, vertebra and normal baby skin covered with vernixcaecosa. There was no mouth, umbilical cord or placenta attached to it⁹.

Outcome and Follow-up: Postoperatively, the

baby was handed over to the family for ritual funeral as requested by family. Histopathological examination (HPE) of the sac enveloping the fetus observed a fibrous cyst wall with focal area lining of mature squamous epithelium with many hair shafts and some muscle in subepithelialstroma. The postoperative period of the patient was uneventful. Alpha-feto protein (AFP) taken 3 months postoperation was normal and the patient has no active complaints during subsequent follow ups⁹.

Conclusion

Fetus in fetu is very rare condition. Before any operation is carried out on a patient, imaging studies should be conducted to differentiate this condition from teratoma. Surgical excision is a curative procedure, and a macroscopic examination of the sac should be done after twin or multiple fetus in fetu are removed. The literature cites less than 200 cases worldwide of twin fetus in fetu.

Source of Funding: Self

Conflict of Interest: Nil

References

1. Grant P, Pearn JH (May 1969). "Foetus-in-foetu". *Med. J. Aust.* 1 (20): 1016–9. PMID 5815070. Hoeffel CC, Nguyen KQ, Phan HT, et al. (June 2000). "Fetus in fetu: a case report and literature review". *Pediatrics.* 105 (6): 1335–44. doi:10.1542/peds.105.6.1335. PMID 10835078.
2. "Journal of Medical Case Reports | Full text | Fetus in fetu : a case report". *Jmedicalcasereports.com*. Retrieved 2012-11-22.
3. Donald G. McNeil Jr. March 21, 2019, on Page A10 of the New York edition with the headline: Remarkable Birth: A Twin Inside a Twin. <https://www.nytimes.com/2019/03/20/health/twins-fetus-colombia.html>
4. Patankar T, Fatterpekar GM, Prasad S, Maniyar A, Mukherji SK: Fetus in fetu: CT appearance--report of two cases. *Radiology.* 2000, 214: 735-737. View ArticlePubMedGoogle Scholar
5. Magnus KG, Millar AJ, Sinclair-Smith CC, Rode H: Intrahepatic fetus-in-fetu: a case report and review of the literature. *J Pediatr Surg.* 1999, 34: 1861-1864. 10.1016/S0022-3468(99)90333-0. View ArticlePubMedGoogle Scholar
6. Senyüz OF, Rizalar R, Celayir S, Oz F: Fetus in fetu or giant epignathus protruding from the mouth. *J Pediatr Surg.* 1992, 27: 1493-1495. 10.1016/0022-3468(92)90480-U. View ArticlePubMedGoogle Scholar
7. Abdurraheem NT, Nasir AA, Abdur-Rahman LO et.al Fetus in fetu-diagnostic criteria and differential diagnosis-a case report and literature review. *J PediatrSurg* 2004;39:616–8.doi:10.1016/j.jpedsurg.2003.12.029PubMedGoogle Scholar
8. Nurudeen Toyin Abdurraheem AbdulasheedA. NasirLukmanO .Abdur-RahmanOluwaseunR. AkanbiMosesO. OlanrewajuMuslimatA. Alada et al.Oralfetus-in-fetu: a case report. *J PediatrSurg Case Rep* 2015; 3:171–.doi:10.1016/j.epsc.2015.02.007
9. SuhasAithalSitharama, BibekanandJindal, Mrudula Kumari Vuriti, Bikash Kumar Naredi, Sriram Krishnamurthy , Deepak Barathi SubramaniaPol *J Radiol.* 2017; 82: 46–49. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5295181/>

Effect of Jacobson's Progressive Relaxation Technique Over Sleep Disturbances and Quality of Life in Chronic Rheumatoid Arthritis

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Abstract

Background: Rheumatoid arthritis is a chronic inflammatory disease of the immune system affecting the synovial tissue of the joint, tendon sheath and bursae. The symptoms are joint pain, stiffness, joint swelling, deformity, functional disability and sleep disturbance. Rheumatoid arthritis is three times more frequent in women than men. There are various study done on Rheumatoid arthritis on their pain management and reducing deformity but there is lack of study on their sleep disturbance and quality of life.

Objective: To find out the effect of Jacobson's progressive relaxation technique on sleep disturbance and quality of life in chronic Rheumatoid Arthritis.

Methodology: Experimental study with a convenient sampling of 30 Rheumatoid arthritis subjects with age group of 20-70 years received Jacobson's progressive relaxation technique 1 session per day for 10 days.

Outcome Measures: Sleep disturbance was evaluated using Pittsburgh sleep quality index (PSQI) and quality of life was evaluated by using Short form health survey-36(SF-36)

Results: Statistical analysis was done by SPSS software version 22, which showed significant improvement in both sleep disturbance and quality of life in chronic Rheumatoid Arthritis.

Conclusion: Thus, Jacobson's progressive relaxation technique has shown significant result in improving sleep disturbance and quality of life in chronic Rheumatoid Arthritis.

Keywords: *Jacobson's progressive relaxation technique, Rheumatoid Arthritis, sleep disturbances, Quality of life.*

Introduction

Rheumatoid arthritis (R.A) is a chronic inflammatory disease of the immune system (Autoimmune disease) which affects the synovial tissue of the joint, tendon sheath and bursae. Its symptoms ranges from joint pain, stiffness, joint swelling, deformity in multiple regions especially in hands and feet, functional disability, erosive synovitis and sleep disturbances.^{1,2}

Rheumatoid arthritis has been one of the most crippling disease affecting mankind because of its numerous manifestations and involvement of multiple joints. Rheumatoid arthritis affects the joints symmetrically, but it is a systemic disease in which anaemia, fatigability, weight loss and fever are prominent feature.

Its three times more frequent in women than men (3:1) and it affects between 0.1 and 0.5% of adults in developed countries.³ The age of onset may be as young as 16 years. The major symptoms of Rheumatoid arthritis also include fatigue and poor sleep quality affecting more than 50-70% of the patients. Poor sleep in Rheumatoid

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Arthritis is contributed to increased pain and fatigue and also associated with depression.⁴

Sleep is naturally recurring state of mind characterized by a temporary loss of consciousness, reduced interaction with surroundings, and a state of inactivity and it can be reversed by an external stimulus. Sleep is important for the functioning of human body and many biological process which are important for the human body which can be impaired without sleep.⁵ Sleep disturbance is the deviation from normal sleep pattern and which may include poor sleep quality, non-restorative sleep, difficulty in falling asleep, early morning awakening, numerous nightly awakenings, fatigue and daytime sleepiness.⁶

As this disease progresses, patient's functional impairment increases which often leads to work disability and it also increases the burden on patient's families, care-givers and society. The daily activity of the patient's also decreases due to pain and fatigue.⁷ The quality of life in Rheumatoid Arthritis is reduced in several ways, such as their physical health, level of independence, environment and personal beliefs.⁸ The quality of life of the patient reduces due to functional impairment in which the patient cannot perform his daily life activity due to pain and fatigue which is most common symptom of rheumatoid arthritis.⁹ The Health related quality of life in Rheumatoid arthritis is reduced and its associated with increased levels of pain, reduced physical activity and disease activity.^{10,11}

Evidences from other studies of chronic disease suggests that number of other factors to have an impact, including gender, body mass index (BMI), age and disease severity.^{12,13,14}

Relaxation is one of the best method to reduce musculoskeletal pain and the symptoms of stress.¹⁵ Jacobson's relaxation technique is also known as progressive relaxation technique. Jacobson's progressive relaxation technique involves contracting and relaxing the muscle. His techniques relax the entire body by releasing muscular tension that accumulates when a person experiences a stressful situation. this technique not only cures taut muscles and cramps, but also reduces the intensity of pain and relieves stress and anxiety.¹⁶

Jacobson demonstrated the deep relationship between muscle, thoughts and emotions which affected the level of muscular tension. This method is based on concentration of attention in a muscular group by paying

attention to the sensation it produces. This technique requires about 15-20 minutes to complete the relaxation technique. It is performed in a dim light room and shouldn't be disturbed by other people and it is done on a floor, on bed or in a chair.

Method

Study Design and Sample: This is an experimental type of study done for 10 days in SRM Medical College Hospital and Research Centre, kattankulathur, Kanchipuram, India. About 30 samples with chronic Rheumatoid arthritis were selected and explained about the procedure and informed consent were obtained and explained them that the information obtained will be kept confidential.

Chronic Rheumatoid arthritis samples between 20-70 years both male and female were included in the study. Samples been treated with hypnotic and anti-depression drugs were excluded from the study.

The samples were evaluated using Pittsburgh Sleep Quality Index (PSQI) and Short Form Health Survey-36 (SF-36) for their sleep quality and Quality of life respectively.

Procedure: A sample size of 30 subjects with age group of 20-70 years, both male and female subjects with a referral from rheumatologist was taken for the study. The subjects with chronic Rheumatoid Arthritis (more than 2 years) were randomly selected for the study.

Jacobson's progressive relaxation technique was clearly explained and taught to the subjects and a trial session was demonstrated to the subjects. The subjects should make them comfortable on the floor, on the bed or in a chair. The subjects were asked to perform this technique in their home in a dim light room, if possible and shouldn't be disturbed by anyone and subjects should switch off their mobile phones. The subjects were asked to perform this technique for 10 days, one session per day and progression is made by repeating about twice per day. The subjects were regularly monitored by telephone.

After 10 sessions of Jacobson's progressive relaxation technique, the post-test was taken immediately. The completed questionnaire was returned, and scoring was done to evaluate the sleep disturbances and quality of life. The scored data was then given for statistical analysis to evaluating the sleep disturbance and quality of life.

Pittsburgh Sleep Quality Index: The Pittsburgh Sleep Quality Index (PSQI) contains 19 self-rated questions and 5 questions rated by the bed partner or roommate (if one is available). Only self-rated questions are included in the scoring. The 19 self-rated questions items are combined to form seven “component” scores, of which has a range of 0-3 points. “0” indicated no difficulty and “3” indicated severe difficulty. The seven components are then added to yield one “global” score, with a range of 0-21 points. “0” indicates no difficulty and “21” indicated severe difficulty in all areas.

Short Form (36) Health Survey: The Short Form (36) Health Survey is a 36-item, patient-reported survey of patient health. It consists of eight scaled scores, which are the weighted sums of the questions in their section. Each question has a score of 0-100, in which zero is equivalent to “maximum disability” and 100 is equivalent to “no disability”. It was reported as easy to understand and acceptable for the respondents from the subjects.

Results

Table 1 shows that the mean value of Pittsburgh Sleep Quality Index (PSQI) score in pre-test is 15.57 and post-test is 9.67, which shows there was a significant improvement in sleep quality among Rheumatoid Arthritis patients treated with Jacobson’s progressive relaxation technique for a period of 10 days.

Table 2 shows the mean value of Short Form-36 health survey (SF-36) score, pre-test is 25.18 and post-test is 51.05 which shows there was a significant increase in Short Form-36 health survey (SF-36) score which indicates a improvement in quality of life among Rheumatoid Arthritis subjects treated with Jacobson’s progressive relaxation technique for a period of 10 days.

Table:1. Pre-Test and Post-Test Mean Values of Pittsburgh Sleep Quality Index (Psqi) Among Rheumatoid Arthritis Patients Treated With Jacobson Relaxation Technique For A Period Of 10 Days (N=30).

Pittsburgh Sleep Quality Index	Mean	N	SD	T-Value	P-Value
Pre-test	15.57	30	0.81	26.63	0.00*
Post-test	9.67	30	0.21		

P value <0.05

According to Table 1, the pre-test mean value of Pittsburgh Sleep Quality Index (PSQI) score is 15.57 and the post-test mean value is 9.67, which shows significant changes in quality of sleep as measured by Pittsburgh Sleep Quality Index (PSQI) score with a P value of 0.00.

Table:2. Pre-Test and Post-Test Mean Values of Short Form-36 Health Survey (Sf-36) Among Rheumatoid Arthritis Patients Treated With Jacobson Relaxation Technique For A Period Of 10 Days (N=30).

Short form-36 Health Survey	Mean	N	SD	T-Value	P-Value
Pre-test	25.18	30	3.19	-21.71	0.00
Post-test	51.05	30	5.79		

P value <0.05

According to Table 2, the pre-test mean value of Short Form-36 Health Survey (SF-36) score is 25.189 and the post-test mean value is 51.059, which shows significant quality of life, with a P value of 0.00.

Discussion

This study determines the effect of Jacobson’s Progressive Relaxation Technique in subjects with chronic Rheumatoid Arthritis.

Rheumatoid Arthritis said to be one of the crippling disease and sleep problem and pain were associated with poor quality of life in Rheumatoid Arthritis patient as stated by **M Purabdollah et al, 2015**.¹⁸

The subjects who fell into the age group of 20-70 years, both genders and who were diagnosed from Rheumatoid Arthritis were selected and the study was analysed on 34 subjects. Four subjects were dropped out from the study due to personal and communication problem. These 30 subjects were treated with Jacobson’s progressive relaxation technique for 10 days.

The results of this study shows that there was a significant improvement in quality of sleep post the management of Jacobson relaxation technique for a period of 10 days(p<0.05). This results goes in hand with

Neriman Temel Aksu et al; (2017) concluded that progressive muscle relaxation prevents a decline in patient-reported sleep quality following pulmonary resection.

Yunping Li et al;(2015) suggested that progressive muscle relaxation practice is effective in improving

anxiety, depression, and the mental health components of Quality of life in patients with pulmonary arterial hypertension.

This can be better explained by the fact that relaxation training brings the body system back into balance by deepening breathing, reducing stress hormones, slowing down heart rate and blood pressure, and relaxing the muscles. In addition to its calming physical effects, research has shown that the relaxation response also increases energy and focus, combats illness, relieves aches and pains, heightens problem-solving abilities, and boosts motivation and productivity.

It is argued that anxiety, worry and depression plays an important role in emergence and development of sleep disturbance in chronic Rheumatoid Arthritis patients. As said above Progressive muscle Relaxation can relieve stress and anxiety thus also improve the Quality of sleep of these patients.

ElhamAmini et al;(2016) concluded that Progressive muscle relaxation program causes a significant improvement of sleep Quality than Aerobic exercises.

C Austad et al;(2016) concluded that sleep disturbance is related to pain, fatigue and disease activity in Rheumatoid Arthritis patients.

So Jacobson may benefit the patients to have a better quality of sleep which indirectly will influence their quality of life which has been proved by the results of this study which states that there was a improvement in short form-36 health survey (SF-36) after training chronic rheumatoid arthritis patients for a period of 10 days($p < 0.05$).

This result goes in hand with **Yildirim et al** who demonstrated that progressive muscle relaxation program caused a significant improvement of Quality Of Life and relieved anxiety among Chronic Renal Failure patients.

Mishra et al (2012) concluded that exercises were more effective in reducing depression and sleep disorders and improve physical functions in cancer patients.

Thus, by all its benefits, this study recommends the use of progressive muscle relaxation technique give patients a comfort and improves the quality of sleep thereby enhances their Quality of Life. Furthermore, the Quality of sleep assessment can be widely practiced

in Chronic Rheumatoid arthritis patients as it has a high influence over Quality of Life of such patient, the improvement of which is the ultimate aim of physiotherapy. Many therapists treat only the pain of the Rheumatoid Arthritis patients and were mostly negligent to the ill effects of sleep disturbances that are quite common among such patients. The sleep disturbance may again have a negative effect on their disease and the physiotherapy management also. So, we physiotherapist should give importance to the sleep disturbances and encourage and build confidence in these patients to practice the relaxation techniques regularly at home.

Conclusion

This study concludes that there was a improvement in sleep and Quality Of Life among chronic Rheumatoid Arthritis subjects after application of Jacobson's progressive relaxation technique for 10 days. This study further recommends that the sleep disturbances assessment and management with Jacobson relaxation technique should be given its importance in Physiotherapy management of Chronic Rheumatoid Arthritis patients.

Ethical Clearance: Obtained from Institutional Ethical committee, SRMIST.

Source of Funding: self

Conflict Of Interest: Nil

References

1. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO 3rd, et al. 2010 rheumatoid arthritis classification criteria: an American college of Rheumatology/European League Against Rheumatism Collaborative initiative. *Ann Rheum Dis* 2010;69:1580-8
2. Luyster FS, Chasens ER, Wasko MCM, Dunbar-Jacob J. Sleep quality and functional disability in patient with rheumatoid arthritis. *J Clin sleep Med* 2011;7:49-55.
3. Mitchell DM. Epidemiology Rheumatoid arthritis, etiology, diagnosis, and treatment. In: utzinger P, Zvalifer N, Geds e editors JB Lippincott Co; 1985
4. Hyphantis TN, Bai M, Siafaka V, Georgiadis AN, et al, psychological distress and personality traits in early rheumatoid arthritis, 2005;23:783-8.
5. M. L. E. Anderson, B. Svensson, and S. Bergman, "chronic widespread pain in patient with rheumatoid arthritis and the relationship between

- pain and disease activity measures over the first 5 years, “ *Journal of Rheumatology*, vol. 40, 12, pp. 1977-1985, 2013.
6. A. M. Ellitt, B. H. Smith, K. I. Penny, W.C. Smith, and W.A. Chambers, “ the epidemiology of chronic pain in the community” *The Lancet*, vol. 354, no.9186, pp. 1248-1252, 1999.
 7. Lambert CM, Hurst NP. Health economics as an aspect of health outcome: basic principle and application in rheumatoid arthritis 1995;34:774-80.
 8. Linde L, Sorensen J, Ostergaard M, Horslev-petersen K, validity reliability of sf-36 in patient with Rheumatoid arthritis. *J rheumatol*2008;35:1528-37.
 9. Kwan Y, Koh E, Leong K, Wee H. association between helplessness, disability, and disease activity with health related quality of life in rheumatoid arthritis patient. *RheumatolInt* 2004.
 10. Hodkinson B, Musenge E, Ally M, Meyer PWA, Anderson R, Tikly M, functional disability and health related quality of life in South Africans with early rheumatoid arthritis. *Scand J rheumatol*2012;41:366-74.
 11. Kwan Y, Koh E, Leong K, Wee H association between helplessness, disability, and disease activity with health-related quality of life among rheumatoid arthritis patient in a multi-ethnic Asian population. *RheumatolInt* 2014. [http://dx. doi. org/10.1007/s00296-013-2938-2](http://dx.doi.org/10.1007/s00296-013-2938-2).
 12. Volz A, Schmid J, Zwahlem M, Kohls S, Saner H, Barth J, Predictors of read-mission and health related quality of life in patient with chronic heart failure: a comparison of different psychological aspects. *J Behav Med* 2011;34:13-22
 13. Faller H, Stork S, Schuler M, Schowalter M, Steinbuchel T, Ertl G, et al. Depression and disease severity as predictors of health related quality of life in patient with chronic heart failure- a structural equation modelling approach. *J card fail* 2009;30:469-76.
 14. Afendy A, Kallman JB, Stepanova M, Younoszai Z, Aquino RD, Bianchi G, et al, predictors of health related quality of life in patient with chronic liver disease. *Aliment Pharmacol Ther*2009;30:469-76.
 15. Delloiagono de paula, A, Compos de Carvalho,. The use of progressive muscle relaxation mtechnique for pain relief in gynaecologu and obstetrics 654-659
 16. fee, R.A.Girdano .d,(1978). The relative effectiveness of three tewch I ques to imducetrophotrophic response 147-157
 17. mogra A L singh G.(1986) Effect of Jacobson relaxation technique on blood pressure level of hypertensive. 68-75
 18. M Purabdollah, rheumatoid arthritis sleep and quality of life. 2015.

Comparison of Therapeutic Ultrasound and Low Level Laser Therapy Over Pain and Scar Health in Post Episiotomy

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Abstract

Background: Episiotomy is a surgical procedure made in the perineum of the gravida in the late second stage of labour in order to facilitate delivery of the fetus. Various studies have been done on episiotomy to relieve pain but there is a lack of study on scar health in episiotomy.

Objective: To find out the effectiveness of therapeutic ultrasound and low level laser therapy over pain and scar health in post episiotomy.

Method: Quasi-Experimental study 10 subjects with age group of 25 to 30 years into two groups (GROUP A & GROUP B). GROUP A (5 subjects) treated with therapeutic ultrasound. GROUP B (5 subjects) treated with low level laser therapy. Outcome measures for pain and scar healing was evaluated using Numerical Pain Rating Scale (NPRS) and Patient and Observer Scar Assessment Scale (POSAS).

Results: There is no statistically significant difference in the post test mean values of Numerical Pain Rating Scale (NPRS) between GROUP-A and GROUP-B with the significant value of 0.216 ($p > 0.05$). There is a significant difference in the posttest mean values of Patient and Observer Scar Assessment Scale (POSAS) between GROUP-A and GROUP-B with the significant value of 0.042 ($p < 0.05$).

Conclusion: This study concludes that low level laser therapy promotes the scar health better than the Therapeutic Ultrasound in episiotomy.

Keywords: Therapeutic Ultrasound, Low Level Laser Therapy, Episiotomy

Introduction

Episiotomy is a surgical procedure made in the perineum of the gravida in the late second stage of labour in order to facilitate delivery of the baby. This procedure is done to widen the introitus and straighten the lower end of birth canal and the incision is made between the anus and vulva. Episiotomy can reduce the amount of

maternal pushing and it also reduces the trauma to the vaginal tissue¹.

Episiotomy was first described by Sir Fielding Ould in the year 1742². Episiotomy is done in more than 90% of vaginal deliveries in India and it is done mostly to primiparous mothers (88.31%)³. The perineum in primiparous mothers is less elastic than the multiparous mothers⁴.

Perineum is very sensitive area, and the muscles are involved in sitting, walking, squatting, urination and defecation⁵. Delivery may lead to overstretching of the vagina, causing tears in the perineal tissue between the vagina and rectum. Perineal tears are more common during childbirth to avoid that episiotomy is done. An

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incision in this region cause pain and discomfort in doing daily activities such as sitting and feeding the baby⁶.

There are two types of incision in episiotomy they are mediolateral and midline incision⁷. The mother who underwent episiotomy will have more blood loss, risk of improper wound healing and increased pain at the time of early puerperium⁸.

Therapeutic ultrasound is given two days after vaginal delivery in order to reduce perineal pain and to promote scar healing. The mechanism of this therapy will improve tissue repair and reduce pain⁹. The biophysical effect of therapeutic ultrasound will promote wound healing, changes in cellular protein synthesis, increased the collagen content, increased blood flow and vascular permeability¹⁰.

The first known trial report for the ultrasound therapy for the relief of pain on the episiotomy incision was published (Foulkes 1980). Therapeutic ultrasound is widely used in physiotherapy to treat soft tissue injuries. Dyson 1987 concluded that ultrasound has a better effect on tissue repair and pain relief in soft tissue injuries.

The waves produced from ultrasound through the propagation of molecular collision and vibration which increased the molecular motion and produce the microfriction between the molecules. The heat generated from friction will increase tissue permeability and facilitates soft tissue healing¹¹.

Low Level Laser therapy is given for two days after delivery to promote scar healing. The application of Low Level Laser therapy was first introduced by Endre Mester in the year 1968¹². Low Level Laser therapy is also known as Low Intensity Low Level Laser Therapy (LLIT), Biostimulative Therapy (BT), Low Level Laser PhotoTherapy (LPT).

Low Level Laser therapy (low-level Low Level Laser therapy L.L.L.T) is the use of red or infra red light which aids in soft tissue healing and helps in relief of pain. The effect of Low Level Laser therapy is photobiostimulation which helps in the production of ATP that gives more energy which makes the tissue to play role in healing process¹³. The mechanism of pain reduction in Low Level Laser therapy is by increasing the local and systemic microcirculation and the synthesis of nitric oxide will improve the blood flow to the particular region¹⁴. The effect on Low Level Low Level Laser therapy on pain relief is due to the action of endorphins

and endogenous pain relievers¹⁵. The various effects of Low Level Laser therapy are anti-inflammatory, anti-edematous, high rates of ATP, increased cellular function and increase in tissue oxygenation and nutrition¹⁶.

The biostimulatory effects of Low Level Laser therapy acts on ulcers, granulomas, burns, wounds and trauma and stimulate the local cell metabolism in damaged tissue¹⁷. Low Level Laser therapy plays a major role in relief of neurological pain, relief of inflammation and oedema and prevention of tissue death¹⁸.

Method

Study Design and Sample: This is a Quasi-experimental type of study done for 3 days in SRM Medical College Hospital and Research Center, Kattankulathur about 10 subjects were included in the study and clearly explained about the procedure and informed consent was obtained and explained them that the information obtained will be kept confidential.

Primiparous women with age between 25 to 30 were included in the study. Numerical Pain Rating Scale (NPRS) and Patient and Observer Scar Assessment Scale (POSAS) were used to assess the pain and scar health and the score is considered as pre-test score. They were randomly assigned into two groups, Group-A and Group-B.

Procedure: Women who were selected for the study, had been explained about the purpose of the study and informed consent form was obtained. Then the assessment was taken from the patient.

Subjects were then divided into 2 groups, Group A (5 subjects), Group B (5 subjects)

Group A: subjects were allotted with the treatment of therapeutic ultrasound.

Group B: subjects were allotted with the treatment of Low Level Laser Therapy.

Group A (5 subjects): Subjects who were treated with ultrasound underwent the following procedure.

The subject was advised to clean herself and the procedure was completely explained to the subject. The subject is then positioned in side lying with lower leg straight and upper leg bent up and supported with pillow covered with mackintosh so that the perineum is visible from back. The therapist stand behind the subject at the

foot end. Proper ethics and safety measures were taken. Ultrasound equipment (Electrocare) was used for this treatment. The head of the ultrasound is covered with condom and gel is applied over the treatment head. Then another condom is filled with water and gel is applied to outside of the condom. The water filled condom is directly placed over the episiotomy area and the treatment is given accordingly for 6 minutes Parameters used

Frequency: 3MHZ

Intensity: 0.5W/cm2

Pulseinterval: 1:1

Duration: 6minutes

Mode: Pulsed mode

Method: water bag method

GROUP B (5 subjects): Subjects who were treated with Low Level Laser Therapy underwent the following procedure

The subject was advised to clean herself and the procedure was completely explained to the subject. The subject is then positioned in side lying with lower leg straight and upper leg bent up and supported with pillow covered with mackintosh so that the perineum is visible from back. The therapist stand behind the subject at the foot end. A piece of sterile cotton was pushed into vagina to preventcontamination of working field by vaginal discharge or blood.

A graduated wooden spatula is used to measure the length of the incision of episiotomy. Low Level Laser therapy machine(Electrocare) was used for this study. The wound exposed to Low Level Laser therapy irradiation of one spot after another using spot size of

0.8cm for 3minutes.

Parameters used are:

Frequency: 2 J/cm2

Duration: 3 minutes

Method: Non contact method

Both the treatment is given for 3days from Post Natal Day (PND) 2,I session a day.

Numerical Pain Rating Scale (NPRS) will be assessed before and after the treatment.

Scar is assessed after 4weeks by using Patient and Observer Scar Assessment Scale (POSAS).

Results

According to Table 1 there is a significant reduction in the mean values of Numerical Pain Rating Scale(NPRS) in Group A treated with Therapeutic Ultrasound and Group B treated with Low Level Laser therapy, but when both groups are compared there is no statistically significant difference in the post test mean values of Numerical Pain Rating Scale(NPRS) between GROUP-A and GROUP-B with the significant value of 0.216 (p>0.05).

According to Table 2 there is a significant reduction in the mean values of Patient and Observer Scar Assessment Scale(POSAS) inGroup A treated with Therapeutic Ultrasound and Group B treated with Low Level Laser therapy, but when both groups are compared there is a significant difference in the post-test mean values of Patient and Observer Scar Assessment Scale(POSAS) between GROUP-A and GROUP-B with the significant value of 0.042 (p<0.05).

Table 1: Comparison of Post-Test Values of Numerical Pain Rating Scale(Nprs) Between Group-A Treated With Therapeutic Ultrasound And Group-B Treated With Low Level Laser Therapy.

Treatment	N	Mean	Std. Deviation	Wilcoxon Signed Ranks	P-Value
THERAPEUTIC ULTRASOUND	5	5.80	0.837	-1.236	0.216
LOW LEVEL LASER THERAPY	5	7.00	1.225		

p>0.05 This table shows p value is greater than 0.05, Hence,there exist no significant difference in Numerical Pain Rating Scale (NPRS) between Group A treated with Therapeutic Ultrasound and Group B treated with Low Level Laser Therapy.

Table 2: Comparison of Post-Test Value of Patient and Observer Scar Assessment Scale(Posas) Between Group-A Treated With Therapeutic Ultrasound and Group-B Treated With Low Level Laser Therapy

Treatment	N	Mean	Std. Deviation	Wilcoxon Signed Ranks	P- Value
THERAPEUTIC ULTRA SOUND	5	113.60	2.191	-2.032	0.042*
LOW LEVEL LASER THERAPY	5	55.60	6.542		

P value <0.05 According to table 2 there is a significant difference (P<0.05) in the post-test mean values of Patient and Observer Scar Assessment Scale(POSAS) between Group A (113.60) and Group B (55.60).

Discussion

This study compares the effectiveness of Therapeutic Ultrasound and Low Level Laser Therapy over pain and scar health in post episiotomy patients.

About 10 subjects who fell in the age group of 25-30 years, satisfied both inclusion and exclusion criteria were included in the study. Group-A (5 subjects) were treated with Therapeutic Ultrasound and Group-B (5 subjects) were treated with Low Level Laser Therapy.

There is a significant reduction (P<0.05) in the mean values of Numerical Pain Rating Scale(NPRS) in Group A subjects treated with Ultrasound and there is a significant reduction (P<0.05) in the mean values of Numerical Pain Rating Scale(NPRS) in Group B subjects treated with Low Level Laser Therapy for three days.

Therapeutic Ultrasound is a high frequency machine which is inaudible and it consist of mechanical vibration. The electrical energy is acoustic energy when the crystals gets deformed and this effect is called piezo-electric effect¹⁹. The tissue permeability is increased due to increased micro-friction between the molecules²⁰.

Therapeutic Ultrasound increase the blood circulation and improves the skin and cell membrane permeability which leads to reduction of pain,removes the waste products and promote wound healing.

EL Hag and coworkers stated the cause for anti-inflammatory effect of Therapeutic Ultrasound as follows, increased protein synthesis, more number of mast cell production. The above causes leads to reduction in swelling and improves the vascular permeability²¹.

Low Level Laser Therapy produces a beam of radiation which differs from the ordinary light. By the end of 1960, **EndreMester**stated that the Low Level Laser therapy can be given for wound healing. The energy production in the Low Level Laser therapy is by

quantum theory.

The Low Level Laser therapy must consist of a lasing medium (solid, crystal or semiconductor), resonating chamber and the energy source. For therapeutic purpose two method of application are used in Low Level Laser therapy such as grid method and scanning method. Low Level Laser therapy is found to be effective in pain reduction both acute and chronic pain by improving the healing process and reducing the swelling.

According to **Dyson and Young 1986**, the low level Low Level Laser therapy is effective for wound healing by increasing the changes and the release of chemical mediators.According to **David Baxter 1994** the energy density plays an important role in pain reduction and promotion of wound healing²².

The results of this study shows that with the Patient and Observer Scar Assessment Scale(POSAS) is found to have a significant effect over scar healing in both Group A treated with Ultrasound and Group B treated with Low Level Laser Therapy for three days.

The effect of Therapeutic Ultrasound on wound healing is due to increase in the growth of the tissues and facilitate repair of soft tissue by the mechanism of acoustic streaming.

In Inflammatory Phase, degranulation takes place in mast cell and release the histamine which leads to the collagen formation. In proliferative phase, Therapeutic Ultrasound promotes wound contraction by development of myofibroblast in that injured region. In remodeling phase the tensile strength of the scar tissue is improved by collagen activity and tissue extensibility.

The effect of Low Level Laser therapy on wound healing is due to absorption of Low Level Laser therapy light by mitochondria which stimulate the electron transport chain and produce AdenosineTriPhosphate(ATP).**Passarella 1988** stated

that Low Level Laser therapy also has an effect on DNA synthesis, cellular activation and granulation tissue formation²³.

When comparing both the groups it was found that there was no statistically significant difference in the reduction of pain between Group A and Group B ($p > 0.05$) which shows that both Ultrasound and Low Level Laser Therapy has similar effect over reduction of pain. According to the statistical analysis which is calculated by Wilcoxon Signed rank Test, there is a significant difference ($p < 0.05$) between both groups in scar health which is assessed by the Patient and Observer Scar Assessment Scale (POSAS) and it was found that GROUP-B subjects treated with Low Level Laser Therapy has a better effect over scar health improvement than the GROUP-A subjects treated with Therapeutic Ultrasound ($p < 0.5$).

Acto myosin plays an important role in myofibroblasts contraction by shrinking the border of the wound which reduce the size of the wound during soft tissue healing.

According to **Tuner and Hode 2002**, Low Level Laser therapy produces a non-thermal effect and is an ideal treatment for wound healing by reducing the pain and promotes tissue healing²⁴. The effect of Low Level Laser therapy in pain reduction is due to its effect on pain relievers such as endorphin and enkephalin.

Both modality has better effect in reducing pain and improving scar health. But this study documents that Group-B (Low Level Laser therapy Therapy) has significant improvement in scar healing than GROUP-A (Therapeutic Ultrasound). According to this study, Low Level Laser Therapy has significant effect on scar health and prevent the complication of dyspareunia.

Conclusion

This study concludes that both Low Level Laser Therapy and Therapeutic Ultrasound is effective in reducing the pain. Low Level Laser Therapy promotes scar health than the Therapeutic Ultrasound. So Low Level Laser Therapy is effective in improving the scar health in post episiotomy.

Ethical Clearance: Obtained from institutional ethical committee.

Source of Funding: Self

Conflict of Interest: Nil

References

1. Kettle C, Dowsell T, Ismail KMK. Continuous and interrupted suturing techniques for repair of episiotomy or second-degree tears. *Cochrane Database System Rev.* 2012;10-11.
2. David M. Who invented the episiotomy? On the history of the episiotomy. *Zentralbl Gynakol.* 1993;188-193.
3. Schuiling KD, Sampselle CM. Comfort in labor and midwifery art. *The Journal of Nursing Scholarship,* 31(1), 1999; 77-81.
4. Tan J, Abisi S, Smith A, Burnand KG. A painless method of ultrasonically assisted debridement of chronic leg ulcers: a pilot study. *EurVascEndovascSurg* 33, 2007; 234-8.
5. Mccandlish R, Perinealtraumaprevention and treatment, *J Midwifery Women's health,* 46 (6), 2001; 396-401.
6. Grant et.al, Ultrasound and PEME treatment for perineal trauma-A Randomized placebo controlled trial. *British Journal of OBGY,* 96, 1989; 15-23.
7. Carter E, During T. *With child birth through the ages,* Edinburgh: Mainstream publishing company Inc, 1986; 1-3
8. Jacob A .A comprehensive text book of midwifery. Jaypee publications, New Delhi, India. 2005; 175-177.
9. Dyson M .Mechanisms involved in therapeutic ultrasound. *Physiotherapy* 73:1987; 116-120.
10. McClaren J. Randomised controlled trial of ultrasound therapy for the damaged perineum. In *Clinical Physics and Physiological Measurement* 1984 Jan 1 Vol.5, No.1; 40-40.
11. Kaufman K .Warm vs cold sitz baths. *Pre-cochrane Reviews:* 2000; 30-30
12. Mester AF, Mester A. Wound healing, Low Level Laser therapy therapy 1, 1989; 7-15.
13. Low and reed., Electrotherapy – photobiostimulation of Low Level Laser therapy: 1997; 212-216.
14. Rane Thakar and Abdul H, "(Sultan Episiotomy and obstetric perineal trauma chapter 17 in best practice in labour and delivery)" Cambridge University Press: 2009; 182.
15. Watban F, Zhang ZY, "(Comparison of the Low Level Laser therapy on wound healing using

- different Low Level Laser therapy wavelengths)". Low Level Laser therapy, 1996;8;127-345.
16. Mester E, Jaszagi-Nagi E, "(Experimentation on the interaction between infrared Low Level Laser therapy and wound healing)". *Studia. Biophys.* 1973; 35;227-230.
 17. Trelles M.A., Rigau J., Sala P., Calderhead G., and Oshiro T., IR diode Low Level Laser therapy in LLLT for knee osteoarthritis. *Low Level Laser therapy* 1991;3;149-153.
 18. Michael R Hamblin and Tatiana N Demidova, "(Mechanisms of low level light therapy)", *Proc. of SPIE*, 2006; 6140, 614001-1.
 19. Ter Haar G basic physics of therapeutic ultrasound. *Physiotherapy* 1987;73;110-113. 22.
 20. Belenger AY Evidence based guide to therapeutic physical agents. Lippincott Williams and Wilkins, Philadelphia, USA. 2002;1-16.
 21. Michlovitz SL, editor. Thermal agents in rehabilitation. Davis Publications; 1990.
 22. David Baxter, Medical Low Level Laser therapy and photomedicine; therapeutic Low Level Laser therapy theory and practice, G. David Baxter, London, Churchill livingstone, 1994;11-19.
 23. Dyson M, Young S., effect of Low Level Laser therapy on wound contraction and cellularity, *Low Level Laser therapy Med Sci.* 1986;1;126-130.
 24. Tuner J, Hode L, "(Medical Indications: Wound Healing. In: Low Level Laser Therapy: Clinical Practice and Scientific Background)". Prima Books: Grangesberg, Sweden ;Prima Books, 2002;189-196.

The Effect of Specific Training on Selected Physiological Variable among Kabaddi Players

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Abstract

Context: The purpose of this study was to find out the effect of specific training on selected physiological variable among school boys kabaddi players from government higher secondary school koomapatti. The age of the subjects ranged from 15 to 18 years. The selected subjects n=30 were divided into one experimental group and one control group at random. The investigator selected a training that is specific training for kabaddi players which improved certain selected physiological fitness variables namely Resting Heart Rate. As the result of field training the physical fitness level of the kabaddi would improve. The experimental group endured the training activities for 6 weeks with a schedule of six days whereas the control group remained with no activities. The data procured in prior and after the training programme was examined. To find out difference between experimental and control group of Resting Heart Rate t-ratio was employed and the level of significance was set at 0.05. The results of the study showed that the Resting Heart Rate of the experimental group was significantly improved than the control group.

Keywords: Specific training, Resting Heart Rate, Kabaddi, Experimental group, Control group

Introduction

Physical events such as scoring goals or crossing a line first often define the result of a sport. However, the degree of skill and performance in some sports such as diving, dressage and figure skating is judged according to well-defined criteria.¹ This is in contrast with other judged activities such as beauty pageants and body building, where skill does not have to be shown and the criteria are not as well defined. Records are kept and updated for most sports at the highest levels, while failures and accomplishments are widely announced in sport news.² Sports are most often played just for fun or for the simple fact that people need exercise to stay in good physical condition. However, professional sport is a major source of entertainment.

Physical Education and Sports: Physical education and training organized instruction in motor activities will contribute to the physical growth, health, and body image of the individual. The historical roots of physical education go back as far as the ancient Chinese who had a well-developed system of exercise and physical training.³

In ancient Greece the Athenians were concerned with both physical and mental development; consequently they accorded gymnastics, sports, and rhythms an important educational role. During the period of the Roman Empire and later during the middle ages, physical education was primarily used as a form of military training. Interest in physical education as a part of the total individual's development was revived during the Renaissance.⁴ It was not until the 19th cent., however, that systems of gymnastics were developed in several European countries, notably Germany, Sweden, and England. During same period gymnastics spread to the United States. Interest in the new system led to a movement to have compulsory physical training in American public schools and to establish

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physical education in colleges and universities. The first department of physical education at an American college was established at Amherst, 1860.

Sports Specific Training: Sports Specific Trainers can help improve strength, flexibility and stamina to improve performance in specific sports.⁵ Options include increasing arm strength for tennis playing or improve strength and core stability providing better balance playing. Sports specific training is all about developing physical conditions to improve performance and skills at a particular sport. Also understanding the needs of the game training practicing at the correct pace in order to meet sports requirements.⁶

Kabaddi: India's efforts to popularize Kabaddi has paid rich dividends as the country has won all the Asian Games gold medals, since the game was introduced in the 1990 Beijing Games. Talking about the techniques of the game, there are two teams that occupy the opposite halves of a field.⁷ In turns, one team sends a 'raider' into the other half, in order to win points. The raider, who goes inside has to touch any one of the teammates from the other team and immediately run back to his line, without even once letting off his breath during the whole raid and chanting the word "kabaddi".⁷ On the other hand, the members of the other team have to grab the raider down before he reaches his line.

Statement of the problem: The purpose of this study was to find out the effect of specific training on selected physiological variable among school boys kabaddi players.

Methodology: To achieve the purpose of these study 30 boys kabaddi players were selected at

government higher secondary school koomapatti. The age of the subjects ranged from 15 to 18 years. The selected subjects were divided into one experimental group and one control group at random. The investigator selected a training that is specific training for kabaddi players which improved certain selected physiological fitness variables namely muscular Resting Heart Rate. As the result of field training the physical fitness level of the kabaddi would improve.

Resting Heart Rate:

Purpose: To measure the subjects' resting heart rate.

Equipments: Stethoscope and stopwatch.

Procedure: The resting heart rate of each subject was recorded in the early morning after getting out of bed and sit at rest comfortably in a chair for few minutes. The resting heart rate was obtained through auscultation i.e. using the bell of the stethoscope is placed to the left of the sternum just above the level of the nipple. Then the stop watch was started with the heartbeat. Counted the first beat as zero and continued for 30 seconds. This procedure was repeated on three separate mornings.

Scoring: Resting heart of the subjects was recorded on three successive mornings. The average of the three recordings was arrived at and recorded as the subjects resting heart rate. The unit of measurement was initially taken for 30 seconds and the beats per minute of the subjects were calculated by doubling the number of beats to arrive at and per minute calculation.

Results and Discussions

Table I: Analysis of 't' ratio for the pre and post test of Control and Experimental Group on Resting Heart Rate

Variable	Group	Mean		SD		Sd Error	Df	't' ratio
		Pre	Post	Pre	Post			
Resting Heart Rate	Control	77.07	77.73	2.81	2.55	0.33	14	2.00
	Experimental	77.33	75.73	4.15	3.73	0.16		9.80*

* Significance at 0.05 level of confidence.

The data analysis done statistically from the table I indicates that the mean values of pre-test of the training groups To find out difference between experimental and control group of Resting Pulse Rate. Difference in two groups t-ratio was employed and the level of significance was set at 0.05. Experimental group pre and post-test

mean value were 77.33, 75.73 respectively. In Control group pre and post-test were mean value was 77.07, 77.73 respectively. In experimental the obtained t-ratio 9.80 was greater than the table value 2.15 so it found to be significant. In control group the obtained t-ratio 2.00 was lesser than the table value 2.15 so it was found to be insignificant.

Discussing on Findings: The result of the study indicates that the experimental group namely training group had significantly improved the selected dependent variables namely Physiological Variable when compared to the control group. It is also found that the improvement caused by training when compared to the control group.

Discussion on Hypothesis: It was hypothesized at the beginning of the study that there would be significant improvement on selected criterion variables such as specific training (physiological variable) due to training for the experimental group as compared to the control group. The present study produced similar results. Hence, the research hypothesis of the investigator was held true.

Conclusions

The results of the study concluded that the Resting Heart Rate of the experimental group was significantly improved than the control group.

Ethical Clearance: Nil

Source of Funding: Self

Conflict of Interest: Nil

References

1. Biju-Sukumar DS, Rajinikanth P. Effect Of Sport Loading Programme On Strength Endurance Among School Level Sprinters. Sports Med. 2017;4(1):27-31
2. Bloomfield J. Australia's sporting success: The inside story. UNSW Press; 2003.
3. Tulchinsky TH, Varavikova EA. The new public health. Academic Press; 2014 Mar 26.
4. Dalleck LC, Kravitz L. The history of fitness: From primitive to present times, how fitness has evolved and come of age. IDEA Heal Fit Source. 2002 Jan 1;20(1):26-34.
5. Kibler WB, Chandler TJ, Uhl T, Maddux RE. A musculoskeletal approach to the preparticipation physical examination: Preventing injury and improving performance. Amer J Sports Med. 1989 Jul;17(4):525-31.
6. Smith DJ. A framework for understanding the training process leading to elite performance. Sports med. 2003 Dec 1;33(15):1103-26.
7. Otis CL, Drinkwater B, Johnson M, Loucks A, Wilmore J. American College of Sports Medicine position stand. The female athlete triad. Med sci sportsexerc. 1997 May;29(5):i-x.

Urinary Intestinal Fatty Acid Binding Protein “IFABP” as a Marker for Gut Maturation in Preterm Babies

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Abstract

Objective: Formula-fed premature babies have a higher incidence of developing necrotizing enterocolitis (NEC) than breast-fed babies which may be caused by breast milk induced gut maturation. The effect of breast milk on maturation of the gut has been widely studied in animal models and recently in humans.

The aim of this study: Is to evaluate the effects of breast-feeding on maturation of the intestine in premature babies by measuring the postnatal values of a specific enterocyte marker which is urinary intestinal fatty acid binding protein (I-FABP).

Method: Maturation of the gut was studied in 60 premature babies (<37 weeks of gestation) without gastrointestinal morbidity. 30 of them were exclusively breast-fed and the other 30 were formula-fed. Urinary I-FABP levels as the measure of gut maturation were measured at 7th, 12th, and 22nd post-natal days.

Results: In breast-fed babies, there was a statistically significant increase in urinary I-FABP levels between 7th and 12th days after birth compared with formula-fed babies (p < 0.01)

Conclusions: The pattern of postnatal changes in urinary I-FABP levels suggests a delayed physiological response causing significantly delayed gut maturation in formula-fed babies compared with breast-fed ones.

Keywords: Breast-feeding, formula feeding, intestinal fatty acid binding protein, gut maturation, mucosal damage, necrotizing enterocolitis.

Introduction

Human milk (HM; milk from the infant's own mother) feedings during the Neonatal Intensive Care Unit (NICU) hospitalization reduce the risk of prematurity-related morbidities in a dose-response manner for very low birth weight babies. ⁽¹⁾

These morbidities include late onset sepsis,

necrotizing enterocolitis, chronic lung disease, retinopathy of prematurity, prolonged NICU hospitalization, increased health care costs, and long-term health and educational problems. ⁽²⁾

Breast milk is a known source of molecules that act synergistically to protect the gut barrier and enhance the maturation of the gut-related immune response. So During the perinatal period, nutrition is the principal contributor for immunological and metabolic development, and microbiological programming. ⁽³⁾

Breast milk is the gold standard for preterm nutrition and influences the development of intestinal microbiota and immune system through its bioactive components. ⁽⁴⁾Preterm infants altered gut microbiota interaction ⁽²⁾ with an immature immunologic intestinal response

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triggers proinflammatory and counter-inflammatory cytokine response. Necrotizing enterocolitis (NEC) is the most common gastro-intestinal emergency in the neonatal intensive care unit (NICU) which is due to excessive inflammatory response against commensal bacteria by the immature intestine following mucosal injury in the postnatal period. ⁽⁵⁾

Its prevalence is largely related to birth weight and gestational age (G.A.) with approximately 1 in 10 very low birth weight infants (<1500 g) developing NEC. ⁽⁵⁾

Breast-fed newborns are protected against NEC development through improved gut maturation and because there is an estimated 3 to 10 folds risk reduction in infants fed with breast milk compared with those fed with formula milk ⁽⁶⁾

Patients and Method: Sixty preterm babies were enrolled in this study, thirty of them were breast-fed preterm babies (Group I) while the other thirty newborns were formula-fed ones (Group II).

All of the babies admitted to the NICU of the Minya University Hospital of children between August 2015 and March 2016 were eligible for participation.

Patients were included if they met the following inclusion criteria: <37 weeks of gestation, first enteral feeding within 7 days after birth, and diet consisting of either exclusively breast milk or exclusively formula milk. The only exclusion criterion was development of significant gastrointestinal pathology during the 30-day study period, defined as disease of the gastrointestinal tract necessitating surgery, antibiotic treatment, cardiopulmonary support, or discontinuation or reduction of enteral feeding.

Initiation of feeding and advancement of feeding volumes were realized according to the local protocol. The standard guidelines consisted of early initiation of oral feeding within few days after birth depending on the infant's gestational age and general condition.

Feeding volume was increased gradually and discontinued if there were signs of feeding intolerance including bilious gastric retentions, abdominal distention, emesis, or bloody stools.

Sample collection: 1-blood samples: 5 ml of venous blood samples were taken for complete blood count, Total and direct bilirubin, and CRP using fully automated chemical auto-analyzer Dimension-ES, USA.

2- Urine samples: Urine samples were collected on the 7th, 12th, and 22th day after birth.

Samples were collected either from a urine bag connected to an indwelling catheter or from a cotton wool swab placed in the diaper and squeezed through a syringe barrel into a collection tube. Samples were then frozen at -20°C till the time of analysis.

Urinary I-FABP levels were measured by ELISA.

Statistical Analysis: The numerical data were presented as means – standard deviations while non numerical data were presented as percentage. Two tailed-tests were used to analyze differences between the two groups.

P-values less than 0.05 were considered statistically significant. The magnitude of correlation was determined by Pearson's correlation coefficient.

All the data were analyzed by statistical package Prism 3.0 (GraphPad software, San Diego, CA, USA). Figures were done by Microsoft Office Excel 2007

Results

In the present study, there was a significant statistical difference between breast-fed and formula-fed preterm babies regarding Duration of NICU admission in days ($p < 0.01^{**}$) which was higher in formula-fed preterm babies compared to breast-fed ones, while there was no significant statistical difference between the two groups of patients regarding gestational age (mean \pm SD 33.1 \pm 2.2, 32.9 \pm 2.1 respectively), sex ($p < 0.01$), and birth weight (mean \pm SD 0.9 \pm 0.7, 0.1 \pm 0.6, -0.97 \pm 0.4 respectively). $p < 0.01$ (Table 1.)

There was significant higher incidence of Comorbidities like respiratory distress and sepsis in formula-fed preterm babies compared to breast-fed ones ($p < 0.01$) for both. Seventy three percent of obese children 26.3% of overweight ones were having NAFLD. (Table 2)

Regarding Signs of feeding intolerance between groups in the form of stopping of feeding, their frequency, and duration, all were significantly higher in formula-fed preterm babies compared to breast-fed ones ($p < 0.01$) for all. Serum platelets were compared to healthy ones (mean \pm SD for ALT 71.3 \pm 21.4, 41.3 \pm 19.1, 30.3 \pm 4.4 and Serum TLC (mean \pm SD for AST 69.8 \pm 24.5, 36.8 \pm 5.5, 30.0 \pm 4.4 respectively) ($p < 0.01$ and

0.05 respectively).staff CRPmean±SD for AST 69.8 ± 24.5 , 36.8 ± 5.5 , 30.0 ± 4.4 respectively) ($p < 0.01$ (Table.3)

There was negative correlation between BMI,weight, cholesterol, TG and ALT and serum visfatin levels. ($p < 0.01$ for all). (Table.4)

Table (1): Demographic data between groups.

Variable	Group (I) Breast fed Babies (n=30)	Group (II) Formula fed Babies (n=30)	P. Value (Sig.)
Gestational age (wks.)	$33.1 \pm 2.2(29-36)$	$32.9 \pm 2.1(29-36)$	0.71 ^{NS}
Sex	Male	12 (40.0%)	0.60 ^{NS}
	Female	18 (60.0%)	
Birth weight (gm)	$1973 \pm 273(1400-2400)$	$1955 \pm 337(1450-2700)$	0.88 ^{NS}
Duration of NICU admission (days)	22.1 ± 4.3	26.0 ± 4.8	< 0.01**

Table (2): Signs of feeding intolerance between groups.

Variable	Group (I) Breast fed Babies (n=30)	Group (II) Formula fed Babies (n=30)	P. Value (Sig.)
Stop Feeding	No	21 (70.0%)	< 0.01**
	Yes	9 (30.0%)	
No. of Episodes	$0.63 \pm 1.06 (0-3)$	$1.83 \pm 1.53(0-5)$	< 0.01**
Duration of Episodes (days)	$0.83 \pm 1.48 (0-5)$	$1.90 \pm 1.54 (0-5)$	< 0.01**
Abd. X-ray Findings for Intolerance	Negative	30 (100.%)	< 0.01**
	Positive	0	

Table (3): Laboratory data between groups

Variable	Group (I) Breast Fed (n=30) (M ± SD)	Group (II) Formula Fed (n=30) (M ± SD)	P. Value (Sig.)
Hb (g/dl)	17.4 ± 2.21	17.3 ± 2.20	0.83 ^{NS}
TLC ($10^9/L$)	10.52 ± 4.73	13.91 ± 4.25	<0.01**
PLT ($10^9/L$)	129.4 ± 37.7	97.7 ± 32.4	<0.01**
Total Bilirubin (mg/dl)	6.80 ± 2.32	6.83 ± 2.43	0.96 ^{NS}
Direct Bilirubin (mg/dl)	0.60 ± 0.25	0.58 ± 0.24	0.76 ^{NS}
Staff (%)	1.78 ± 1.68	8.47 ± 4.83	<0.01**
CRP	Negative	21 (70.0%)	<0.01**
	Positive	9 (30.0%)	

Table (4): Comparison between groups regarding IFABP level at different postnatal days.

Variable	Group (I) Breast Fed (n=30) (M ± SD)	Group (II) Formula Fed (n=30) (M ± SD)	P. Value (Sig.)
IFABP (7 th day), (ng/l)	3807 ± 319	3040 ± 722	<0.01**
IFABP (12 th day), (ng/l)	3999 ± 735	3262 ± 552	<0.01**
IFABP (22 th day), (ng/l)	3731 ± 828	3414 ± 942	0.17 ^{NS}
P. value (Sig.)	0.28 ^{NS}	0.16 ^{NS}	-

Discussion

FABPs is a set of widely expressed cytoplasmic proteins with small molecular weight and excellent organ specificity, which are immediately secreted into the systemic circulation upon the damage of cells⁽⁷⁾

As a member of the FABPs family, FABP2, which is a *FABP2* gene encoding protein, accounts for up to 2% of the cytoplasmic proteins in the mature enterocyte, and it is responsible for the intake alongside with the transport of polar lipids like fatty acids from the lumen of the small bowel.⁽⁸⁾

FABP2 is a water soluble cytosolic protein with a small molecular weight of 14-15 kDa, and it is initially located in the mature enterocytes of the small intestine. FABP2 is also named as intestinal-type FABP (I-FABP).⁽⁹⁾

Because of its small molecular size, FABP2 is believed to be delivered to the circulation immediately upon the loss of the integrity of the cell membrane and filtering of the glomerulus with a renal excretion of 28% and a considerable half-life of 11 minutes. So, it is supposed to be detectable in urine.⁽¹⁰⁾

Thus, varying FABP2 expressions in the urine could exactly reflect the severity of the cell damage to the intestinal epithelia, making it possible to use FABP2 as a trustable indicator of the disease progression⁽¹¹⁾.

This study was carried out to assess the diagnostic utility of the urinary I-FABP levels as a new marker for gut maturation in breast-fed preterm neonates compared to formula-fed ones.

In the present study, breast-fed babies and formula-fed ones showed no significant statistical difference regarding gestational age ($p=0.71$), sex ($p<0.60$) and birthweight ($p<0.88$). These findings agreed with the study of Kostan W2014 who stated that there were no significant differences in GA, birth weight, or sex between the 2 groups; however, there was a trend of lower median GA in the breast-fed group.

Our study shows that Prematurity was the primary reason for admission to the NICU in all of the babies and that the duration of NICU admission in days was higher in formula-fed preterm babies compared to breast-fed ones ($p<0.01$).

The results of our study show a significant higher

incidence of Co-morbidities like respiratory distress and sepsis in formula-fed preterm babies compared to breast-fed ones ($p<0.01$) for both. This agrees with the study of⁽¹²⁾ who explained the beneficial effects of breast milk and its immunomodulatory and anti-inflammatory effect, and high concentrations of secretory immunoglobulin A, CD14, transforming growth factor- β , erythropoietin, and interleukin-10 in breast milk.

In our study, total volume of enteral feedings was recorded every day to investigate whether the type of feeding correlated with feeding intolerance. Feeding intolerance is defined as episodes of discontinuation of enteral feeding or frequency and cumulative amount of gastric retentions.

We found that signs of feeding intolerance including feeding stoppage, number of episodes, and duration of those episodes were significantly higher in formula-fed preterm babies compared to breast-fed ones ($p<0.01$) for all. This could be explained by that early breast milk feedings, especially colostrum, promote the growth, maturation, and protection of the gut epithelial border.

In agreement with our study,⁽¹³⁾ explained the mechanisms by which breast-feeding improves intestinal maturation. For example, analogues of growth factors or human milk oligosaccharides. The preterm infant's high need for trophic factors should be taken into account. Added to that, his study underlines the importance of breast milk use in preterm infants.

Our results also agree with the study of⁽¹⁴⁾ who found that human milk feedings have been shown to stimulate healthy gut microflora, reduce intestinal permeability, and interfere with the translocation of bacteria from the gut lumen to the mucosa, and appear to be the most critical as VLBW infants transition from intrauterine (e.g., swallowing amniotic fluid) to extrauterine nutrition in the early post-natal period.

Commercial formulas may have a separate detrimental impact on these processes during these early postnatal exposure periods, via up-regulation of inflammatory processes, GIT epithelial cell toxicity, and other mechanisms.⁽¹⁵⁾

Ethics Approval and Consent to Participate: The study was conducted according to the declarations of Helsinki and approved from the faculty of medicine scientific committee in Minia

University (No: 116-5-2016): Written consents were obtained from patients and/or caregivers.

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Conflict of Interest: The authors declare that there is no conflict of interests.

References

- 1- Meier, P. P., Engstrom, J. L., Patel, A. L., Jegier, B. J., & Bruns, N. E.. Improving the use of human milk during and after the NICU stay. *Clinics in perinatology*, (2010); 37(1), 217-245]
- 2- Fullerton, B. S., Hong, C. R., Velazco, C. S., Mercier, C. E., Morrow, K. A., Edwards, E. M., ... & Jaksic, T.. Severe neurodevelopmental disability and healthcare needs among survivors of medical and surgical necrotizing enterocolitis: a prospective cohort study. *Journal of pediatric surgery*, (2018); 53(1), 101-107]
- 3- Mills, S., Stanton, C., Lane, J. A., Smith, G. J., & Ross, R. P.. Precision nutrition and the microbiome, Part I: Current state of the science. *Nutrients*,(2019) 11(4), 923]
- 4- Collado, M. C., Cernada, M., Neu, J., Pérez-Martínez, G., Gormaz, M., & Vento, M.. Factors influencing gastrointestinal tract and microbiota immune interaction in preterm infants. *Pediatric research*, (2015)77(6), 726]
- 5- Maheshwari, A., Corbin, L. L., & Schelonka, R. L.. Neonatal necrotizing enterocolitis. *Research and Reports in Neonatology*, (2011)1, 39]
- 6- Cilieborg, M. S., Boye, M., & Sangild, P. T.. Bacterial colonization and gut development in preterm neonates. *Early human development*, (2012)88, S41-S49]
- 7- Briana DD, Liosi S, Gourgiotis D, Boutsikou M, Baka S, Marmarinos A, et al. Cord blood intestinal fatty acid-binding protein (I-FABP) in full-term intrauterine growth restricted pregnancies. *J Matern Fetal Neonatal Med* 2012;25:2062-2065
- 8- Aydemir C, Dilli D, Oguz SS, Ulu HO, Uras N, Erdeve O, et al. Serum intestinal fatty acid binding protein level for early diagnosis and prediction of severity of necrotizing enterocolitis. *Early Hum Dev* 2011;87:659-661
- 9- Evennett NJ, Hall NJ, Pierro A, Eaton S. Urinary intestinal fatty acid-binding protein concentration predicts extent of disease in necrotizing enterocolitis. *J Pediatr Surg* 2010;45:735-740.
- 10- Reisinger KW, Derikx JP, Thuijls G, van der Zee DC, Brouwers HA, van Bijnen AA, et al. Noninvasive measurement of intestinal epithelial damage at time of refeeding can predict clinical outcome after necrotizing enterocolitis. *Pediatr Res* 2013;73:209-213
- 11- Thuijls G, Derikx JP, van Wijck K, Zimmermann LJ, Degraeuwe PL, Mulder TL, et al. Non-invasive markers for early diagnosis and determination of the severity of necrotizing enterocolitis. *Ann Surg* 2010;251:1174-1180.
- 12- Walker A. Breast milk as the gold standard for protective nutrients. *J Pediatr* 2010;156:S3-7.
- 13- Quigley MA, Henderson G, Anthony MY, et al. Formula milk versus donor breast milk for feeding preterm or low birth weight infants. *Cochrane Database Syst Rev* 2007CD002971
- 14- Taylor SN, Basile LA, Ebeling M, Wagner CL. Intestinal permeability in preterm infants by feeding type: Mother's milk versus formula. *Breastfeed Med*. 2009 Mar; 4(1):11-5. [PubMed:19196035]
- 15- Newburg DS. Innate immunity and human milk. *Journal of Human Lactation*. 2005

Relationship Individual Factors with Sickness Absence in Hospital

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Abstract

Background: Workers in health industries are more likely to have health problems. Health problems may result in sickness absence. High rate of sickness absence can decrease productivity and consumer satisfaction.

Objectives: To analyse individual factors with types of sickness absence.

Method: Retrospective study design. Data collection was done using secondary data in the form of sickness absence data report of hospital in 2017. A binary logistic regression test was used to identify the significance of correlation of age, sex, years of service and marital status correlation with types of sickness absence.

Results: Of 416 workers, 100 people submitted 163 sickness absence letter with the total of 653 days. Women workers with age range of 26-45, who were married and with 5 years of service were the group with the most sickness absence. Short term sickness absence was the most common type. The results of multivariate binary logistic regression showed that age (p value = 0.659 and Exp (B) = 0.783), sex (p value = 0.929 and Exp (B) = 0.945), years of service (p value = 0.620 and Exp (B) = 0.866), marital status (p value = 0.773 and Exp (B) = 0.837) variables were not significant.

Conclusion: There is no significant relationship between individual factors and type of sickness absence.

Keyword: Sickness absence, workers, hospital

Introduction

Based on Canadian Institute for Health Information (CIHI) in 2000, workers in health care are 1.5 times more likely to call in sick or leave work on disability compared to workers in industries other than health care. The average duration of 11.8 days of sickness absence is higher than workers in other fields which is 6.7 days.⁽¹⁾

Hospital workers sickness absence results in not only decreased productivity but also affect consumer

satisfaction. This is supported by the study of Duclay et al (2015) conducted in a hospital in France, concluding that the attendance of the hospital staff correlated with patient satisfaction in the hospital.⁽²⁾

Unhealthy workers are prone to sickness absence. Sickness absence is divided into 2 types. Short term sickness absence (fewer than 4 days) and long term sickness absence (longer than 4 days). Short term sickness absence is more common than the long term one. Long term sickness absence is generally caused by serious or severe illness.⁽³⁾ It is important therefore to identify individual correlation factors with the types of sickness absence.

The objective of this study is to analyse the individual correlation factors with the types of sickness absence of workers in hospital X in 2017.

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Method

This type of research is an observational analysis study with a retrospective research design. The population is workers who call in sick in hospital in Malang, Indonesia. During the period of 2017, the total number of workers was 416 people with 100 workers submitted sickness absence, amounting to 163 sick letters (spell) and 653 days of sickness absence. The research variables studied included the characteristics of workers, namely age, sex, years of service and marital status, and types of sickness absence. Data collection was carried out using secondary data in the form of hospital worker's sickness absence data in 2017. The data obtained were analyzed descriptively using cross tabulation. Binary logistic regression test was used to test the significance of parameters in a multivariable manner.

Findings: The frequency distribution of hospital workers by age can be seen as follows (see Table 1). Based on table 1 it can be seen that 56 people (56%) who submitted sickness absence were in the age group between 26 to 45 years.

Table 1: The Frequency Distribution of Workers by Age in Hospital in 2017

Age	Total (n)	Percentage (%)
17-25	36	36
26-45	56	56
>45	8	8

Table 2: shows that 79 workers (79%) who called in sick were women.

Table 2: The Frequency Distribution of Workers by Sex in Hospital in 2017

Sex	Total	Percentage (%)
Women	79	79
Men	21	21

Table 3 shows that 73 workers (73%) who called in sick were married.

Table 3: The Frequency Distribution of Workers by Marital Status in Hospital in 2017

Status	Total	Percentage (%)
Married	73	73
Unmarried	27	27

Table 4: Shows that 61 workers (61%) who called in sick had years of service of less than 5 years (see Table 4).

Table 4: The Frequency Distribution of Workers by Years of Service in hospital in 2017

Years of Service	Total	Percentage (%)
0 – 5 years	61	61
6 – 10 years	13	13
11 – 15 years	13	13
16 – 20 years	9	9
>20 years	4	4

Most of the workers (79%) submitted short term sickness absence (see Table 5).

Table 5: The Frequency Distribution of Workers by Attendance in Hospital in 2017

Attendance	Total (n)	Percentage (%)
Short term	79	79
Long term	21	21

Nagelkerke R Square in Table 6 shows a value of 0.16 or 16%. This means that the dependent variable can be explained by 16% independent variables. That is, all independent variables affect the dependent variable simultaneously in the range of 16%, while 84% are influenced or explained by variables not included in this study.

Table 6: Model parameter estimation test

Step	-2 Log Likelihood	Cox & Snell R Square	Nagelkerke R Square
1	101,728 ^a	,011	,016

It can be seen in Table 7 that the p-value (sig.) is more than 0.05, meaning that age, years of service, marital status and sex not significantly influence the types of sickness absence.

Table 7: Univariable Significance Test Results

	S.E.	P Value	Exp(B)	95% C.I.for EXP(B)	
				Lower	Upper
Age	,554	,659	,783	,264	2,322
Years of Service	,291	,620	,866	,490	1,530
Marital Status	,618	,773	,837	,249	2,809
Sex	,637	,929	,945	,271	3,295
Constant	1,402	,793	,692		

Discussion

As many as 56% of workers who submitted sick letters were aged 26-45 years. This is consistent with a cross sectional study conducted on 1200 workers by Sorevi et al (2013) at Mazandaran university hospital, where the frequency of sickness absence was most common among workers aged 38 - 41 years.⁽⁴⁾ Likewise, the study conducted by Isah et al (2008) concluded that the number of sickness absence was significantly correlated with the age of workers.⁽⁵⁾

Of the 100 people who submitted sick letters, 79% of them were women. This is consistent with a 602 nurse cross sectional study in Brazil in 2008-2012 conducted by Marques et al (2015) which stated that 92.9% of sickness absence were female nurses.⁽⁶⁾ According to Kurniawidjaja (2010), female workers, especially those who are married, are more often called in sick because they have multiple roles, that is, aside from work duties, they also have to provide domestic services to their children and husbands, plus the role of educating children so that they have no problems in their studies.^(6,7)

About 73% of those who called in sick were married. According to Kurniawidjaja (2010), sickness absence of married workers is related to household problems such as divorce, children and workload. In fact, women who are married have a higher sickness absence or absenteeism in general, and non-medical factors are thought to contribute.⁽⁷⁾

Workers with the years of service less than 5 years submitted most sick letters, amounting to 61%. This is consistent with the research of Linggarwati et al (2017) which stated that workers with short years of service will be more likely to be absent which may be because

they are still adjusting to the environment and workplace conditions. Workers who have worked for years have better attendance because they do not need to adjust to the environment or working conditions.⁽⁸⁾ According to Kurniawidjaja (2010), workers with longer years of service usually have fewer sickness absence than those who have worked for less than a year, presumably because older workers have better working relationships.⁽⁷⁾

79% of workers submitted short term sickness absence. This is in accordance with Kurniawidjaja's opinion which stated that 80-90% of sickness absence are short-term ones. Usually, short-term sickness absence is acute and mild in nature, such as diarrhea, red eye disease, common cold or sore throat. However, if it occurs 12 times or more in one year, for example 3 to 6 times in 3 months, the risk factors and pattern need to be analyzed both medically and non-medical.⁽⁷⁾ The study conducted by Tripathi et al (2010) on 385 nurses in India concluded that two-thirds of sickness absence were short-term absences and this was attributed to the low morale of workers.⁽⁹⁾

Based on variable statistical test, age, years of service, gender and marital status did not significantly influence the types of sickness absence. This was consistent with studies conducted by Mollazadeh et al (2018) in hospital workers in Iran, which concluded that there was no correlation between sex and marital status with workers' absenteeism.⁽³⁾ This result is also supported by a research conducted by Linggarwati (2017) concluding that sickness absence does not have a significant relationship with age, gender, years of service and level of education. From the results of statistical tests, the variables of age, years of service, gender and marital status have an effect of about 16%, while 84% are influenced or explained by variables not included in this study.⁽⁸⁾ According to Kurniawidjaja (2010) there are 3 factors influencing sickness absence, which are individual factors, geographical factors and organisational factors.⁽⁷⁾ The unanalysed factors of this study include geographical factors, comprising of climate, ethnicity, epidemic, insurance system, retirement age. While organisational factors include company scale, work type, occupational hazard, work shift, personal policy, health facility and industrial relationship. While the individual factors that have not been analyzed from this study are job satisfaction, distance of travel to work, social activities.

Conclusions

Based on the results of the analysis it can be concluded that there is no significant relationship between individual factors with the types of sickness absence. Limitations in this study are limited to only a few individual factors. Subsequent research will be better if it is complemented by the inclusion of variables of organizational factors and geographical factors in the analysis of sickness absence.

Conflict of Interest Statement: The authors of this research declare that there is no conflict of interest related to this study.

Because it uses secondary data. This study does not use ethical tests

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References

1. Donovan TL, Moore KM, VanDenKerkhof EG. Employee absenteeism based on occupational health visits in an urban tertiary care Canadian hospital. *Public Health Nurs.* 2008;
2. Duclay E, Hardouin JB, Sébille V, Anthoine E, Moret L. Exploring the impact of staff absenteeism on patient satisfaction using routine databases in a university hospital. *J Nurs Manag.* 2015;
3. Mollazadeh M, Saraei M, Mehrdad R, Izadi N. Sickness absenteeism of Healthcare Workers in a Teaching Hospital. *Hosp Pract Res.* 2018;3(1):6–10.
4. Mohseni Saravi B, Kabirzadeh A, Rezazadeh E, Khariki MF, Asgari Z, Bagherian Farahabadi E, et al. Prevalence and causes of medical absenteeism among staff (case study at mazandaran university of medical sciences: 2009-2010). *Mater Sociomed.* 2013;
5. Isah EC, Omorogbe VE, Orji O, Oyovwe L. Self-reported absenteeism among hospital workers in benin city, Nigeria. *Ghana Med J.* 2008;
6. Marques D de O, Pereira MS, Souza ACS e, Vila V da SC, Almeida CCO de F, Oliveira EC de. Absenteeism – illness of the nursing staff of a university hospital. *Rev Bras Enferm.* 2015;68(5):876–82.
7. Kurniawidjaja LM. *Teori dan Aplikasi Kesehatan Kerja.* Penerbit Universitas Indonesia; 2010.
8. Linggarwati YP, Nawawinetu ED. The Correlation of Individual Factors with Absenteeism Among Textile Industry Workers in Surabaya (PT X) During 2013. *J Vocat Heal Stud.* 2017;
9. Tripathi M, Mohan U, Verma R, Masih L, Pandey HC. Absenteeism among nurses in a tertiary care hospital in India. *Natl Med J India.* 2010;

Climate Variability and Dengue Hemorrhagic Fever in Surabaya, East Java, Indonesia

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Abstract

Background: Dengue hemorrhagic fever is an arboviral infectious disease that has occurred frequently as an extraordinary event due to its fast spread and lethal potential in Indonesia. The vector *Aedes aegypti* is sensitive to climate variability. This study determines the relationship between climate variability and dengue hemorrhagic fever in Surabaya, East Java, Indonesia from 2009 to 2017.

Subject and Method: This study used the monthly dengue hemorrhagic fever incidence obtained from the Surabaya Health Office and the monthly climate variability parameters (average temperature, rainfall, humidity) obtained from the Indonesian Agency for Meteorology, Climatology and Geophysics and website www.worldweatheronline.com. Data analysis was done using One-Sample *Kolmogorov Smirnov Test* and Spearman non-parametric correlation test.

Results: The results showed a correlation between all three climate variability parameters with dengue hemorrhagic fever incidence (average temperature $p < 0.05$, $r = -0.603$; rainfall $p < 0.05$, $r = 0.407$; humidity $p < 0.05$, $r = 0.7$).

Conclusion: Average temperature is negatively correlated to dengue hemorrhagic fever incidence, while rainfall and humidity are positively correlated to dengue hemorrhagic fever incidence. This study shows preliminary evidence on the correlation of climate variability and dengue hemorrhagic fever in Surabaya, East Java, Indonesia.

Keywords: *Climate variability; dengue hemorrhagic fever incidence; average temperature; humidity; rainfall; Surabaya*

Background

Dengue fever (DF), an infectious disease, and its more severe manifestation dengue hemorrhagic fever (DHF) are the fastest emerging arboviral infectious disease in tropical and subtropical countries. It is estimated 2.5

billion people are at risk of dengue infection, while an estimated 50 million dengue infections occur worldwide with 500 thousand people requiring hospitalization for DHF annually¹.

The first reported cases of DHF in Indonesia occurred in Jakarta and Surabaya in 1968². The incidence rate has increased ever since with expanding endemic regions and has affected most of the provinces in East Java^{3,4}. Surabaya was recorded as the province with the highest DHF incidence rate in East Java back in 2012³, with very high coping range index (CRI) levels in 2007-2009 and 2011-2012⁵.

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DF and DHF are caused by dengue viruses (DENV), which form the dengue complex in the genus *Flavivirus*, family *Flaviviridae*. This self-limited, systemic viral infection is caused by four antigenically related viruses (DENV 1-4) found circulating in the tropical and subtropical regions of the world^{6,7} and transmitted by the female *Aedes aegypti* and *Aedes albopictus* mosquito species. As a tropical country, Indonesia with a monsoonal wet season and a dry season provide an optimum habitat to support the breeding of *Aedes aegypti* mosquitoes and spread of its virulent infection⁸. Climate variability plays an important role in the epidemiology of vector-borne diseases That affects human health and spread of diseases. It is a complex study that requires a thorough understanding of the links with the climate and disease⁹. Examples of the climatic variables included in climatic factors are qualitatively the temperature, humidity and rainfall^{10,11}.

Further quantitative analysis needs to be done to understand dengue dynamics with climate¹³. There is no specific treatment available to treat the virus and efforts to curb dengue transmission in South-East Asia region are not largely successful¹. Recent findings also found an increasing trend for global dengue epidemic potential in temperate regions over time¹⁴.

To date, there are only a few research studies¹⁵ done on the effect of climatic variables on the spread of DHF in Surabaya. Therefore, the aim of this study is to investigate the relationship between climate variability and dengue transmission in Surabaya, to be able to plan effective vector control and DHF surveillance programs to prevent the endemicity of DHF in Surabaya.

Subjects and Method: This study was an ecological descriptive study with a retrospective time-series analysis approach. This study was conducted in Surabaya, a city area with 326.37 km²¹⁶, with a sample size of 2,862,406 inhabitants.

The secondary data DHF cases and climatic data from 2009 to 2017 were collected. DHF case incidence data diagnosed based on WHO clinical criteria and obtained from the Surabaya City Health Office. Climatic data which were the average temperature, rainfall and humidity were collected from the Indonesian Agency for Meteorology, Climatology and Geophysics and the public online website www.worldweatheronline.com.

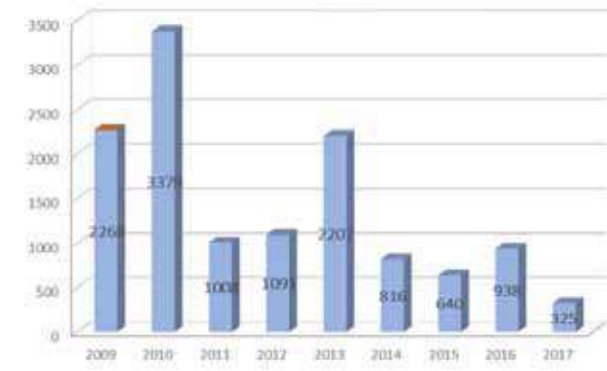
SPSS statistical software package version 16.0 was used for the statistical analysis. One-Sample *Kolmogorov Smirnov* Test was used to evaluate the cumulative distribution function for the data. The Spearman non-parametric correlation test was used to examine the relationship between monthly climatic data and DHF incidence.

Results

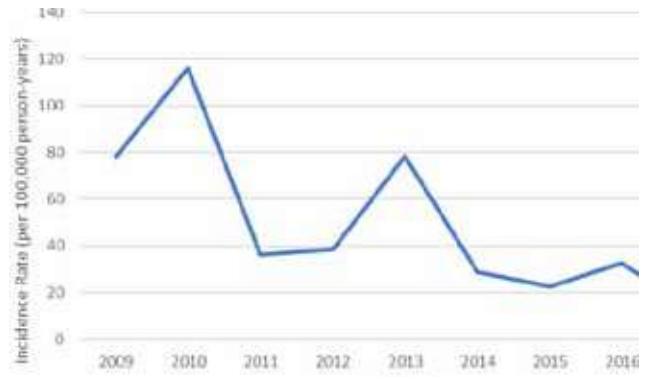
1. Profile of Dengue Hemorrhagic Fever Incidence from 2009 to 2017 in Surabaya, Indonesia

During the study period from 2009 to 2017, there were 12,672 dengue hemorrhagic fever (DHF) cases reported (Figure 1 (a)), with the highest in 2010 (3379 cases, IR of 116 per 100,000 person-years), and the lowest in 2017 (325 cases, IR of 11.3 per 100,000 person-years). Total DHF cases and IR incidence rate (Figure 1 (b)) had sudden increases in 2013 and 2016, while CFR (Figure 1 (c)) was the highest in 2014 (2.1) and lowest in 2009 (0.3).

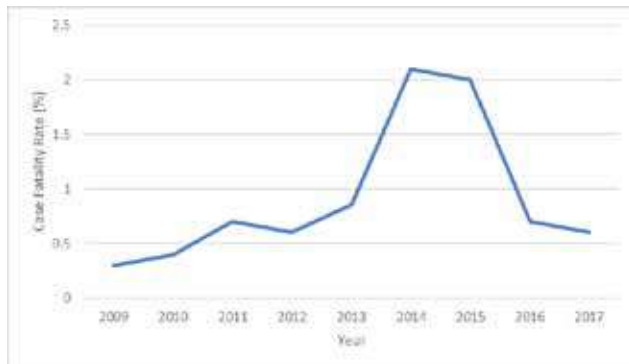
DHF cases recorded were highest from March to May and were the lowest in September (Figure 1 (d)). Monthly DHF cases fluctuated similarly to the monthly rainfall (Figure 1 (f)) and monthly humidity (Figure 1 (g)), while the monthly average temperature had a low thermal variation of less than 10 degree Celsius (Figure 1 (e)).



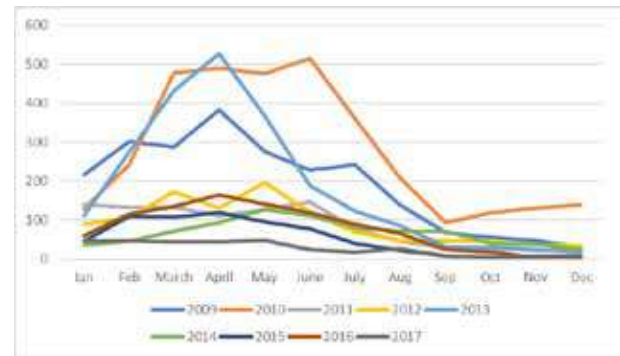
(a)



(b)



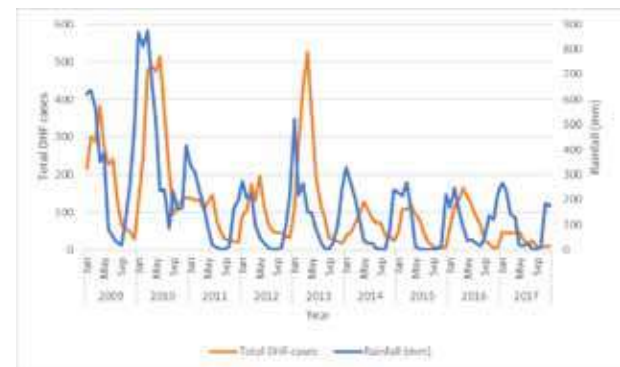
(c)



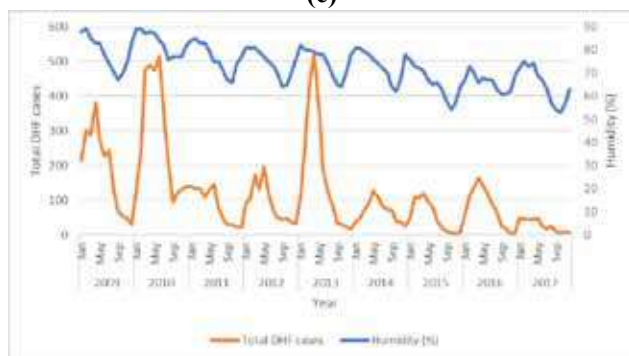
(d)



(e)



(f)



(g)

Figure 1: Profile of DHF cases from 2009 to 2017 in Surabaya, Indonesia (a) Annual total DHF cases (b) Incidence rate (IR) of DHF cases (c) Case fatality rate (CFR) of DHF cases (d) Monthly total DHF cases (e) Monthly average temperature and monthly DHF cases (f) Monthly rainfall and monthly DHF cases (g) Monthly humidity and monthly DHF cases

2. Relationship between Climate Variability and Dengue Hemorrhagic Fever

The One-Sample *Kolmogorov Smirnov* Test showed that the monthly average temperature, monthly rainfall, monthly humidity and monthly total DHF cases from 2009 to 2017 were not in normal distribution (p -value = 0.000).

Spearman non-parametric correlation test found significant correlations (p = 0.01) between monthly average temperature and monthly total DHF cases (r = -0.603); between monthly rainfall and monthly total DHF cases (r = +0.407); and between monthly average humidity and monthly total DHF cases (r = +0.700).

Discussion

1. Profile of Dengue Hemorrhagic Fever Incidence from 2009 to 2017 in Surabaya, Indonesia:

It is difficult to say whether the DHF case profile in Surabaya from 2009 to 2017 has improved compared to previous decades due to the fluctuating trend pattern of DHF cases over the past 50 years².

The “down sloping” trend of DHF incidence in recent years could be due to the effective surveillance and vector control programs carried out by the Surabaya City health officials¹⁷. Thermal fogging, mass larviciding, insecticides, and health awareness programs were reasonably successful in eradicating dengue transmission¹⁸. However, the intermittent spikes of CFRs over the study period could be due to the lack of awareness amongst the community albeit effective government mosquito-control regimes¹⁹. The complex dynamics of climate also influenced the ecology and caused increased vector density after rainy seasons in Indonesia¹¹.

2. Relationship Between Climate Variability and Dengue Hemorrhagic Fever:

Ae. aegypti population dynamics are sensitive to changes in temperature, and the survival of the species increased in general when temperatures increased^{30,31}. Kramer and Ebel found that adult mosquito survival rates were linked with lower temperatures³² while Lambrechts et al. found that vector competence is reduced in *Ae. aegypti* for flaviviruses when the mean temperature fluctuations are above 18°C, and increases when the mean temperature fluctuations are below 18°C³³. Increased rainfall increases the potential breeding sites of *Aedes* mosquitoes³⁴, leading to an increased propagation of mosquitoes, increased

vector density¹⁰, and increased risk of dengue virus transmission. This relationship is unclear though because *Ae. aegypti* is a domesticated species that breeds indoor primarily³⁵. However, it is possible that the domestication process of mosquitoes may increase its competence to transmit human virus³⁶, because the oviposition behavior of vectors in different environments still remain unknown³⁷. Flooding may also increase the vector densities and increase dengue virus transmission rate³⁸⁻⁴⁰. This is because more breeding conditions of *Aedes* mosquitoes are formed when the increased water levels during floods recede⁴¹.

The rising humidity influences the feeding pattern of *Aedes* mosquitoes, increasing the survival and lifespan of the mosquitoes³⁴. Humidity was also found to be the most reliable indicator in dengue incidence models due to its more stable impact on dengue incidence²⁷. Several studies found significant correlations between humidity and dengue cases with seasonal periodicities^{22,42}. However, there is cautioning to interpret the results of this climate variable due to its biological causation from rainfall and temperature⁴². This is because the humidity is influenced by the rainfall and temperature of a region.

3. Limitations of Study: The limitations of this study are the unconfirmed and underreported DHF cases, and the mosquito spatial distribution abundance and virulence. Other determinants not studied were the non-climatic factors socioeconomic development, vector control capacity, surveillance programs, drainage cleaning programs in Surabaya, herd immunity for DENV, increased human mobility, altered human-host interaction, demographic changes and regional climate phenomenon such as ENSO.

4. Implications of Research: The findings of this study will provide new evidence on the relationship between climate variability and DHF in Surabaya in recent years and may aid in the development of disease prediction models in the future. The application of these findings into public health measure designs may help mitigate the transmission risk of dengue disease.

Conclusion

From our findings, it is concluded there is a significant correlation between climate variability and DHF incidence in Surabaya, East Java, Indonesia from 2009 to 2017. The application of these findings into public health measure designs may help mitigate the transmission risk of dengue disease.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflict of interest.

Ethical Clearance: This study has received ethical clearance from the Ethical Review Committee of the Faculty of Medicine, Universitas Airlangga and the Department of National Unity, Politics and Community Safety of Surabaya (*BAKESBANGPOL*)

Reference

1. WHO. Comprehensive Guidelines for Prevention and Control of Dengue and Dengue Haemorrhagic Fever. SEARO Technical Publication; 2011. doi:10.1017/CBO9781107415324.004.
2. Karyanti MR, Uiterwaal CSPM, Kusriastuti R, et al. The Changing Incidence of Dengue Haemorrhagic Fever in Indonesia: A 45-year Registry-Based Analysis. *BMC Infect Dis.* 2014;14(1):412. doi:10.1186/1471-2334-14-412.
3. East Java Province Health Office. 2012 East Java Province Health Profile. 2012th ed. East Java Province: East Java Province Health Office; 2012. http://dinkes.jatimprov.go.id/userfile/dokumen/1380615402_PROFIL_KESEHATAN_PROVINSI_JAWA_TIMUR_2012.pdf.
4. Simmons CP, Farrar JJ, van Vinh Chau N, Wills B. Dengue. *N Engl J Med.* 2012;366(15):1423-1432. doi:10.1056/NEJMra1110265.
5. Akhtar R. Health Adaptation Scenario and Dengue Fever Vulnerability Assessment. In: Rais Akhtar, ed. *Climate Change and Human Health Scenario in South and Southeast Asia*. Springer; 2016:290. doi:10.1007/978-3-319-23684-1.
6. Lambrechts L, Scott TW, Gubler DJ. Consequences of The Expanding Global Distribution of *Aedes Albopictus* for Dengue Virus Transmission. *PLoS Negl Trop Dis.* 2010;4(5). doi:10.1371/journal.pntd.0000646.
7. Beasley D, Barrett A. The Infectious Agent. In: G P, SL H, eds. *The Infectious Agent. Dengue*. Vol. 5. Imperial College Press; Covent Garden, London, UK; 2008:29-73. https://books.google.co.id/books?id=M127CgAAQBAJ&pg=PA29&lpg=PA29&dq=The+Infectious+Agent.+by+beasley&source=bl&ots=vcM-W8tTO_&sig=tDIHr16--cLQ_teBtQnd9xtellA&hl=en&sa=X&ved=0ahUKEwiHsz96KbXAhUKs48KHYNB9oQ6AEISzAI#v=onepage&q=The Infectious Agent. by be.
8. WHO. Dengue: Guidelines for Diagnosis, Treatment, Prevention, and Control. *Spec Program Res Train Trop Dis.* 2009:147. doi:WHO/HTM/NTD/DEN/2009.1.
9. Epstein PR. Climate Change and Emerging Infectious Diseases. *Microbes Infect.* 2001;3(9):747-754. doi:10.1016/S1286-4579(01)01429-0.
10. Xu L, Stige LC, Chan K, et al. Climate Variation Drives Dengue Dynamics. *Proc Natl Acad Sci U S A.* 2017;114(1):113-118. doi:10.1073/pnas.1618558114.
11. Naish S, Dale P, Mackenzie JS, McBride J, Mengersen K, Tong S. Climate Change and Dengue: A Critical and Systematic Review of Quantitative Modelling Approaches. *BMC Infect Dis.* 2014;14(1):167. doi:10.1186/1471-2334-14-167.
12. Costa EAPDA, Santos EMDM, Correia JC, Albuquerque CMR De. Impact of Small Variations in Temperature and Humidity on The Reproductive Activity and Survival of *Aedes aegypti* (Diptera, Culicidae). *Rev Bras Entomol.* 2010;54(3):488-493. doi:10.1590/S0085-56262010000300021.
13. Semenza JC, Menne B. Climate Change and Infectious Diseases in Europe. *Lancet Infect Dis.* 2009;9(6):365-375. doi:10.1016/S1473-3099(09)70104-5.
14. Liu-Helmersson J, Stenlund H, Wilder-Smith A, Rocklöv J. Vectorial Capacity of *Aedes aegypti*: Effects of Temperature and Implications for Global Dengue Epidemic Potential. *PLoS One.* 2014;9(3):10. doi:10.1371/journal.pone.0089783.
15. Yudhastuti R, Satyabakti P, Basuki H. Climate Conditions, Larvae Free Number, DHF Incidence in Surabaya Indonesia. *J US-China Public Adm.* 2013;10(11):1043-1049. https://s3.amazonaws.com/academia.edu.documents/34419333/JUCPA_Volume_10_Number_11_November_2013.pdf?AWSAccessKeyId=AKIAIWOWYYGZ2Y53UL3A&Expires=1509976793&Signature=QTUa15mhyRhKszb4NatAOBAtedw%3D&response-content-disposition=inline%3B filename%3DJUCPA_Vo.
16. Ministry of Health Republic of Indonesia. Indonesian Health Profile. (drg. Rudy Kurniawan MK;, Boga Hardhana, S.Si M;, Yudianto, SKM MS, eds.); 2017.

17. Kusriastuti R, Sutomo S. Evolution of Dengue Prevention and Control Programme in Indonesia. Vol 29.; 2005. <https://pdfs.semanticscholar.org/6061/a77e16a69fce0c16c07f1243756e9b940ca9.pdf>. Accessed September 27, 2018.
18. Prasittisuk C, Andjaparidze AG, Kumar V. Current Status of Dengue/Dengue Haemorrhagic Fever in WHO South-East Asia Region. Vol 22.; 1998. http://apps.searo.who.int/PDS_DOCS/B0640.pdf. Accessed September 27, 2018.
19. Ahmad K. Dengue Death Toll Rises in Indonesia. *Lancet*. 2004;363(9413):956. doi:10.1016/S0140-6736(04)15829-7.
20. Thammapalo S, Chongsuwiatwong V, McNeil D, Geater A. The Climatic Factors Influencing The Occurrence of Dengue Hemorrhagic Fever in Thailand. *Southeast Asian J Trop Med Public Health*. 2005;36(1):191-196. <http://www.ncbi.nlm.nih.gov/pubmed/15906666>. Accessed September 19, 2018.
21. Lowe R, Bailey TC, Stephenson DB, et al. Spatio-Temporal Modelling of Climate-Sensitive Disease Risk: Towards An Early Warning System for Dengue in Brazil. *Comput Geosci*. 2011;37:371-381. doi:10.1016/j.cageo.2010.01.008.
22. Descloux E, Mangeas M, Menkes CE, et al. Climate-Based Models for Understanding and Forecasting Dengue Epidemics. Anyamba A, ed. *PLoS Negl Trop Dis*. 2012;6(2):e1470. doi:10.1371/journal.pntd.0001470.
23. Silva FD, Santos AM dos, Corrêa R da GCF, Caldas A de JM. Temporal Relationship Between Rainfall, Temperature and Occurrence of Dengue Cases in São Luís, Maranhão, Brazil. *Cien Saude Colet*. 2016;21(2):641-646. doi:10.1590/1413-81232015212.09592015.
24. Su GLS. Correlation of Climatic Factors and Dengue Incidence in Metro Manila, Philippines. *Ambio*. 2008;37(4):292-294. <http://www.ncbi.nlm.nih.gov/pubmed/18686509>. Accessed December 12, 2017.
25. United Nations. Urban Solid Waste Management: Surabaya, Indonesia. In: *Cities and Sustainable Development: Lessons and Experiences from Asia and the Pacific*. New York: United Nations Publication; 2003:48-56. https://books.google.co.id/ks?id=RUZpW3pDnlgC&pg=PA48&lpg=PA48&dq=surabaya+experiences+near+constant+temperatures&source=bl&ots=bUzINxq78U&sig=umBomM0bvfMliCrOJ80f3vSfX34&hl=en&sa=X&ved=2ahUKewiM19ia_dvdAhWJvI8KHRmgCRIQ6AEwBXoECAAQAQ#v=onepage&q&f=false. Accessed September 28, 2018.
26. Wu X, Lang L, Ma W, et al. Non-Linear Effects of Mean Temperature and Relative Humidity on Dengue Incidence in Guangzhou, China. *Sci Total Environ*. 2018;628-629:766-771. doi:10.1016/J.SCITOTENV.2018.02.136.
27. Xu H-Y, Fu X, Lee LKH, et al. Statistical Modeling Reveals the Effect of Absolute Humidity on Dengue in Singapore. Barrera R, ed. *PLoS Negl Trop Dis*. 2014;8(5):e2805. doi:10.1371/journal.pntd.0002805.
28. Thi Diem Phuong L, Thi Tuyet Hanh T, Sinh Nam V. Climate Variability and Dengue Hemorrhagic Fever in Ba Tri District, Ben Tre Province, Vietnam during 2004–2014. *AIMS Public Heal*. 2016;3(4):769-780. doi:10.3934/publichealth.2016.4.769.
29. Chompoosri J, Thavara U, Tawatsin A, Anantapreecha S, Siriyasatien P. Seasonal Monitoring of Dengue Infection in *Aedes Aegypti* and Serological Feature of Patients with Suspected Dengue in 4 Central Provinces of Thailand. Vol 42.; 2012. https://www.researchgate.net/profile/Padet_Siriyasatien/publication/230868218_Seasonal_Monitoring_of_Dengue_Infection_in_Aedes_aegypti_and_Serological_Feature_of_Patients_with_Suspected_Dengue_in_4_Central_Provinces_of_Thailand/links/09e4150592208d590b000. Accessed September 28, 2018.
30. Ng K, Chaves LF, Tsai K, Chuang T. Abundance in A Dengue Transmission Hotspot , Compared to A Coldspot , Within Kaohsiung. *Insects*. 2018;9(3):1-16. doi:10.3390/insects9030098.
31. Grech MG, Sartor PD, Almirón WR, Ludueña-Almeida FF. Effect of Temperature on Life History Traits During Immature Development of *Aedes aegypti* and *Culex quinquefasciatus* (Diptera: Culicidae) from Córdoba City, Argentina. *Acta Trop*. 2015;146:1-6. doi:10.1016/J.ACTATROPICA.2015.02.010.
32. Kramer LD, Ebel GD. Dynamics of Flavivirus Infection in Mosquitoes. *Adv Virus Res*. 2003;60:187-232. <http://www.ncbi.nlm.nih.gov/pubmed/14689695>. Accessed September 24, 2018.

33. Lambrechts L, Paaijmans KP, Fansiri T, et al. Impact of Daily Temperature Fluctuations on Dengue Virus Transmission by *Aedes aegypti*. *Proc Natl Acad Sci U S A*. 2011;108(18):7460-7465. doi:10.1073/pnas.1101377108.
34. Focks DA, Haile DG, Daniels E, Mount GA. Dynamic Life Table Model for *Aedes aegypti* (Diptera: Culicidae): Analysis Of The Literature and Model Development. *J Med Entomol*. 1993;30(6):1003-1017. <http://www.ncbi.nlm.nih.gov/pubmed/8271242>. Accessed September 20, 2018.
35. Banks I, Brey PT, Hill N, et al. Risk Factors for the Presence of *Aedes aegypti* and *Aedes albopictus* in Domestic Water-Holding Containers in Areas Impacted by the Nam Theun 2 Hydroelectric Project, Laos. *Am J Trop Med Hyg*. 2013;88(6):1070-1078. doi:10.4269/ajtmh.12-0623.
36. Powell JR, Tabachnick WJ. History of Domestication and Spread of *Aedes aegypti*--A Review. *Mem Inst Oswaldo Cruz*. 2013;108 Suppl(Suppl 1):11-17. doi:10.1590/0074-0276130395.
37. Abreu FVS de, Morais MM, Ribeiro SP, Eiras ÁE. Influence of Breeding Site Availability on The Oviposition Behaviour of *Aedes aegypti*. *Mem Inst Oswaldo Cruz*. 2015;110(5):669-676. doi:10.1590/0074-02760140490.
38. Jiménez-Sastré A, Boldo-León X, Priego-Álvarez H, Quevedo-Tejero E, Zavala-González MA. Geographic Distribution of Dengue Fever Cases in Flooded Zones from Villahermosa, Tabasco, in 2010. *Rev Chil Infectología*. 2012;29(1):32-36. doi:10.4067/S0716-10182012000100005.
39. Anyamba A, Small JL, Britch SC, et al. Recent Weather Extremes and Impacts on Agricultural Production and Vector-Borne Disease Outbreak Patterns. Ikegami T, ed. *PLoS One*. 2014;9(3):e92538. doi:10.1371/journal.pone.0092538.
40. Brown L, Murray V. Examining The Relationship Between Infectious Diseases and Flooding in Europe: A Systematic Literature Review and Summary of Possible Public Health Interventions. *Disaster Heal*. 2013;1(2):117-127. doi:10.4161/dish.25216.
41. Hashizume M, Dewan AM, Sunahara T, Rahman MZ, Yamamoto T. Hydroclimatological Variability and Dengue Transmission in Dhaka, Bangladesh: A Time-Series Study. *BMC Infect Dis*. 2012;12(1):98. doi:10.1186/1471-2334-12-98.
42. Do TTT, Martens P, Luu NH, Wright P, Choisy M. Climatic-Driven Seasonality of Emerging Dengue Fever in Hanoi, Vietnam. *BMC Public Health*. 2014;14(1):1078. doi:10.1186/1471-2458-14-1078.

Associations Between TNF- α and Interleukin-18 and ADIPOQ Gene Polymorphisms in Iraqi Obese Women Patients with Polycystic Ovary Syndrome

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Abstract

Context: Polycystic ovary syndrome has always been an enigma, and it still continues to be. In addition to an ovulatory subfertility, women with PCOS show an increased danger of pregnancy complications, obesity, so the effect of this issue isn't simply constrained to reproductive age, however all through life. A total of (128) samples (50 normal Weight and 78 obese groups). Those samples were collected from the Kamal Al-Samarraie hospital, Ministry-of Health in Baghdad-Iraq from April 2017- August 2017. The aim of this present study was to detect association from polymorphism ADIPOQ gene (rs12495941) with risk of Polycystic ovary syndrome for Iraqi women patients and compare between ADIPOQ gene of Iraqi population with gene bank of NCBI. Examine Interleukin-18(IL-18), Tumor necrosis factor alpha (TNF- α) of Polycystic ovary syndrome Iraqi women patients. TNF- α , and IL-18 showed significant change ($p < 0.05$) in Obese with PCOS and low weight with PCOS groups when comparing with control group. followed by no-significant change ($p > 0.05$) when comparing between Obese without PCOS and low weight with PCOS groups, also shows significant change ($p < 0.05$) when comparing between low weight with PCOS and control group. The results show substitution three Transition A>G and G>A, six Transversion T>G, T>A, and C>A, showed 98% identified with a standard in Gene Bank from patients group while having 100% identified with a standard in Gene Bank with the control group.

Keywords: Polycystic ovary syndrome, Interleukin-18(IL-18), Tumor necrosis factor alpha (TNF- α), ADIPOQ gene.

Introduction

Polycystic ovary syndrome is the most well-known endocrinopathy influencing reproductive aged women. While some women may present symptomatic and others asymptomatic, it does affect women physically, psychologically, metabolically, endocrinologically and reproductively⁽¹⁾. The status was first portrayed in 1935 by the American gynecologists Irving F Stein and

Michael L Leventhal, both working at the Department of Obstetrics and Gynecology, Michael Reese Hospital, Chicago, USA from whom its original name of Stein-Leventhal syndrome was taken, they described the clinical, the macroscopic characteristics and histological features of PCOS for the first time⁽²⁾. TNF α is a dominant pro-inflammatory cytokine vital for immunity to infections and expressed mainly in monocytes, macrophages and adipose tissue. However, its extravagant production is contributory in chronic inflammation and disease pathology⁽³⁾. Studies on reproductive biology have proven that these pro-inflammatory cytokines promote ovarian function and the processes of ovulation, fertilization, and implantation in women with PCOS⁽⁴⁾. Moreover, TNF- α can also play an important role in the development of cardiovascular disease. A higher

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levels of TNF- α were reported to be connected with an increased risk of future myocardial infarction ⁽⁵⁾. IL-18 is a potent pleiotropic cytokine, member of the IL-1 family, ambidextrous to induce IFN gamma, GM-CSF, TNF alpha and IL-1 in immunocompetent cells, so as to activate death by lymphocytes, and to up-organize the expressing of chemokine and their receptors ⁽⁶⁾. Adiponectin is encoded by the gene ADIPOQ situated in the chromosomal area 3q27. It comprises of three exons and two introns, ⁽⁷⁾. Human adiponectin is encoded by the 16-kb gene recognized as ACDC (adipocyte C1q and collagen field containing gene). ACDC is situated in a district of chromosome 3 that has been appeared to contain a quantitative trait locus (QTL) connected to phenotypes identified with metabolic disorder ⁽⁸⁾. Several single-nucleotide polymorphisms (SNPs) and mutations of the ADIPOQ gene were shown in Japanese and Europe populations to be associated with obesity ⁽⁹⁾.

Materials and Method

Samples Collection: This case-control study involves of a total (128) samples (50 normal Weight and 78 obese groups) . Those samples was collected from the Kamal Al-Samarraie hospital, Ministry-of Health in Baghdad-Iraq from of April 2017- August 2017. Five milliliters of blood was collected from each patient and control then separate 2ml into EDTA tube and 3ml into gel tube after waiting for a minute centrifuged the tube at 3000 rpm for 5 min.

Measurements: Enzyme-linked immunosorbent assay (ELISA) were utilized to estimate the serum level of Human IL-18 ELISA Kit, and Tumor necrosis factor ELISA Kit according to the manufacturer’s instructions (bioaimscientific, and MabTag) respectively.

PCR Amplification: The DNA was extracted by utilizing (Geneaid DNA Mini Kit) according to manufacturer’s instructions, primer used in this study were ADIPOQ gene (rs12495941) sense F: (5'-TAGTGAGCCGAGATTGTGC -3') and a anti sense primer R: 5'-(TCCTTAGGCATGTAGCTTCC 3') obtained from AlphaDNA company (Xian Chang Sun *et al.*, 2017) . The PCR amplification is performed in a total volume of 25 μ l containing 1.5 μ l DNA, 12.5 μ l Green Master Mix PCR (Promega, USA), 1 μ l of each primer 10 pmol then nuclease-free water is added into a tube to a total volume of 25 μ l. Thermo cycling conditions were as follows: initial denaturation at 4 min at 94 $^{\circ}$ C, followed by 28 cycles of denaturation 94 $^{\circ}$ C for

30 sec, annealing at 62 $^{\circ}$ C for 30 sec, extension at 72 $^{\circ}$ C for 30 sec and a final extension of 72 $^{\circ}$ C for 5min. The PCR products were separated on 1% agarose gel. The gel is left to run for 60min with a 70volt/65 mAmp current. Following electrophoresis, visualization was conducted with a UV trans illuminator after ethidium bromide staining. The sequencing of ADIPOQ gene (rs12495941) gene was performed at Macrogen, utilizing their ABI 3730xl genetic analyzer (Applied Bio systems, US).

Statistical Analysis: The Statistical Analysis System-SAS (2014) program was utilized to impact of various factors in study parameters.. Least noteworthy contrast LSD test (ANOVA) was utilized to analyze between method between various factors in this study.

Result and Discussion

The levels of TNF-alpha , and IL-18 showed significantly change (p<0.05) in Obese with PCOS and low weight with PCOS groups when comparing with control group. followed by no-significant change (p>0.05) when comparing between Obese without PCOS and low weight with PCOS groups , also shows significant change (p<0.05) when comparing between low weight with PCOS and control group. As seen in table (1).

Table (1): Levels of TNF-alpha, IL-18 ,in PCOS women and healthy controls.

Parameters Groups	TNF-alpha (ng/ml) (mean \pm SD)	IL-18 (pg/ml) (mean \pm SD)
Group 1 (Obese with PCOS)	A 1.2040 \pm 0.5796	A 26.139 \pm 3.660
Group 2 (low weight with PCOS)	B 0.5674 \pm 0.0655	B 12.832 \pm 0.266
Group 3 (Obese without PCOS)	B 0.6426 \pm 0.0517	B 12.391 \pm 0.297
Group 4 Healthy control	C 0.3456 \pm 0.0852	C 3.040 \pm 0.377
LSD	0.209	3.275
P-value	0.0073	0.0069
Significant	Significant	Significant

*different letters mean significant difference

Adipose tissue discharges a cytokine called TNF-a which is a key component in mediating IR ⁽¹⁰⁾. This cytokine not only stimulates IR but also causes HA and is present in follicular development. It therefore plays a part in the pathophysiology of PCOS. Development of

IR in humans has been linked to hyper expression of the TNF-a in muscle and adipose tissues through decreasing tyrosine kinase activity in the insulin receptors. Our test results corroborated those of⁽¹¹⁾. In their experiment they found that there were significant differences between PCOS patients in serum TNF-a and insulin. ⁽¹²⁾found that TNF-a levels in PCOS patients were significantly higher than those in controlled studies. When ^(13,14) carried out tests they found that women with PCOS exhibited higher levels of IL18 than controlled groups. In both the aforementioned studies the level of IL18 correlated to the insulin sensitivity index. More recent tests have shown that there is no difference in IL18 between obese PCOS and the obese control group. This reveals that when obesity is controlled, the PCOS effect disappears completely ⁽¹⁵⁾ posits that in the future, studies should classify subjects according to BMI classes so as to better highlight the independent association among IL18 and PCOS⁽¹⁶⁾.

One and a half µl of genomic DNA was used for each PCR reaction. A conventional PCR protocol was utilized to analyze simultaneously the presence of ADIPOQ gene(rs12495941). The presence of the ADIPO gene(rs12495941) was identified by 360bp, as shown in figure(1).

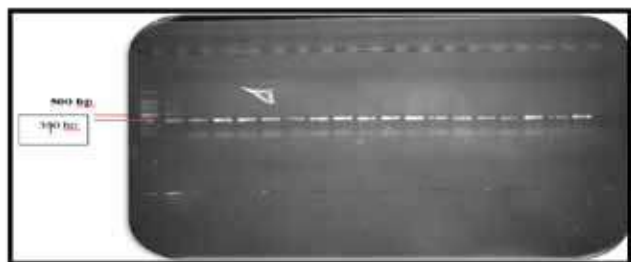


Figure (1): Amplified fragment of Adiponectingene ((RS:12495941)after electrophoresis on agarose gel (2%) for 1x TBE buffer for 1:30 hours. M: DNA ladder (100bp).

The repeat of nucleotide the amplified product of ADIPOQ gene (rs12495941) gene by direct sequencing. Our sequences were compared with the reference sequence from in national center biotechnology information(NCBI) Gene Bank.

After alignment of product amplification of ADIPO gene for patients group having three Transition one A>G and two G>A in Locations (15655, 15679,and 15685nucleotide)respectively, six Transversion T>G, C>A, and fourT>A in Locations (15429,15719, 15671, 15713, 15715, 15731nucleotide) under sequence ID: NG_021140.1, and have number score (685) bits, and expect (0.0). From the Gene Bank, found that part of ADIPOQ gene having 98% compatibility with standard in Gene Bank as shown in Figure(2), and table(2).

Table (2): Represent type of polymorphism of ADIPOQ gene.

Sequence ID	Nucleotide	Location	Type of substitution
ID: NG_021140.1	T>G	15429	Transversion
	A>G	15655	Transition
	T>A	15671	Transversion
	G>A	15679	Transition
	G>A	15685	Transition
	T>A	15713	Transversion
	T>A	15715	Transversion
	C>A	15719	Transversion
	T>A	15731	Transversion

Homo sapiens adiponectin, C1Q and collagen domain containing (ADIPOQ), RefSeqGene on chromosome 3 Sequence ID: NG_021140.1

Score	Expect	Identities	Gaps	Strand
685 bits(759)	0.0	393/402(98%)	0/402(0%)	Plus/ Plus

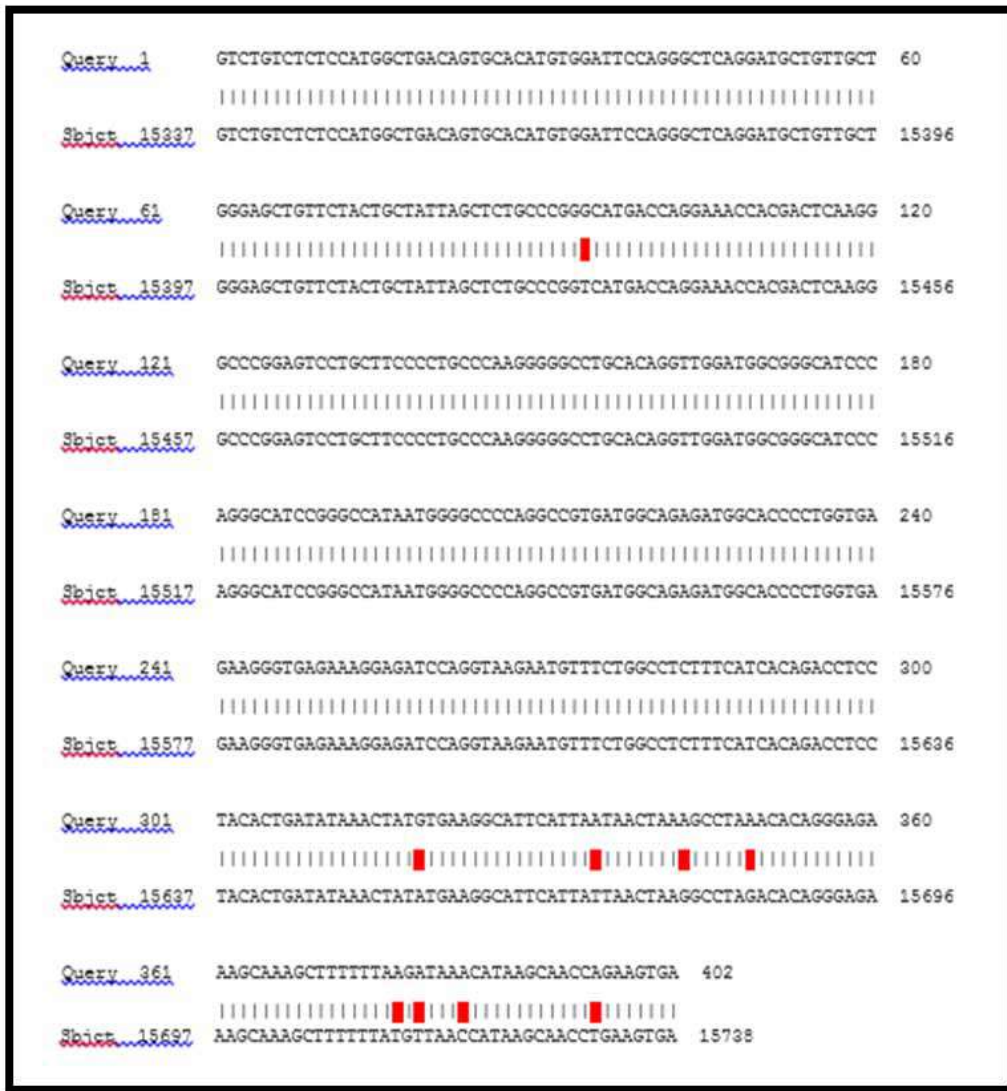


Figure (2): Alignment analysis of ADIPOQ gene of patients group with Gene Bank of NCBI. Query represents from the sample; Subject represents a database of National Center Biotechnology Information (NCBI).

Compatibility of 100% in Gene Bank ADIPOQ gene as shown in figure (3) under sequence ID: NG_021140.1, and have number score (430) bits, so no recorded change noticed from the Gene Bank in ADIPOQ gene for control group.

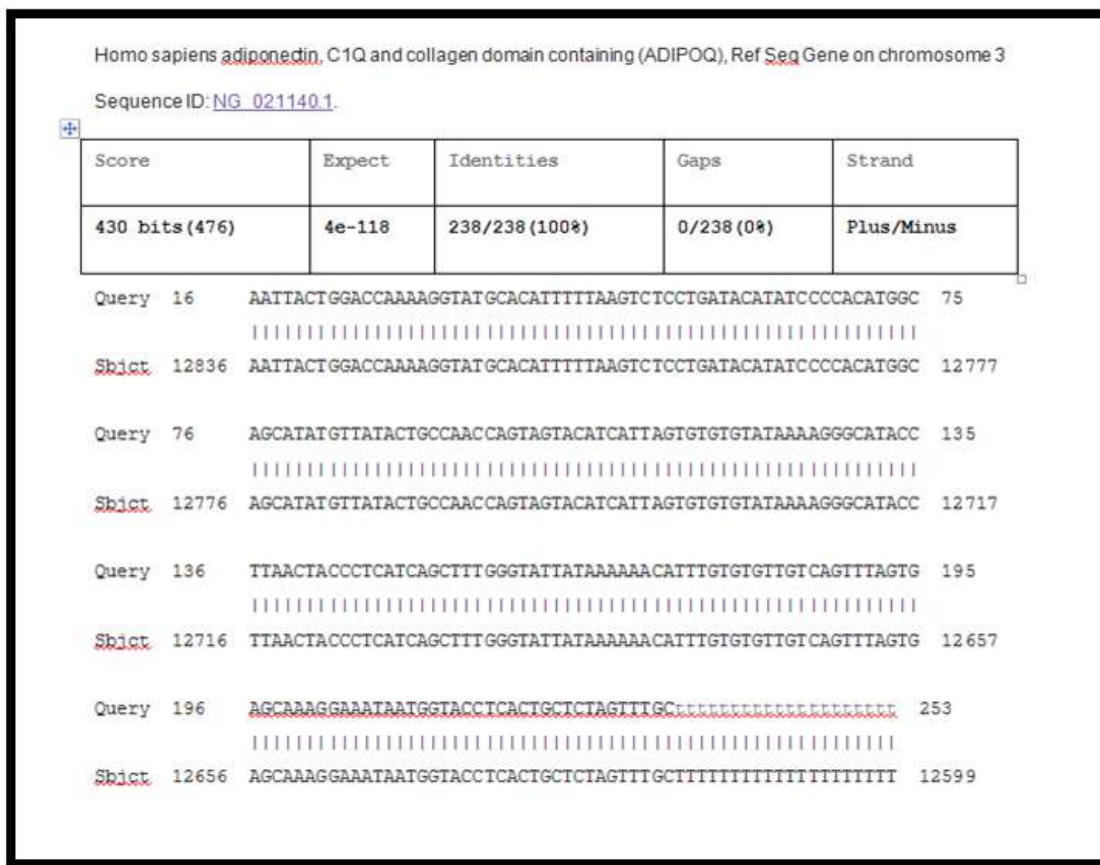


Figure (3): Alignment analysis of ADIPOQ gene of Control group with Gene Bank of NCBI. Query represents from the sample; Subject represents a database of National Center Biotechnology Information (NCBI).

Conclusions

Our study concluded in patients of Polycystic ovary syndrome is increased as compared to healthy controls as evidenced by increased (TNF- α , IL-18) in patients group. ADIPOQ gene having 98% compatibility from patients group while having 100% compatibility of the control group with a standard in Gene Bank

Conflict of Interest: There is no conflict of interest among the authors.

Funding: Self

Ethical Clearance: This study is ethically approved by the Institutional ethical Committee.

References

1. Brady C, Mousa SS, Mousa SA. Polycystic ovary syndrome and its impact on women’s quality of life: More than just an endocrine disorder. Drug, healthcare and patient safety. 2009;1:9.
2. Stein IF. Amenorrhea associated with bilateral polycystic ovaries. Am J Obstet Gynecol. 1935;29:181-91.
3. Chen L, Deng H, Cui H, Fang J, Zuo Z, Deng J, Li Y, Wang X, Zhao L. Inflammatory responses and inflammation-associated diseases in organs. Oncotarget. 2018 Jan 23;9(6):7204.
4. Zangeneh FZ, Naghizadeh MM, Masoumi M. Polycystic ovary syndrome and circulating inflammatory markers. International Journal of Reproductive BioMedicine. 2017 Jun;15(6):375.
5. Popa C, Netea MG, Van Riel PL, Van Der Meer JW, Stalenhoef AF. The role of TNF- α in chronic inflammatory conditions, intermediary metabolism, and cardiovascular risk. Journal of lipid research. 2007 Apr 1;48(4):751-62.
6. Coondoo A. Cytokines in dermatology—a basic overview. Indian journal of dermatology. 2011 Jul;56(4):368.

7. Labib M, Green B, Mohamadi RM, Mephram A, Ahmed SU, Mahmoudian L, Chang IH, Sargent EH, Kelley SO. Aptamer and antisense-mediated two-dimensional isolation of specific cancer cell subpopulations. *Journal of the American Chemical Society*. 2016 Feb 22;138(8):2476-9.
8. Kissebah AH, Sonnenberg GE, Myklebust J, Goldstein M, Broman K, James RG, Marks JA, Krakower GR, Jacob HJ, Weber J, Martin L. Quantitative trait loci on chromosomes 3 and 17 influence phenotypes of the metabolic syndrome. *Proceedings of the National Academy of Sciences*. 2000 Dec 19;97(26):14478-83.]
9. Kaur H, Badaruddoza B, Bains V, Kaur A. Genetic association of ADIPOQ gene variants (-3971A>G and+ 276G> T) with obesity and metabolic syndrome in North Indian Punjabi population. *PloS one*. 2018 Sep 28;13(9):e0204502.
10. Sun X, Wu X, Duan Y, Liu G, Yu X, Zhang W. Family-based association study of rs17300539 and rs12495941 polymorphism in adiponectin gene and polycystic ovary syndrome in a Chinese population. *Medical science monitor: international medical journal of experimental and clinical research*. 2017;23:78.
11. Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, Janssen OE, Legro RS, Norman RJ, Taylor AE, Witchel SF. Criteria for defining polycystic ovary syndrome as a predominantly hyperandrogenic syndrome: an androgen excess society guideline. *The Journal of Clinical Endocrinology & Metabolism*. 2006 Nov 1;91(11):4237-45.
12. Thathapudi S, Kodati V, Erukkambattu J, Katragadda A, Addepally U, Hasan Q. Anthropometric and biochemical characteristics of polycystic ovarian syndrome in South Indian women using AES-2006 criteria. *International journal of endocrinology and metabolism*. 2014 Jan;12(1).
13. Gao L, Gu Y, Yin X. High serum tumor necrosis factor-alpha levels in women with polycystic ovary syndrome: a meta-analysis. *PloS one*. 2016 Oct 20;11(10):e0164021.
14. Escobar-Morreale HF, Villuendas G, Botella-Carretero JI, Alvarez-Blasco F, Sanchon R, Luque-Ramirez M, San Millan JL. Adiponectin and resistin in PCOS: a clinical, biochemical and molecular genetic study. *Human Reproduction*. 2006 May 4;21(9):2257-65.
15. Zhang YF, Yang YS, Hong J, Gu WQ, Shen CF, Xu M, Du PF, Li XY, Ning G. Elevated serum levels of interleukin-18 are associated with insulin resistance in women with polycystic ovary syndrome. *Endocrine*. 2006 Jun 1;29(3):419-23.
16. Kaya C, Pabuccu R, Berker B, Satiroglu H. Plasma interleukin-18 levels are increased in the polycystic ovary syndrome: relationship of carotid intima-media wall thickness and cardiovascular risk factors. *Fertility and sterility*. 2010 Mar 1;93(4):1200-7.

The Effect of Ladder Training on Selected Physical Variable among College Men Football Players

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Abstract

Context: The purpose of this study was to find out the Effect of ladder training on selected physical and physiological variables among college men football players. In order achieve the purpose of the study the thirty players from G.T.N Arts College and S.B.M College of Engg in Dindigul were taken as subjects. The age groups of the subjects were between 17 to 25 years. Thirty men football players were selected and the subjects were divided into two groups consist of 15 subjects. G.T.N Arts College acted as experimental group (group I) S.B.M College of Enggs acted as Control group (group II). Each subject was oriented in the procedure to the administration of the test. The subjects were formed a random group design consisting of Ladder training given to experimental group and control group, of 15 each, the control group not given any kind of Ladder training. After the experimental period of six weeks in progression, post test scores were obtained from all the two groups. The differences between initial and final scores on physical variable considered as the effect of Ladder training on subjects. The mean differences were tested for significance using 'F'-ratio set at 0.05. The result of the study reveals that ladder training would positively improve the college men football player Physical variable significantly.

Keywords: Ladder training, Speed, Football, Experimental group, Control group

Introduction

Physical Education is one of the most ancient arts of the humanities. In its broadest interpretation physical education is defined as the art and science of voluntary purposeful and active human movement.¹ It is clear that physical education is concerned with a fundamental mode of human expression.² Physical education and training organized instruction in motor activities will contribute to the physical growth, health, and body image of the individual. The historical roots of physical education go back as far as the ancient Chinese. 2500B.C, who had a well-developed system of exercise and physical training.

Fitness: Fitness is the ability to live a full and balanced life. The totally fit person has a healthy and

happy outlook on life. Fitness is the young man's absolute necessity.³ It breeds self-reliance and keeps man mentally alert. Physical fitness is essential for human beings to adjust well with his environment as his mind and body are in complete harmony.

Physical Fitness: The term "Physical" refers to movement, whereas the prefix "bio" is added to illustrate the biological importance of these three abilities.⁴ Physical Fitness is one's richest possession. It cannot be purchased. It has to be earned through a daily routine of physical exercises. It is self-evident that the fit citizens are a nation's best assets and weak ones its liabilities. Physical fitness is necessary for achieving success in sports without a high level of physical fitness and individual will not be able to withstand the stress and strain caused to the body by various games and sports. To achieve success in the international competitions and to attain high sports performance superior physical fitness is a must. Physical Fitness is the development and maintenance of strong physique and sound functioning of organs to the end.⁵

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Sports Training: It must be understood on a wider sense since physical exercises undoubtedly are the principle means to improving performance. But the sports performance is improved by other means also which should be included in the concept of sports training. Such means, which are most commonly used along with physical exercise, are theoretical instructions, discussions, and tasks of observations, physiotherapeutic measures for recovery from fatigue, psycho regulative procedures and so on.⁶

Ladder Training: The agility ladder is a time tested and proven effective tool for improving our footwork.⁷ The training effect is similar to jump rope, but with several advantages. First, agility ladder training is multi – directional. In most sports, we are not staying in one sport. We are moving forward, sideways and sometimes backwards, second, our feet are also allowed to move independently more complex patterns than jumprope allows. And third, the cycle time can be result is that you can train your feet to move quickly through complex footwork patterns. The benefits to any ground based sport are huge.

Statement of the Problem: The purpose of this study was to find out the Effect of ladder training on selected physical variable among college men football players.

Methodology: In order achieve the purpose of the study the thirty players from G.T.N Arts College and S.B.M College of Engg in Dindigul were taken as subjects. The age groups of the subjects were between 17 to 25 years. Thirty men football players were selected and the subjects were divided into two groups consist of 15 subjects. G.T.N Arts College acted as experimental group (group I), S.B.M College of Engg acted as Control group (group II). The subjects were formed a random group design consisting of Ladder training given to experimental group and control group, of 15 each, the control group not given any kind of Ladder training. After the experimental period of six weeks in progression, post test scores were obtained from all the two groups. The differences between initial and final scores on physical variable considered as the effect of Ladder training on subjects. The mean differences were tested for significance using ‘F’-ratio.

Administration of Test: Speed(50 meters)

Purpose: The aim of this test is to determine acceleration and speed.

Equipment: Measuring tape, stop watch, Chunnam, score sheet, subject, whistle, 10m thread, timer, pen etc.

Procedure: Maximum 50 meters standard track in 6 or 8 line, Warm up, including some practice. Standing position (hands cannot touch the ground), with one foot in front of the other. The front foot must be behind the starting line. Once the subject is ready and motionless, the starter gives the instructions “set” then “go”. The tester should provide hints for maximizing speed (such as keeping low, driving hard with the arms and legs) and the participant should be encouraged to not slow down before crossing the finish line.



Scoring: Two trials are allowed, and the best time is recorded to the nearest 2 decimal places.

The table 1 showed that the pre test mean values on speed of ladder training group and control group are 7.76 and 7.73 respectively. The obtained ‘F’ ratio 0.15 for pre test mean was less than the table value 4.20 for df 1 and 28 required for significance at 0.05 level of confidence on speed. The post-test mean values on speed of ladder training group and control group are 6.72 and 7.27 respectively. The obtained ‘F’ ratio 5.81 for post-test mean was greater than the table value 4.20 for df 1 and 28 required for significance at 0.05 level of confidence on speed. The adjusted post-test means of ladder training group and control group are 6.71 and 7.28 respectively. The obtained ‘F’ ratio 10.13 for adjusted post-test mean was greater than the table value 4.21 for df 1 and 27 required for significance at 0.05 level of confidence on speed.

The adjusted post mean values of ladder training group and control group on speed are graphically represented in the Figure 1.

Table 1: Analysis of Co-variance for the Pre, Post and Adjusted Post Test Mean Values for Ladder Training Group and Control Group on Speed

Test	Ladder Training Group	Control Group	Source of Variance	Sum of square	Df	Mean Square	'F' ratio	Table Value
Pre Test Mean	7.76	7.73	Between	0.009	1	0.009	0.15	4.20
			With in	17.525	28	0.626		
Post Test Mean	6.72	7.27	Between	2.296	1	2.296	5.81*	4.20
			With in	11.070	28	0.395		
Adjusted Post Test Mean	6.71	7.28	Between	2.447	1	2.447	10.13*	4.21
			With in	6.520	27	0.241		

*Significant at 0.05 level of confidence.

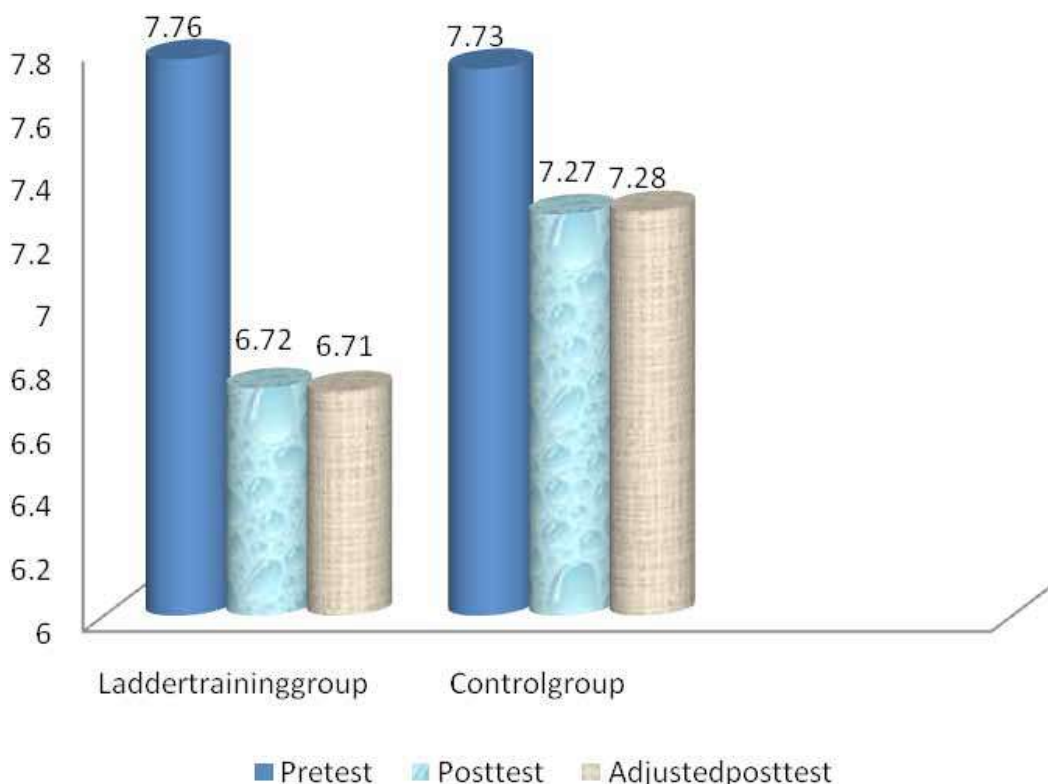


Figure 1: Bar Diagram Showing the Pre, Post and Adjusted Mean Values of Ladder Training Group and Control Group on Speed

Discussing on Findings: The goal of the investigation is to find whether there is any effect on those selected variables in the effect of Ladder training and further to find improvement on training group. The obtained 'F' ratio showed that there was significant difference between experimental groups and control group in performance of speed.

Discussion on Hypotheses: It was hypothesized that there would be a significant difference in selected physical variables on speed. The results of the study

revealed that there is a significant difference in selected physical variables on speed due to effect of Ladder training. Hence the investigator hypothesis was accepted.

Conclusions

The result of the study reveals that ladder training would positively improve the college men football player Physical variable significantly.

Ethical Clearance: Nil

Source of Funding: Self

Conflict of Interest: Nil

References

1. Markula-Denison P, Pringle R. Foucault, sport and exercise: Power, knowledge and transforming the self. Routledge; 2007 Jan 24.
2. Ekman P. An argument for basic emotions. *Cog & Emo.* 1992 May 1;6(3-4):169-200.
3. Robertson S, Zwolinsky S, Pringle A, McKenna J, Daly-Smith A, White A. 'It is fun, fitness and football really': a process evaluation of a football-based health intervention for men. *Qual Res Sport, Exerc and Health.* 2013 Nov 1;5(3):419-39.
4. Winter DA. Biomechanics and motor control of human movement. John Wiley & Sons; 2009 Oct 12.
5. McArdle WD, Katch FI, Katch VL. Exercise physiology: nutrition, energy, and human performance. Lippincott Williams & Wilkins; 2010.
6. Pennebaker JW. The psychology of physical symptoms. *Springer Sci & Bus Media*; 2012 Dec 6.
7. Brown L, Ferrigno V, editors. Training for speed, agility, and quickness, 3E. *Human Kin*; 2014 Nov 13.

C2 Lateral Mass Vertebrae Anthropometry for Evaluating C2 Straight Lateral Mass Screw Fixation

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Abstract

Background: The cervical vertebra is an important vertebra as there are blood vessels in its surroundings from the brain to the entire vertebrae. Cervical injury has the most fatal consequences when it occurs as high as C1-C2. If instability occurs in the C1-C2 vertebrae and atlantoaxial joints, the procedure of surgical techniques include cervical arthrodesis or spinal fusion. C2 straight lateral mass fixation is one technique that can be used for fixation in patients with spinal cord compression and anomalous vertebral artery by inserting shorter screws in the lateral mass of the C2 vertebrae from the posterior direction. There have been not many references similar to the present study of anatomy to discover the screw characteristics needed in this technique.

Aim: This study aimed to identify the length of the lateral mass in the C2 vertebra for the purposes of the C2 straight lateral mass screw fixation technique.

Method: This research was an observational descriptive study with cross sectional design that observed the results of cervical CT-Scan. Observation was made using the RadiAnt DICOM Viewer application and measurements were based on a sagittal cross section. The length was measured from the posterior parallel to the posterior longitudinal ligament (PLL). The initial mean was measured on the right and left side; afterwards, the final mean is the total mean of both sides.

Result: From 10 samples, there were mean long lateral masses of C2 vertebrae on the right side of 13.511 ± 1.081 millimeters, the left side of 13.444 ± 1.396 millimeters, and the final mean of $13.48 \pm 1,216$ millimeters. It was rounded to an average of 13.5 ± 1.2 millimeters.

Discussion: The line parallel to the posterior longitudinal ligament (PLL) is more posterior than the line parallel to the foramen transversum wall which causes the measured length to be shorter. This is useful for the C2 straight lateral mass screw technique as it avoids the possibility of lesions in the vertebral artery.

Conclusion: The average lateral mass length in the population of Surabaya is 13.5 ± 1.2 millimeters.

Keywords: *Lateral Mass Vertebrae C2, C2 Straight Lateral Mass Screw Fixation*

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Introduction

The cervical vertebrae consist of 7 bone spaces, namely C1-C7.¹ The cervical vertebra has a transverse foramen in each segment through which the vertebral artery passes.² The vertebral artery is tasked with vascularizing the brain; hence, cervical vertebrae injuries

and failure to identify can cause serious complications.³ The most fatal consequences can occur in the upper cervical area, both in the crania cervical junction and in the C1-C2 vertebrae.⁴ This is because the anatomical structure of the C1 and C2 vertebrae is unique and has a close relationship with the vertebral arteries.⁵ Cases of C1-C2 injuries that have dislocations should be surgically removed.⁶ The principles of cervical vertebrae surgery are stabilization and prevention of nerve decompression, optimizing the results of actions, and avoiding complications that may occur if non-surgical measures are performed.⁷

Cervical arthrodesis is a surgical treatment that unites one vertebra with another vertebra.⁸ This technique can be performed on any cervical vertebra in accordance with the location of the injury. Fusion of vertebrae as high as C1-C2 is used for fusion due to instability in the C1-C2 vertebrae and atlantoaxial joint.^{9, 10}

Because of their unique and biomechanical properties, most cervical vertebrae stabilization studies have focused on modification of fixation in C2 vertebrae.¹¹ Trans-articular fixation resulted in limitations on flexion and extension movements.¹² Meanwhile, the C2 pedicle technique by Harm further reduces the risk of lesions in the vertebral artery compared to the Magerl technique; however, it is still not possible to be used in patients who have anomalies in the vertebral artery.¹³ The C2 laminar screw technique is used to avoid lesions in the vertebral artery¹⁴, but this technique is not recommended for patients who require laminectomy to decompress the spinal cord.¹⁵

To explore the contraindications to the C1-C2 technique, a study in Japan stated that there were 238 (24.4%) cases accompanied by the incidence of compression of the cervical spinal cord¹⁶ and another study asserted that of 200 patients, there were 66 patients with High-Riding Vertebral Artery (HRVA) and 90 patients with narrow pedicles after being detected using thinly-sliced pedicular-oriented CT (TPCT).¹⁷ The high number of these two numbers makes it possible for both conditions to occur in an individual; consequently, other techniques are needed for patients with the mentioned condition.

C2 straight lateral mass fixation is one technique that can be used for fixation in patients with these two conditions. Fixation is performed by inserting shorter sized screws in the lateral mass of the C2 vertebrae from

the posterior direction, as is the case in Korea which reduces the risk of bleeding in HRVA patients with C2 fixation by using shorter screws.¹⁸ To date, there are not many references regarding this technique, therefore further studies on the anatomy of the C2 vertebrae are needed to support this fixation technique. Many modifications have been made to avoid complications. This is carried out by changing the entry point of the screw and the direction of screw installation.¹⁹ These modifications can affect the required screw characteristics, such as length and diameter.

Method

This study aimed to measure anthropometric C2 lateral mass vertebrae from the lateral side for the C2 straight lateral mass screw fixation technique in order to determine the appropriate screw requirements and minimize complications that can occur. An observational analytic with cross-sectional approach was used.

Sample: The research samples were the results of the CT scan taken from the Mitra Keluarga Darmo Satelit Hospital, Surabaya in the period of August-November 2017. The sampling technique was conducted by using total sampling with the inclusion criteria of CT scan results as high as vertebrae C1-C7, while the exclusion criteria included CT Scan results with abnormalities of vertebral anatomy as high as C1-C7 and patients who are not domiciled in Surabaya.

Research Instrument and Data Analysis: The instrument used to measure the CT scan result was RadiAnt DICOM Viewer Application version 4.1.6. The length of the lateral mass of the C2 vertebra was measured at the point of 3 millimeters superior to the facet line, median lateral mass, and anterior-superior direction parallel to the facet until the posterior longitudinal ligament (PLL). The PLL boundary point was initially marked. Afterwards, the length was measured on the slice showing the lateral mass picture from the posterior to the marked point. The initial mean was calculated on the right and left sides; then, the final mean was obtained from both sides. The measurement results were then processed using Microsoft Excel 2016.

Result

The total CT scan results sampled in this study were 10. Observation of radiology results was carried out for 1 week to determine the mean lateral mass in each sample. Lateral mass is the mass located in both right and left

lateral of C2 vertebrae. The length of the C2 vertebrae lateral mass was measured from the sagittal cross section at the point of 3 millimeters superior to the facet line, median lateral mass, anterior-superior direction parallel to the facet to the PLL limit.

Referring to the observation results, it was obtained the mean lateral mass of C2 vertebrae from 10 samples of 13.511 ± 1.081 millimeters with a minimum value of 12.006 millimeters and a maximum value of 15.496 millimeters. Whereas, the mean lateral mass of the C2 vertebrae from 10 samples was 13.466 ± 1.396 millimeters with a minimum value of 11.343 millimeters and a maximum value of 15.630 millimeters (Table 1). The mean left and right lateral mass of the C2 vertebrae obtained a mean total of 13.448 ± 1.216 millimeters with a minimum value of 11.334 millimeters in both sides and a maximum value of 15.630 millimeters in both sides (Table 2).

Tables

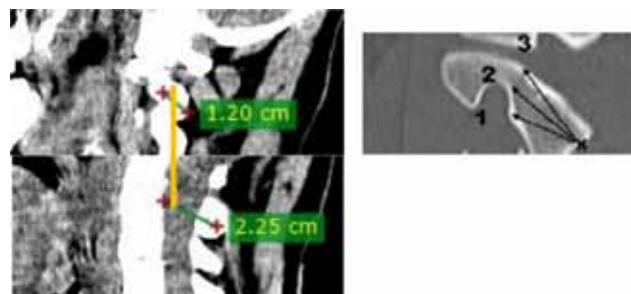
Table 1: The Length of C2 Vertebrae Lateral Mass

No	The Length of Right Lateral Mass (mm)	The Length of Left Lateral Mass (mm)
1	12.443	11.343
2	14.618	15.213
3	14.412	13.765
4	12.982	13.863
5	13.601	13.755
6	13.303	14.205
7	12.006	12.005
8	12.631	12.130
9	15.496	15.630
10	13.624	12.754
Mean	13.511	13.466
Min	12.006	11.343
Max	15.496	15.630
SD	1.081	1.396

Table 2: The Mean of C2 Vertebrae Lateral Mass Length

Mean	Length (mm)
Right	13.511
Left	13.466
Total mean	13.488
Min	11.343
Max	15.630
SD	1.216

Picture 1: (a) Measurement of lateral mass from posterior as high as PLL, (b) The marker points parallel to PLL, (c) The measurement limit based on a research in Los Angeles (Hoh, et al., 2010)



(Picture)

Discussion

C1-C2 Trans-articular Screw Fixation is the technique that produces the most rigid outcome.¹² The entry point of this technique is at 2-3 millimeters superior-lateral from the facet to the axial isthmus in medial,¹² then, it is forwarded to the C1 lateral mass. C1-C2 joints are very functional in rotational movements and with a little flexion-extension. Hence, the fixation in this area will cause limitations on flexion-extension movements, lateral swelling, and rotational movements. The screw mounting direction of this technique reduces freedom of movement in all directions so as to achieve a state of high stability. This technique can also prevent slippage between segments.²⁰ This technique is also an indication for C1-C2 instability due to rheumatoid arthritis, odontoid process fracture, os odontoideum, C1-C2 arthrosis.¹² This technique is contraindicated for the condition of vertebral artery anomalies in segments as high as C1-C2, axial isthmus that is too small, deformities in segments as high as C1-C2, prominent kyphosis in the cervical-thoracic junction, and destruction of the atlas bone lateral mass.

C2 Pedicle Screw Fixation connects the vertebral body with the posterior component of the atlas bone. The screw is mounted obliquely from the pediculus to the vertebral body.¹⁵ The advantage of this technique is that it can protect joints between C1-C2. In addition, it is possible to remove the screw after stability returns to restore movement to C1-C2. Compared with the trans-articular technique, this technique further reduces the risk of injury to the vertebral arteries.¹³ The technique is indicated for C1-C2 instability caused by trauma, tumors, and inflammation, for non-fusion odontoid process fractures, unstable Jefferson fractures, and repair

in failed odontoid screw fixation.¹³ Contraindications are if there are anatomic variations in the vertebral artery.¹³

The entry point of the screw in the C2 Laminar Screw Fixation technique is between the spinous and lamina process, and is directed across the direction of the lamina on the contralateral side.²¹ This technique is intended for 20% of patients who have anatomic anomalies that are contraindicated in trans-articular screw or pedicular screw techniques, because there is a risk of vertebral artery injury.²² If there is a condition that requires decompression of the spinal cord, laminectomy of the axis bone is needed and this technique cannot be performed.¹⁵

C2 Pars Screw Fixation has the same entry point and direction as the trans-articular technique. The difference with the trans-articular technique is the depth of screw fixation that does not go through the atlas bone.¹⁵

Based on the results of the study, there have been no similar results from other references to the present study. However, a study with a similar concept was conducted in Los Angeles regarding the lateral mass of the C2 vertebra that used the same entry point and direction as this study and produced an average of 17.0 millimeters on both sides.²³ A case study conducted in Egypt on the evaluation of the efficacy and safety of C2 pars/pedicle screws also has a different number from this study, which used a screw with a size of 16 millimeters for the C2 vertebrae.²⁴

The difference in results among studies can be caused by several factors. A factor that may be influential is the anterior border of the measurement. Measurements performed in research in Los Angeles was started from the posterior to the point before the transverse foramen wall,²³ which is different from this study which has a limit to the point parallel to the PLL. Observation results show that the line parallel to the PLL is more posterior than the line parallel to the transverse foramen wall. This causes the length measured in this study is shorter. This is useful for the C2 straight lateral mass screw technique because it avoids the possibility of lesions in the vertebral artery (Picture 1).

Another factor that might influence differences in results is morphological variation in each different population. A previous study conducted in India has shown that the average antero-posterior length of the right and left C2 vertebrae superior facets were 16.61 ± 1.33 millimeters and 16.70 ± 1.49 millimeters respectively.⁵

This result is different from a similar study conducted in Turkey with an average of 17.5 ± 14 on the right side and 17.5 ± 1.5 on the left side.²⁵ Specific references regarding differences in the lateral mass length of the C2 vertebrae were not found. However, the differences in the results of the two studies above may allow for differences in the lateral mass.

Limitation: There are several limitations in this study. A factor from the author that might be influential is the lack of accuracy in the measurement process. The small number of samples is also a disadvantage in this study. Retrieval of data in only one hospital is presumed to be insufficient to describe the lateral mass length of the entire population in Surabaya.

Conclusion

The mean of C2 vertebrae lateral mass length is 13.5 ± 1.2 millimeters.

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Ethical Clearance: This study received a certificate of ethical clearance from ethical commission of Faculty of Medicine, Universitas Airlangga Indonesia.

References

1. Panchbhavi VK. Neck Anatomy 2015 [cited 2017 13 November]. Available from: <https://reference.medscape.com/article/1968303-overview#showall>.
2. Windsor RE. Cervical Spine Anatomy 2017 [cited 2017 13 November]. Available from: <https://emedicine.medscape.com/article/1948797-overview#showall>.
3. Hertner GL. Cervical Spine Acute Bony Injuries in Sports Medicine 2017 [cited 2017 13 November]. Available from: <https://emedicine.medscape.com/article/94234-overview#showall>.
4. Davenport M. Cervical Spine Fracture Evaluation 2017 [cited 2017 13 November]. Available from: <https://emedicine.medscape.com/article/824380-overview#showall>.
5. Singla M, Goel P, Ansari MS, Ravi KS, Khare S. Morphometric Analysis of Axis and Its Clinical Significance -An Anatomical Study of Indian Human Axis Vertebrae. Journal of clinical and

- diagnostic research : JCDR 2015;95:AC04-9.
6. Marcon RM, Cristante AF, Teixeira WJ, Narasaki DK, Oliveira RP, de Barros Filho TE. Fractures of the cervical spine. *Clinics* 2013;6811:1455-61.
 7. Alves PL, Martins DE, Ueta RH, Del Curto D, Wajchenberg M, Puertas EB. Options for surgical treatment of cervical fractures in patients with spondylotic spine: a case series and review of the literature. *Journal of medical case reports* 2015;9:234.
 8. Peng B, DePalma MJ. Cervical disc degeneration and neck pain. *Journal of pain research* 2018;11:2853-7.
 9. Bourdillon P, Perrin G, Lucas F, Debarge R, Barrey C. C1-C2 stabilization by Harms arthrodesis: indications, technique, complications and outcomes in a prospective 26-case series. *Orthopaedics & traumatology, surgery & research : OTSR* 2014;1002:221-7.
 10. De Iure F, Donthineni R, Boriani S. Outcomes of C1 and C2 posterior screw fixation for upper cervical spine fusion. *Eur Spine J* 2009;18 Suppl 1Suppl 1:2-6.
 11. Ghostine SS, Kaloostian PE, Ordookhanian C, Kaloostian S, Zarrini P, Kim T, et al. Improving C1-C2 Complex Fusion Rates: An Alternate Approach. *Cureus* 2017;911:e1887.
 12. Winking M. Posterior Transarticular C1/C2 Screw Technique. In: Vieweg UV, Grochulla F, editors. *Manual of Spine Surgery*. Berlin: Springer; 2012. p. 187-94.
 13. Schultz C. C1-C2 (Harms) Technique. In: Vieweg U, Grochulla F, editors. *Manual of Spine Surgery*. Berlin: Springer; 2012. p. 195-8.
 14. Ma W, Feng L, Xu R, Liu X, Lee AH, Sun S, et al. Clinical application of C2 laminar screw technique. *Eur Spine J* 2010;198:1312-7.
 15. Joaquim AF, Riew KD. Axis Screw Fixation – A Step-by-Step Review of the Surgical Techniques. *Arq Bras Neurocir* 2017;36:101-7.
 16. Nagata K, Yoshimura N, Muraki S, Hashizume H, Ishimoto Y, Yamada H, et al. Prevalence of cervical cord compression and its association with physical performance in a population-based cohort in Japan: the Wakayama Spine Study. *Spine* 2012;3722:1892-8.
 17. Wajanavisit W, Lertudomphonwanit T, Fuangfa P, Chanplakorn P, Kraiwattanapong C, Jaovisidha S. Prevalence of High-Riding Vertebral Artery and Morphometry of C2 Pedicles Using a Novel Computed Tomography Reconstruction Technique. *Asian spine journal* 2016;106:1141-8.
 18. Park YS, Kang DH, Park KB, Hwang SH. Posterior atlantoaxial screw-rod fixation in a case of aberrant vertebral artery course combined with bilateral high-riding vertebral artery. *Journal of Korean Neurosurgical Society* 2010;484:367-70.
 19. Mohamed E, Ihab Z, Moaz A, Ayman N, Haitham AE. Lateral mass fixation in subaxial cervical spine: anatomic review. *Global spine journal* 2012;21:39-46.
 20. Turel M, Kerolus M, Traynelis V. Machined cervical interfacet allograft spacers for the management of atlantoaxial instability. *Journal of Craniovertebral Junction and Spine* 2017;84:332-7.
 21. Finn MA, Schmidt MH. Occipital Cervical Stabilization with Rod-Screw Systems. In: Vieweg U, Grochulla F, editors. *Manual of Spine Surgery*. Berlin: Springer; 2012. p. 181-5.
 22. Siemionow K, Janusz P, Mardjetko S. The Four Fixation Points of the Axis: Technique and Case Report. *International journal of spine surgery* 2018;125:611-6.
 23. Daniel JH, Charles YL, Michael YW. A radiographic computed tomography-based study to determine the ideal entry point, trajectory, and length for safe fixation using C-2 pars interarticularis screws. *Journal of Neurosurgery: Spine SPI* 2010;126:602-12.
 24. Eshra MA. C2 pars/pedicle screws in management of craniocervical and upper cervical instability. *Asian spine journal* 2014;82:156-60.
 25. Sengul G, Kadioglu HS. Morphometric Anatomy of the Atlas and Axis Vertebrae. *Turkish Neurosurgery* 2006;162:69-76.

Preferred Learning Method of Undergraduate Medical Students

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Abstract

Background: Learning style is the way students begin to focus, internalize and remember new and difficult information. Identifying the learning styles of medical students will enable the faculty to use appropriate Teaching and Learning method to increase the grasping ability of students. Purpose of the study was to assess the preferred learning styles of medical students by using VARK questionnaire .

Method: This was a cross-sectional study based on the VARK (Visual, Auditory, Read & write and Kinesthetic)questionnaire done among 414 medical students of Subharti Medical College Meerut UP. The VARK questionnaire was administered to 1st year 86(20.7%), 2nd year 91 (22%), 3rd year 116 (28%), and final year 121 (29.3%) students. The students were categorized as visual learner, auditory, read/write or kinesthetic, depending on the predominant option they chose.

Results: Of the total 414 medical students participated in the study. 24.1%,25.8%,14.2% and 5.70% were unimodal, bimodal, trimodal and quarimodal modality as their preferred modality of learning. Among the unimodallearners the percentages of students who preferred visual(20%), auditory (35%), reading/writing (12%), kinesthetic (33%). AV(29.9%) followed by AK(26.1%) were most preferred bimodal modalities of learning. AVK(44.1%) was most preferred trimodal modality of learning. There was no significant difference among different year of medical students for preferredunimodal modalities of learning (p=0.55), different bimodal modalities of learning (p=0.9) and different trimodal modalities of learning.

Conclusions: Audio visuals which includes short movies, video clips and animated versions are most preferred modalities for exciting and interesting learning. Kinesthetic learning which includes ECE (early clinical exposures) role plays, case presentation, simulations etc works more on affective and psychomotor component of learning and gives a better understanding, adds meaningfulness to the topic and renders a long lasting memory. A teaching session which includes all the modalities makes a strong, positive and permanent impression on a students mind about the subject.

Keywords: Visual, Auditory, Read and write Kinesthetic (VARK) Teaching and Learning style, medical students.

Introduction

Medical education is a continuous process which requires both students and instructors to update themselves regularly. There are several challenges medical education is facing, one of which is imparting a large amount of knowledge within a limited time period in a manner it is effectively retained, interpreted and remembered by a student. This has resulted in important changes in the field of medical education, with a shift

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from conventional teaching to the use of problem-based, student-centered and interactive learning. Most medical curricula have implemented creative method of teaching and learning to changeable degrees. [1] Students in a medical college belong to different socioeconomic and cultural backgrounds, have varied prior educational experiences, different levels of competencies, and perhaps even different preferential method of learning. Teaching is a process of presentation of knowledge while learning is many times multi-factorial and depends on the mind-set of each individual student. Students have different preferences when it comes to the assimilation and processing of the information. [2] Learning habit of a learner means how he processes information and it varies with each individual. Learning results in gain of knowledge and skills. If the method of information delivery to the learner suits their particular learning habit, they learn even better. [3]

Three learning habits have been identified according to the VARK model as visual, auditory and kinesthetic. Another learning habits added to this, the Read- write habit (VARK model) and this was developed by Fleming and Bonwell. Fleming's learning habit inventory is the most commonly used model of learning which is also known as VARK questionnaire. [4] The VARK is a tool that categorizes learning habit according to Visual, Auditory, Read/write or kinesthetic modes as indicated on a simple preference survey. [5] The VARK

questionnaire is a 13-item, self-reported, multiple-choice questionnaire that can be completed within a time span of 10–15 minutes. The VARK questionnaire was selected for the assessment of learning habits in our study because it is a concise, simple survey Questionnaire, and was pre-validated by the peer group. [6]

Material and Method

This was a cross-sectional study based on the VARK questionnaire among the medical students of Subharti Medical College, Meerut, UP. The study was done after obtaining the permission from the institutional ethics committee. All the volunteer students from first to final year MBBS participated in the study after written informed consent. The VARK learning styles assessment questionnaire was administered. Students were given a time of 15 minutes to fill the questionnaire. The students were categorized as visual learner, auditory, read/write, kinesthetic depending on the predominant option they chose. If they opted a single sensory preference they were considered as unimodal, two as bimodal, three as trimodal and all four as quadrimodal. Their learning styles were analyzed by using frequency and proportions. Chi square test was used. A 'p' value of <0.05 was considered as statistically significant. The aim of this study was to describe learning styles of medical students in Subharti Medical College, Meerut UP.

Results

Figure 1. Showing distribution of students according to year of MBBS

Number of students



Distribution of the total 414 students participated in the study according to year of MBBS is given in figure 1. More students were from third and final year as compared to first and second year because in last two years intake of students was less in college.

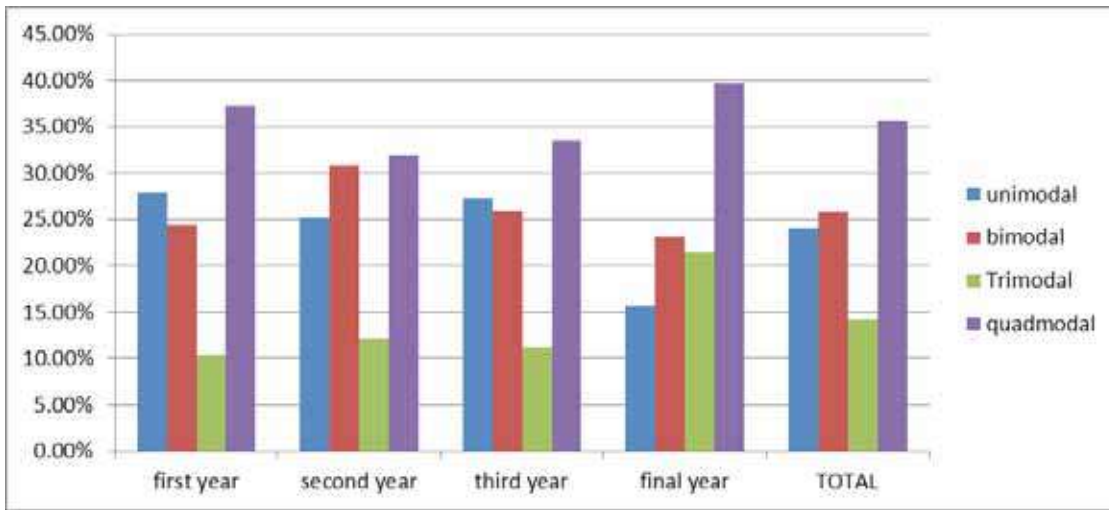


Figure 2. Graph showing the distribution of students according to preferred modality of learning.

Distribution of preferred modality of learning and year of MBBS is in figure 2. Quadrimodal modality was most preferred among all the years. There was no significant difference among different year of medical students for modality of learning (p=0.11)

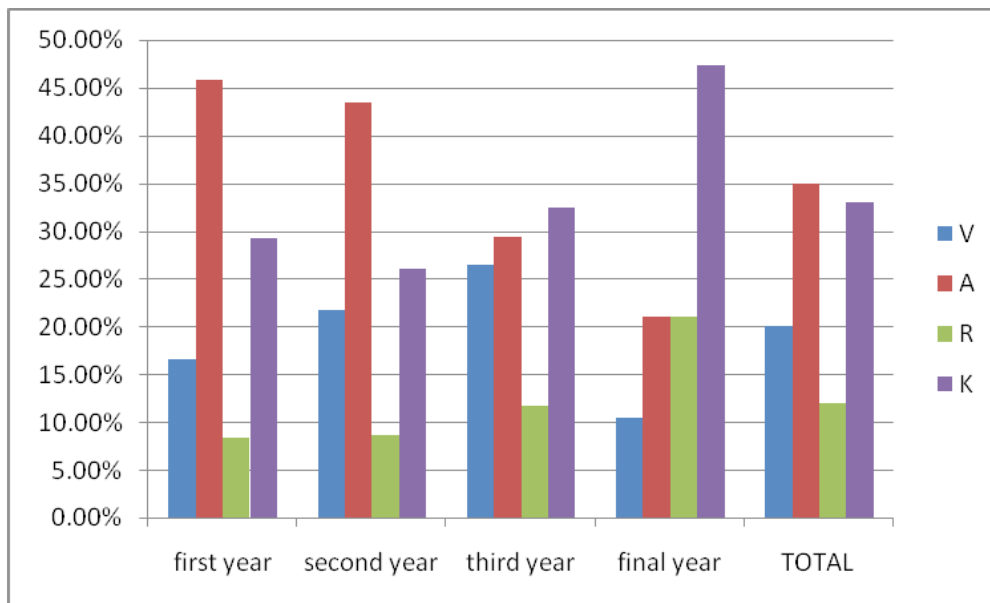


Figure 3: Graph showing distribution of students according to preferred UNIMODAL modality of learning

Among the unimodal learners the percentages of students who preferred visual (20%), auditory (35%), reading/writing (12%), kinesthetic (33%) shown in figure 3. Auditory was most preferred in first and second year while kinesthetic was more chosen in third and final year.

Table 1: Table showing distribution of students according to preferred BIMODAL modality of learning.

	AV	VR	VK	AR	AK	RK
First Year	23.80%	9.50%	19.00%	14.30%	23.80%	9.50%
Second Year	32.10%	10.70%	21.40%	3.60%	25.00%	7.10%
Third Year	33.30%	6.60%	20%	3.30%	26.60%	10.70%
Final Year	28.60%	7.10%	7.10%	17.90%	26.70%	10.7%
Total	29.90%	8.40%	16.80%	9.30%	26.10%	9.30%

The distribution of learning preferences among bimodal modality of learning is shown in table 1.AV followed by AK comes out to be most favorite among all the years.

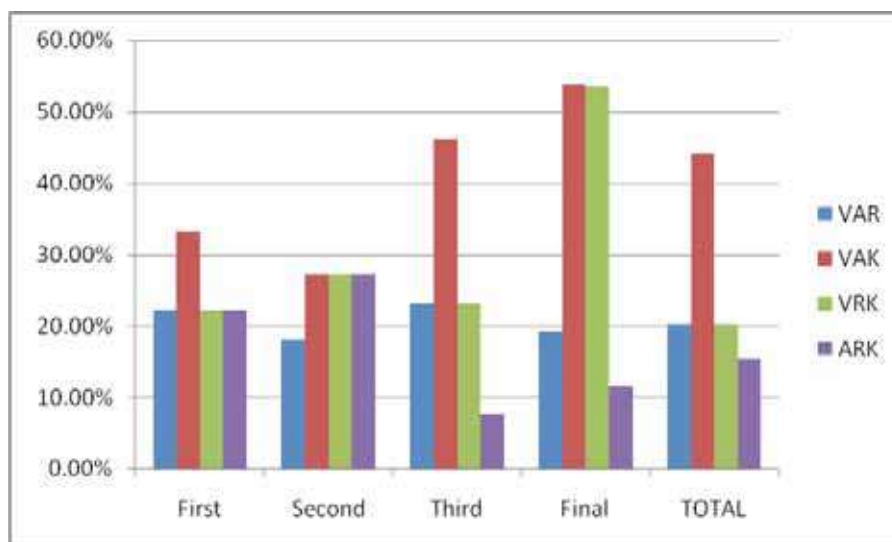


Figure 4: Graph showing distribution of students according to preferred TRIMODAL modality of learning.

The distribution of learning preferences among trimodal modality of learning is shown in figure 5. VAK is most preferred among all the student across different year of MBBS.

There was no significant difference among different year of medical students among different modalities of learning ($p=0.11$), different unimodal modalities of learning ($p=0.55$), different bimodal modalities of learning ($p=0.9$).

Discussion

VARK questionnaire was used in our study to assess the preferred modality of learning among undergraduate medical students. Awareness about the learning styles helps the faculty in identifying and solving the learning problems and also helps reduce the frustration levels of students. Current situation demands the transition from the passive traditional didactic lectures to problem-based learning and to achieve this, the faculty needs to apply multiple teaching method which suit the different learning preferences for a better outcome. Method which promote thinking and improve problem solving as well as decision-making abilities should be used. Students learn in different ways using variety of method to convert the information into long term memories.

In our study, the VARK questionnaire was administered to 1st year 86(20.7%), 2nd year 91 (22%),

3rd year 116 (28%), and final year 121 (29.3%) students. The students were categorized as visual learner, auditory, read/write or kinesthetic, depending on the predominant option they chose. Of the total 414 students participated in the study the distribution according to year of MBBS is given in figure 1. Distribution of preferred modality of learning and year of MBBS is in figure 2. there was no significant difference among different year of medical students for modality of learning ($p=0.11$). Among the unimodal learners the percentages of students who preferred visual (20%), auditory (35%), reading/writing (12%), kinesthetic (33%) shown in figure 3. The distribution of learning preferences among bimodal modality of learning is shown in figure 4. The distribution of learning preferences among trimodal modality of learning is shown in figure 5. There was no significant difference among different year of medical students among different modalities of learning ($p=0.11$), different unimodal modalities of learning ($p=0.55$), different bimodal modalities of learning ($p=0.9$) and different trimodal modalities of learning ($p=???$). if we compare first and second year students with third and final year students we found there was an increase in preference for kinesthetic modality of learning as medical student reaches third and final year it may be because of introduction of more clinical or patient based activities in last two years.

In a study done by Navin R et al (2013), 55% of

the medical students preferred using a single sensory modality while learning i.e., they had unimodal learning preferences, while the rest 45% preferred using two or more sensory modalities i.e., they were multimodal.^[7] A study conducted by Chinmay S, et al. (2013) in Bhavnagar Medical College revealed that among 1st year MBBS students, the highest preference was given to Aural followed by Kinesthetic, Read/Write and Visual.^[8] In a study done by Usha GS et al (2013) suggested that final MBBS students the most preferred mode was visual.^[9]

Visual learners process information best through agents like graphs, flow charts and pictures. Aural learners process and internalize information by listening to lectures, attending tutorials etc. The Read/write learners are the students who like to take notes verbatim and reread these repeatedly. Finally, the kinesthetic learners like to acquire information through experience and practice. They prefer to learn information that has some connection to the reality.^[10] In the present day scenario, majority of the medical students have preference for several learning habits, and yet medical faculties teach predominantly in a single mode i.e. the lecture. Listening to lectures is basically a passive learning method that encourages mere memorization and note-taking as the means of assimilating knowledge.^[11]

In our study for bimodal modality of learning AV(29.9%) followed by AK(26.10%) were most preferred among all the years. Videoclips, short movies and animated movies creates interest in subject and explains the topic in comprehensive manner. While kinesthetic modality which includes case presentations, role plays adds to affective and psychomotor component of learning and if its mixed with AV modality the combination may makes a strong, positive and permanent impression on a student's mind about the subject.

Many of the studies have shown that the teaching method that caters to multiple modalities of learning styles, enhances performance by the students. Some of the strategies that can be included for the benefit of students in academics are Objective Structured Clinical/ Practical Examination (OSCE/OSPE), integrated teaching, e-learning, early clinical exposure to patients in OPDs and wards, increasing use of models, lending the hand-outs of power point presentations, audio recording of lectures, and computer assisted learning. Discussion in class, cooperative learning exercises, role-plays, simulations, debates, and games are active learning strategies that can be used which promotes

enthusiasm and motivation. It involves thinking through reasoning and improves problem solving and decision making skills which can be improved from the beginning of the course itself. Teaching method should include combinations of audio visual aids to help them shift from unimodal to multimodal learning style. Hence it is thought that discussion in class role play and debates can be introduced to the students as they enter the course to make them multimodal learners.

Conclusion

Multimodal way of teaching and learning is most preferred among all the students across different stages of their medical education. Students prefer more of a method which includes their active participation in the subject and hence creates curiosity about the topic. Audio visuals which includes short movies, video clips and animated versions

are most preferred modalities for exciting and interesting learning. Kinesthetic learning which includes ECE (early clinical exposures) role plays, case presentation, simulations etc works more on affective and psychomotor component of learning and gives a better understanding, adds meaningfulness to the topic and renders a long lasting memory. A teaching session which includes all the modalities makes a strong, positive and permanent impression on a student's mind about the subject. This will make the educational experience more fruitful and productive.

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Ethical Approval: Research work approved from the ethical Committee of Subharti Institution of Medical Sciences

References

1. Koh GC, "The effects of problem based learning during medical school on physician competency: a systematic review.," CMAJ, vol. 178, no. 1, p. 34-41., 2008.
2. Prithish Kumar IJ, Michael SA. Understanding your student: Using the VARK model. J Postgrad Med 2014;60;183-6.
3. Sadler-Smith E, Smith PJ. Strategies for accommodating individuals' styles and preferences inflexible learning programs. British Journal of

- Education Technology. 2004;35:395-412.
4. Fleming N. VARK: a Guide to Learning Habits. Available from: URL:[http://www.vark-learn.com/documents/TheVARK Questionnaire.pdf](http://www.vark-learn.com/documents/TheVARK%20Questionnaire.pdf).
 5. Fleming ND. Teaching and Learning Habits: VARK strategies. Christchurch, New Zealand: N.D. Fleming Bedford TA. Learning Habits: A Review of Literature. Toowoomba, Australia: OPACS, the University of Southern Queensland; 2006.
 6. Dýnakar C, Adams C, Brýmer A, Sýlva MD. Learning preferences of caregivers of asthmatic children. *Journal of Asthma*. 2005;42:683-7.
 7. Navin R, Suganthi V, Suzanne MD. Learning preferences of students studying Physiology in South India. *IOSR Journal of Dental and Medical Sciences* 2013;7:15-9.
 8. Chinmay S, Shailesh P, Jaswin D, Hemant M. Learning Habits Evaluation of First M.B.B.S. Students of Bhavnagar Medical College. *Int J MedSci Public Health*. 2012;1:81-6
 9. Usha GS, Kutty K, Vinutha Shankar MS, Nachal A. Changes in the learning styles in Medical students during the MBBS course. *Int J of Scientific and Research publications*. 2012;2:1-4.
 10. Marcy V. Adult Learning Styles: How the VARK learning style inventory can be used to improve student learning. *Perspective on Physician Assistant Education. Journal of the Association of Physician Assistant Programs*. 2001;12(2).
 11. Endorf M, McNeff M. The adult learner: five types. *Adult Learning*. 1991;2:20-5.

Effect of Smoking & Alcohol on Hypertension in Various Professionals a: Cross Sectional Study

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Abstract

Objective: To study the effect of smoking & alcohol on hypertension in various professionals.

Method: A cross sectional study was done from 1st August 2015 to 30th August 2017 in district Bareilly. A Predesigned & Pretested questionnaire was used comprising of demographic data, alcohol & tobacco use. Three types of professionals were included in this study: Doctors, Managerial staff, School teachers from the teaching institutions.

Results: The Smoking history among professional groups found that majority of doctors (67.70%) were smokers followed by managerial staff (60%) and school teachers (30%) & p-value (<0.001) was found statistically significant. Alcohol consumption history among professional groups found that majority (60%) doctors were alcoholic followed by (43.08%) managerial staff and (30%) school teachers and p-value (<0.001) was found statistically significant.

Conclusion: In this study among professional groups the association of hypertension with alcohol and smoking was found highly significant. The odds of developing high blood pressure and its adverse consequences in professional groups can be minimized by promoting a healthy lifestyle.

Keywords: Hypertension, Professional, Bloodpressure

Introduction

Hypertension also known as high or raised blood pressure is a global public health issue. It is a major risk factor for stroke and coronary heart diseases and is a major contributor to the onset and progression of chronic heart failure and chronic kidney failure.¹ The global prevalence of raised blood pressure defined as systolic and/or diastolic blood pressure $\geq 140/90$ mmHg in adults aged 18 years and over was around 22% in 2014. The number of hypertensive individuals is anticipated to n

early double from 118 million in 2000 to 213 million by 2025.²

In India, hypertension is the leading non communicable disease risk and estimated to be attributable for nearly 10 per cent of all deaths. Even the majority of those who are diagnosed do not get treated to control the blood pressure. Smoking is a strong independent risk factor for cardiovascular diseases. Smoking causes an immediate increase in blood pressure and heart rate that persists for more than 15 minutes after one cigarette. People who smoke show higher ambulatory blood pressure levels than non-smokers.

Some studies have shown that the use of oral snuff or smokeless tobacco may predispose a person to higher systolic and diastolic blood pressures and significantly increase the risk for myocardial infarction.³

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Epidemiological data shows a linear relationship between alcohol consumption and hypertension prevalence. Reducing alcohol consumption can lower systolic blood pressure by an average of 3.8 mmHg in patients with hypertension.⁴ Hypertension is more common amongst people from upper social class because of the presence of multiple factors such as sedentary jobs, lack of physical activity, rich diet, alcohol intake, smoking, and tobacco use. Boden-Albala and Sacco reported a study & found that especially current smoking was found to be a crucial and extremely modifiable independent determinant of stroke.⁵ McNagny et al conducted a study to find the association of cigarette smoking and Hypertension in African Americans significantly which were more likely to be current smokers and less compliant with medication when compared with controlled hypertensive.⁶ Zilkenet et al study showed the relationship between alcohol consumption and blood pressure (BP) in healthy normotensive men with daily consumption of red wine, dealcoholized red wine or beer. The only way to curb the problem of hypertension is by its prevention.

Keeping this in view the present study was done to find out the effect of smoking & alcohol and its impact on hypertension among three professional groups, doctors, school teachers and managerial staff of Bareilly, Uttar Pradesh.

Objective: To study the effect of smoking & alcohol on hypertension in various professionals.

Material and Method

Study Design: This cross sectional study was done in three professional groups; doctors, school teachers and managerial staffs from 1st August 2015 to 30th August 2017. **Study Tool:** A Predesigned & Pretested questionnaire comprising of alcohol use & tobacco use was prepared in English language after reviewing the available literature. **Study Area:** The cross sectional study was done in district Bareilly, Uttar Pradesh. **Study Population:** The study was done in three professional groups i.e. doctors, school teachers and managers working on regular basis in the institutions. **Sampling technique:** The study subjects were selected randomly from three professional groups.

Inclusion Criteria: All individual willing to participate from each profession, have been included in the study.

Exclusion Criteria: Subjects with co-morbid

conditions were not included in the study. Subjects not willing to participate were also excluded.

Sample Size Estimation: According to a study conducted by Ramachandran et al⁷ on young physicians in India, the Using prevalence of hypertension 35.6%. Absolute error was taken as 5% and the required sample size was 352. The Sample size is rounded to 390. The study includes 3 professional groups i.e. doctors, school teachers and managerial staff. Therefore the total sample size is divided into 3 parts and 130 sampling units are assigned to each professional group.

- **Current Smoker:** An adult who has smoked 100 cigarettes in his/her lifetime and who currently smokes cigarettes.⁸
- **Alcoholic:** An adult who were consuming alcohol regularly at the time of interview.

Result

The Smoking history among professional groups found that majority of doctors (67.70%) were smokers followed by managerial staff (60%) and school teachers (30%). Whereas majority of school teachers (70%) were non smokers followed by managerial staff (40%) and doctors (32.30%) and p-value (<0.001) was found statistically significant.

Alcohol consumption history among professional groups found that majority (60%) doctors were alcoholic followed by (43.08%) managerial staff and (30%) school teachers and p-value (<0.001) was found statistically significant.

Hypertension among professionals with smoking habit found that 68.46% doctors, 69.23% school teachers and 74.62% managerial staff were hypertensive with smoking habit. Whereas 17.69% doctors, followed by 14.62% school teachers and 8.46% managerial staff was hypertensive with non smoking habit. A p-value <0.001 was found to be statistically significant among all professionals.

Hypertension with alcohol habit among professional groups found that 56.92% doctors, 26.16% school teachers and 31.54% managerial staff was hypertensive with alcoholic habit. Among all study subjects 38.21% were hypertensive with alcoholic habit. 60% school teachers, 51.54% managerial staff and 29.22% doctors were found hypertensive who was non alcoholic. Among all study subjects 46.92% were hypertensive with non

alcoholic habit. The association between professional groups with habit of alcohol was found significant by χ^2 test and p-value came out to be 0.000 for doctors and 0.009 for managerial staff, while insignificant for school teachers with p-value 0.825. The association among all study subjects and alcohol was found insignificant with p-value 0.621.

Table 1: Association of hypertension with smoking habit among various professional groups

Smoking habit	Doctors (130)		School teachers (130)		Managerial staff (130)		Total	
	HTN N (%)	Non HTN N (%)	HTN N (%)	Non HTN N (%)	HTN N (%)	Non HTN N (%)	HTN N (%)	Non HTN N (%)
Smoker	89 (68.46)	5 (3.85)	90 (69.23)	7 (5.38)	97 (74.62)	5 (3.85)	276 (70.77)	17 (4.36)
Non smoker	23 (17.69)	13 (10)	19 (14.62)	14 (10.77)	11 (8.46)	17 (13.07)	53 (13.59)	44 (11.28)
Total	112 (86.15)	18 (13.85)	109 (83.85)	21 (16.15)	108 (83.08)	22 (16.92)	329 (84.36)	61 (15.64)
p-value	0.001		0.001		0.001		0.001	
χ^2	20.690		22.535		48.676		86.430	

Table 2. Association of hypertension with alcohol habit among various professional groups

Alcohol habit	Doctors		School teachers		Managerial staff		Total	
	HTN N (%)	Non HTN N (%)	HTN N (%)	Non HTN N (%)	HTN N (%)	Non HTN N (%)	HTN N (%)	Non HTN N (%)
Alcoholic	74 (56.92)	4 (3.08)	34 (26.16)	5(3.84)	41 (31.54)	15 (11.54)	149 (38.21)	24 (6.15)
Non alcoholic	38 (29.23)	14 (10.77)	78 (60)	13 (10)	67 (51.54)	7 (5.38)	183 (46.92)	34 (8.72)
Total	112 (86.16)	18 (13.84)	112 (86.16)	18 (13.84)	108 (83.08)	22 (16.92)	332 (85.13)	58 (14.87)
p-value	0.001		0.825		0.009		0.621	
χ^2	12.424		0.049		6.807		0.245	

Discussion

The present study showed association of hypertension with alcohol habit among professional groups and found that 56.92% doctors, 26.16% school teachers and 31.54% managerial staff were hypertensive with alcoholic habit. Among all study subjects 38.21% were hypertensive with alcoholic habit. Whereas 29.23 doctors followed by 60% school teachers and 51.54% managerial staff were hypertensive with non alcoholic habit. Among all study subjects 46.92% were hypertensive with non alcoholic habit. A highly statistical significant difference was found by applying by chi square test and p-value came out to be 0.000 in doctors, 0.825 in school teachers and 0.009 for managerial staff. Among all study subjects a significance was found with p-value 0.621 which is similar to the findings of study reported by Zilkenet al

⁹relationship between alcohol consumption and blood pressure (BP) in healthy normotensive men with daily consumption of red wine, dealcoholized red wine or beer. The results of the study showed that both red wine and beer significantly (P<0.05) increased systolic BP i.e. 2.9 and 1.9 mm Hg.

In this present study association of hypertension among professionals with smoking habit found that 68.46% doctors, 69.23% school teachers and 74.62% managerial staff were hypertensive with smoking habit. Whereas 17.69% doctors, followed by 14.62% school teachers and 8.46% managerial staff was hypertensive with non smoking habit. A chi-square test for significance was applied and p-value <0.001 was found that is highly significant among all professionals which is similar to the findings of McNagney et al ⁶studied

the association of cigarette smoking and hypertension in African Americans (221 subjects). 86 patients had uncontrolled HTN (mean BP=192/106 mm Hg) and were significantly more likely to be current smokers and less compliant with medication when compared with controlled hypertensive. BodenAlbala and Sacco (2000)⁵ study reported that smoking has been associated with increasing risk of hypertension, diabetes, hyperlipidemia and cardiac diseases.

Conclusion: In this study among professional groups the association of hypertension with alcohol and smoking was found highly significant. The odds of developing high blood pressure and its adverse consequences in professional groups can be minimized by promoting a healthy lifestyle with emphasis on nutrition aspects, reduced salt intake to less than 5 g of salt per day, avoiding excessive use of alcohol & Stopping tobacco use and exposure to tobacco products. It is recommended to follow medical advice and prescribed medications for lowering blood pressure.

Conflict of Interest: Nil

Source of Funding: Self

Ethical Clearance: Institutional Ethical committee Sri Ram Murti Smarak Institute Of Medical Sciences Bareilly Uttar Pradesh.

References

1. Hypertension Gale Encyclopedia of Medicine. 2008. [cited August 1 2017] Available from: [Internet] <http://medicaldictionary.thefreedictionary.com/hypertension>
2. Non communicable disease Situation and Response: WHO South East Asia region New Delhi. 2011
3. Steyn K, Bradshaw D, Norman R, Laubscher R, Saloojee Y. Tobacco use in South Africans during 1998. *J Cardiovascular Risk* 2002;9: 161–70.
4. Dickinson HO, Mason JM, Nicolson DJ, Campbell F, Beyer FR, Cook JV. Lifestyle interventions to reduce raised blood pressure: a systematic review of randomized controlled trials. *J Hypertension* 2006; 24:215-33.
5. Albala B, Sacco RL. Lifestyle factors and stroke risk Exercise, alcohol, diet, obesity, smoking, drug use, and stress. *Curr Atheroscler Rep.* 2000;2(2):160-166
6. McNagny SE, Ahluwalia JS, Clark WS, Resnicow KA. Cigarette smoking and severe uncontrolled hypertension in inner city African Americans. *Am J Med.* 1997; Aug;103(2):121-7
7. Ramachandran A, Chamukuttan A, Yamuna SA, Murugesan N. High prevalence of cardiometabolic risk factors among young physicians in India. *The Journal of the Association of Physicians of India.* 56;17-20.
8. National centre for health statistics centre for disease control and prevention. Saving lives, protecting people. U.S. Department of Health and Human Services. Available from [INTERNET] www.cdc.gov/nchs/nhis/tobacco_glossary.htm
9. Zilkens RR, Burke V, Hodgson JM, Barden A, Beilin LJ, Puddey IB. Red Wine and Beer Elevate Blood Pressure in Normotensive Men. *Journal Hypertension AHA.* 2005;45:874-879.

Credibility of Health Care Advertising: An Empirical Understanding of its Multi-dimensional Structure and Scale Validation with Special Reference to Children's Health Food Drinks

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Abstract

Context: Advertising techniques need to be transformed based on the observations of the perceptions of consumers since they can be the directional force to any advertising aimed at those groups. The study fruitfully provides an empirical understanding about the multiple components of advertising credibility of consumer healthcare products. One of the major tasks undertaken in this research was to develop a scale which is statistically reliable and valid to measure advertising credibility in the current marketing environment of Kerala with special reference to children's health drinks.

Keywords: Advertising credibility, corporate credibility, endorser credibility, message content credibility, consumer health care, health food drinks.

Introduction

The tough competition in the market and large volume of advertisements make the consumers confused regarding purchase decision making. There is a tendency in the minds of consumers to distrust advertising and to doubt about the genuineness of producers and products. Sometimes they feel exploited by the advertisers. This often results in the failure of advertisements and loss of money. The opportunity for consumers to raise voice and file complaints against non-credible/misleading advertisements again increases the risk of facing legal actions. According to Rodgers and Moore¹, advertisements that lack credibility, are often ignored or avoided by consumers. Hence knowledge about the perceived credibility of advertisements and consumer

psychology may help the advertisers and marketers to avoid mistakes and adopt the right advertisement tactics. In fact, from a careful review of past-related works the researcher could observe that still gaps existed in areas of existing knowledge related to advertising credibility in terms of variables, dimensions, scales, sample, context etc. The previous studies conducted in this area approached advertising credibility with limited dimensions and items. Therefore, this paper attempts to develop a valid scale to measure Advertising Credibility. Children's Health Food Drinks segment is opted to study the dimensions and structure of perceived advertising credibility.

Credibility of Advertising: Credibility has been identified as one of the most important characteristics of a persuasive message which frequently affect the result of persuasive messages^{1,2}. Advertising credibility can be defined as "the extent to which the consumer perceives claims made about the brand in the ad, to be truthful and believable"^{3,4}. Rodgers and Moore¹ argue that the advertisements those lack credibility are generally ignored or avoided by consumers. According to Lafferty

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and Goldsmith⁵, irrespective of media type, advertising credibility is a crucial inspiration for creation of attitude and subsequent behaviors.

Dimensions of Advertising Credibility: Perceived credibility of an advertisement is influenced by numerous factors, especially by the firm's credibility, the credibility of the person who brings a message⁶ and the credibility of the information content⁷. As per the literature advertising credibility has three components:

Advertiser / Corporate Credibility: Corporate credibility is defined as "the extent to which consumers believe that a firm can design and deliver products and services that satisfy customer needs and wants"⁸, and has been found to have direct, positive impacts on attitude toward the ad, attitude toward the brand, and purchase intention^{2,6,9}.

Endorser Credibility: An endorser is an individual, recognized by the public and uses this recognition on behalf of a consumer good, by appearing with it in an advertisement¹⁰. Endorser credibility in this research indicates a term used to specify a communicator's positive characteristics and trustworthiness that affect the receiver's acceptance of a message^{6,11}. Endorser credibility is further be classified into three: -'Expertise', 'Trustworthiness' and 'Attractiveness'^{6, 9,11}.

Message Content Credibility: Quality of message or argument is another important determinant of ad credibility. In a study Austin and Dong¹² tried to determine if the sender along with the message would have any impact on the total credibility of the information. They concluded that the perceived credibility of the information is more influenced by the message than by the sender.

Objectives of the Study:

1. To understand the structure of perceived advertising credibility
2. To develop and validate a multi-dimensional scale for measuring perceived advertising credibility

Research Methodology: Exploratory and descriptive research design and survey approach have been used for the study. A preliminary study was conducted to understand the dimension structure of advertising credibility which comprised a focus group interview and pilot study. The sample for the focus

group interview consisted of 50 mothers of children between 5-15 years old, and who are the consumers of CHFD and who watch TV commercials and 6 experts from advertising industry and 4 experts from marketing research. The in-depth interviews with 50 respondents were conducted and the as the second stage a pilot study was conducted by collecting responses from 50 respondents from Kochi, a South Indian City, and ensured the reliability of the instruments used for data collection.

The children's health food drinks (CHFD) industry is selected for studying the credibility of advertising communication. The CHFD brands selected for the study are Horlicks, Bournivita, Complan and Boost. The sample for the study was taken from the six corporations of Kerala state namely Kozhikode, Trichur, Kochi, Kollam, Kannur and Thiruvananthapuram. The mothers of children between 5-15 years were surveyed. For the selection of the wards (divisions) under study and for the selection of the sample respondents from the wards, multistage random sampling is used. The 2011 census document and 2015 voters list of the corporation were taken as sampling frame. The research instruments included structured questionnaires, advertisement story board and recorded TV commercials. The mothers were informed to respond to the questions related to the advertisements of their most preferred children's health drink brand. A total of 1252 responses were used for data analysis.

Measurement Tool Development: The results of focus interview and literature review gave insights in to the dimensions that should be highlighted in the study. After identifying the three relevant dimensions of ad credibility (corporate credibility, endorser credibility and message-content credibility) through focus interview, the items from validated scales used in the previous research were taken to construct the scale for advertising credibility. To measure corporate credibility 7 item scale is used based on the scale developed and validated by Newell and Goldsmith¹³. The endorser credibility measurement (13 items) was based on the scales of Ohanian, R.¹¹ and Goldsmith, et al.⁶. The message/content credibility scale is developed based on the measures of Kemp, Deena G.¹⁴, McKenzie and Lutz⁴ and Wang¹⁵ and focus group study.

Data Analysis and Discussion: The verification and cleaning of the collected data was done initially. Verification of Missing Values was done using

frequency test, Outliers using Z-scores, Normality and Randomness using Kolomogorov-Smirnov test with Lillefors significance correction. Skewness and kurtosis are used to ensure non-normality doesn't exist to a problematic level. Durbin- Watson statistics was found 2.046 thus established independent observations and "Runs" test was used to confirm randomness. Content validity is ensured through extensive literature review which helped also in the development of the constructs¹⁶. In this research a pilot study is conducted to ensure that the content validity concept is not violated. Criterion-related validity is ensured by using a common scale (five-point Likert scale) for measurement throughout the questionnaire.

Exploratory Factor Analysis: The next step in the scale validation procedure is to discover the dimension structure of perceived advertising credibility using the EFA. After considering the pilot study results, eliminated 3 items and finally 27 scale items have been used to measure advertising credibility. Exploratory factor analysis (Maximum Likelihood) was done using varimax rotation and the items with loading above 0.5 are taken while items with low loading were dropped. To assess the internal consistency a reliability test was conducted. Following Nunnally's suggestion¹⁷ it is ensured that for all the constructs the Cronbach alpha coefficients were greater than 0.70.

The KMO Measure was 0.940 and the Bartlett test was significant with $p < 0.001$. The Chi-square value of 14267.39 with 351 degrees of freedom affirmed the quality of data for further analysis and served as basis for factorization. The EFA provided four components with an 'Eigen value' greater than 1, which together explained over 54.013 percent of the variance. The items used to measure Advertising credibility is shown in Table 1.

After EFA the factor structure evolved with four dimensions. The 27 items used in the scale were classified into 4 dimensions such as Corporate credibility, Message-content credibility, Endorser credibility- Trustworthiness and Endorser credibility- Attractiveness which is given in Table 2. The single dimension endorser credibility is divided into two subgroups here - 'trustworthiness of endorser' and 'attractiveness of endorser'. The themes behind the items were the basis for naming the factors. The factors extracted in each case are given in tables below with Cronbach alpha coefficients.

Confirmatory Factor Analysis Using Warp PLS

5.0: The CFA was done to confirm the factor structure model of Advertising credibility construct. The main objective of conducting confirmatory factor analysis is to check the model fit ie., whether the predefined model is fit with the observed data. Confirmatory factor analysis tested the construct validity of Advertising credibility using Warp PLS 5.0 software as it is the most advanced research tool. The results for the measurement model of Advertising credibility showed an acceptable fit.

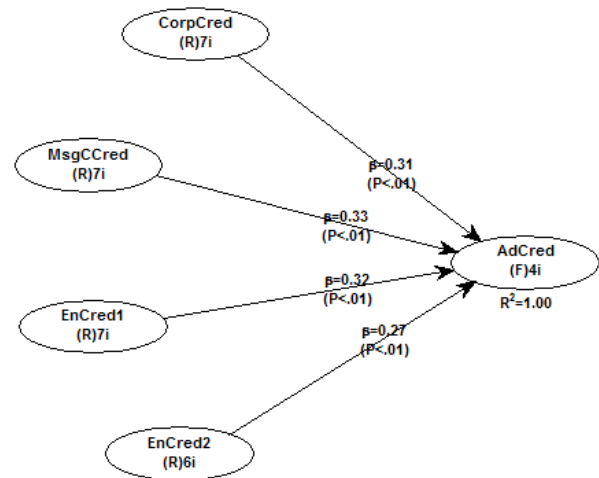


Figure 1: CFA Model - Advertising Credibility

The various fit criteria are reported below: Average path coefficient/APC=0.308, $P < 0.001$ and Average R-squared/ARS=1.000, $P < 0.001$ which was found significant. Average adjusted R-squared/AARS=1.000, $P < 0.001$. AVIF=1.876 which is acceptable if ≤ 5 and ideally ≤ 3.3 . TenenhausGoF/GoF=0.744, which should be ≥ 0.1 , ≥ 0.25 , ≥ 0.36 for small, medium and large effects respectively. Sympton's paradox ratio SPR=1.000 which is acceptable if ≥ 0.7 , ideally = 1. R-squared contribution ratio (RSCR)=1.000 which can be accepted if ≥ 0.9 , ideally = 1. The other fit criteria are given in Tables 4 and Table 5.

Results

The combined loadings and cross loadings of every indicator is significant as p-value is less than 0.05. P values less than 0.05 are desirable for reflective indicators. The indicator weights for latent variables are 0.314, 0.336, 0.318, 0.267 for corporate credibility, message-content credibility, endorser credibility-trustworthiness, endorser credibility-attractiveness, respectively.

The reliability of reflective constructs has been established as all composite reliability coefficient and Cronbach alpha values were above 0.7. For formative constructs, reliability is not a crucial consideration. It is noticed that all average variance extracted values were > 0.5, p- values of the loadings were <0.05. The loadings were equal to or >0.5 and cross loading were <0.5. Thus, the convergent validity of reflective indicators is

established. The convergent validity of the formative construct. Advertising credibility is also affirmed by observing that the corresponding AVE was > 0.5 and VIF found <0.5 for all formative indicators and weights were significant at p-value less than 0.05. Since the square root of the average variance extracted was higher than any of the correlations involving that latent variable, the discriminant validity also was confirmed.

Table 1: Measures of Advertising Credibility.

Item code	Items used in the advertising credibility scale	Item code	Items used in the advertising credibility scale
CC1	The Company has great amount of experience.	EC1	The persons appeared in the ad seems Trustworthy
CC2	The Company is skilled in what they do.	EC2	The persons appeared in the ad seems Dependable
CC3	The Company has great expertise.	EC3	The persons appeared in the ad seems to be Honest
CC4	The Company does not have much experience	EC4	The persons appeared in the ad seems Reliable
CC5	The Company is honest.	EC5	The persons appeared in the ad seems Sincere
CC6	I trust the Company.	EC6	The persons appeared in the ad are knowledgeable
CC7	The Company makes truthful claims	EC7	The persons appeared in the ad are Experienced
MC1	The information about the Product is Truthful	EC8	The persons appeared in the ad seems Qualified
MC2	The health care communication is believable	EC9	The persons in the ad are Skilled
MC3	The overall presentation of the matter is convincing	EC10	The persons in the ad seems Classy
MC4	The communicated message is clear and understandable	EC11	The persons in the ad seems Elegant
MC5	The ad is informative	EC12	The persons in the ad looks Attractive
MC6	The content and presentation are ethical	EC13	The persons in the ad are Beautiful
MC7	The communication by the characters seemed unbiased		

Table 2: Factors extracted after EFA

Sl. No	Factor name	Items	No. of Items	Cronbach's alpha
1	Corporate Credibility	CC1,CC2,CC3,CC4, CC5,CC6,CC7	7	0.849
2	Message Content Credibility	MC1,MC2,MC3,MC4, MC5,MC6,MC7	7	0.837
3	Endorser Credibility-Trust worthiness	EC1,EC2,EC3,EC4, EC5, EC6, EC7	7	0.85
4	Endorser Credibility- Attractiveness	EC8,EC9,EC10,EC11, EC12, EC13	6	0.841

Table 3: Various Quality criteria for CFA Model

Advertising Credibility Dimensions	Composite Reliability Coefficients	Cronbach's Alpha Coefficients	Average Variances Extracted
Corporate Credibility (R)7i	0.886	0.849	0.527
Message Content Credibility (R)7i	0.877	0.837	0.506
Endorser Credibility-Trust worthiness (R)7i	0.886	0.85	0.527
Endorser Credibility- Attractiveness (R)6i	0.883	0.841	0.558

Table 4: Correlation among L.Vs. with square roots. of AVEs

Correlations among L.Vs. with sq. rts. of AVEs					
	CorpCre	MsgCCre	EnCred1	EnCred2	AdCred
CorpCre	0.726	0.648	0.539	0.435	0.719
MsgCCre	0.648	0.711	0.671	0.459	0.705
EnCred1	0.539	0.671	0.726	0.434	0.718
EnCred2	0.435	0.459	0.434	0.747	0.696
AdCred	0.719	0.705	0.718	0.696	0.807

Note: Square roots of AVEs are shown on the diagonals.

Conclusion

Measuring and building credibility in advertising communication lessens consumer’s doubt about the intension of marketers and enhances the advertising effects which will positively contribute to an increase in sales. This again will save the companies from the possible legal actions invited by the non-credible advertisements. The empirical investigation into the dimensionality of ad credibility after confirmatory factor analysis, revealed four ad credibility dimensions containing 27 ad credibility attributes.

The factor construction developed after EFA had items with adequate loadings and less conflicting cross loadings. All the 27 items could be classified into 4 dimensions such as Corporate credibility, Message-content credibility, Endorser credibility- Trustworthiness and Endorser credibility- Attractiveness. Almost all the dimensions identified as significant contributors to ad credibility. The CFA model of Advertising Credibility came out as good model with adequate fit and satisfied other quality parameters. This research contributes valid output to equip corporates and their ad agencies to assess the perceived credibility of their advertisement and to study its linkage with other brand related and purchase related variables. Based on such studies they can frame suitable advertising and marketing strategies. Since health is a sensitive issue, consumers are less willing to take risk and involvement in information search for healthcare products is more. This also highlights the need for a credible communication from society’s point of view.

Ethical clearance: The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5).

Source of Funding: Self

Conflict of Interest: Nil

References

1. Rodgers S. L, Moore J. J. An Examination of Advertising Credibility and Skepticism in Five Different Media Using the Persuasion Knowledge Model. Proceedings of the conference of the American Academy of Advertising. 2005; 10-18: ISBN:0931030307
2. Choi S. M., Rifon N. J. Antecedents and Consequences of Web Advertising Credibility: A Study of Consumer Response to Banner Ads. Journal of Interactive Advertising. 2002;3(1).
3. Cottea J., Coulterb R. A., Moore M. Enhancing or disrupting guilt: the role of ad credibility and perceived manipulative intent. Journal of Business Research. 2005; 58: 361– 368.
4. Mac Kenzie S. B., LutzR. J. An Empirical Examination of the Structural Antecedents of Attitude Toward the Ad in an Advertising Pretesting Context. Journal of Marketing. 1989; 53 (2):48-65.
5. Lafferty B. A., Goldsmith R. E. Corporate Credibility’s Role in Consumers’ Attitudes and Purchase Intentions When a High versus a Low Credibility Endorser Is Used in the Ad. Journal of Business Research. 1999;44: 109-116.
6. GoldsmithR. E., LaffertyB. A. & Newell S. J. The Impact of Corporate Credibility and Celebrity Credibility on Consumer Reaction to Advertisements and Brands. Journal of Advertising. 2000; 29(3): 43-54.
7. Gardete P. Cheap-Talk Advertising and Misrepresentation in Vertically Differentiated Markets. Marketing Science. 2013; 32: 609-621.

8. Keller K.L. Branding Perspectives on Social Marketing”, in *NA - Advances in Consumer Research*. 1998; 25, eds. Joseph W. Alba & J. Wesley Hutchinson, Provo, UT : Association for Consumer Research: 299-302.
9. Abdul Majid, M.A. The Impact of Source Credibility on Yemeni Male Consumers’ Attitudes Toward Print Advertisement, Brand attitudes and Purchase Intention of Head Cover Product: The moderating role of Brand Familiarity, PhD Thesis, University Sains Malaysia.2009.
10. Byrne A. Whitehead M. & Breen S. The naked truth of celebrity endorsement. *British Food Journal*.2003; 105(4/5): 288-296.
11. Ohanian R. Construction and Validation of a Scale to Measure Celebrity Endorsers’ Perceived Expertise, Trustworthiness, and Attractiveness. *Journal of Advertising*.1990; 19(3): 39-52.
12. Austin, E.W., Q. Dong. Source V. Content Effects on Judgments of News Believability. *Journalism Quarterly*.1994; 71(4): 973–8.
13. Newell, S.J., Goldsmith, R. E. The development of a scale to measure perceived corporate credibility. *Journal of Business Research*.2001; 52: 235-247.
14. Kemp, D. G. Source credibility and public information campaigns: The effect of audience evaluations of organizational sponsors on message acceptance. Graduate Theses and Dissertations.2007; <http://scholarcommons.usf.edu/etd/2241>.
15. Wang, A. Advertising Engagement: A Driver of Message Involvement on Message Effects, *Journal of advertising Research*. 2006.
16. Reji Kumar, G. Study on linkage between customer expectation, service quality perception customer satisfaction and related behavioral intentions in banking context, Anna University, Chennai.2011.
17. Nunnally, J. C. *Psychometric Theory* (2nd ed.). 1978. New York, NY: McGraw-Hill.

Service Quality Perceptions to Wards Health Insurance Products

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Abstract

Context: A healthy and competent workforce is the biggest asset of any nation and therefore, it is an important objective of every progressive government to ensure health for all. In this regard, insurance is the backbone in managing the risk of the country. In today's globalised world of fierce competition, providing a quality service to the customers is the key for existence and success of any business. Service quality or quality of service is said to be a function of three variables, viz., expectation, perception and performance. The main objective of this paper is to identify the service quality of health insurance products and services offered by the public and private health insurance companies and to identify the key factors contributing to the service quality. The study is based on primary data. The gaps between perception and expectation scores on various dimensions of service quality of health insurance products have been captured by the SERVQUAL tool.

Keywords: Insurance, Health, SERVQUAL, Dimensions, Service quality

Introduction

Health is a state of physical, mental, social well being and not merely the absence of disease or infirmity. Providing a security net for ensuring availability of quality and affordable healthcare to the population is the prime goal every nation aspires for. According to NFHS – 3, in spite of the emergence of a number of health insurance programmes and health schemes, only 2 percent of households in Assam reported that they have any kind of health insurance that covers at least one member of the household. But some evidences show that steadily the health insurance coverage is increasing. It may be because of the fact that people become aware of the high health care cost, incoming of the private players in insurance field and government health care/insurance schemes along with involvement of community based health insurance schemes. Assam

now stands at the threshold of transition of the industry to the next level. Health insurance would be one of the key tools to supplement and compliment the present health financing options.¹The Health Insurance Company's main aim to create an ideal environment for health insurance business with a satisfied customer at the core. Three core areas are identified namely service quality, customer satisfaction and role of hospitals for studying the marketing perspective in health insurance. Parasuraman, Zeithaml and Berry (1990) mention that service quality is an extrinsically perceived attribution based on the Customer's experience about the service that the Customer perceived through the service encounter.²

Objectives: To find out the gap between expectation and perception score in health insurance product service quality.

Research Questions: In order to guide the study and achieve the above objective, the following research questions are formulated

1. How is the service delivered by the health insurance providers perceived by their customer and does it meet the expectations of their customers?

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2. Which dimension is doing well among all five dimensions in health insurance sector?

Data Sources and Methodology: The geographical location for the present study has been selected purposively as Tinsukia district of Assam. The district is further stratified into development blocks. Tinsukia district has seven developmental blocks namely, Guijan, Hapjan, Itakhuli, Kakopothar, Margherita, Saikhuwa and Sadiya. Since the study is mainly concentrated in rural areas, thus the top three blocks namely Margherita, Kakopothar and Hapjan have been selected as these blocks have highest number of rural population respectively. In the next step, one Gaon Panchayat (GP) from each sample block having the highest population is taken as sample GP. Again Lekhapani GP of Margherita block, Kakojan GP of Kakopothar block, Hatijan GP of Hapjan block has highest number of rural population in their respective block. Thus these three GPs are selected as sample GP. 10% of the total villages of each sample GPs have been taken as sample villages. Lastly a total of 208 households have been selected for the field survey. A five pointlikert type scale is used in this study to evaluate the 5 health insurance service quality dimensions. Respondents were asked to provide ratings of both expectation and perceptions on the provided statements related to service quality. The service quality statements

used in the study were rated by using five pointlikert scale with 1 indicating 'strongly disagree', 2 indicating 'disagree', 3 indicating 'neutral', 4 indicating 'agree', and 5 indicating 'strongly agree'. Thus the difference obtained from subtracting the expectation scores from the perception score revealed the gap between customer's expectation and their perception of the service quality. The study period has been selected from May – July 2019. Respondents are basically the customers of New India Insurance Company (Public Sector Insurance Company) and Bajaj Allianz (Private Sector Insurance Company). According to the SERVQUAL tool, services quality of health insurance companies can be measured by the gap between expectations and perceptions of consumers on 5 dimensions of service quality namely reliability, assurance, responsiveness, professionalism and fairness in dealings.³

Reliability Gap: Reliability implies the ability to perform promised service dependably and with accuracy. Reliability is connected to the consistency of performance and dependability on the service. Here it is determined if the company give the service in the right way the first time and keeps to its promises every time.⁴ The term reliability refers to the ability of a health insurance company to consistently perform according to its specifications.

Table 1: Mean score/Standard deviation of perception and expectation on Reliability:

Reliability Attributes	Mean of perception score (P)	SD of perception score	Mean of expectation score (E)	SD of expectation score	Gap score P - E
The company gives all the required information	2.2260	0.94	3.2596	1.04	-1.0336
The company pointed out the best choice for me	1.6875	0.76	2.4087	0.78	-0.7212
I feel more confident when I purchase a policy	2.4087	0.82	3.1971	0.96	-0.7884
The Company's promises are reliable.	2.0529	0.85	2.9904	1.01	-0.9375
The company is consistent in providing quality services	2.1250	0.93	3.3317	0.94	-1.2067
Total	2.10002	0.86	3.0375	0.946	-0.93748

Source: Compiled from field survey

The table 1 shows the mean and standard deviation on the reliability dimension in the service quality of insurance policy holders about their companies. The total mean score and standard deviation on the perception on reliability attributes towards the service quality of insurance companies are 2.10002 and 0.86 respectively and for reliability expectation scores it is 3.0375 and 0.946. It is found that the mean perception

score for 'feeling more confident when they purchase a policy is highest i.e. 2.4087 whereas it is highest for the fifth attribute which is related to consistency in providing quality service i.e. 3.3317. Again for all four statements on reliability, it is seen that the mean expectation scores are greater than the mean perception scores which shows some difference in magnitude of gap score among the five items. It can be noted that attribute

2 has the lowest mean gap score (-0.72) which is related to “pointing out of Best Choice for the customer by the health insurance company. It indicates that people are comparatively less dissatisfied in this attribute than the other four attributes. Again attribute 5 has the highest mean gap score (-1.2067) which is related to consistency in providing quality service.

Assurance Gap: Assurance means that employees’ behavior will give customers confidence in the firm and that the firm makes customers feel safe.⁵ It also means that the employees are courteous and have the necessary knowledge to respond to customers’ questions.

Table 2: Mean score/Standard deviation of perception and expectation on Assurance:

Assurance Attribute	Mean of Perception Score (P)	SD of Perception Score	Mean of Expectation Score (E)	SD of Expectation Score	Gap Score (P – E)
I feel that I can always trust this company	2.1827	0.89	2.4471	0.88	- 0.2644
The company follows the motto “Customer is the king”.	2.3510	0.91	2.5481	0.89	-0.1971
The company gives sincere commitment in servicing The claims	2.3077	1.02	3.0625	0.85	-0.7548
The company deserves recommendation for new Customers	2.1346	0.78	2.8976	0.76	-0.763
Company gives more importance to the satisfaction of customers rather than profit gain.	2.673	0.95	2.956	1.78	-0.283
Total	2.32988	0.91	2.78228	1.032	-0.4524

Source: Compiled from field survey

It can be observed that the process execution time and kind and politeness of the employees are noticeable factors contributing to the average assurance gap. Employee’s expertise and knowledge on the company’s operations hold a big hand in satisfying the customers in terms of service quality. Efficient and knowledgeable employees are always a big boon for any organization. It can be noted that, out of all the attributes for assurance, attribute 7 i.e. “The company follows the motto customer is the king” has the lowest mean gap score (-0.1971) In terms of expectation, attribute 6 i.e. “I feel that I can always trust this company” has lowest mean, whereas in

terms of perception attribute 9 i.e. “Company gives more importance to the satisfaction of customers rather than profit gain” has lowest mean gap score. Few respondents think that some of the staffs appear not to be quick and efficient, as they tend to make errors or ask seniors to help them.

Responsiveness Gap: his means that the employees of a service firm are willing to help customers and respond to their requests as well as to inform customers when service will be provided and then give prompt service.

Table 3: Mean score/Standard deviation of perception and expectation on Responsiveness:

Responsiveness Attribute	Mean of Perception Score (P)	SD of Perception Score	Mean of Expectation Score (E)	SD of Expectation Score	Gap Score (P – E)
The Company tries to understand the specific needs.	2.4327	0.91	3.3798	0.96	-0.9471
The company actively responds to The inquiries regarding policy matters.	2.4423	0.96	3.3173	0.91	-0.875
The company timely informs us about the new offers.	2.4663	0.93	3.6587	0.99	-1.1924
The company properly informs me as and when my policy becomes due.	2.9758	0.94	3.7564	0.94	-0.7806
Information provided by the company is always Accurate.	2.5477	0.89	3.0567	0.96	-0.509
Total	2.57296	0.926	3.43378	0.952	-0.86082

Source: Compiled from field survey

This table 3 shows the perception and expectation gap score of various responsiveness attributes. It is evident the attribute 15 i.e. “Information provided by the company is always accurate” has lowest gap score (-0.509). It can be noted that, out of all the attributes for responsiveness, attribute 11 i.e. “The Company tries to understand the specific needs” has the lowest overall mean gap score (2.4327) In terms of expectation, attribute 6 i.e. “I feel that I can always trust this company” has lowest mean, whereas in in terms of expectation attribute 15 i.e. “Information provided by the company is always accurate” has lowest mean gap score. It is seen that in all cases policy holders are not satisfied.

Professionalism Gap: Professionalism is defined as the strict adherence to courtesy, honesty and responsibility when dealing with policy holders or stakeholder in the business environment.

Table 4: Mean score/Standard deviation of perception and expectation on Professionalism

Professionalism Dimension	Mean of Perception Score (P)	SD of Perception Score	Mean of Expectation Score (E)	SD of Expectation Score	Gap Score (P – E)
The company gives the correct information about the service charges and related charges	2.5962	0.86	3.2981	0.82	-0.7019
The company timely informs any new Government Regulations regarding policies	2.7163	0.84	3.4760	0.88	-0.7597
I never felt any communication problem	2.7429	0.81	3.6399	0.85	-0.897
The company tries to avoid probable conflict	2.6754	0.87	3.7462	0.90	-1.0708
Total	2.6827	0.845	3.54005	0.8625	-0.85735

Source: Compiled from field survey

The above table4 deals with the mean and standard deviation on the professionalism of service quality received by policy holders of the insurance policy. The total mean score and standard deviation on the perception professionalism dimension in the service quality of Health Insurance Company are 2.6827 and

0.845 respectively, whereas in case of expectation professionalism dimension the mean score and standard deviation are 3.54005 and 0.8625 respectively. Among the four attributes of professionalism dimension attribute 19 i.e “ The company tries to avoid probable conflict” has highest mean gap score (-1.0708) and attribute 16 i.e

“The company gives the correct information about the service charges and related charges” has least gap score (-0.7019)

Fairness in Dealings: Factors consist of trustworthiness, believability and honesty comes under

the fairness dimension of any service organization. It means to the level the company has the customers’ best interest at heart and job. Factors that affect the fairness are the company name and fame, reputation, personal characteristics and the degree to which the company is connected to intersections with customers.

Table 5: Mean score/Standard deviation of perception and expectation on Fairness in dealings

Fairness in dealings	Mean of Perception Score (P)	SD of Perception Score	Mean of Expectation Score (E)	SD of Expectation Score	Gap Score (P – E)
The company openly discusses the problems	2.5962	0.86	3.2981	0.82	-0.7019
The company has an effective Grievance Redressal mechanism	2.7163	0.84	3.4760	0.88	-0.7597
Company tries to solve the problems at the office level itself	2.8521	0.88	3.8546	0.90	-1.0025
The company handles the conflicts as speedy as possible	2.9745	0.85	3.8123	0.89	-0.8378
Total	2.784775	0.8575	3.61025	0.8725	-0.825475

Source: Compiled from field survey

The table 5 shows that the total mean score and standard deviation on the perception fairness dimension in the service quality of Health Insurance Company are 2.784775 and 0.8575 respectively, whereas in case of expectation fairness dimensions the mean score and standard deviation are 3.61025 and 0.8725 respectively. It is found that the mean perception and expectation score for ‘Company openly discusses the problems’ are 2.5962 and 3.2981 respectively for insurance policy holders, perception and expectation mean score for ‘The company has an effective grievance redressal mechanism’ are 2.7163 and 3.4760 respectively for insurance policyholders, perception and expectation mean score for “Company tries to solve the problems at the office level itself” are 2.8521 and 3.8546 respectively for insurance policy holders, the perception and expectation

mean score for “The Company handles the conflicts as speedy as possible” are 2.9745 and 3.8123 respectively for insurance policy holders. It is evident the attribute 20 i.e. “The company openly discusses the problems” has lowest gap score (-0.7019). It can be noted that, out of all the attributes for fairness dimension, attribute 22 i.e. “Company tries to solve the problems at the office level itself” has the highest mean gap score (-1.0025). The policyholders feel that all the activities starting from the fixation of premium and claim settlement is not fair and scientific. It demands for more transparency in dealings so that the grievances can be reduced. Seamless movement of information and integration of different stakeholders in health insurance is necessary in this direction.⁶

Gap score for the overall dimension of health insurance services:

Table 6: Mean and gap score for the overall dimension of health insurance services

Dimension	Perception Score	Expectation Score	Gap Score
Reliability	2.10002	3.0375	-0.93748
Assurance	2.32988	2.78228	-0.4524
Responsiveness	2.57296	3.43378	-0.86082
Professionalism	2.6827	3.54005	-0.85735
Fairness in Dealings	2.784775	3.61025	-0.825475

Source: Compiled from field survey

As most of the responses were negative, indicating significant shortfall in meeting customer expectations across all service areas and dimensions of health insurance policies. It is clear that reliability gap (-0.93748) which is highest followed by responsiveness gap (-0.86082), Professionalism gap (-0.85735), fairness in dealings gap (-0.825475), assurance gap (-0.4524). This entire gap can be reduced by minimal promise and maximum performance thus leading to customer satisfaction.

Conclusion:

The health insurance sector has undergone many changes after the adoption of new economic policy which is based on privatization, globalization and liberalization. Customer is the king in the present day market. Today the customer's service preference and demands are keep on changing at a rapid speed. The aim of the health insurance providers is to make the customers comfortable and happy. Health insurance companies should not only have to satisfy the customer but should also trigger to the attitude of the customers towards their insurance company. Each company follows different procedure. So, it is very difficult for the customer's to follow all these procedures. Personal communication is the most influencing medium considered for taking health insurance selection decisions by the policy holders. Customer retention in health insurance is beneficial to both the company and insured in many ways. Immediate attention is needed from the part of the companies to check the percentage of people renewing the policy from the same company.

Ethical Clearance: It is a review article.

Source of Fund: Self.

Conflict of Interest: Nil

References

1. Amsavani, R. and Gomathi S. A study on Satisfaction of Mediclaim Policyholders with special reference to Coimbatore City. *RVS Journal on Management*. 2013; 6 (1):10-23.
2. Parasuraman, A. Berry, L. and Zeithaml, V. SERVQUAL: a multi item scale for measuring customer perception of SQ. *Journal of Retailing*. 1988; 64 Spring: 12 – 40
3. Parasuraman, A. Berry, L. and Zeithaml, V. Refinement and Reassessment of SERVPERF scale, *Journal of Retailing*. 1991;67 (4): 420 - 450
4. Machnes, Y. The Demand for Private Health Care under National Health Insurance: The Case of the Self- Employed. *The European Journal of Health Economics*. 2006; 7(4): 265-269.
5. Buchmuller, T.C. and R.G. Valletta a. The Effects of Employer- Provided Health Insurance on Worker Mobility. *Industrial and Labour Relation Review*. 1996; 49(4): 39-55.
6. Syed Falaknaaz. Innovative Managed Care model to be launched on a pilot scale. *Journal of Express Health Care Management*. 2005 April; 35-46.

Unwed Mother: A Socio-Legal Study

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Abstract

Context: This research evaluated the effects of a social support program on young unwed mothers. Measures of social support, stress, affect, and life events were compiled by 15 program participants and 15 matched controls before and after the program six months later. The results showed significant increases in the size of the family and friend network for program participants relative to controls. Also, program participants reported more involvement in work and school and maintained a high level of positive affect significantly more than controls. The two groups did not differ in reported levels of stress. The implications of the findings for future research and program development were discussed.

Keywords: *Public Health Social Support Health Psychology Program Development Positive Affect*

Introduction

The trends in major research traditions show that the unwed motherhood has been well researched from a variety of disciplinary perspectives in the west especially in the countries like the United States of America, Canada, and UK. From a positivist theoretical paradigm, there are ample amount of research literature available that looked at single parenthood, unwed motherhood, teenage parenthood from descriptive to experimental, from retrospection to prospective, from cross sectional to longitudinal data at local and national levels. However, the phenomenon of illegitimacy or out of the wedlock pregnancy is not new; the recent time has shown a sharp increase as a direct effect of changing family systems in terms of its structure, stability and functioning. Though, the gravity of the phenomenon was well realized in western countries since 1950s and 1960s, and attracted a large amount of research interests from diverse disciplinary perspectives- public health, mental health, demographers, sociologists, anthropologists and social

work.

In developing countries like India, where family structure and functioning were relatively firm and stable, had been remained as a protective shield from teenage motherhood. However, India's intensive urbanization induced by the scientifically planned and politically accelerated economic development redefined the basic tenets of family relationships and its fundamental properties such as stability and functioning. These fundamental changes had produced a wide range of impacts on interpersonal and intrapersonal relationship contexts in individuals, families and communities and in the broader Indian society.

Teenage pregnancy today, is a widely acknowledged common public health problem worldwide, whereas the problems presented by the pregnant unwed teenagers are among the most difficult and perplexing issues faced by those who work in the fields of health, education and social services (Saran, 1999). No society is immune to teenage pregnancy and it affects every society-developed and developing alike. There is a growing awareness that early child bearing has multiple consequences in terms of maternal health, child health and over all well-being of society (WHO, 2004). Illegitimate pregnancies may have multiple traumatic impacts on the teenager, her boyfriend, her family, her community and ultimately on her yet to-be-born child. Therefore, pre-marital or teenage

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pregnancies is a crucial area of scientific exploration and examination in the context when no segment of society is immune to the causes and effects of the out-of-wedlock teenage pregnancy. Each year the extent of this problem grows. The statistics from worldwide indicate a substantial increase of unwed mothers that warrant multi-disciplinary research response. This trends suggest that the proportion of the adolescent population involved in increased sexual activities were so large that sexually active teenagers can no longer be considered socially deviant, a dominant view of Christian west.

Defining Unwed Motherhood: Does the term unwed mothers include all typologies of single parent women? For this, the researcher critically review the existing research literatures to identity the pattern, characteristics, nature, functions, and inclusiveness of existing definitions that deal with illegitimate pregnancy and subsequent child rearing and family management. In fact, socio-cultural and economic contexts of the society wherein teenage pregnancy takes places set the answers for many of these questions and these answers may vary widely across socio-cultural and economic contexts where teenagers live. There were efforts to define the term unwed mothers from both western and eastern socio-cultural contexts that uniquely responded to sensitive socio-cultural fabric of the society that accommodate these unwed mothers.

An unwed mother is a girl or woman (13-35 Years) who is not legally married to a man by whom she has conceived a child. She may be pregnant or has already delivered a child, whereas the single parent family is defined as a family in which either the father or mother has primary responsibility for bringing up children with only occasional or no contact with the spouse. The single parent family can be formed through death, divorce or separation”.

There were isolated efforts to define the concept of unwed mothers and unwed motherhood in the context of aboriginals or tribes, though the purpose was to operationalize the concept that was amenable for empirical investigations, these definitions were limited in conceptual clarity and for inclusiveness of diverse typologies of unwed mothers found in the unique tribal social context that often overlaps¹.

Such typologies may include unwed mothers who married later, widows who have single/multiple sexual relationships and gave birth to children, deserted tribal

women who gave birth to children in later sexual relationship outside wedlock relationships etc. Thus, it was operationalized towards an effort to define the term unwed tribal mother as a tribal woman or girl who conceived or/and gave birth to one or more children outside the wedlock of marriage by a man of same tribe, or man of other tribe or a man of non-tribel (Jose *et al.*, 2010a). In this definition, the purpose was to define the term “*unwed tribal mothers*” operationally where in emphasis was given only to pregnancy or delivery of children outside wedlock relationships². This definition is silent about a variety of typologies such as widows who delivered children outside of further wedlock relationships, or tribal women who were impregnated in pre-marital sexual relationships subsequently got into to wedlock relationships either with same or other men. A common thread that passes across all types of single parents was the functional aspect i.e., parenting. This was exclusively shouldered by women often with no help either from by whom they were impregnated or from their own families.

Socio-Demographic aspects of Unwed Motherhood: The existing evidence suggests that socio-demographic variables are critical onto the pathways to unwed motherhood while there is a paucity of evidences on socio-demographic pre-dispositions of unwed mothers, from Indian socio-cultural scenario. Thus, current study mostly relied on western empirical literature in order to depict a broader socio-demographic picture of unwed mothers. Sylvia has studied using two socio-economic variables such as the median income of all families and the percentage of families on welfare. US census data was used for this study with a conceptualizing a negative correlation between median income and teenage birth rates. This conceptualization was happened in the background that nationwide study of never-married women aged 15-19, which revealed that an inverse relationship between family income and sexual experience³. But a positive relationship between family socioeconomic status and a teenager’s likelihood of using contraception was also found in that study with an implication that —wealthier teenagers are not only less likely to be sexually active, but they also have easier access to contraceptive services, and are more likely to use them. Subsequent studies have also shown that wealthier family’s teenagers are more likely to use contraceptives and abortion services.

After examined the association with pre-existing characteristics and teenage pregnancy showed no

statistical associations between the demographic, economic, and educational characteristics of the teenage mothers at registration and whether or not they had a rapid subsequent pregnancy. The variables studied were age, number of years of residence in New Haven, number of parents in the household, total number of persons in the household, ordinal position, number of previous pregnancies, socioeconomic quartile, welfare status, educational goals, or whether or not they were in the age appropriate grade in schools. The authors attributed or explained these extremely surprising results on lack of associations as a result of homogeneity of the study group on many of these variables. The author further reported that this was partly due to the nature of the program (based in a hospital clinic) and partly to the research design (all who participated had to meet the study 29 criteria) Among the pre-existing characteristics, only school status at registration was correlated significantly with subsequent pregnancy those in school were less likely to become pregnant again by 15 months postpartum⁴. However, this result cannot be treated as conclusive because existing studies show strong influence of socio-demographic and economic variables in out of the wedlock pregnancies.

Psychological Aspects of Unwed Motherhood:

Identity of unwed mothers: The adolescence is a developmental stage characterized by multi-faceted event involving every aspect of an individual whereas the identity formation is the critical aspect. The sexuality becomes a dominant feature and makes adolescents prone to risky behaviour that would likely to results in becoming sexually active during early teenage and even in pregnancy. Such incidence is expected to bring a cascade of events that can negatively affect the main social contexts. The impact of pregnancy on the life of unmarried adolescents in the local context, has found that pregnancy as a stressful event that changes an adolescent's life completely⁵. Important aspects like financial dependence, negative self-image, sudden responsibilities and changes in aspirations are highlighted. Practical and emotional support was identified as critical for the young mothers' well being; without adequate help they are likely to flounder.

Self Concept and Self Esteem: The term self-concept is a general term used to refer to how someone thinks about or perceives themselves. Lewis (1990) suggests that development of a concept of self has two aspects: (1) The Existential Self is —the most basic part

of the self-scheme or self-concept; the sense of being separate and distinct from others and the awareness of the constancy of the self'. (2) The Categorical self, having realised that he or she exists as a separate experiencing being, the child next becomes aware that he or she is also an object in the world. Just as other objects including people have properties that can be experienced (big, small, red, smooth and so on) so the child is becoming aware of him or herself as an object which can be experienced and which has properties. Carl Rogers believes that self-concept has three different components. They are the view you have of yourself (Self image), how much value you place on yourself (Self esteem or self-worth) and what you wish you were really like (Ideal self). Self-efficacy as a concept refers to being able to picture yourself achieving what it is you want to achieve at the level you want to achieve it. As Bandura had put it, self-efficacy refers to people's convictions about their own capabilities for successfully executing a course of action that leads to a desired outcome.

Low self concept had been shown to be associated with adolescent pregnancy and has been associated with decreased attendance at prenatal and post natal care and with repeat pregnancy. Self-efficacy is another factor that can be predicted to influence the prenatal care. Social cognitive theory conceptualizes human functioning as a reciprocal interaction between personal factors such as self-efficacy and outcomes of expectancies, environmental factors, and behaviours⁶. Hence, self-efficacy refers to the people's confidence to regulate their motivation, thought process, emotional state, and social environment to effect a given behaviour. Hence guided by social cognitive theory, a peer-centred mastery model group intervention was designed. The programme focused on modelling and rehearsal skills to achieve **(a)** increase knowledge about pregnancy **(b)** prepare for childbirth **(c)** work with self care systems **(d)** including hospitals, clinics and physicians and nurses **(d)** enable expectant mothers to assess her own and her babies' health **(e)** prevent an unplanned repeat pregnancy **(f)** improve health self care. 262 pregnant adolescents were randomly assigned to either experimental or control groups of 6-8 participants. Experimental groups were provided peer-centered mastery model group intervention by nurse-midwives.

Family and Social Responses to Unwed Motherhood: Familial and societal reactions to unwed pregnancy and individuals were reviewed. Literature search has revealed that a limited number

of studies were available with this focus which was in aboriginal context. Such studies discussed that typical reactions of the alleged father to the news of the pregnancy would be annoyance, fear, anger and a desire to escape from the entire situation. Another set of reactions to pregnancies were the boys would react proudly when they learned of their prospective parenthood, and would offer to marry their pregnant girlfriends. Reviewing the responses of men by whom tribal girls in Kerala were impregnated. They placed responsibility and blame of out of the wedlock pregnancy on the victims, denied fatherhood of the conceptions, persuaded women to go for abortion and also refused the responsibility of household and children rearing. It was also reported that men were forced to provide financial security for households and child rearing in the context where they were questioned either by formal and non-formal institutions of justice⁷. The same study revealed that unwed mothers live through a series of positive and negative emotions and psychological responses in their initial periods of pregnancy while some of them felt very happy because during initial periods because they enjoyed their men's support and physical proximity. These mothers reported that, by being impregnated, they could find new meaning for their life and relationships. However, this was not the case for many other unwed mothers. They learned about their pregnancy with shock, disbelief and denial and experienced uncertainty about future, became fearful, felt giddy and weak. Some of them experienced anger towards self which were associated with occasional suicide ideation and actual suicidal attempts. Many perceived that every one stopped loving them and are left alone.

Legal perspectives/Human Rights: Social norms and legal systems that encourage or do not censure men's multiple sexual partners are likely to leave many of the women who become mothers through such unions economically vulnerable. Few men have sufficient wealth to adequately support multiple families and invest equally in each mate and her offspring, yet men continue to father children with multiple partners (Saran, 1999). In addition, structural violence in the forms of stigmatization and discriminations coupled with sexual harassment and violence is likely to restrict women's ability to seek legal redress and even deny access to or fare treatment from locally available non-formal judicial systems. For example, when men responsible for pregnancies deny or refuse to shoulder the responsibility of fatherhood, cases are often filed in police stations, not even reaches to the courts. But most

of the time, such cases are settled outside courts with nominal financial assistance and a promise to bear a share of the household and child rearing expenses by men. However, instances are many wherein ongoing financial support for household and child rearing simply remain as promises. As these men suddenly move away from women, contacts also do not exist in many cases where these promises remain unfulfilled. Hence, investigations need to focus on the process and outcomes of both institutional and non-institutional conflict resolutions models in practice that govern the lives of women because very minimal knowledge base is available in this regard (Jose *et al.*, 2010c). Similarly, a few social activists and a very limited number of NGOs have taken up the issue on their agenda but they too could not do much to stop the exploitation, resulting inadequate civil society response to facilitate and strengthen access to socially marginalized women's groups. Thus, it is vital to identify what are the capacity building needs of civil society organizations and strengthening them to effectively respond to human rights concerns.

Conclusion

Most of the research studies found out that the crucial problems which tribal communities face today in India are illiteracy, poor health, and poverty, lack of landholdings, unemployment and cultural diffusion. While compiling researches on the status of tribal women with regard to freedom of marriage and family, it is inferred that even though they are struggling for existence, they do not have much difficulties than that of non-tribal women, might be because of the equal status they have enjoyed with men in the social structure of the tribal societies, but they are marginalized within tribal communities in socio economic and political spheres.

A few studies which have been conducted in this field, found many psychological and social factors as the reason for unwed motherhood. Majority of the tribal women were exploited by persons from outside the community and studies found that, the psychological problems are high among the unmarried mothers.

There is meager research on the Quality of Life of single parent and the available studies on quality of social life shows that marital status significantly influenced quality of social life. This is implied that unwed tribal mothers were more likely to enjoy less quality social life than married mothers and unwed mothers who later married.

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Reference

1. Bhatia, B.D, Chandra, R. Adolescent mother - an unprepared child, Indian Journal of Maternal and Child health. 1993 Jul-Sep;4(3):67-70.
2. Cohen S., M. Burge. Partnering: A New Approach to Sexual and Reproductive Health, 2000 New York: UNFPA.
3. Chapin, J.R .Adolescent sex and mass media: A developmental approach. Adolescence, 2000 35(140),799-811.
4. Hurlock Elizabeth. Developmental Psychology A Life Span Approach. 5th Edition, Tata McGraw Hill Publishing Company Ltd, N. Delhi, 2002.221-251p.
5. Family Planning Association of India, Planned parenthood, Vol.3 March 2004,p.3.
6. Jessy John. Life Skills Development Programme for the mental Health of Juvenile in Kerala, India. Loyola Journal of social Sciences, Vol. 22 (2), Jul-Dec 2008.
7. Alan Guttmacher Institute. Teenage pregnancy: the problem that hasn't gone away. 1981, New York.

Association of Epicardial Adipose Tissue Thickness with Resting and Post-Exercise Cardiac Output in Overweight and Obese Individuals

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Abstract

Background: Epicardial adipose tissue is known to have adverse effect on local coronary health, cardiac structure and function. Echocardiography has shown to be a reliable method to measure the adipose thickness.

Aim: To study the association between epicardial adipose tissue thickness with resting and post-exercise test cardiac output.

Method: A cross-sectional study of 26 overweight and obese subjects in the age group of 20 to 50 was included. Epicardial adipose tissue thickness was measured using M-mode echocardiogram. Resting and post exercise cardiac output, ejection fraction and heart rate recovery were measured during sub-maximal exercise on treadmill.

Results: There was no significant correlation of epicardial adipose tissue thickness with resting and post-exercise cardiac output, ejection fraction and heart rate recovery.

Conclusion: Cardiac output, Ejection fraction at rest and post - exercise, also Heart rate recovery were not affected by epicardial adipose tissue thickness of less than 4mm.

Keywords: Epicardial adipose tissue, cardiac output, sub-maximal exercise test, body mass index, overweight and obesity, echocardiography

Introduction

Overweight and obesity are considered as major risk factors for cardiovascular diseases, diabetes, degenerative diseases and cancers.¹ There is an increase in morbidity and mortality resulting from obesity due

to lifestyle changes in Indians.² Cardiovascular and metabolic diseases are found to be more prevalent in obese individuals with increased visceral adipose tissue.³ Epicardial adipose tissue (EAT) is the fat located between the myocardium and visceral pericardium⁴. EAT is found to have influence on local coronary artery health^{5,6}. It is the true visceral fat depot of the heart. Increased amount of EAT is associated with abnormal cardiac morphology as it adds to the weight of the ventricles which may further restrict the contraction of heart and pumping ability^{7,8}. EAT has been shown to be very closely related to intra-abdominal adiposity, a marker of entire body visceral adiposity, according to

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various magnetic resonance imaging studies. It is well known that visceral adiposity rather than subcutaneous adiposity is more responsible for health risks associated with fat deposition in humans.^{9,10}

Even though the gold standard method to measure EAT thickness is MRI, echocardiography has shown to be a reliable method to measure the adipose thickness. Epicardial fat thickness is measured on a free wall of the right ventricle from both parasternal long – and short- axis views. The largest amount of epicardial fat is usually seen at this right ventricular free wall site. Epicardial adipose tissue is usually seen as an echo-free or if it is massive, hyper-echoic space.^{11, 12} Stroke volume can also be measured using echocardiography. Excess VAT has a detrimental effect on sub-maximal aerobic capacity.¹³ Fick's principle states that VO_2 peak will occur when the maximal arterio-venous oxygen difference and the cardiac output (CO) reach their maximum during an exercise test.¹⁴ Thus, VO_2 peak is directly related to the maximal arterio-venous oxygen difference and CO. CO has been recognized as the most important measurement in the assessment of cardiac pump function and overall hemodynamic function.¹⁵ The influence of increased amount of epicardial adipose tissue thickness on the cardiac function is unknown. The aim of the study is to determine the association between epicardial adipose tissue thickness and resting and post-exercise cardiac output.

Method and Materials:

A cross-sectional study of 26 subjects with convenience was conducted at Cardiology department, Kasturba Hospital, Manipal. The participants of age between 20 to 50 years with $BMI \geq 24.9 \text{ kg/m}^2$, both male and female sedentary individuals (who exercise less than 3 Times/week) were included. The participants with any known respiratory and musculoskeletal conditions, those on regular medications were excluded from the study

Approval from the University Ethical Committee was obtained, following which a verbal advertisement was given among all staff and students of the constituent colleges of University. Participants went for a complete cardiac evaluation to rule out any undiagnosed cardiac conditions and then subjects were recruited as per the inclusion and exclusion criteria. A written informed consent was obtained from all the eligible subjects. Procedure was explained to the subjects and following data were documented: Age(years), height(cm),

weight(kg), $BMI(\text{kg/m}^2)$, body fat percentage and the baseline characteristics like EAT thickness(mm), Heart rate(bpm), Stroke volume(ml/beat), Ejection fraction(%) were measured in the left lateral decubitus position.

A single cardiovascular technician measured EAT thickness, SV using 2-D, B-mode echocardiography, with a Trans-thoracic, parasternal view [long – axis measurement of EAT thickness and apical 4- chambered method for stroke volume (which was calculated using the formula: end diastolic volume {EDV} – end systolic volume {ESV})]. And the EF was measured using M-mode parasternal long-axis view. Subjects were then allowed to walk on the treadmill for 2 minutes to familiarize the instrument. Then test was conducted on the treadmill according to stages of Balke protocol (as per mentioned in the appendices). Test was terminated when the subjects complained of fatigue or reached 75 – 85% of Maximum heart rate (HRmax). The termination criteria for the study include fatigue, onset of angina or angina-like symptoms, significant decrease in SBP of 20mmHg or more, light-headedness, confusion, ataxia, pallor, cyanosis, nausea, or signs of severe Peripheral circulatory insufficiency, excessive increase in BP systolic >260mmHg, diastolic >115mmHg, also when subject requested to stop test for whatever reason and the equipment failure. Immediately after cessation of the test, subjects were made to lie on the left lateral position as before to measure SV and EF, within the first minute and simultaneously HRR was measured at 0, 1st, 3rd, 5th minute. The data was analyzed using SPSS version 19. Pearson's correlation was used to correlate EAT with BMI and body fat percentage, EAT with resting and post exercise cardiac output and ejection fraction, EAT with heart rate recovery. Heart rate recovery pattern was analyzed using repeated measures ANOVA

Results

There was a significant difference in the resting and post-exercise cardiac output. There was a moderate correlation between epicardial adipose tissue thickness and body mass index, but no significant correlation was found between EAT and total body fat percentage. There was a significant rise in heart rate during the first minute of recovery, but it did not return to baseline by the 5th minute of recovery. However, there was no significant correlation found between epicardial adipose tissue thickness and heart rate recovery

Figure:1. A) Procedure of echocardiographic measurement of EAT thickness, SV, EF (resting and post-exercise) in the left lateral decubitus position. B) 2-D, B-mode transthoracic Parasternal view, long axis measurement of EAT thickness.

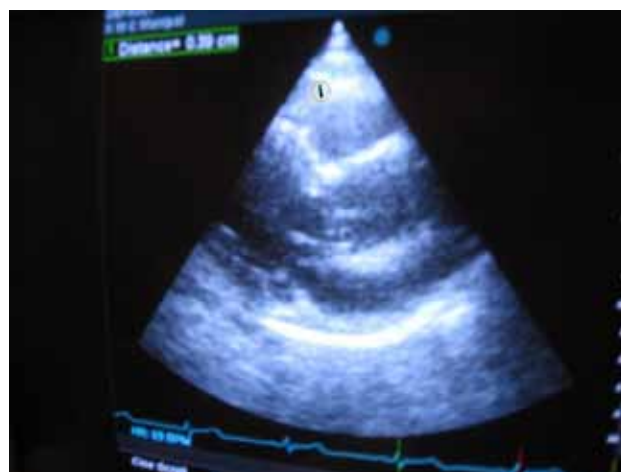


(A)

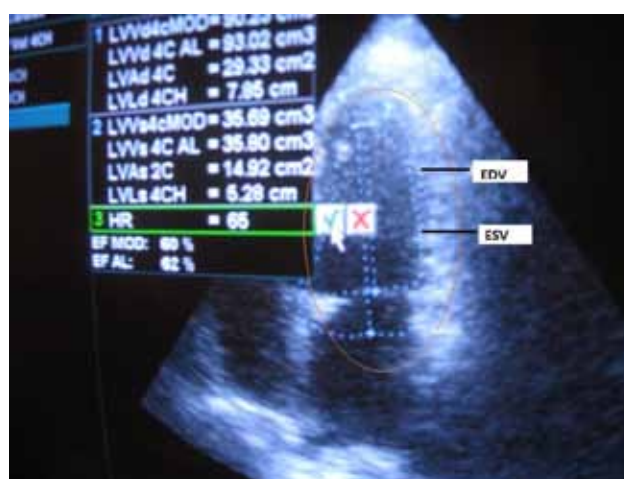


(B)

C). B-mode echocardiographic, parasternal view, long axis measurement of EAT showing thickness of 3.9 mm (marked area).D) Measurement of SV using and apical 4-chambered method (SV=EDV- ESV)



(C)



(D)

Table: 1. Demographic characteristic of subjects from age group 20-50 years.

	Mean ± SD (n=26)
Age(year)	27.46±8.78
BMI (kg/m ²)	30.16±4.41
Body fat percentage	38.35±5.6
EAT thickness (mm)*	2.58±0.447

°BMI – Body Mass Index *EAT- Epicardial Adipose Tissue

Table: 2. Comparison of resting and post-exercise cardiac output and ejection fraction

	Resting (L/min) Mean ±SD	Post-exercise (L/min) Mean ±SD	p value
Cardiac output	3.30±0.8	6.8±1.8	<0.05
Ejection fraction	66.5±3.6	74.5±2.9	<0.05

Table: 3. Correlation of BMI and body fat percentage with epicardial adipose tissue thickness

	r	p value
BMI & EAT	0.424	0.015
Total body fat % and EAT	0.183	0.186

Discussion

This study was conducted to determine the influence of EAT thickness on cardiac function. Increased amount of EAT is known to have a potential active role in the development of cardiovascular and metabolic disorders.¹⁶ But whether excess amount of EAT thickness influences the cardiac function is not known.

In the present study, we investigated the influence of EAT thickness on CO, EF and HRR. We found that all the participants in the present study were under the categories of overweight and obese (Class1 & 2) Indian subjects. The EAT values obtained in the present study were relatively low (1.9mm -3.9mm) [n=26] in comparison with African American (n=50) & Non – Hispanic white (n=106) population (6.7- 8.9mm).^{17, 18} We found a moderate correlation between overweight as well as class1 and class 2 obesity with EAT thickness. We could not study the subjects in class 3 obese category.

In our study, a linear increase in the resting and post-exercise cardiac output and ejection fraction was found. It is known that the aerobic capacity is directly proportional to cardiac output and arterio-venous oxygen difference.¹⁹ It has been shown that higher cardiac output in response to exercise testing in overweight people compared with normal –weight people may be explained by higher stroke volume. It is also shown that large differences in VO₂ peak values in general population are due primarily to large differences in maximal stroke volume.^{20, 21}

EAT can substantially modulate the cardiac morphology and function.²² Ejection fraction and stroke

volume are good indicators of cardiac function. In this study we found no significant correlation between EAT thickness less than 4mm and resting and post-exercise cardiac output and ejection fraction. We did not find literature on association of EAT thickness with cardiac output and ejection fraction.

Heart rate recovery is a predictor of future cardiovascular events and indicates the autonomic function of the body.²³ We found no significant correlation between EAT thickness and HRR. HRR in the first minute was dropped by more than 20 beats per minutes (mean HRR was 28 bpm), indicating normal autonomic function. However, baseline values were not achieved within the fifth minute. In the study conducted by Kim et al, there was a blunted heart rate response in the 1- and 2- minute of recovery. And the cardiorespiratory fitness which was assessed as VO₂ peak was also reduced in obese men.²⁴ This study suggests that EAT thickness of less than 4mm does not affect the cardiac function and aerobic capacity was not affected by EAT thickness in overweight, as well as class 1 & 2 obese subjects.

The exact relationship of EAT thickness with cardiac output could not be established because of small sample size and also because of EAT thickness was not more than 4mm. Further studies are required to focus on larger sample size with wider age group distribution. Future research should include all categories of overweight and obesity. There was no significant correlation between epicardial adipose tissue thickness and resting and post-exercise cardiac output. Cardiac output, Ejection fraction at rest and post - exercise, also Heart rate recovery were not affected by epicardial adipose tissue thickness of less than 4mm.

Conclusion

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Conflict of Interest: The authors hereby declare that there is no conflict of interest with regards to the content in the manuscript

References

1. Pi-Sunyer FX. Health implications of obesity. The American journal of clinical nutrition. 1991 Jun 1;53(6):1595S-603S.
2. Gopalan C. Rising Incidence of Obesity, Coronary Heart Disease and Diabetes in the Indian Urban

- Middle Class. *World Review of Nutrition and Fitness*. 2001;90:127-43.
3. Matsuzawa Y, Nakamura T, Shimomura I, Kotani K. Visceral fat accumulation and cardiovascular disease. *Obesity research*. 1995 Dec;3(S5):645S-7S.
 4. Talman AH, Psaltis PJ, Cameron JD, Meredith IT, Seneviratne SK, Wong DT. Epicardial adipose tissue: far more than a fat depot. *Cardiovascular diagnosis and therapy*. 2014 Dec;4(6):416.
 5. Mahabadi AA, Massaro JM, Rosito GA, Levy D, Murabito JM, Wolf PA, O'Donnell CJ, Fox CS, Hoffmann U. Association of pericardial fat, intrathoracic fat, and visceral abdominal fat with cardiovascular disease burden: the Framingham Heart Study. *European heart journal*. 2009 Jan 9;30(7):850-6.
 6. Payne GA, Kohr MC, Tune JD. Epicardial perivascular adipose tissue as a therapeutic target in obesity-related coronary artery disease. *British journal of pharmacology*. 2012 Feb;165(3):659-69.
 7. Petta S, Argano C, Colomba D, Cammà C, Di Marco V, Cabibi D, Tuttolomondo A, Marchesini G, Pinto A, Licata G, Craxì A. Epicardial fat, cardiac geometry and cardiac function in patients with non-alcoholic fatty liver disease: association with the severity of liver disease. *Journal of hepatology*. 2015 Apr 1;62(4):928-33.
 8. Iacobellis G, Ribaldo MC, Leto G, Zappaterreno A, Vecci E, Di Mario U, Leonetti F. Influence of excess fat on cardiac morphology and function: study in uncomplicated obesity. *Obesity research*. 2002 Aug;10(8):767-73.
 9. Flüchter S, Haggi D, Dinter D, Heberlein W, Kühl HP, Neff W, Sueselbeck T, Borggreffe M, Papavassiliu T. Volumetric assessment of epicardial adipose tissue with cardiovascular magnetic resonance imaging. *Obesity*. 2007 Apr;15(4):870-8.
 10. Nelson AJ, Worthley MI, Psaltis PJ, Carbone A, Dundon BK, Duncan RF, Piantadosi C, Lau DH, Sanders P, Wittert GA, Worthley SG. Validation of cardiovascular magnetic resonance assessment of pericardial adipose tissue volume. *Journal of Cardiovascular Magnetic Resonance*. 2009 Dec;11(1):15.
 11. Iacobellis G, Willens HJ. Echocardiographic epicardial fat: a review of research and clinical applications. *Journal of the American Society of Echocardiography*. 2009 Dec 1;22(12):1311-9.
 12. Iacobellis G, Willens HJ, Barbaro G, Sharma AM. Threshold values of high-risk echocardiographic epicardial fat thickness. *Obesity*. 2008 Apr;16(4):887-92.
 13. Dubin J, Wallerson DC, Cody RJ, Devereux RB. Comparative accuracy of Doppler echocardiographic method for clinical stroke volume determination. *American heart journal*. 1990 Jul 1;120(1):116-23.
 14. Wagner PD. An integrated view of the determinants of maximum oxygen uptake. In *Oxygen transfer from atmosphere to tissues 1988* (pp. 245-256). Springer, Boston, MA.
 15. de Divitiis OR, Fazio SE, Petitto M, Maddalena G, Contaldo F, Mancini M. Obesity and cardiac function. *Circulation*. 1981 Sep;64(3):477-82.
 16. Iacobellis G, Sharma AM. Epicardial adipose tissue as new cardio-metabolic risk marker and potential therapeutic target in the metabolic syndrome. *Current pharmaceutical design*. 2007 Jul 1;13(21):2180-4.
 17. Yerramasu A, Dey D, Venuraju S, Anand DV, Atwal S, Corder R, Berman DS, Lahiri A. Increased volume of epicardial fat is an independent risk factor for accelerated progression of sub-clinical coronary atherosclerosis. *Atherosclerosis*. 2012 Jan 1;220(1):223-30.
 18. Pierdomenico SD, Pierdomenico AM, Cuccurullo F, Iacobellis G. Meta-analysis of the relation of echocardiographic epicardial adipose tissue thickness and the metabolic syndrome. *The American journal of cardiology*. 2013 Jan 1;111(1):73-8.
 19. Stringer WW, Hansen JE, Wasserman K. Cardiac output estimated noninvasively from oxygen uptake during exercise. *Journal of Applied Physiology*. 1997 Mar 1;82(3):908-12.
 20. Ogawa T, Spina RJ, Martin 3rd WH, Kohrt WM, Schechtman KB, Holloszy JO, Ehsani AA. Effects of aging, sex, and physical training on cardiovascular responses to exercise. *Circulation*. 1992 Aug;86(2):494-503.
 21. Vella CA, Paul DR, Bader J. Cardiac response to exercise in normal-weight and obese, Hispanic men and women: implications for exercise prescription. *Acta physiologica*. 2012 May;205(1):113-23.

22. Petta S, Argano C, Colomba D, Cammà C, Di Marco V, Cabibi D, Tuttolomondo A, Marchesini G, Pinto A, Licata G, Craxì A. Epicardial fat, cardiac geometry and cardiac function in patients with non-alcoholic fatty liver disease: association with the severity of liver disease. *Journal of hepatology*. 2015 Apr 1;62(4):928-33.
23. Cole CR, Blackstone EH, Pashkow FJ, Snader CE, Lauer MS. Heart-rate recovery immediately after exercise as a predictor of mortality. *New England journal of medicine*. 1999 Oct 28;341(18):1351-7.
24. Kim MK, Tanaka K, Kim MJ, Matsuo T, Tomita T, Ohkubo H, Maeda S, Ajisaka R. Epicardial fat tissue: relationship with cardiorespiratory fitness in men. *Medicine and science in sports and exercise*. 2010 Mar;42(3):463-9.

Factors Affecting Risk of Cardiovascular Diseases among Hotel Employees in Udupi District, Karnataka

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Abstract

Context: Several research has indicated the increasing morbidity and mortality across the globe. Diet, lifestyle habits, stress are the most common risk factors associated with cardiovascular disease (CVD) risk. Hotel employees have been reported to have increased workload and stress which increases their risk to CVD related morbidity and mortality. This paper is a pilot study of the cross-sectional research study undertaken to identify risk factors associated with CVD risk among hotel employees in Udupi district of Karnataka. A structured questionnaire was used to elicit information pertaining to medical history, lifestyle habits, stress, sleep, bowel toxicity, inflammation and pain, blood glucose, blood lipids, diet, blood pressure and weight status. Research identified abnormal blood sugar levels, lipid profile, high blood pressure, high waist circumference and lifestyle habits like smoking and alcohol consumption as common risk factors among hotel employees. Over 69% had moderate to high risk of CVD due to the above mentioned risk factors. A good diet and lifestyle management can modify these risk factors and reduce risk of CVD among hotel employees.

Keywords: CVD risk, modifiable risk factors, hotel employees, diet and lifestyle habits, stress

Introduction

According to the Global Burden of Disease study age-standardized estimates (2010), closely a quarter (24.8%) of deaths in India are attributable to CVD. The age-standardized CVD death rate of 272 per 1,00,000 population in India is greater than the global average of 235 per 100,000 population⁽¹⁾. Cardiovascular diseases affect Indians a decade earlier and in their most productive midlife years as compared to the people of European ancestry^(2,3). High blood glucose, blood

pressure, body mass index (BMI), and serum cholesterol have been recognized as foremost metabolic risk factors driving this epidemic⁽⁴⁾. Nutritional, behavioral, and developmental risk factors together with diet, smoking, alcohol use, and physical activities have also been identified as major underlying determinants of CVD risks⁽⁵⁾.

Dietary practices, physical activity requirements, and job-related stress differ among different occupational groups. Due to a deviation in lifestyle factors across job-related groups, some occupations are at higher risk of metabolic risk factors and consequent non-communicable diseases^(6,7). Although there are abundant researches on the CVD risk factors in connection with various industries and occupations, there is scarcity of research on the prevalence and antecedents of CVD risk factors among hospitality employees.

Earlier, occupational health was related more on physical and chemical hazards in an occupational setting

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rather than cardiovascular and other non-communicable diseases that are often thought to be connected with the lifestyle of a person rather than her/his occupation. This is true for hospitality despite being an industry that produces and/or serves food including fast food that is linked to obesity. Prolonged disease risk factors among hotel employees need to be studied and this study one such effort to understand the present status of well-being among the employees of hotels. Within the hotel industry, jobs can be further classified as managerial, executive, clerical, administrative, skilled, semi-skilled, and un-skilled labor. It was initially assumed that upper grades are more at risk because of managerial desk level jobs but later it was realized that occupations may also act independent of these transitional behavioral risk factors. Junior job levels have been associated with greater chances of mortality due to coronary artery disease. Lower occupational levels are associated with low income and minor social recognition. People with low socio-economic status are more susceptible to conditions of ill-health and frequently do not have resources to manage with the consequences of diseases ensuing in discrepancies in health. Hence this study includes employees across the various departments of classified star category hotels in Udupi district. It targets to obtain the risk factors prevalent among hotel employees.

Methodology: A cross-sectional study was conducted a part of pilot study with the aim of identifying factors associated with risk of cardiovascular diseases among hotel employees. Institutional Ethics committee approval was obtained from Institutional Ethics Committee – Kasturba Hospital, Manipal. This paper is a pilot study involving 26 hotel employees in Udupi District who were assessed using a structured interview schedule. Informed consent was taken from all participants before collecting the data. The interview schedule consisted of sociodemographic information, medical history, CVD risk assessment questionnaire⁽⁸⁾, physical activity, workload and stress. Physical activity level was calculated using Mets and classified as per ICMR classification. Blood pressure and biochemical tests like blood glucose level and lipid profile, anthropometric measurements like height, weight, waist circumference and hip circumference was assessed with due precautions. CVD risk assessment questionnaire comprised of medical history, lifestyle habits, stress, sleep, bowel toxicity, inflammation and pain, blood glucose, blood lipids, diet, blood pressure and weight

status. Based on the sum of score obtained in each of this components, each participant was classified as Low risk (score=88 to 100; RR<1), Moderate risk (Score= 101 to 220; RR= 1-3), High risk (Score= 221 to 350; RR= 3-5), Very high risk (Score \geq 351; RR>5). Data thus collected was coded and analyzed using SPSS (v. 16.0).

Findings:

General Information: Table 1 represents general information of participants. Most of the hotel employees were males (84.6%) and belonged to the age group of 30-40 years of age. About of 76.9% of the participants were Hindus followed by 19.2% Christians and remaining (3.8%) were Muslims. Most of the participants were married (92%).

Medical History: None of the participants had a history of CVD or diabetes. About 7.7% of participants' mothers history of cardiovascular disorders followed by 11.5% of fathers who has history of cardiovascular disorders. About 15.4% of the participants had history of type 2 diabetes mellitus among both parents.

Lifestyle Habits: It is recommended to undertake moderate intensity activity for at least 5-6 days per week. Only 11.5% of the participants were involved in exercise as per the standard recommendations. About 34.6% were involved in moderate intensity activity but the frequency of performing exercise was less than 3 times per week. About 30.8% were sedentary activity. This pilot study revealed that most of the subjects were involved in moderate exercise but the frequency per week was less for most of the participants. Physical activity level as recorded as calculated using their activities and the corresponding mets indicates that most of them fall under sedentary or light activity (78.3%) followed by 15.4% of the participants who were moderately active and only 3.8% who were vigorously active. About 42.3% had adequate sleep of 7-8 hours however 15.4% of them snored during sleep.

Majority of the participants (84.6%) never smoked whereas the remaining participants (15.4%) smoked less than 20 cigarettes a day. About 19.2% were exposed to passive smoking which is equally considered to be dangerous as first hand smoke.

Most of the participants (57.7%) never consumed alcohol while 23.1% consumed 1 drink daily followed by 7.7% who consumed about 2 drinks per day and about 11.5% who consumed more than 3 drinks per day.

Bowel Toxicity: About 15.4% of the participants complained of bowel related symptoms like lower abdominal pain, bloating, constipation, diarrhea, foul smelling stools etc. Only 3.8% of participants were on oral contraceptives pill for more than 6 months in the last one year. Similarly, only 7.6% of the participants consumed antibiotics for more than 2 weeks.

Inflammation and Pain: Only 7.7% of participants reported signs of inflammation like wheezing, sneezing whereas 3.8% complained of heart palpitations or headache after consuming certain foods.

Blood Sugar: About 11.5% of the participants were diabetics of which only 3.8% reported signs of hypoglycemia like energy level dropping, craving for sweets or chocolates or experience headache or lack of concentration that is relieved by eating.

Biochemical Assessment: Lipid profile, blood glucose level was assessed. About 50% of the participants showed low HDL level whereas, 80.8% showed high LDL, 69.2% showed elevated serum cholesterol level and all participants had a high triglycerides.

Cardiovascular Disorders Risk Assessment

Table 1 Cardiovascular risk assessment of Hotel employees

Modifiable risk factors	Priority based on the score	Percent
Cardiovascular History	Low priority (0-30)	96.2
	High priority (51 and above)	3.8
Lifestyle	Low priority (-35 to -10)	30.8
	Medium priority (-9 to 21)	46.2
	High priority (22 and above)	23.1
Stress	Low priority (-19 to 20)	100.0
Sleep	Low priority (0-5)	69.2
	Medium priority (6 -11)	19.2
	High priority (12 and above)	11.5
Bowel Toxicity	Low priority (0-3)	76.9
	Medium priority (4 -9)	19.2
	High priority (10 and above)	3.8
Blood sugar	Low priority (0-19)	46.2
	Medium priority (20-49)	34.6
	High priority (50 and above)	19.2
Inflammation and Pain	Low priority (0-19)	96.2
	Medium priority (20-42)	3.8
Diet	Low priority (-19 to 6)	92.3
	Medium priority (7 to 13)	7.7
Lipids	Low priority (-15 to 9)	7.7
	Medium priority (10 to 34)	38.5
	High priority (35 and above)	53.8
Blood Pressure	Low priority (0-9)	42.3
	Medium priority (10-29)	26.9
	High priority (30 and above)	30.8
Weight Management	Low priority (0-11)	69.2
	Medium priority (12-25)	7.7
	High priority (26 and above)	23.1
CVD Risk	Low risk (score=-88 to 100; RR<1)	30.8
	Moderate risk (Score= 101 to 220; RR= 1-3)	50.0
	High risk (Score= 221 to 350; RR= 3-5)	15.4
	Very high risk (Score >=351; RR>5)	3.8

Data pertaining to cardiovascular history, lifestyle, stress, sleep, bowel toxicity, blood sugar, inflammation and pain, diet, blood lipids, blood pressure and anthropometric measurements were scored and classified to prioritize based on risk of cardiovascular disorders (Table 1). These findings showed 50% of the participants in the moderate risk, 15.4% high risk, 3.8% very high risk and about 30.8% were classified under low risk of CVD.

Gender wise comparison of CVD risk clearly indicated that females had either low (25%) or moderate risk (75%) of CVD whereas among the males, the CVD risk was distributed across the risk classification with a highest percentage showing moderate risk (45.5%) followed by 31.8% with low risk, 18.2% with high risk and 4.5% with very high risk of CVD.

Discussion

It is evident from the result that personal history or family history is not a risk for hotel employees in South Canara. Family history has been studied for many years as an independent risk factor for CVD risk and mortality⁽⁹⁾. Very few participants performed exercised as per recommendations. American College of Sports Medicine and the Centers for Disease Control and Prevention recommends 30 minutes of moderate intensity activity for atleast 5 days in a week or 20 minutes of vigorous intensity activity for atleast 3 days in a week. Sedentary lifestyle or not performing exercise besides the regular routine is considered as a major risk factor for chronic diseases like heart disease⁽¹⁰⁾.

The study clearly showed that although most of them never smoked, they were exposed to passive smoking. Passive smoking negatively affects the coronary circulation causing increased risk of endothelial dysfunction among healthy non-smokers⁽¹¹⁾ and also precipitates acute manifestations of CVD⁽¹²⁾. Alcohol is yet another risk factor that has been reported to cause mortality. Among the participants who consume alcohol, only a few had the habit of bingeing. Although, moderate consumption of wine and beer has cardio-protective effects on both CVD patients and healthy people, binge drinking can cause increased morbidity and mortality⁽¹³⁾.

Some of the participants had gastrointestinal symptoms indicating dysbiosis. Dysbiosis is a change in gut microbiota which has been speculated to play a role in cardiovascular health⁽¹⁴⁾. Consuming antibiotics over a long period of time affects gut microbiota⁽¹⁵⁾ thereby

increasing risk of CVD⁽⁶⁾. Inflammation increases WBC count which is an independent predictor of CVD risk⁽¹⁶⁾. A small number participants reported signs of inflammation like wheezing, sneezing etc. An elevated triglycerides, LDL and a low HDL poses an increased risk of CVD⁽¹⁷⁾.

Most of the participants in low priority for cardiovascular history, stress, sleep, bowel toxicity, blood sugar, inflammation and pain, dietary habits, blood pressure and weight. Most of the participants did not have either personal history or family history of CVD and diabetes. Disturbed sleep is a common symptom that is associated with stress. Since most of the participants were not affected by stress, sleep was also not affected. The main focus of treatment has to focus on abnormal lipid levels and weight status. Abnormal weight status is a risk factor for CVD related death⁽¹⁸⁾.

Majority of the participants were falling in moderate to high risk attributed to abnormal blood glucose, lipid profile, obesity and blood pressure. The study also highlighted a higher risk of CVD among male as compared to females. This risk can be attributed to difference in physical activity, stress, sleep, diet pattern, blood glucose and lipid abnormalities between the gender.

Conclusion

Most of the hotel employees are young adults and also they had a low family history of CVD. The risk of CVD due to these non-modifiable risk factors is not influential. The most common risk factors identified were abnormal blood sugar levels, lipid profile, high blood pressure, high waist circumference and lifestyle habits like smoking and alcohol consumption. Over 69% had moderate to high risk of CVD due to the above mentioned risk factors. The intervention strategies should focus on these modifiable risk factors with an aim to reduce risk CVD risk. A good diet and lifestyle management can modify these risk factors and reduce risk of CVD among hotel employees.

To conclude in general, a research base specific to hotel employees in India is essential to assist employees at all levels to become aware of the risks associated as well as provide basic training to employees periodically. Seek treatment interventions by association with primary health care centers for additional training in the management of CVD. We may need more resources and facilities to tackle the health risks associated with CVD

due to the socio-economic differentials through capacity building and awareness programs and involvement of all stakeholders.

Conflict of Interest: Authors declare no conflicts of interest

Source of Funding: Self

Ethical Clearance: The research has been approved by the Kasturba Medical College and Kasturba Hospital Institutional Ethics Committee, Manipal.

References

1. Prabhakaran D, Jeemon P, Roy A. Cardiovascular Diseases in India: Current Epidemiology and Future Directions. *Circulation*. 2016; 133⁽¹⁶⁾:1605–20.
2. Joshi SR, Anjana RM, Deepa M, Pradeepa R, Bhansali A, Dhandania VK, et al. Prevalence of dyslipidemia in urban and rural India: The ICMR-INDIAB study. *PLoS One*. 2014; ----
3. Xavier D, Pais P, Devereaux P, Xie C, Prabhakaran D, Reddy KS, et al. Treatment and outcomes of acute coronary syndromes in India (CREATE): a prospective analysis of registry data. *Lancet*. 2008;371(9622):1435–42.
4. Danaei G, Lu Y, Singh GM, Carnahan E, Stevens GA, Cowan MJ, et al. Cardiovascular disease, chronic kidney disease, and diabetes mortality burden of cardiometabolic risk factors from 1980 to 2010: A comparative risk assessment. *Lancet Diabetes Endocrinol*. 2014;2⁽⁸⁾:634–47.
5. Lim SS, Vos T, Flaxman AD, Danaei GKS, Adair-Rohani H, Amann M, Anderson HR, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380(9859):2224–60.
6. Allman-Farinelli MA, Chey T, Merom D, Bauman AE. Occupational risk of overweight and obesity: An analysis of the Australian Health Survey. *J Occup Med Toxicol*. 2010; 5⁽¹⁾:1–9.
7. Bonauto DK, Lu D, Fan ZJ. Obesity Prevalence by Occupation in Washington State, Behavioral Risk Factor Surveillance System. *Prev Chronic Dis*. 2014; 11⁽¹⁵⁾:1–9.
8. Clinic SNH and LS. Cardiovascular Risk Assessment Questionnaire. 2015. 1–12.
9. O'Reilly D, Holbrook A, Blackhouse G, Troyan S, Goeree R. Cost-effectiveness of a shared computerized decision support system for diabetes linked to electronic medical records. *J Am Med Informatics Assoc*. 2012; 19⁽³⁾:341–45.
10. Haskell WL, Lee IM, Pate RR, Powell KE, Blair SN, Franklin BA, et al. Physical activity and public health: Updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Medicine and Science in Sports and Exercise*. 2007; 39:1423–34.
11. Otsuka R, Watanabe H, Hirata K, Tokai K, Muro T, Yoshiyama M, et al. Acute effects of passive smoking on the coronary circulation in healthy young adults. *J Am Med Assoc*. 2001; 286⁽⁴⁾:436–41.
12. Raupach T, Schäfer K, Konstantinides S, Andreas S. Secondhand smoke as an acute threat for the cardiovascular system: A change in paradigm. *European Heart Journal*. 2006; 27: 386–92.
13. Chiva-Blanch G, Arranz S, Lamuela-Raventos RM, Estruch R. Effects of wine, alcohol and polyphenols on cardiovascular disease risk factors: Evidences from human studies. *Alcohol*. 2013;48⁽³⁾:270–7.
14. Ahmadmehrabi S, Tang WHW. Gut microbiome and its role in cardiovascular diseases. *Current Opinion in Cardiology*. 2017;32:761–6.
15. Modi SR, Collins JJ, Relman DA. Antibiotics and the gut microbiota. *Journal of Clinical Investigation*. American Society for Clinical Investigation. 2014; 39:4212–8.
16. Brown DW, Giles WH, Croft JB. White blood cell count: An independent predictor of coronary heart disease mortality among a national cohort. *J Clin Epidemiol*. 2001;54⁽³⁾:316–22.
17. Castelli WP. Lipids, risk factors and ischaemic heart disease. *Atherosclerosis*. 1996; 124:S1-9.
18. Stajic D, Djonovic N. Cardiovascular diseases: Risk factors. *Med Cas*. 2017; 50⁽²⁾:43–8.

Comparative Evaluation of Depth of Cure of Bulk: Fill Composite Resin and Alkasite Restorative Material by Vicker's Hardness Test

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Abstract

Background: This study evaluates depth of cure (hardness ratio) of a bulk-fill resin composite and an alkasite material in self cure and dual cure mode and compares and evaluates the Vicker's hardness and depth of cure of a bulk-fill resin composite and an alkasite material in self cure and dual cure mode.

Materials and Method: A dual-cure alkasite material and a bulk-fill composite resin were divided into three parts: Group A- bulk-fill resin composite, Group B- self-cured alkasite material and Group C- light-cured alkasite material. The samples were prepared in a stainless steel split mould of 6mm height and 4mm diameter. Vicker's hardness testing was performed to evaluate depth of cure of 4mm at three levels of 0mm, 2mm and 4mm.

Results: The statistics were analyzed using SPSS Software and One- way ANOVA and Post Hoc tests. The data obtained revealed that Cention N showed the greatest depth of cure in dual cure mode.

Conclusion: Most dual cure restorative materials exhibit better strength post light-curing compared to only the self-cure mode.

Keywords: alkasite, bulk-fill resin, composite, depth of cure, Vicker's hardness

Introduction

The rationale of this study was to compare and evaluate the claimed depth of cure of 4mm of bulk-fill restorative materials; an alkasite cement cured by itself and dually, with a bulk-fill composite resin.

Resin based composites require isolation, necessary steps for enamel and dentin etching, priming, and

bonding, and the gold standard thickness of each increment of 2 mm. However, deeper preparations with 2-mm increments are time consuming and relatively technique sensitive. The validation for this incremental technique is to warrant the penetration of the curing light deeply enough to initiate and complete the curing of the resin, apart from reducing the shrinkage and shrinkage-induced stress associated with polymerization of resin based composites. Recently, the introduction of resin-based bulk-fill composites claim to fill cavities up to 4–6 mm immediately.

Dental bulk-fill resins are increasing in demand, but the clinicians doubt that the in-depth cure may be insufficient. An alternative is possible through newer dual-cured resin based composites that not only save critical clinical time but also provide bioactive properties. Apart from new photo-initiators¹, the given

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techniques improve the depth in light-cured bulk-fill resin based composites by reducing the filler–matrix interface by enlarging the filler size² and decreasing the amount of pigments. Apart from fast curing and sufficient strength in large increments, modern bulk-fill resin based composites also necessitate the need for an additional feature to make it more acceptable, namely, bioactivity or self-adhesiveness.³

The increasing demand for a quick restorative procedure with light-cured, bulk-fill composites raises a doubt whether an adequate depth of cure will be achieved.⁴ This factor, along with the trial to offer an aesthetic, basic filling material has proved to be the motivation for the launch of several dual-cure resin based composites in the market, that are also appropriate for a bulk-filling procedure. The bulk fill resin materials also concentrate on bioactive properties that intend to prevent tooth demineralization by releasing acid-neutralizing ions and aid in remineralization. For this sole purpose, one method implemented the addition of alkaline fillers in a methacrylate resin matrix, by introducing a new material category—the alkasites.⁵

Dual-curing resin based composites consists of mixing two components together, each of which, consists of a different initiator system. Currently, dual-cure resin based composites have been mainly used in modern dentistry for core build-up and cementation. However, it needed to be confirmed whether the self-curing polymerization reaction was enough not only in case of impeded light transmittance, but also in the absence of light. On comparing the features of resin based bulk fill composites that were either self-cured or dual-cured, it was found that the impact of light irradiation depended on the final material ranging from no- impact to high-impact.⁶ Hence, the concluding factor for a newer dual-cured alkasite cement, apart from its caries preventive ability, is the duration it takes to set, the adequacy of its mechanical properties and early strength, the degree of conversion in depth, and the impact on the properties of the final material with additional light-curing.

The polymerization that is light-initiated facilitates the curing of a material on demand, whereas the polymerization procedure through a redox activation occurs slowly in comparison and may not be conducive enough for a quick restorative procedure that is generally required in modern clinics. The time required to set the material in question should be calculated and adjusted to the required time of a regular clinical treatment, even in

the absence of light. Furthermore, the higher refractive index of alkaline fillers when compared to regular silicate glass fillers may alter the filler/resin refractive index match that is crucial for better light transmission for optimum depth. The result would be a more dense material that is able to camouflage the oral cavity or the tooth's structural discolorations effectively rather than the one obtained through several translucent, light-cured, bulk-fill resin based composites.

Materials and Methodology: A dual-cure alkasite material (Cention-N, Ivoclar Vivadent AG, Schaan, Liechtenstein) and a bulk-fill composite resin (Filtek™ Bulk-Fill Posterior Restorative material, 3M™ ESPE, St. Paul, USA) were selected for the study.

The materials were divided into three parts: Group A - bulk-fill resin composite, Group B - self-cured alkasite material and Group C - light-cured alkasite material.

A stainless steel split mold of height 6mm and diameter 4mm was used to prepare 10 Samples from each group.

Group A (Cention N – Self Cure): Powder and liquid was dispensed onto a paper pad in the ratio of about 4.6:1, mixed for about 45-60s and condensed into the mold. They were retrieved after 5 minutes of setting time.

Group B (Filtek Bulk-Fill): The samples were condensed into the mold and cured for 20 seconds with blue LED Light Source.

Group C (Cention N – Dual Cure): The powder and liquid was mixed and the cement loaded into the mold to be cured. The samples were cured for 20 seconds with blue LED Light Source (Kerr Demi™ Ultra Ultracapacitor- 1200 mW/cm²) and were retrieved immediately after the curing cycle was complete. The samples were all thermocycled (Thermocycler SD Mechatronik, GmbH Dental Research Equipment, Germany) for 5,000 cycles at 5°C and 55°C (dwelling time: cold bath, 30 seconds; hot bath, 30 seconds)

The Depth of cure was measured by Vicker's Hardness Testing Machine (MMT- X7A, Matsuzawa Co., Ltd., Japan).

Results

The statistics were analyzed using SPSS Software

16.0. One- way ANOVA statistical tests were done to compare the three groups and on achieving statistically significant results, Post Hoc test was done.

The results obtained (Table I): showed that Group C (Cention N- Dual Cure) had manifested the most coveted results in comparison to the other two groups. Group C showed best results at all three levels of 0mm, 2mm and 4mm.

Group C had the highest VHN value of 65.08 followed by Group B at 54.63 and lastly group C, at 43.87 and the surface layer of 0mm. Even at the claimed depth of 4 mm, Group C did better with the VHN value of 49.86.

Table 1: Vicker’s Hardness Numbers of Group A, B, C at 0, 2 and 4 mm.

Group	Depth	Sample Size (n)	Mean	Standard Deviation
Group A – Cention N - Self Cure				
	0 mm	10	43.87	0.881
	2 mm	10	39.94	0.910
	4 mm	10	32.45	0.820
Group B – Filtek Bulk- Fill				
	0 mm	10	54.63	0.834
	2 mm	10	48.23	0.824
	4 mm	10	41.35	0.921
Group C – Cention N- Dual Cure				
	0 mm	10	65.08	0.820
	2 mm	10	57.31	0.748
	4 mm	10	49.86	0.625
The mean difference is significant at $p < 0.05$.				

Discussion:

Currently, bulk-fill resin based composite materials has gained popularity among practitioners owing to the comparative simplicity of the procedure.

Manufacturers, with the help of advanced technology, relate the modifications in the filler content and/or organic matrix as their claim in the main advancement of bulk-fill composite materials i.e, namely increased depth of cure, which probably results from higher translucency, and low polymerization shrinkage stress

Cention N contains an acyl phosphine oxide initiator (Norrish type1 initiator) which requires just one component for radical formation and the

photoinitiator, Ivocerin. The presence of this leads to faster polymerization of the resin material and causes better conversion of the monomer to polymer which may have lead to the results developed in this study. Cention N also contains UDMA, DCP, and an aliphatic/aromatic UDMA; which has claimed faster cross-linking of the methacrylate monomers to a high polymer network density and may be responsible for the better depth of cure.⁷

A self-curing material with options for light-curing outlook is the substance of analysis. Although the initiation rate can be very high in the light-curing mode, its significant drawback maybe the fact that the saturation of light energy in depth is quite low. In order to improve this, the alkasite was modified and a redox activation containing a copper salt, a peroxide and a thiocarbamide was added in the powder component.⁷

The use of restorative and viscous composite resins has demonstrated that greater depth of cure up to 4 mm is more effective.^{8, 9} It has been found that filler size and content in dental composites may reduce light penetration and this, in turn, has an effect on the depth of the cure.^{10,11} The pigments present in shaded composite materials have a direct impact on the depth of cure since these are dense particles that hinder the penetration of light and decrease the degree of polymerization at greater depths while a cavity is being treated.¹²

Filtek Bulk-Fill claims to contain AFM (addition-fragmentation monomers) that react with the methacrylate to keep the physical features of the material intact. The kind of monomers being used have an effect on the Methacrylate composites as they have the ability to shrink in varying degrees during polymerization. Filtek Bulk Fill Posterior Restorative consists of two new methacrylate monomers; their properties have served as a catalyst to gain lower polymerization stress that is necessary for better results.

Filtek bulk fill (bulk fill viscous composite) has shown a higher degree of conversion than the conventional viscous composite. Probably the reduced filler volume fraction is convenient compared to the less viscous conventional composite.¹³ The composition of 4 high molecular weight monomers, viz. Bis-GMA, Bis-EMA, UDMA and procrlyate in Filtek bulk fill facilitates a higher conversion and Depth of cure . Filtek bulk fill flow composites contain a proprietary monomer equivalent to Bis-GMA and patented as Procrlyat

resin.¹⁴ Procrlyat is a high molecular weight monomer with low viscosity similar to Bis-GMA but with a lower viscosity, the lack of pendant hydroxyl groups is the only difference between Bis-GMA and Procrlyate.¹⁵

The decreased hydrogen bonding potential is due to the lack of hydroxyl group which reduces the viscosity of the monomer. Also Bis-EMA and UDMA are high molecular weight monomers with low viscosity so the manufacturers adjust the proportions of the 4 high molecular monomers to decrease viscosity and create hard cross link network.¹⁶

The monomer aromatic dimethacrylate (AUDMA) with a high molecular weight is responsible for reducing the number of reactive groups in the resin. Polymerization stress is caused mainly due to two factors – the shrinkage in the volume and the stiffness in the developing and final polymer matrix. However, AUDMA is capable of combating both these factors.

Another distinctive methacrylate characterizes a class of compounds called addition-fragmentation monomers (AFM). The AFM reacts like any other methacrylate by forming cross-links between the adjacent polymer chains during the process of polymerization. The third reactive site of the AFM splits into fragments during polymerization. This process provides a technique to relax the developing network that results in greater relief from the stress caused. The fragments, however, still preserve the feature that can not only allow them to react with each other but also with other reactive sites of the developing polymer. Thus the physical features of the polymer are retained along with relief from stress.

Conclusion:

Under the limitations of this study, Cention N showed best depth of cure when tested by the Vicker's Hardness Test in dual cure mode. Filtek bulk fill also showed coveted results while maintaining a desirable depth of cure. In self-cure mode, Cention N may not achieve enough curing and we recommend that the alkasite material be used along with light curing protocols.

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Conflicts of Interest: There are no conflicts of interest with this study.

Ethical Clearance: This was an in vitro dental material based study and did not require ethical clearance from the ethical committee.

References

1. Ilie N. Comparative Effect of Self-or Dual-Curing on Polymerization Kinetics and Mechanical Properties in a Novel, Dental-Resin-Based Composite with Alkaline Filler. Running Title: Resin-Composites with Alkaline Fillers. *Materials*. 2018;11(1):108.
2. Moszner N. State of the art: Photopolymerization in dentistry. Ivoclar Vivadent Report. Liechtenstein: Ivoclar Vivadent AG. 2013 Jul;19.
3. Ilie N. Impact of light transmittance mode on polymerisation kinetics in bulk-fill resin-based composites. *Journal of dentistry*. 2017 Aug 1;63:51-9.
4. Tarle Z, Attin T, Marovic D, Andermatt L, Ristic M, Tauböck TT. Influence of irradiation time on subsurface degree of conversion and microhardness of high-viscosity bulk-fill resin composites. *Clinical Oral Investigations*. 2015 May 1;19(4):831-40.
5. Ilie N. Comparative Effect of Self-or Dual-Curing on Polymerization Kinetics and Mechanical Properties in a Novel, Dental-Resin-Based Composite with Alkaline Filler. Running Title: Resin-Composites with Alkaline Fillers. *Materials*. 2018;11(1):108.
6. Ilie N, Simon A. Effect of curing mode on the micro-mechanical properties of dual-cured self-adhesive resin cements. *Clinical Oral Investigations*. 2012 Apr 1;16(2):505-12.
7. Cention N – Ivoclar Vivadent Brochure <http://www.ivoclarvivadent.in/en-in/p/all/cention-n>.
8. Lazarchik DA, Hammond BD, Sikes CL, Looney SW, Rueggeberg FA. Hardness comparison of bulk-filled/transtooth and incremental-filled/occlusally irradiated composite resins. *The Journal of prosthetic dentistry*. 2007 Aug 1;98(2):129-40.
9. Jackson RD. New posterior composite materials improving placement efficiency. *Compendium of continuing education in dentistry (Jamesburg, NJ: 1995)*. 2012 Apr;33(4):292-3.
10. DeWald JP, Ferracane JL. A comparison of four modes of evaluating depth of cure of light-activated composites. *Journal of Dental Research*. 1987 Mar;66(3):727-30.
11. Ferracane JL. Correlation between hardness and

- degree of conversion during the setting reaction of unfilled dental restorative resins. *Dental Materials*. 1985 Feb 1;1(1):11-4.
12. Garcia D, Yaman P, Dennison J, Neiva GF. Polymerization shrinkage and depth of cure of bulk fill flowable composite resins. *Operative dentistry*. 2014 Jul;39(4):441-8.
 13. Zorzin J, Maier E, Harre S, Fey T, Belli R, Lohbauer U, Petschelt A, Taschner M. Bulk-fill resin composites: polymerization properties and extended light curing. *Dental materials*. 2015 Mar 1;31(3):293-301.
 14. Yokesh CA, Hemalatha P, Muthalagu M, Justin MR. Comparative evaluation of the depth of cure and degree of conversion of two bulk fill flowable composites. *Journal of clinical and diagnostic research: JCDR*. 2017 Aug;11(8):ZC86.
 15. Elhawary AA, Elkady AS, Kamar AA. Comparison Of Degree Of Conversion And Microleakage In Bulkfill Flowable Composite And Conventional Flowable Composite (An In Vitro Study). *Alexandria Dental Journal*. 2016 Dec 15;41(3):336-43.
 16. Filtek™ Bulk Fill Flowable Restorative. 3M. 2012. Available at: <http://multimedia.3m.com/mws/media/7923190/filtek-bulk-fill-flowable-restorative.pdf>

Health Implications on Consumption of Food at Fast Food Outlets in Chennai

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Abstract

Context: The recent lifestyles of youngsters has changed in such a way that, it led to an impact on their dietary patterns. Nowadays youngsters prefer to go for the food which is available in fast food outlets, although these foods are high in caloric content, sugar, salt and fat some of which will also laden with preservatives, there is a great demand for this foods and the expansion of multinational fast foods are the evidence for its growth. The health implication starts with overweight and hypertension which will reduce the life span. Foods prepared at fast food outlets will be at extreme heat to complete the cooking process. Fast foods have become a prominent feature of the diet among youngsters and the main reason is fast food outlets deliver food quickly which is convenient to lifestyle in metro cities and also in developing countries. A balanced and nutritional diet is required to have a healthy life and it is a responsibility of fast food outlets to full fill the dietary requirements of consumers. The objective of the paper is to highlight the health implications on consuming food and beverages with high calorific value, inadequate cooking, food laden with colorings and additives.

Keywords: *Fast Foods, Food contamination, Inadequate cooking, Food Additives, Health implications.*

Introduction:

The fast food outlets in Chennai have been grown to the max in the recent trend that is because of the people lifestyle with the convenience on receiving food. The foods that are prepared from fast foods outlets will consist high nutritional value with high calories, sugar and fat, and it will lead to various health implications. Consuming food at fast food outlets leads to cardio metabolic disorders and this is considered as a global health issue in recent trend¹. Fast food has strong association with the development of type2 diabetes and cardiovascular morbidity and mortality in adults ². There are too much of calories found in foods like Fats,

salt and sugar, has insufficient vitamins, minerals, and protein. Food is a basic need for survival and that has to be in proper ratio according to age and type of work to have a better health, irregular balance in food consumption will leads to bad nutritional value and that will spoil the proper functioning of the body to regulate³. In recent trends snacks such as pizza, burgers, tacos, Fried chicken Club sandwiches, and instant noodles; in addition kebabs fall under the fast food category. Fast food has strong association with the development of type2 diabetes and cardiovascular morbidity and mortality in adults. Food is a basic requirement for human survival; it helps in living healthy. Food and beverage is a basic commodity which fills stomach with satisfaction and makes us happy and emotionally satisfies with taste. Especially after the globalization fast food outlets has grown faster in cities, especially in Chennai. The foods which are deep fried have high calories because it fully cooked in fat such as vanaspathi, coconut oil, and ghee, some of the foods have already laden with more calories, Mutton & Chicken kebabs, Kentucky French Chicken, Crumb fried

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chicken, Nuggets and croquette are the ultimate sources of unsaturated fatty acids, increasing hypertension, and it leads to blocking arteries on the arterial walls of the heart⁴. Because mainly these foods are fried in full of fat with intense heat due to which there is a substance produced carcinogen acts as a cancer causing agent. In addition it is being served with Acrylamide substance that damages the nervous system; they are also laden with sodium that increases the risk of hypertension and heart diseases. Mutton kebabs, samosas and Patties, from food outlets contain high amounts of unsaturated fatty acids. Foods prepared from margarines, cheese spreads, and frying oils to preserve the food for longer duration will become unhealthy⁵. Consuming high calorie foods causing health implications, Fast food outlets are using some additives and colourings which are harmful to health. Fast food items are tastier, but the effects on the health are detrimental⁶.

Noodles are most commonly consumed in western countries and it is prepared from unleavened dough. However in today's trend the instant noodles are easy to prepare and it is easy to cook and serve⁷, by added preservatives with the addition of certain sodium additives, due to high carbohydrates and sodium it is detrimental to health, as well as it is not containing required proteins, fibre, vitamins. Noodles are coated with wax kind of substances like Propylene glycol and added with MSG (monosodium glutamate) which is not advised for regular consumption⁸, It has harmful effects like hypertension, cancer and harmful to health. Foods prepared with preservatives the main reason is to avoid the formation of bacteria in longer storage, The action of preservatives not only preventing the food from spoilage as well as they also can prevent you from pleasure of healthy life⁹. The main effects of food preservatives on the body will be in various degrees with type of preservative added with the food and it also have changes with age and health of a person. The major effects of preservatives are breathing difficulties reducing the preservatives from diet will have relief from diseases like asthma and the another effect will be the behavioural changes in recent years most of the foods contains preservatives and it mainly affects the young generation like children's are becoming more hyperactive the major cause is consumption of foods with preservatives and additives¹⁰. Preservatives are also containing a substance called carcinogens which has harmful effects when it gets digested it leads to cancer. The rural areas produced foods recipes have

both nutritional and medicinal values¹¹. Food habit in Chennai among students and youngsters had a tremendous change in the past two decades the most preferred foods are from fast food outlets which have high calorific value, salt and sugar content¹². In spite of great attention in gathering nutritional needs for daily consumption in order to attain good healthy life style, most of the youngsters are not particular about their food and disregard with their healthy food¹³.

Materials and Method

The quantitative and qualitative method of Statistical analysis is carried out by collecting the data's for this research. A total of 140 questionnaires were distributed randomly among the consumers of fast food in Chennai, out of which only 125 were completed and used for analysis. This study was carried out from June 2018 to August 2019 at fast food outlets in Chennai. The Statistical Package for Social Sciences (SPSS 24 version) is used for data analysis and the data comparisons was conducted after the collection of data's from youngsters, who consume food at fast foods in Chennai. Secondary Data has been collected by literature survey.

Results & Discussions

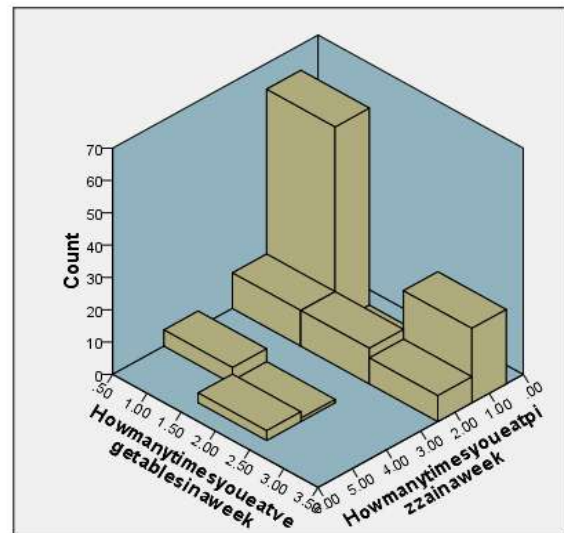


Figure 1: Comparison on consumption of Vegetables with Pizza in a week

In Figure 1: It shows the association in consumption of pizza with vegetables, the results having the value 1 shows as 1 to 2 times consumption in a week, value 2 for more than three times and 3 denotes daily consumption, at this juncture youngsters shows their

interest on consumption of pizza minimum twice in a week comparatively similar with the consumption of vegetables. As well as some of the consumers are aware with health implication on consuming pizza thereby consumption is reduced to twice in a month with the value 4 and also by value 5 indicates that youngsters stopped consuming pizza. The majority is similar for pizza and vegetables with by value 1 twice in a week and the daily consumption of vegetables with the value 3 has an elevation, shows the awareness of health between the consumers.

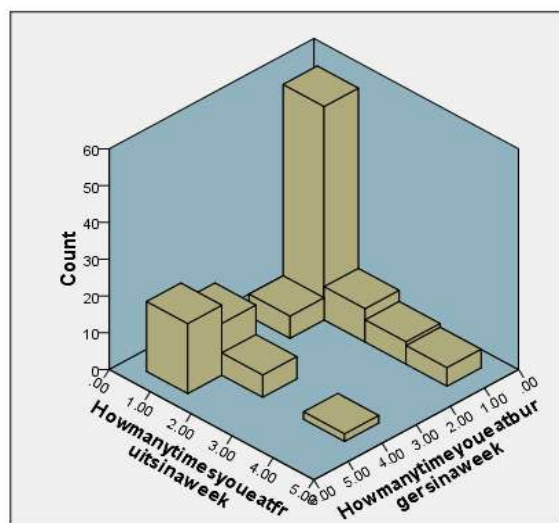


Figure 2: Comparison on consumption of Fruits with Burgers in a week

The Figure 2: Illustrates the comparison between the consumption of burgers with fruits among youngsters in a week, with the value 1 indicating once or twice, 2 for more than three times and 3 stands for daily consumption. Here the results are similar as in the case of consumption of pizza and vegetables, the majority shows once or twice for consumption of fruits and burger in a week and simultaneously only few have habits of consuming fruits in daily basis also it denotes even after knowing the health implications youngsters are addicted to fast foods.

The food choices depend on the age especially youngster’s shows higher interest in consuming foods from fast food outlets, the correlation study between nature of job and food habits are showing the majority youngsters preferring fast food outlets is significant with Pearson correlation coefficient, r , .261 for fried chicken and wish to be regular for consuming pizza with

the statistically significant ($r = -084$) this value shows that youngster from heart of the city is mostly addicted with fast foods by having P-value = .003, shows that youngsters are frequently consuming fried chicken.

The consumption of pizza shows relatively in high frequency with the p-value .350 as it is one of the most popular Italian foods around the globe and the comparison between consumption of vegetables and pizza shows the majority of the consume pizza regularly than vegetables simultaneously many youngsters not consuming fruits regularly by having lesser ratio of consumption in Chennai from more than two decades it is considered as an easily available food¹⁴. The pizza is loaded with cheese, sauce and also with meat will not get easily digested, due to high calories with fats and other mineral leads to acidity¹⁵. The basic topping for the pizzas are tomato sauce and it will not go with people who have acidity complaints because tomatoes have high acidic content. The Main reason for acidity is due to people tends to eat more number of pizzas, by substituting their normal diet with pizza like the consumption of sweet has coefficient $r = .0005$ with p-value .955. However there are various views related with the consumption of pizza in daily life like the ingredients added shows it is a healthy food with so many herbs and vegetables meat and milk products, especially when it is baked with the dietary needs. The stunning taste of pizza makes people to feel why to stop eating it. The major reason is it is heavily added with sodium and carbohydrates; cheese that has high calorie counts a cause of hypertension¹⁶, cardiovascular disease and obesity. Consuming pizza regularly will lead to poor health, results in health implications.

The consumption of burger among youngsters are in regular basis may become detrimental to health the majority of youngsters are consuming burgers with coefficient $r = -.121$ with p-value .178. The Burgers are mostly rich in dietary cholesterol. It will raise levels of cholesterol in your blood and that leads to hypertension and it became a harbinger for heart disease, this study also show that the consumption of meat also frequent for the consumers who consume burgers with the coefficient $r = .363^{**}$ with a p-value .000 shows a greater significance, furthermore a double hamburger contains 25.2 grams of saturated fat, and **193** milligrams of cholesterol that increases the percent of the daily calorific value in diet. By consuming a single-patty stuffed with a burger you can reduce 3.5 grams of saturated fat and 26 milligrams of cholesterol. Generally burgers are with the blend of mayonnaise, meat, cheese, patty and deep fried bacon

added with sauces rich in sugar and sodium, and they tend to raise the cholesterol and sodium levels. So burgers are considered as one of the worst junk foods with more than 1000 calories in each serving which can be raised or reduced according to the preference of a consumer.

The correlation between consumption of sweets and pizza shows the results coefficient $r = .005$ with a p-value .955 has a higher significance on consumption of Junk food and a most favourite sweet dish of youngsters like Donuts; it is mostly sprinkled or spayed with many colourful and delicious toppings like chocolate, jam and appetizing sugar Candies, due to blending of these ingredients along with the unsaturated oils, sugar and dough fried in intense heat, when fried they release harmful cancer causing substance carcinogens and the unsaturated fatty acids causing harmful effects on the body and the consumption of meat and sweets also has the value ($r = -.047$) with a p-value .600 shows the significance of consumers. The frequent consumption of these foods will elevate the sugar and cholesterol levels.

Conclusion

This study reveals the food habits among youngsters are mostly related with consumption of foods like pizza, burgers and deep fried meat from fast food outlets^{15, 16}. Hence awareness to the fast foods consumer is required and the fast food outlets should have alternatives on their food which have proper nutritional values and without preservatives, food colouring, and food additives. In addition medical practitioners need to know about that these kinds of eating habits are the cause of major diseases which are generally affecting the people in Chennai. The fast food outlets and food handlers should focus on hygiene standards and the nutritional value of the food which in turn help the community to grow with health. Food safety education is essential for food handlers and consumers as poor food habits result in food related diseases. The findings suggest that in modern business trend, it is difficult to stop the foods which are available from the market easily but consumers can opt for the foods which have good nutritional value, pastries are made out of rich milk cream and it is delicious when it is combined with sponge cake, and cake is one of the perfect choices for desserts¹⁰. Yet, an enticing piece of cake contains sugar and fat combined with all-purpose flour rich in carbohydrates that contain high calories causing high blood glucose levels in the body. Likewise the fresh cream is topped on sponge cake added

with chocolate, flavouring essence and some colouring agents are having harmful effects on health when it is frequently consumed.

Ethical Clearance: Not required for this article.

Conflicts of Interest: Conflict of interest declared none.

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References

1. Zahra Bahadoran, Parvin Mirmiran and Fereidoun Azizi, Fast Food Pattern and Cardiometabolic Disorders: A Review of Current Studies, Journal of Health Promotion Perspectives; Volume5,(4)., 2016: pp. 231–240.
2. Mohammad Hossein Rouhani, Maryam Mirseifinezhad, Nasrin Omrani, Ahmad Esmailzadeh, and Leila Azadbakht. Fast Food Consumption, Quality of Diet, and Obesity among Isfahanian Adolescent Girls. Journal of Obesity, Volume 2012, (2012) pp. 1-8.
3. 1: Ruano-Rodríguez C, Serra-Majem L, Dubois D. Assessing the impact of dietary habits on health-related quality of life requires contextual measurement tools. Front Pharmacol. 8;6:101 (2015) May. doi: 10.3389/fphar.2015.00101. eCollection 2015. PubMed PMID: 26005420; PubMed Central PMCID: PMC4424859.
4. Datar, Ashlesha and Nancy Nicosia. “Junk Food in Schools and Childhood Obesity” Journal of policy analysis and management : [the journal of the Association for Public Policy Analysis and Management] vol. 31,2 (2012): 312-337.
5. Shridhar G¹, Rajendra N^{2,3*}, Murigendra H¹, Shridevi P¹, Prasad M³, Mujeeb MA¹, Arun S¹, Neeraj D³, Vikas S³, Suneel D³ and Vijay K, Modern Diet and its Impact on Human Health, Journal of Nutrition & Food Sciences, doi: 10.4172/2155-9600.1000430.
6. KSillah, EAGriffiths, SAPritchard, RSwindell, CMWest, RPage, and IMWelch¹ Clinical Impact of Tumour Involvement of the Anastomotic Doughnut in Oesophagogastric Cancer Surgery, Volume: 91 Issue: 3, April 2009, pp. 195-200
7. Balaji Arumugam, Suganya A, Saranya Nagalingam, Suveka V. Fast food addiction – The

- junk enslavement. *Journal IAIM*, 2015; 2(1): 62-70. ISSN: 2394-0026 (P) ISSN: 2394-0034 (O)
8. Niaz, et al, Extensive use of monosodium glutamate: A threat to public health? *EXCLI journal*, (2018). 17, 273–278. Doi: 10.17179/excli2018-1092.
 9. Ashraf A. Mostafa, et al., Antimicrobial activity of some plant extracts against bacterial strains causing food poisoning diseases, *Saudi Journal of Biological Sciences*, Volume 25, Issue 2 (2018) pp. 361–366.
 10. in-H e ho, MD; et. al., Long-Term Use of Preservatives on Rat Nasal Respiratory Mucosa: Effects of Benzalkonium Chloride and Potassium Sorbate, *Journal TheLaryngoscope*, Volume 110, Issue 2, February 2000, Pages 312-312.
 11. Preetam Sarkar et, al., Traditional and ayurvedic foods of Indian origin, *Journal of Ethnic Foods*, Volume 2, Issue 3: 2015, 97-109.
 12. J De Irala-Estévez, et, al., A systematic review of socio-economic differences in food habits in Europe: consumption of fruit and vegetables, *European Journal of Clinical Nutrition*, volume 54 (2000) pp 706–714.
 13. Kim HK, Kim JH, Jung HK. A comparison of health related habits, nutrition knowledge, dietary habits, and blood composition according to gender and weight status of college students in Ulsan. *Korean Journal of Nutrition*; 45(4): 2012 336-346.
 14. Masset G, Mathias KC, Vlassopoulos A, Mölenberg F, Lehmann U, Gibney M, et al. Modeled Dietary Impact of Pizza Reformulations in US Children and Adolescents. (2016) pp 1-13.
 15. Lordan, Ronan et al. “Dairy Fats and Cardiovascular Disease: Do We Really Need to be Concerned” *Foods (Basel, Switzerland)* volume 7 Issue 3. 2018. pp. 1-21.
 16. Liu, Ann G et al. “A healthy approach to dietary fats: understanding the science and taking action to reduce consumer confusion.” *Nutrition journal* vol. 16, 1 53. 30 Aug. 2017, doi:10.1186/s12937-017-0271-4

Study to Evaluate Prevalence, Knowledge and Awareness of Needle Stick Injury among Dental and Nursing: Under Graduate Students

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Abstract

Introduction: Blood borne pathogens such as Human Immunodeficiency Virus, Hepatitis B and C viruses are commonly transmitted through needle stick injuries (NSI). Health care workers are the most commonly affected group of people. This study was conducted to test the prevalence, knowledge and awareness among the Dental and Nursing students.

Material and Method: Cross sectional study was done among dental and nursing students. Data was collected through questionnaire and analyzed. Total 410 students participated in the survey, (160 Dental students and 250 Nursing) students.

Results: The nursing students were affected frequently by NSI compared to dental students. 82.76% nursing students while only 22.23% dental students reported the incidence of NSI to the institutional health care department.

Conclusion: The prevalence of NSI was higher in nursing students compared to dental students. Both dental and nursing students lacked the knowledge and awareness about the NSI reporting. Reinforcement of the importance of reporting NSI, knowledge about the management of the same, following the guidelines of universal precautions and proper biomedical waste disposal method especially of the sharps and needles through formulated training programs designed for students would considerably reduce the risk of NSI and transmission of infection.

Keywords: Occupational, hazard, risk, Infection, transmission

Introduction

The national institute of occupational safety and health, USA, defines NSIs as those caused by needles such as hypodermic needles, blood collection needles, intravenous stylets and needles used to connect parts of intravenous drug delivery system.^[1] Health workers including doctors, nurses, technicians, assistants and

trainees are susceptible to the injuries inflicted by contaminated needles/sharp objects. Serious blood borne pathogens, such as human immune deficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV) can be transmitted from these injuries.^[2-4]

According to the WHO, 16000 HCV, 66000 HBV and 1000 cases of HIV may have occurred worldwide in the year 2000 among health care workers through their exposure to NSIs.^[5,6] NSIs mostly occur during disposal of used needles (23.7%), during administration of parental injection or infusion therapy (21.2%), drawing blood (16.5%), re-capping needles after use (12%) and handling linen or trash containing uncapped

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needles (16.1%).^[7] The annual occupational risk of HIV transmission was estimated at 0.27% for health workers. Among surgeons, the risk was 0.7% (more than twice as high) if no special protective measures were taken.^[8] The risk of exposure to occupational hazards is expected to be higher for un-experienced individuals, working in a new environment, such as dental and nursing students during their clinical training. The objective of this study was to assess prevalence, knowledge and awareness of NSIs among the undergraduate dental and nursing students at a tertiary care hospital.

Materials and Method

A cross-sectional questionnaire based survey was conducted among dental and nursing students, after the due approval of institutional ethical committee. Keeping in mind that trainees who are exposed to the clinical work will be prone for NSIs, only third and final year students and Interns (B.D.S.) in faculty of dentistry and second, third and final year (B.Sc.) nursing students were included in the study. A self-administered questionnaire was given to the participants, which included questions designed to evaluate prevalence and assess knowledge and awareness about NSIs among the students. The questionnaire included general information about the needle stick injury, method of disposal of sharps and possible risk of diseases due to improper handling and disposal. Those who volunteered to participate in the survey were asked to read the instructions carefully and respond truly to the questions.

Results

Total of 410 participants, including 160 dental and 250 nursing students completed the questionnaire. The incidence of reported NSI was 18.53% (n=76). Nursing students (23.2%) were almost twice as affected as compared to the dental students (11.25%), which was statistically significant (p=0.0036).(table 1) Although the respondents were well aware of the protocol of reporting NSIs, out of 76 exposures, 24 (31.57%) were not reported. Number of dental students not reporting NSIs was 14 (77.77%), which was much higher as compared to nursing students (n=10, 17.24%).(table 2)

All the dental students participating in the study had knowledge of universal precautions and reportedly used gloves when examining or treating patients, whereas 4% (n=16) nursing students did not compulsorily use gloves

while examining patient. 97.5% (n=156) dental students and 65.6% (n=164) nursing students practised recapping of needle after use. Most of the students used single handed method for re-capping the needle (89.7%,n=140) dental and 91.4% (n=150) nursing students).(table 3)

Our study shows poor knowledge among students regarding immediate management of NSIs. Only 18.75% dental and 20% of nursing students were aware of the correct method of using soap and water at the site of exposure after NSI. This correct answer received the lowest response (19.51%) which was extremely significant according to chi square test (p<0.0001; chi square value=35.104).(table 4) About 66.25% dental and 56.8 % nursing students had the knowledge about pathogens that can be transmitted through NSIs (which was statistically significant; p<0.0001 chi square value=59.667). (table 5) 62% were aware that the risk of transmission of HBV was maximum through NSIs. In this study 61.46% of the participants had taken the HBV vaccination out of which 20.83% dental students and 46.15% nursing students had tested for anti-HBs antibodies after hepatitis B vaccination. 94.63% of students were aware of need of bio-medical waste disposal to avoid accidental NSIs.

Table 1: NSI among students

	Dental	Nursing	Total
Affected	18 (11.25%)	58 (23.2%)	76 (18.53%)
Unaffected	142	192	334
Total	160	250	410

Table 2: NSI reported to the health care department.

	Dental	Nursing
Reported	4 (22.23%)	48 (82.76%)
Not reported	14 (77.77%)	10 (17.24%)

Table 3: Knowledge about universal precaution and safety guidelines

	Dental	Nursing
Wear gloves	160 (100%)	234(96%)
Don't wear gloves	0	16
Recap needle	156 (97.5%)	164 (65.6%)
Don't recap needle	4	86
Single hand method	140 (89.7%)	150 (91.4%)
Double hand method	16	14

Table 4: knowledge of immediate measures taken after NSI.

	Dental	Nursing
Squeeze/suck the blood	34	62
Wash with only water	50	104
Wash with soap water	30 (18.75%)	50 (20%)
Wash with alcohol	20	0
No response	26	34

Table 5: Knowledge of disease transmitted by NSI

	Dental	Nursing
Hepatitis B	24	6
Hepatitis C	0	4
HIV	14	86
Tuberculosis	0	0
All of above	106 (66.25%)	142 (56.8%)
No response	0	12

Discussion:

WHO has estimated that the occupational exposure of health care workers to diseases such as hepatitis B and hepatitis C is 40%, while that of the HIV infections is 2.5%.^[9] 90% of the occupational exposure is reportedly due to NSI. The actual data regarding the NSI in India is insufficient.^[10,11,12,13] The importance of occupational health and safety of trainees have been systemically ignored by the medical fraternity, with very limited research conducted in this field.^[9,14-15] Trainees are at even greater risk due to their limited clinical experience and hence are known to be a high-risk subgroup.

Various studies have shown a low incidence of reporting of NSIs.^[17-20] In a study of sharps injuries among health-care workers in Taiwan, Shiao et al. discovered that 87% of health-care workers sustained at least one NSI, but only 18% incidents were reported.^[21] The findings of our study show that 11.25% dental students had NSI, out of which 22.23% was reported. Nursing students showed higher incidence of NSIs, out of which 82.76% cases were reported. Inexperience is possibly an important factor that contributes to high incidence of NSI among trainees/students. The possibility of high risk of NSI among students may also be attributed to increased stress, resulting in anxiety.^[22,23] The incidence of NSI was almost double in nursing students as compared to dental trainees. The likely reason of the same may be greater amount of exposure of nursing students to hospital and ward setup.

In the present analysis 57.5% of the dental students and 84.8% of nursing students were aware of the standard precaution and post exposure prophylaxis guideline. 97.5% dental students had the habit of recapping the needle and 89.74% used the single handed technique. While among the nursing students 65.6% had the habit of recapping the needle and out of them 91.46% used single hand method. The overall result shows that as a technique for safe needle recapping, 70.73% followed the single handed technique while the 26.82% followed double handed technique. Several studies have shown recapping to be an important cause of NSI.^[24-27] All training programs emphasize that recapping of needles after use is not to be done and if it is to be done then use single handed technique has to be followed.^[28,29] Double handed recapping of needle between the procedures is considered extremely hazardous, with much higher risk of NSI. Present recommendation for recapping needle is to use: single handed scoop method or using needle capping device.^[30]

The average risk of HIV infection after a needle stick or direct mucosal cut exposure to HIV-infected blood is 0.3%.^[31] The health worker vaccinated against Hepatitis C has lower risk of transmission (0-3 %), as compared to hepatitis B, that is stated as 7-30%. Risk of transmission of hepatitis B infections are more likely and commonest after NSIs.^[32] In our study knowledge among dental and nursing students about the pathogens that can be transmitted by needle-stick injury was inadequate. A similar study to evaluate the prevalence and nature of needle stick injuries among nursing students showed that although all the participants were aware of the fact that hepatitis B and C can be transmitted by NSI, over 20% were not aware that infections other than hepatitis B & C can also be transmitted by needle-stick injuries.^[33]

As the risk of transmission of hepatitis B is most common with NSI, vaccination against it is highly desirable among the health care professionals. Vaccination regimen followed for the hepatitis B is three-dose regimen where second dose is taken after 1 month followed by third dose after 6 months. Minimum time interval between 1st dose and 2nd dose is 4 weeks, and between 2nd and 3rd dose is 8 weeks.^[34,35] In the present study 60% of dental students and 62.4% nursing students were vaccinated against Hepatitis B. A need for strict implementation of vaccination programme for the vulnerable population including the nursing and dental trainees can significantly lower the risk of transmission of infections due to NSI.

For prevention of the sharps injuries it is an important to practice proper bio-medical waste disposal method. Needles and sharps from the hospital waste should be disposed properly and care must be taken while handling them. The handlers must use protective ware including hand gloves and eye glasses.^[36] In our study 93.75% dental students and 91.53% nursing students were aware of the proper biomedical waste disposal method and the fact that improper disposal method can cause infection due to sharps/needles and blades. It is recommended to use needle cutters before disposing of injection equipment and the use of sharp boxes which has to be replaced when two- third full.^[37] These practices can definitely reduce the chance of sharps injuries to the bio-medical waste handlers, health care providers including the trainees. Reinforcement of the importance of reporting NSI, knowledge of prompt management of the same, adherence to guidelines of universal precautions and proper waste disposal method through formulated training programs designed for medical, dental and nursing trainees/students would considerably reduce the risk of NSI and transmission of infection.

Conclusion

Ethical Clearance: Taken from Institution Ethical committee of KIMSUDU, Karad.

Source of Funding: Study conducted under 'Student Project of KIMSUDU.

Conflict of Interest: None

References

1. Ali A, Ali T, Ghazi A, Khan MY, Ali Z; Needle stick injury and associated factors among medical students, *Pak J Surg.* 2008;24(3):145-49.
2. Gerberding JL. Incidence and prevalence of human immunodeficiency virus, hepatitis B virus, hepatitis C virus and cytomegalovirus among health care personnel at risk for blood exposure: final report from longitudinal study *J Infect Dis* 1994;170:1410-7.
3. Lanphear BP, Linnenamn CC, Cannon CG, DeRonde MM, Pendy L, Kerley, LM, Hepatitis C virus infection in health care workers: risk of exposure and infection. *Infect control hospi Epidemiol* 1994; 12:214-9.
4. Shah SM, Merchant AI, Dosman JA, Percutaneous injuries among dental professionals in washington state. *BMC Public Health* 2006; 6:214-74.
5. Atenstaedt R, Payne S, Roberts R, Russell T, Russell D et al. (2007) Needle-stick injuries in primary care in Wales. *J Public Health* 29: 434-440.
6. .Nee L, Lim H, Huak Y, Bachok D (2002) Analysis of sharp injury occurrences at a hospital in Singapore. *Int J Nurs Pract* 8: 274-281.
7. Rita D, Makki DG, Epidemiology of needle stick injuries in hospital personnel. *Amj med* 1981; 70:928-32.
8. Gumdokha F.I, Bwrege, Z.A and Dolmans W.M.V. Dolmans occupational exposure to the risk of HIV infection among health care workers in mwanza region, rural and remote health 9:1185 united. Republic of Tanzansa bulletin of the world health Organization. *World hlth org*,1997;75:133-140.
9. Shah R. Mehta HK, Fancy M, Nayak S, Donga BN. Knowledge and awareness regarding needle stick injuries among health care workers in tertairy care hospital in Ahemdabad, Gujrat. *Nat J Com Med* 2010;1:93-6.
10. Simonsen L, Kane A, Lloyd J, Zaffran M, Kane M. Unsafe injections in the developing world and transmission of bloodborne pathogens: a review. *Bull World Health Organ* 1999;77:789-800.
11. Sagoe-Moses C, Pearson RD, Perry J, Jagger J. Risks to health care workers in developing countires. *NEngl J Med* 2001;345(7):538-41
12. Murlidhar S, Singh PK, Jain RK, Malhotra M, Bala M. Needle stick injuries health care workers in a tertairy care hospital of India. *Indian J Med Res* 131, March 2010, pp 405-410
13. Tadesse M, Tadesse T. Epidemiology of needlestick injuries among health-care workers in Awassa City, Southern Ethiopia. *Trop Doct.* 2010 Apr;40(2):111-3. doi: 10.1258/td.2009.090191
14. Smith DR, Mihashi M, Adachi Y, Shouyama Y, Mouri F, Ishibashi N, Ishitake T: Organizational climate and its relationship with needle stick and sharps injuries among Japanese nurses. *Am J Infect Control* 2009, 37(7):545-550.
15. Salehi A, Garner P: Occupational injury history and universal precautions awareness: a survey in Kabul hospital staff. *BMC Infectious Diseases* 2010 10(1):19.
16. Hamory BH. Under reporting of needle stick injuries in a university hospital. *Am J Infect control*

- 1983;63:445-51
17. Shiao JSC, Hung MC, Yang YJ, Guo LYL. Needlestick and sharps injuries among nursing personnel in southern Taiwan. *Chinese J Occup Med* 1997;4:93e100.
 18. Shiao JSC, Guo YL, McLaws ML. Estimation of the risk of bloodborne pathogens to health care workers after a needlestick injury in Taiwan. *Am J Infect Control* 2002;30:15-20.
 19. Guo YL, Shiao JSC, Chuang YC, Huang KY. Needlestick and sharps injuries among health care workers in Taiwan. *Epidemiol Infect* 1999;122:259e65.
 20. Hung MC, Shiao JSC, Chuang YC, Huang KY, Gupo YL. The prevalence of sharps injury, blood and body fluids exposure among emergency department staffs in Taiwan. *Chinese J Pub Health* 1999;18:66e76
 21. Shiao JSC, Chuang YC, Ko WC, Huang KY, Guo YL. The prevalence of needle-stick and sharp object injuries at a medical center in Taiwan. *NICJ* 1997;4:203e14.
 22. Lee J J, Kok S H, Cheng S J, Lin L D, Lin C P. Needlestick and sharps injuries among dental healthcare workers at a university hospital *J Formos Med Assoc* (2014) 113, 227e233
 23. Askarian, Malekmakan I. The prevalence of needle stick injuries in medical, dental, nursing and midwifery students at the university teaching hospitals of Shiraz, Iran,. *Indian J Med Sci.* 2006;60(6):227.
 24. National Institute for Occupational Safety and Health [Internet]. Preventing needlestick injuries in health care setting. NIOSH. [cited 2019 Mar 28] Available at: <http://www.cdc.gov/niosh/2000-108.html>.
 25. World Health Organization [Internet]. Pruss-Ustun A, Rapiti E, Hutin Y. Sharps injuries: Global burden of disease from sharps injuries to health-care workers. (WHO Environmental Burden of Disease Series, No. 3). [cited 2019 Mar 28] Available from: https://www.who.int/quantifying_ehimpacts/publications/en/sharps.pdf?ua=1
 26. Kermod M, Jolley D, Langkham B, Thomas MS, Crofts N. Occupational exposure to blood and risk of bloodborne virus infection among health care workers in rural north Indian health care settings. *Am J Infect Control* 2005;33:34-41.
 27. Ebrahimi H, Khosravi A. Needlestick injuries among nurses. *J Res Health Sc* 2007;7:56-62.
 28. Pournaras S, Tsakris A, Mandraveli K, Faitatzidou A, Douboyas J, Tourkantonis A. Reported needlestick and sharp injuries among health care workers in a Greek general hospital. *Occup Med (Lond)* 1999;49:423-6.
 29. Adegboye AA, Moss GB, Soyinka F, Kreiss JK. The epidemiology of needlestick and sharp instrument accidents in a Nigerian hospital. *Infect Control HospEpidemiol* 1994;15:27-31.
 30. Occupational safety and environmental health [Internet]. Laboratory standard operating procedure for: needle recapping and handling. [Cited 2019 Mar 28] Available from:
 31. Petty, T.J. When the unthinkable Happens: Post Exposure Prophylaxis of HIV Contaminated Percutaneous Injuries. *J Can Dent Assn* 1999. 65:293-294
 32. Germanaud J, Causse X, Dhumeaux D. Transmission of hepatitis C by accidental needle stick injuries. Evaluation off the risk. *J PubMed* 1994 jun 18;23(23):1078-82.
 33. Khan RY, Correspondence to Dr. Ghulam F. Knowledge, Attitude and Practice among nursing students on needle stick injury Sheikh Zayed Hospital. *P J M H S* 2013;7:357-60.
 34. Poland GA, Jacobson RM. Clinical practice: prevention of hepatitis B with the hepatitis B vaccine. *N Engl J Med.* 2004 Dec 30;351(27):2832–2838. [PubMed]
 35. Adoga MP, Pennap G, Akande BO, Mairiga JP, Pechulano S, Agwale SM. Evaluation of recombinant DNA hepatitis B vaccine in a vaccinated Nigerian population. *J Infect Dev Ctries.* 2010 Nov 24;4(11):740–744.
 36. Recommendations for preventing transmission of human immunodeficiency virus and hepatitis B virus to patients during exposure-prone invasive procedures. *Morbidity and Mortality Weekly Report*. 1991 July; 40(RR08):1-9.
 37. Occupational Safety and Health Administration [Internet]. OSHA fact sheet-Protecting yourself when handling contaminated sharps. [cited 2019 Mar 28] Available from: https://www.osha.gov/OshDoc/data_BloodborneFacts/bbfact02.pdf.

Effect of Mental Imagery Technique on Balance in Postmenopausal Women with Postural Disturbance: A Randomized Controlled Trial

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Abstract

Background: Decreased blood estrogen after menopause causes decreased the sensitivity of higher centers because of impaired postural control in postmenopausal women which can increase the risk of fall.

Objective: To find the effect of mental imagery technique on balance in postmenopausal women with postural disturbance.

Method/Design: 32 PMW who met the inclusion criteria were enrolled in the study. Subjects were allocated in two groups of 16 each into an experimental and control group. Berg balance scale and Balance error scoring system were taken before the start of the intervention and at the end of four weeks. According to the allocated group, BT was given to Group A and BT + MI to Group B thrice a week for four weeks.

Results: There was a significant improvement in Group B in BESS, with p-value <0.01. Comparison between the group indicates the individuals treated with a combination of BT with MI technique significantly improved better than those individual treated with BT alone. Comparison of the mean difference of BBS score between the two groups A and B was not statistically significant.

Conclusion: On comparing the mean difference of BEES it can be concluded that MT along with conventional BT is beneficial for postmenopausal women with postural disturbance when compared to conventional balance training alone.

Keywords: Balance exercise, Post-menopause, Mental Imagery

Introduction

Balance by the term is defined as the dynamic process where the body has the capability to maintain equilibrium.¹ Along with advance in age, the female reproductive system undergoes changes leading to menopause which is associated with balance issue.^{2,3}

Menopause is the term used when a women experience last menstrual flow and it can be judged only retrospectively.⁴ When there is stoppage in production of hormones by women's ovaries it causes cessation of menstrual periods and when there is no menstrual period for 12 months, it is known as menopause.⁵ In India, the mean age of menopause in women is 46.02 years.⁶ Risk of fall in PMW is due to loss of balance and increased body sway, so fall prevention management by focusing on exercises aiming to improve balance has to be routinely done.⁷

There are various treatment and techniques to treat balance and MI is one of them.^{8,9} The illustrative practice of physical activity in the absence of any visible

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muscular movements is known as MI.¹⁰

In PMW, estrogen decreases slowly in the blood which leads to decreased calcium absorption by the bone which reduces its density. Non-contractile collagen tissue, tendon attaches muscles to bone which helps in creating movement at the joint by transferring muscle force from the belly. In menopause even muscle mass decreases. So because of decreased muscle mass and bone density, there will be muscle weakness and osteoporosis. Which causes postural issues thereby affecting postural component of balance which leads to increased fall risk. Decreased blood estrogen causes decreased sensitivity of higher centers because of impaired postural control. As sensitivity by the cortex decreases the load on gaining feedback and information from associated structures of maintaining balance like the vestibular system and cerebellum increases. So this leads to a decrease in their threshold.^{11,12,13} Which is permanently stored in memory so it will not be so easy to correct balance disorder until the central mechanism and peripheral structures are corrected. Studies have shown that balance is disturbed in PMW due to the reduction in estrogen hormone.^{14,3} Various studies have shown that resistance training, aerobic exercises balance training with feedback are proved to be effective in maintaining the hormonal level in PMW.^{15,16} MI which targets the central circuits proved to be effective in balance training in individuals with stroke and geriatric population.^{9,17}

To best of our knowledge, there is dearth in the literature that effect of MI on balance in PMW hence in this study we are aiming to identify the problem and are trying to correct it by focussing on the periphery and moulding the central circuits. Thus purely concentrating on central and postural components of balance this will help the women who are in risk at initial stages.

Method

Participants: Current study was a prospective randomised clinical trial carried out in Tertiary Hospital of India between May 2018 to April 2019. Thirty-two healthy postmenopausal women subjects, recruited among women employees were recruited. After obtaining the ethical clearance from the Institutional Ethical Committee, the trial was registered in the Clinical Trial Registry of India (CTRI/2018/06/014493) and an informed consent was taken from the patients. Inclusion criteria were the following: 1) women between the age group of 45 - 64 years; 2) Having amenorrhoea

> 12 months; 3) normal or corrected to normal vision; 4)Willing to participate in the study; 5) absence of neurological and orthopaedic disorders; 6) Balance disturbance BBS < or = 52.

Training Design: The participants were randomly assigned to 2 groups: BT (balance training) and BT + MI (Balance training with Mental Imagery). A computerized random list generator (random.org) provided the randomization list. All groups were trained for four weeks, three days per week. Outcome measure BBS¹⁸ and BESS¹⁹ were taken on the first day and after 12 sessions of intervention.

A total of 7 challenging balance exercises performed by participants, for example tandem walking, reach out, one leg standing, Raising the knee rapidly while standing, perturbation training (reactions), (anticipatory), standing on foam surface (see Fig. 1 for examples), were used for BT group. Each single exercise lasted 5 min. BT with MI group underwent auditory screening prior to the session for hearing threshold limit check-up. Subjects who were able to hear within normal threshold limit were only taken in the study. After that subjects were given same balance exercises as BT group for 20 minutes and 10 minutes of MI with the help of auditory stimulus using head phone (SENNHEISER HD 206 and iPod shuffle). Considering balance exercises, and mental imagery, both group underwent sessions lasting 30 min. (figure 1 and 2)

Mental Imagery: Subject was asked to sit on a chair in a sound proof closed room and headphone for auditory stimulus (the hearing level 40dBHL). Listening to the auditory stimulus the subject imagined without any movement externally.

First Week: Walking

- Relax, sit comfortably with well back support and slowly close your eyes.
- Inhale deep breath and then gently exhale out the breath, Inhale and exhale deeply. Repeat inhale and exhale 2-3 times.
- Think about a safe and peaceful place, look at green plants outside and feel great climate, try to visualize a clear view.
- Now your eyes look relaxed, and your body is calm.
- Now its time for your muscles contraction
- Presume that you are on a chair and there is a

cooking area next room.

- Contract foot muscles then thigh muscles then lower leg and finally hip muscles.
- Now you have to stand and feel that your legs are trying to initiate a forward movement to go kitchen by lifting your one leg at a time, flexing your knee and hip.
- Attempt to imagine in slow motion the movement which you are performing by balancing yourself and stay relaxed like that till the end of the session. Good going
- You have to walk ahead with attention, feel that you are opening the shelf which is higher in the kitchen.
- Now you are not able to reach normally so you are trying to stand on your toes and balancing yourself to get the things from the shelves and finally you are able to get it.
- Now after getting it you kept it down on the kitchen slab.
- Relax and make yourself comfortable now you have to go to the previous room.
- Promptly we are getting to the previous surrounding of here, listen to the sonances around you. Accompany my count starting backwards 5 to 1,

when I say 1 please open your eyes. 5...4,...3,...2,...1.

Mental Imagery practice was continued in increasing activity and complexity of tasks with the Corresponding weeks.¹⁷

The same training was performed with increasing level of exercise difficulty. The same physiotherapist, blinded to baseline assessment, trained subjects during the exercises.

Statistical Analysis: To compare BBS and BESS before and after the intervention within the group paired t-test was used. The between- group comparison was performed by using independent sample “t” test. The p-value < 0.05 was considered as significant. All data were analysed using the software SPSS 23.

Results

The groups were similar at baseline in terms of demographic variables (age and BMI). Moreover, no significant differences in balance performance were found between the group at T0 (see Table 1,2,3,4)

Comparison of mean difference of BBS score between group A and B was not statistically significant.

However, mean difference on BESS between group A and B was statistically significantly.

	BT	BT+MI	p- value
Sample(n)	16	16	-
Age (years)	52.44±3.31	53.06±3.27	0.595
BMI (kg/m ²)	23.05±3.38	24.5±2.89	0.202
Balance measures			
BBS (Pretest)	50.50±0.816	50.94±1.063	0.202
BESS (Pretest)	44.31±4.222	41.81±4.764	0.127

Table 1: Demographic characteristics of the participants and Balance variable at baseline.

Outcome measure	Mean S.D	Mean difference	95% CI for the difference		t- value	df	p- value	
			Lower	Upper				
BBS	Pre	50.47±0.83	-4.133	-4.823	-3.443	-12.848	14	<0.01*
	Post	54.60±1.18						
BESS	Pre	44.13±4.30	14.267	11.751	16.782	12.163	14	<0.01*
	Post	29.87±4.32						

(* indicates significant) (SD= Standard Deviation, CI= Confidence Interval, df= Degree of freedom)

Table 2: Within-group comparison of BBS and BESS at the end of 12 sessions of Group A

Outcome measure		Mean± S.D	Mean difference	95% CI for the difference		t- value	df	p- value
				Lower	Upper			
BBS	Pre	50.94±1.06	-4.50	-4.935	-4.065	-22.045	15	<0.01*
	Post	55.44±0.96						
BESS	Pre	41.81±4.76	30.375	27.355	33.395	21.439	15	<0.01*
	Post	11.44±5.95						

(* indicates significant) (SD= Standard Deviation, CI= Confidence Interval, df= Degree of freedom)

Table 3: Within-group comparison of BBS and BESS at the end of 12 sessions of Group B

Outcome measure		Mean± S.D	Mean difference±SD	95% CI for the difference		t- value	df	p- value
				Lower	Upper			
BBS	BT GroupA)	-4.13±1.24	0.366±0.375	-0.402	1.1355	0.975	29	0.337
	BT+MI (GroupB)	-4.50±0.81	0.366±0.381	-0.419	1.153	0.962	23.9	0.345
BESS	BT (GroupA)	14.26±4.54	-16.10±1.85	-19.89	-12.31	-8.69	29	<0.01*
	BT+MI (GroupB)	30.37±5.66	-16.10±1.83	-19.87	-12.34	-8.75	28.3	<0.01*

(* indicates significant) (SD= Standard Deviation, CI= Confidence Interval, df= Degree of freedom)



Figure 1: Mental Imagery



Figure 2: Standing in foam surface

Discussion

Findings of the present study within the group analysis shows there is significant difference in both the outcome measures (BBS and BESS) in both the group. Whereas between the group analysis for BBS and BESS (Pre and Post) at the end of 12 sessions. Comparison of BBS score between the groups shows there is no statistically significant difference in favour of any group. However, in case of BESS, comparison between the group indicates the individuals treated with combination of BT with MI technique significantly improved better than those individual treated with BT alone.

In this study we can see significant difference only in the BESS because it consists of more complex tasks than BBS. In BESS foam surface is also used were as there is no such component in the BBS which measures the balance in foam surface. The subjects with upper limit of BBS score (48-52) were included in the study which made the subjects to have less scope for improvement on BBS whereas there was more space for improvement on BESS

Steadman et al. (2003)²⁰, who found that balance training program for only six weeks significantly improves balance, mobility, confidence, and quality of life in patients with balance problems. By this study to promote reflex muscular activation patterns which

is necessary for balance seems to be adequate in four weeks for PMW.

A study conducted by Warner LA (1988)²¹ systematic review was conducted on mental imagery and its potential for physiotherapy where it was concluded physical practice combined with mental practice is effective so implementation of this method of treatment is beneficial as Mental imagery doesn't require any sophisticated equipment in similar way Asmita K et al⁸(2014) conducted a study effect of Mental Imagery on Balance in Young Adults were result showed better balance in the group with MI and BT after 4 weeks program at a rate of 3 times/week. A comparative study conducted by Tomar J⁹(2014) in Geriatric Population where result showed that mental imagery provides additional benefits to conventional physiotherapy and the author concludes that embedded mental imagery may hence be an important therapeutic tool to improve balance in elderly.

As BT along with MI was given in younger and older population but in this study it is given in postmenopausal women were the findings shows better improvement in the group after combination of conventional physiotherapy balance training with MI.

Based on the results the clinical implication of the study is that MI training can be included in the routine balance training for PMW with balance disturbance.

Conclusion

The result of the present study concludes that there was significant difference between the group receiving conventional balance training and the group receiving mental imagery and conventional balance training in postmenopausal women with postural disturbance.

On comparing the mean difference of BEES it can be concluded that MT along with conventional BT is beneficial for postmenopausal women with postural disturbance when compared to conventional balance training alone.

Conflict of Interest: None

Source of Funding: Self

References

1. Carolyn K, Lynn AC. Therapeutic exercise foundation and techniques. Fifth ed. New Delhi: Jaypee Brothers Medical Publishers (p) Ltd; 2007:251-69.
2. Ersoy Y, Mac Walter R, Durmus B, Altay Z, Baysal O. Predictive Effects of Different Clinical Balance Measures and the Fear of Falling on Falls in Postmenopausal Women Aged 50 Years and Over. *Gerontology* 2009;55(6):660-65.
3. Hanan S. El-Mekawy, Dalia M. Kamel, Magda S. Moursi, et al. Effect of Balance Training on Postural Stability in Obese Postmenopausal Women. *Bulletin of Faculty of Physical Therapy, Cairo University* 2007;12(2):159-67.
4. Margaret P, Jill M. *Physiotherapy in obstetrics and gynaecology*. New Delhi: Jaypee Brothers Medical Publishers (p) Ltd; 1994
5. The Menopause Years (FAQ047) [document on the Internet]. The American College of Obstetricians and Gynecologists; 2015 May [cited 2018 Jan 9]. Available from: <https://www.acog.org/Patients/FAQs/The-Menopause-Years>
6. Ahuja M. Age of menopause and determinants of menopause age: A PAN India survey by IMS. *Journal of Mid-life Health*. 2016;7(3):126.
7. Cangussu L, Nahas-Neto J, Petri Nahas E, et al. Evaluation of postural balance in postmenopausal women and its relationship with bone mineral density-a cross sectional study. *BMC Musculoskeletal Disord*. 2012;13(1).
8. Asmita K, Jenesis D, Unnati P, et al. The effect of Mental Imagery on Balance in Young Adults. *Indian Journal of Physiotherapy and Occupational Therapy - An International Journal*. 2014;8(3):38.
9. Tomar J, Chauhan V. Comparative Study of Mental Imagery, Embedded Mental Imagery and Balance Training in Improving Balance Control Ability in Geriatric Population. *European Academic Research* 2014;2(9):12359-82.
10. Driskell J, Copper C, Moran A. Does mental practice enhance performance?. *Journal of Applied Psychology*. 1994;79(4):481-492.
11. Hall J, Guyton A. *Textbook of medical physiology* eleventh edition. Edinburgh: Elsevier Saunders; 2006:1012-18
12. Kochi MN, Marques NR, Da GDC, et al. Impact of First 10 Years of Post Menopause on Muscle Function, Muscle Mass and Bone Mineral Density in Adult Women. *J OsteoporPhys Act*. 2015;03(03)

13. Ekblad S, Lönnberg B, Berg G, et al. Estrogen Effects on Postural Balance in Postmenopausal Women Without Vasomotor Symptoms. *Obstetrics & Gynecology*. 2000;95(2):278-83.
14. Darlington C, Ross A, King J, et al. Menstrual cycle effects on postural stability but not optokinetic function. *Neuroscience Letters*. 2001;307(3):147-50.
15. Gunendi Z, Ozyemisci-Taskiran O, Demirsoy N. The effect of 4-week aerobic exercise program on postural balance in postmenopausal women with osteoporosis. *N. Rheumatol Int*. 2008;28(12):1217-22.
16. Copeland J, Tremblay M. Effect of HRT on hormone responses to resistance exercise in postmenopausal women. *Maturitas*. 2004;48(4):360-71.
17. Monika C. Effectiveness of Mental Practice Combined with Physical Practice in the Treatment of Post Stroke Patients. *Journal of Novel Physiotherapies*. 2014;04(03).
18. Felicity AL, Shyle FH, Mackintosh. Functional balance assessment of older community dwelling adult. *The internet journal of allied health sciences and practice* 2007; 5(4):1-11.
19. Bell D, Guskiewicz K, Clark M, et al. Systematic Review of the Balance Error Scoring System. *Sports Health*. 2011;3(3):287-95.
20. Steadman J, Donaldson N, Kalra L. A Randomized Controlled Trial of an Enhanced Balance Training Program to Improve Mobility and Reduce Falls in Elderly Patients. *Journal of the American Geriatrics Society*. 2003;51(6):847-852.
21. Warner L, McNeill M. Mental Imagery and Its Potential for Physical Therapy. *Physical Therapy*. 1988;68(4):516-21.

An Observational Study on Factors Associated with Pre-Eclampsia/Gestational Hypertension among Pregnant Women Attending a Tertiary Care Hospital at Udupi

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Abstract

Introduction: Pre-Eclampsia and Gestational Hypertension are often categorised under the complicated hypertensive disorders in pregnancy. The present study was carried out to observe the maternal age distribution, family history of hypertension, blood group distribution, gravida status, gestational age at delivery and baby weight distribution among healthy pregnant women and pregnant women with PE/GH attending a tertiary care hospital at Udupi district.

Methodology: After obtaining the consent from pregnant women fulfilling the criteria for the study, details on maternal age distribution, family history of hypertension, blood group distribution, gravida status, gestational age at delivery and baby weight distribution were obtained from the patient records. Healthy pregnant were defined as those who had no complications in pregnancy till delivery and cases were defined as the ones who developed GH/PE anytime after 20 weeks of gestation.

Results: The present study identified that among Control 16.7% and among Case 29% had family history of hypertension. Larger percentage of women had blood group of O+ among control whereas it was B+ among case. Among Case, 48.6% women delivered at ≤ 37 weeks. The babies born to Control women had a birth weight of 3.07 ± 0.38 kg as compared to babies born to women with Gestational Hypertension/Pre-eclampsia which was 2.6 ± 0.32 kg.

Conclusion: The study could identify the distribution pattern of maternal age, family history of hypertension, blood group, gravida status, gestational age at delivery and baby birth weight and among healthy pregnant women and pregnant women with PE/GH attending a tertiary care hospital at Udupi district.

Keywords: Maternal Age, Family History of Hypertension, Blood Group, Gravida Status, Gestational Age at Delivery, Birth Weight.

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Introduction

Pre-Eclampsia and Gestational Hypertension are often categorised under the complicated hypertensive disorders in pregnancy¹. Various risk factors have been identified for PE. Age of the mother during conception is the most discussed risk factor. PE reported to occur mostly if the maternal age is to the extremes of

reproductive age (< 18 y or >35 y)². A family history of PE indicates that genetics play a role in the genesis of PE³. On a national based cross sectional study on “Prevalence and risk factors for PE in Indian women”, it was observed that, in India more than half of the women recruited in the study (55.6%) had features of PE. However, the higher rates (>70%) were observed in the states of Uttarakhand, Bihar, Jharkhand, Kerala and a peak higher rate in Tripura (87.5%)⁴. Women with PE are at higher risk of delivering preterm. The present study was carried out to observe the maternal age distribution, family history of hypertension, blood group distribution, gravida status, gestational age at delivery and baby weight distribution among healthy pregnant women and pregnant women with PE/GH attending a tertiary care hospital at Udupi district.

Methodology: The project proposal, patient information sheet and patient consent were approved by the Institutional Ethics Committee. This study with a case control design and duration of three and half years was carried out in the Department Obstetrics and gynaecology Department of Dr TMA Pai Hospital, Udupi. After obtaining the consent from pregnant women fulfilling the criteria for the study, details on maternal age distribution, family history of hypertension,

blood group distribution, gravida status, gestational age at delivery and baby weight distribution were obtained from the patient records. Healthy pregnant were defined as those who had no complications in pregnancy till delivery and cases were defined as the ones who developed GH/PE anytime after 20 weeks of gestation. Statistically the sample size was calculated as Case: Control in 1:3 ratio. Thus, 41 cases and 124 controls were used for the observational study.

Results

Maternal age distribution among the Case-Control subjects recruited in the study: Among the Control (n=124), 10 women (8.2%) were between 18-22 years of age, 34 women (27.1%) were in the age group of 23-25 years, 60 (48.4%) were in the age group of 26-30 years, 19 (15.6%) were between 31-35 years and only 1 woman (0.8%) had age greater than or equal to 36 years.

Among the Case group (n=41), it was observed that, 4 women (9.8%) were between 18-22 years of age, 7 women (17.1%) were in the age group of 23-25 years, 19 women (46.3%) were in the age group of 26-30 years, 7 (17.1%) were between 31-35 years and 4 women (9.76%) were above the age of 36 years.

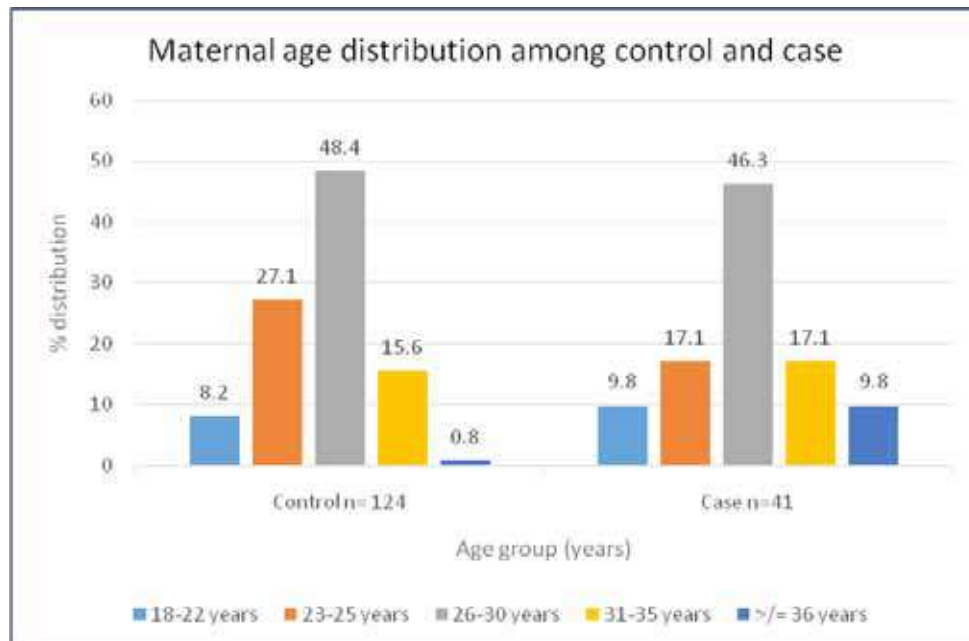


Fig.1. Maternal age distribution among the Case and Control

The mean maternal age among Control was 27.02±3.6 whereas among Case was 28.5±4.7.

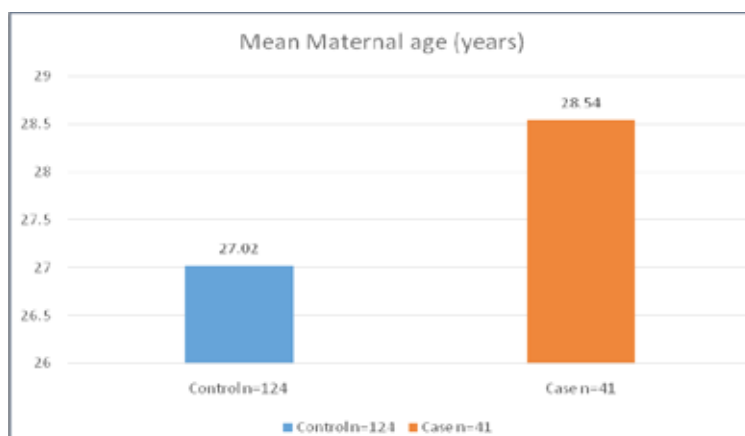


Fig. 2. Mean maternal age of Case and Control

Family history of hypertension among the Case- Control subjects recruited in the study: Among Control 21 women (16.7%) had family history of hypertension whereas among Case 12 women (29%) had family history of hypertension.

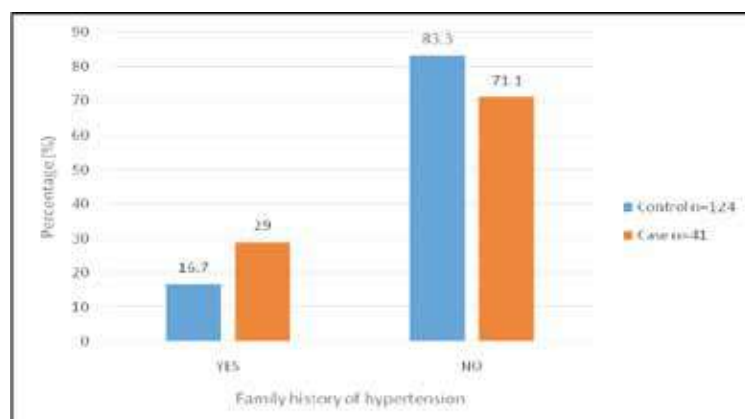


Fig. 3. Family history of hypertension among Case and Control

Blood group distributions among the Case- Control subjects recruited in the study: Among the Control 32 women were A+ (25.9%), 2 were A- (1.8), 24 were B+ (19.6%), 1 was B- (0.9%), 11 were AB+ (8.9%), none were AB- 0%, 47 were O+ (37.5%) and 7 were O- (5.4%). Among Case, 4 women were A+ (10.3%), 1 was A- (2.6%), 14 were B+ (33.3%), 1 was B- (2.6%), 5 were AB+ (12.8%), 1 was AB- (2.6%), 13 were O+ (30.7%) and 2 were O- (5.1%).

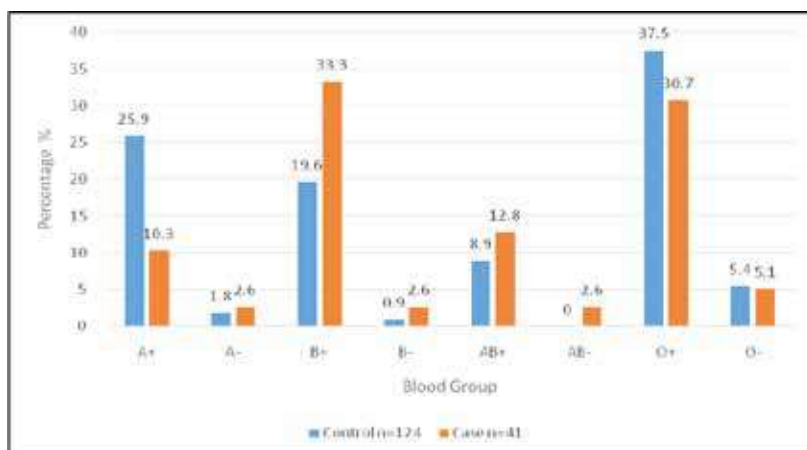


Fig. 4. Blood group distribution among Case and Control

Gravid status among the Case- Control subjects recruited in the study: Among Control and Case, 75 (60.3%) and 26 (62.5%) women respectively were primigravid, 30(24.1%) and 7(17.5%) were gravida 2; and 19 (15.5%) and 8(20%) were gravid 3 and more respectively.

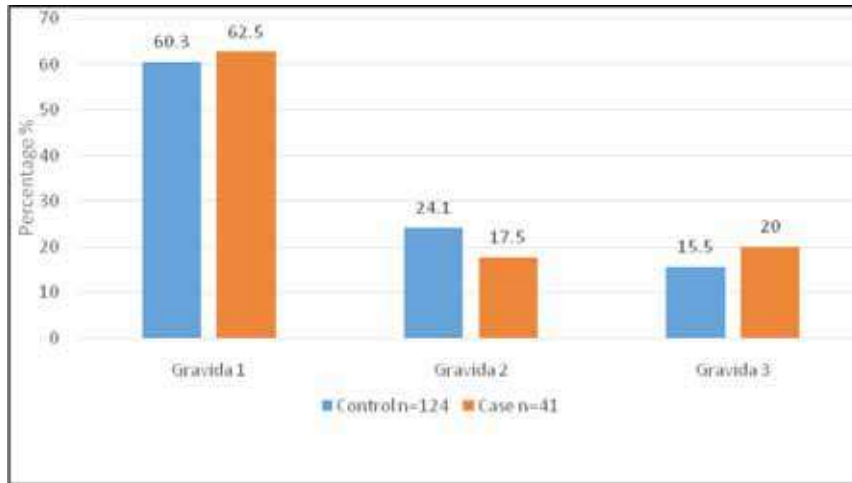


Fig. 5. Gravid status among Case and Control

Gestational age at delivery among the Case- Control recruited in the study: Among Control 20 women (16.4%) delivered at ≤ 37 weeks, 41 women (32.7%) delivered at 38 weeks, 36 women (29.1%) delivered at 39 weeks and 27 women (21.8%) at ≥ 40 weeks.

Among Case, 21 women (48.6%) delivered at ≤ 37 weeks, 9 women (22.9%) delivered at 38 and 39 weeks each and 2 women (5.7%) at ≥ 40 weeks.

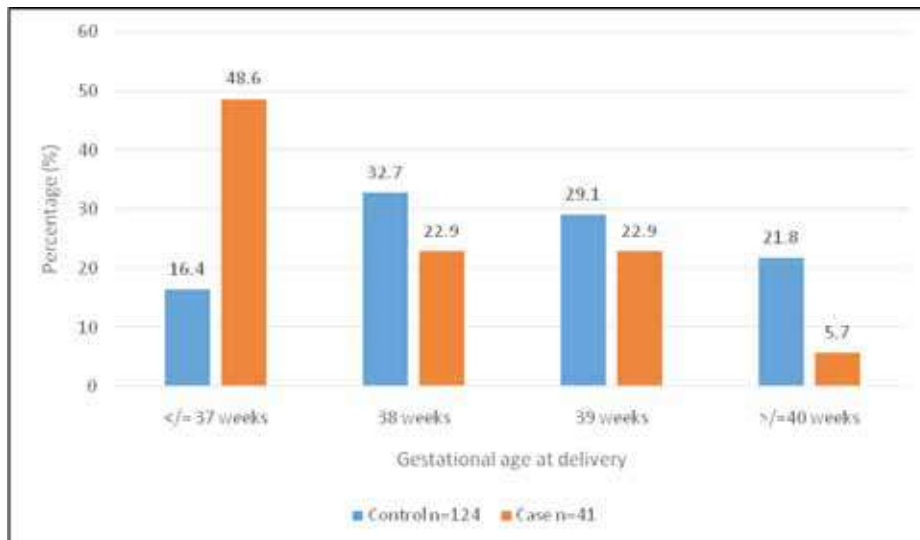


Fig. 6. Gestational age at delivery among Case and Control

Baby birth weight distribution among the Case Control subjects recruited in the study: The babies born to Control women had a birth weight of 3.07 ± 0.38 kg as compared to babies born to women with

Gestational Hypertension/Pre-eclampsia which was 2.6 ± 0.32 kg. It was observed that there is statistically significant difference between the baby birth weight of Control and Case.

Discussion

Maternal age is a risk factor for PIH. In the present study, it was observed that a larger proportion of women who developed the disease were in the age group of 26-30 years. Maternal age does not consistently show an association with risks of gestational hypertensive disorders⁵. However, maternal body mass index influences the association of maternal age with incidence of hypertension in pregnancy. In a study, PIH group had large proportion of women with age >30 years as compared to the control group⁶. However, maternal age is not consistently associated with the risks of gestational hypertensive disorders. Maternal body mass index might influence the association between maternal age and the risk of PIH⁵. Increased maternal age is associated with increased incidence of PIH. The risk increased in the age group above 40 years⁷.

In the current study it was observed that among Control 16.67% only had family history of hypertension whereas among Case 28.95% had family history of hypertension. There is increased risk of hypertensive disorders in pregnancy in women who had previous history of PE and family history of hypertension and PE⁸. Family history of hypertension and diabetes is often associated with genetic and behavioural susceptibility to the genesis of PE⁹.

In the present study, we observed that the proportion of women with B+ blood group were more in the PE/GH group. However, Clark P and Wu O (2008) reported that, there is no association existing between the blood group types and incidence of PE¹⁰. Studies have reported that AB+ blood group were at higher risk of developing hypertension in pregnancy and O+ was at lowest risk^{11,12}. It is also reported that, A or AB blood types, but not B, were at a higher risk of PE compared with O type individuals¹³.

Gravida number is also identified as yet another causative factor for PIH. In our study it was observed that among the primigravid, there was larger incidence of hypertension. Also it was observed that, there were a relatively larger proportion of women in gravid 3 and above in the hypertensive group as compared to Control. Primigravidis associated with higher incidence of PIH¹⁴.

We also observed lower birth weight in babies born to women in the hypertensive disorder group as compared to the control group. However, the birth weight of the babies was above the cutoff of 2.5kg defined for

low birth weight. In the current study, majority of the mothers in hypertension group delivered at ≤ 37 weeks as compared to Control where it was 38 and 39 weeks¹⁵. In their study pre-eclamptic women who delivered ≤ 37 weeks, had statistically significantly lower birth weight babies whereas babies born to women who delivered ≥ 37 weeks did not have a difference as compared to the control group.

Conclusion

The study could identify the distribution pattern of maternal age, family history of hypertension, blood group, gravida status, gestational age at delivery and baby birth weight among healthy pregnant women and pregnant women with PE/GH attending a tertiary care hospital at Udupi district.

Conflict of Interest: There is no conflict of interest among the authors.

Ethical Clearance: The project proposal, patient information sheet and patient consent were approved by the Institutional Ethics Committee.(IEC 290/2013)

Source of Funding: The study was funded by Manipal Academy of Higher Education, Manipal.

References

1. Turpin CA, Sakyi SA, Owiredu WK, Ephraim RK, Anto EO. Association between adverse pregnancy outcome and imbalance in angiogenic regulators and oxidative stress biomarkers in gestational hypertension and preeclampsia. *BMC pregnancy and childbirth*. 2015 Aug 25;15(1):1.
2. Bansode BR. Managing Hypertension in Pregnancy. *Medicine update*. 2012;22:150-6.
3. Cnossen JS, van der Post JA, Mol BW, Khan KS, Meads CA, terRiet G. Prediction of pre-eclampsia: a protocol for systematic reviews of test accuracy. *BMC pregnancy and childbirth*. 2006 Oct 19;6(1):1.
4. Agrawal S, Walia GK. Prevalence and Risk Factors for Symptoms Suggestive of Pre-Eclampsia in Indian Women. *J Womens Health, Issues Care* 3. 2014;6:2.
5. Gaillard R, Bakker R, Steegers EA, Hofman A, Jaddoe VW. Maternal age during pregnancy is associated with third trimester blood pressure level: the generation R study. *American journal of hypertension*. 2011 Sep 1;24(9):1046-53.

6. Jasovic-Siveska E, Jasovic V, Stoilova S. Previous pregnancy history, parity, maternal age and risk of pregnancy induced hypertension. Bratisl Lek Listy. 2011;112(4):188-91.
7. Liu X, Ruan Y, Liu Y, Zhang W. Relationship between maternal age and hypertensive disorders in pregnancy. Zhonghua Yi Xue Za Zhi. 2015 Jan 6;95(1):19-22.
8. Ordas AM, Gomez AR, Benito MH, Luis MF, Hernandez RS, Cotera FA. Gestational Hypertension: Risk Factors, Clinical And Laboratory Findings: PP. 32.294. Journal of Hypertension. 2010 Jun 1;28:e538.
9. Qiu C, Williams MA, Leisenring WM, Sorensen TK, Frederick IO, Dempsey JC, Luthy DA. Family history of hypertension and type 2 diabetes in relation to preeclampsia risk. Hypertension. 2003 Mar 1;41(3):408-13.
10. Clark P, Wu O. ABO (H) blood groups and preeclampsia: A systematic review and meta-analysis. Thrombosis and haemostasis. 2008;100(3):469-74.
11. Lee BK, Zhang Z, Wikman A, Lindqvist PG, Reilly M. ABO and RhD blood groups and gestational hypertensive disorders: a population-based cohort study. BJOG: An International Journal of Obstetrics & Gynaecology. 2012 Sep 1;119(10):1232-7.
12. Reshmarani, Veena H. C, Amruta Bernal. Association between ABO Blood Group and Pregnancy Induced Hypertension. Sch. J. App. Med. Sci., 2014; 2(6C):3054-3056
13. Phaloprakarn C, Tangjitgamol S. Maternal ABO blood group and adverse pregnancy outcomes. Journal of Perinatology. 2013 Feb 1;33(2):107-11.
14. Gunnlaugsson SR, Geirsson RT, Snaedal G, Hallgrímsson JT, Gunnlaugsson S. Incidence and relation to parity of pregnancy-induced hypertension in Iceland. Acta obstetrica et gynecologica Scandinavica. 1989 Jan 1;68(7):599-601.
15. Xiong X, Demianczuk NN, Saunders LD, Wang FL, Fraser WD. Impact of preeclampsia and gestational hypertension on birth weight by gestational age. American journal of epidemiology. 2002 Feb 1;155(3):203-9.

The Effect of Specific Training on Selected Physical Variable among Kabaddi Players

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Abstract

Context: The purpose of this study was to find out the effect of specific training on selected physical variable among school boys kabaddi players. The age of the subjects ranged from 15 to 18 years. The selected subjects n=30 were divided into one experimental group and one control group at random. The investigator selected a training that is specific training for kabaddi players which improved certain selected physical fitness variables namely muscular strength. As the result of field training the physical fitness level of the kabaddi would improve. The experimental group endured the training activities for 6 weeks with a schedule of six days whereas the control group remained with no activities. The data procured in prior and after the training programme was examined. To find out difference between experimental and control group of Muscular strength t-ratio was employed and the level of significance was set at 0.05. The results of the study showed that the muscular strength of the experimental group was significantly improved than the control group.

Keywords: Specific training, Muscular strength, Kabaddi, Experimental group, Control group

Introduction

A sport is an organized, competitive, entertaining and skillful physical activity requiring commitment, strategy and fair play in which a winner can be defined by objective means.¹ It is governed by a set of rules or customs. In sports the key factors are the physical capabilities and skills of the competitor when determining the outcome winning or losing. The physical activity involves the movement of people, animals and/or a variety of objects such as balls and machines or equipment. In contrast, games such as card games and board games, though these could be called mind sports and some are recognized as Olympic sports,

require primarily mental skills and only mental physical involvement.²

Physical Education is one of the most ancient arts of the humanities. In its broadest interpretation, Physical Education is defined as the art and science of voluntary purposeful and active human movement.³ It is clear that Physical Education is concerned with a fundamental mode of human expression. Likewise it is an essential form of non – verbal communication which can be communicated very effectively depending and does, express a wider range of emotions while participating in a group towards the activities of Sports Specific Trainers can help improve strength, flexibility and stamina to improve performance in specific sports.⁴ Options include increasing arm strength for tennis playing or improve strength and core stability providing better balance playing golf.

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Specific Fitness: Specific or task-oriented fitness is a person's ability to perform in a specific activity with a reasonable efficiency. For example sports or military service. Specific training prepares athletes to perform

well in their sports.⁵ Examples are 400 m sprint in a sprint the athlete must be trained to work an aerobically throughout the race.

Sport Training: Sport training is done for improving sports performance. The sports performance as any other type of human performance is not product of one single system or aspect of human personality. On the contrary it is the product of the total personality of the sports person. The personality of a person has several dimensions for example physical, physiological, social and psychic.

Sports Specific Training: Sports specific training is all about developing physical conditions to improve performance and skills at a particular sport.⁶ Also understanding the needs of the game training practicing at the correct pace in order to meet sports requirements.

Kabaddi: The game Kabaddi includes quick movement along with a great deal of bending, dodging, quick turns, kicks and twists. The participant in Kabaddi requires substantial muscular strength to grasp hold of opponents or to oppose the hold of opponents and get away from them. The skill includes the movements to be understood and carefully practiced during long period, as in any other well ordered game so that participants not only play better but also get satisfaction in plying Kabaddi.⁷

Statement of the Problem: The purpose of this study was to find out the effect of specific training on selected physical variable among school boys kabaddi players.

Methodology: To achieve the purpose of these study 30 boys kabaddi players were selected at government higher secondary school koomapatti. The

age of the subjects ranged from 15 to 18 years. The selected subjects were divided in to one experimental group and one control group at random. The investigator selected a training that is specific training for kabaddi players which improved certain selected physical fitness variables namely muscular strength. As the result of field training the physical fitness level of the kabaddi would improve.

Test Administration of Muscular Strength:

(SIT-UPS (1- min))

Purpose: To measure the endurance of the abdominal muscles.

Equipment: The only equipment required is a mat and yardstick.

Direction: From a lying position on the back, the performer flexes his knees over the yardstick while sliding his heels as close to his seat as possible. The yardstick should be held tightly under the knees until the performer is instructed to slowly slide his feet forward. At the point where the yardstick drops to the mat, the tester marks the hard line and seat line to indicate how for the feet should remain from the seat during the bent-knee sit-ups exercise. The hands are clasped behind the head, and the subject raises the trunk by lifting first the head, then the shoulders, and then the back. Each trial by performing five sit-ups for the testers before proceeding with the time trails. The time limits are observed.

Scoring: The completion of one complete curl up (up and back) counts as one. The sit-up must be performed correctly for it to be counted. For the tempo tests, the test is continued until the subject cannot maintain the rhythm or has reached the target number for the test.

Table 1: Analysis of ‘t’ ratio the pre and post test for Control and Experimental Group on Muscular strength

Variable	Group	Mean		SD		Sd Error	Df	‘t’ ratio
		Pre	Post	Pre	Post			
Muscular strength	Control	17.47	17.00	2.03	2.04	0.43	14	1.07
	Experimental	17.60	20.80	2.20	2.65	0.17		18.33*

* Significance at 0.05 level of confidence.

Table 1: presents the difference between experimental and control group of Muscular strength. Difference in two group's t-ratio was employed and the level of significance was set at 0.05. Experimental group pre and post-test mean value were 17.60, 20.80 respectively. In Control group pre and post-test were mean value was 17.47, 17.00 respectively.

In experimental the obtained t-ratio 18.33 was greater than the table value 2.15 so it found to be significant. In control group the obtained t-ratio 1.07 was lesser than the table value 2.15 so it was found to be insignificant. Figure 1 shows the pre and post test mean values of control and experimental group on muscular strength.

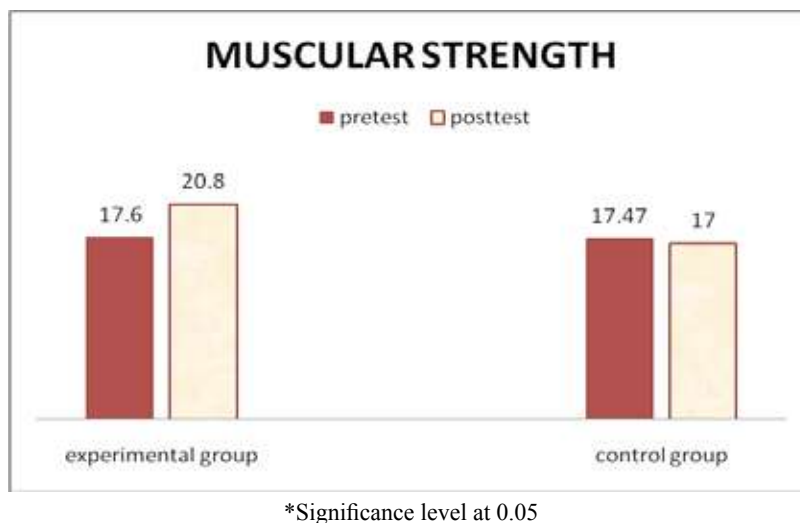


Figure 1: Bar Diagram Shows the Pre and Post Test Mean Values of

Control and Experimental Group on muscular strength:

Discussing on Findings: The result of the study indicates that the experimental group namely specific training group had significantly improved the selected dependent variables namely Physical Variable- muscular endurance when compared to the control group. It is also found that the improvement caused by specific training when compared to the control group.

Discussion on Hypotheses: It was hypothesized at the beginning of the study that there would be significant improvement on selected criterion variables such as specific training (physical variable) due to training for the experimental group as compared to the control group. The present study produced similar results. Hence, the first research hypothesis of the investigator was held true.

Conclusions

The results of the study concluded that the muscular strength of the experimental group was significantly improved than the control group.

Ethical Clearance: Nil

Source of funding: Self

Conflict of Interest: Nil

References

1. Caillois R. Man, play, and games. University of Illinois Press; 2001.
2. Koster R. Theory of fun for game design. "O'Reilly Media, Inc."; 2013 Nov 8.
3. Manley AF. Physical activity and health: Rep Surg Gen. Diane Publishing; 1996.
4. Kloubec JA. Pilates for improvement of muscle endurance, flexibility, balance, and posture. J Stren & CondRes. 2010 Mar 1;24(3):661-7.
5. Fernandez J, Mendez-Villanueva A, Pluim BM. Intensity of tennis match play. British jlsports med. 2006 May 1;40(5):387-91.
6. Côté J, Baker J, Abernethy B. Practice and play in the development of sport expertise. Hb sport psyc. 2007 Jan 1;3:184-202.
7. Murthy V. Common injuries in kabaddi play and their prevention with the help of biomechanics. Int J Phy Edu Sports and Health. 2016;3(4):78-81.

Effect of Selected Yogic Practices on Aerobic Capacity and Anaerobic Power of School Girls

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Abstract

Context: The objective of the present study was to find out the effect of selected aerobic capacity and anaerobic power of sedentary school girls of west Bengal. Subject: twenty five(n=25) sedentary school students were randomly selected as subjects for this study from Atulia Neta Adharsha Vidyapath, North 24 paraganas. The age ranged from 16-18 years. The study was confined in a single experimental group and no control group was considered. In the present study of aerobic capacity and anaerobic power were two variables. Aerobic capacity were measured in terms of maximum oxygen consumption during excersice i.e. VO2 max. Aerobic capacity & anaerobic power were measured respectively by Queens College Step Test and Margaria-kalamenanaerobic power test. A structured yogic training was intervened for six week. Mean and Standard deviation statistical procedure was carried out. The mean of different variables were compared by using t-test statistical significance was tested at 0.05 levels. The results highlighted that there were the significant difference in aerobic capacity between pre and post treatment condition. On the other hand a significant difference was found in anaerobic power between the pre and post treatment condition.

Keywords: Aerobic capacity, Anaerobic power, Oxygen consumption, Yogic training, t-test

Introduction

Aerobic (cardiovascular) capacity is one of the most important components of physical fitness. The other components are muscular strength and endurance, and flexibility and low-back function.¹ Cardiovascular fitness is measured as the amount of oxygen transported in the blood and pumped by the heart to the working muscles and as the efficiency of the muscles to use that oxygen. Increasing cardiovascular fitness means increasing the capability of the heart and the rest of the cardiovascular system in their most important task, to supply oxygen and energy to your body.²

Having good cardiovascular fitness has many health benefits. For example, it decreases your risk of cardiovascular diseases, stoke, high blood pressure, diabetes and other diseases, cardiovascular fitness is best improved by activities, which employ large muscle groups working dynamically. Such activities include walking, running, jogging, swimming, skating, cycling, climbing and cross- country skiing.

Anaerobic power is energy that is stored in muscles and that can be accessed without use of oxygen.³ There are two systems utilize this type of power, the phosphogern system and the lactic acid system. Human beings use this form of energy in short burst that cannot be sustained for longer than about two minutes.⁴ Considering the research work in this field it concluded that very little effort has been taken so far to find the effect of yoga practice aerobic capacity and anaerobic power on sedentary school children.⁵ Accordingly the project is planned to iniative research work related to the effort of selected yogic practice aerobic capacity and anaerobic power of school children from west Bengal.⁶

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Materials and Method:

Subjects: A total no of twenty five (N=25) healthy female having age ranged between 18 years were randomly selected as subjects for the present study from, Atuli A Netaaji, Adharth Vidyapith, Norht 24 Paraganas of west Bengal. They were basically the students of classes XII of the institution. The study was approved by Institutional Ethical Committee. The study was confined into a single experimental group and no control group was considered.

Experimental Protocol: A six weeks yogic training schedule(5 days in a week), study on 25th January up to march 1st week, were intervened on the subject by the researcher the help of instructress, bend and other coaching professionals. Yoga classes were offered five per week, from 8.00-9.00 a.m. for 8 weeks, Saturday-Sunday was considered as rest day of certified yoga instructor led all classes. Each yoga session consisted of 15 minutes of warm-up exercise. The warm-up program focused on slow, dynamic muscular movements, which consist of dynamic lunge shoulder and arm circles, neck rolls, standing forward bend two. The training program was prolonged for 50 minutes of asana, (yoga postures), and 10 minutes relaxation in savasana. The selected names of asana were scheduled as follows. Pranayamas focused on the quality and ease of breath and isometric muscular contraction. Table 1 presents the training schedule given to the students.

Variable Studied: In this project three variables were studied viz.:

1. Aerobic capacity in terms of VO₂ max-Queens College Step Test
2. Anaerobic power- Margaria Anaerobic Power Test or Margaria-Kalamen Power Test.

Measuring Procedure: Height and weight are measured by Anthropometric rod and weighing machine (Tanita, Model: BC-554). To measure aerobic capacity in terms of max Queen's College Step Test (QCST) was administrated on all the selected subjects in pre as well as post treatment condition.

Prediction of Vo₂ Max: In brief the step was performed using a stool of 16.5 inches height. Stepping was done for a total duration of 3 minutes at the rate of 24 cycles per minute which was set by a metronome. After completion of the exercise, the subjects were used

to remain standing comfortably and the carotid pulse was measured from the fifth to the tenth second of the recovery period. This 15 second pulse rate was converted into beats per minute(15 sec pulse rate x 4) and the value thus obtained was put in the following equation predict VO₂ max in ml/kg/min, as proposed by McArdle et al., 1986.

$10 \text{ max (ml/kg/min)} = 65.81 - (0.1847 \times \text{pulse rate in beats per min})$

Prediction of Anaerobic Power: The students ready at the starting line 6 meters in front of the first step. On the command "GO", the students sprints to and up the flight of steps, bring three steps at the time (stepping on the 3rd, 6th and 9th steps), attempting to go up the steps as fast as possible. The time to get from the 3rd step to the 9th step is recorded (either using the stop watch or using switch mats placed on the 3rd and 9th steps), starting when the foot was in first in contact with the 3rd step and stopped when the foot contacts the 9th step. Allow three tills of the test, with 2-3 minute, recovery between each trial. Anaerobic power (Watts) calculated from the formula below, where P= Power (Watts), M=Body Mass (kg), D= Vertical Distance, between steps 3 & 9 (meters), T= Time (Seconds), 9.8 is the constant of gravity.

$$\text{POWER} = P = M \times D \times 9.8 / t$$

The unit of power in S.I system was Jule/second or watts.

Instrument and Tools: Following instruments and tools were used for collecting the data: 1) staircase 12-16 stairs (15-20cm), 2) weight scale, 3) steeping bench (16-17"), 4) Metronome and 5) stopwatch.

Statistical Analysis: In the present study for the sake of analysis of data mean and standard deviation of the variables were calculated. To find out significant difference of mean between the pre and postintervention in different variables statistical t-test was used. The significant of means were tested at p<0.005 level of confidence. For statistical calculations excel Spread Sheet of windows version 7 will be used.

Results and Discussion

The mean standard deviation of obtained data belongings to height and weight of collegiate women have been presented in Table-1.

Table 1:- Training Schedule

DAYS	TOTAL TIME- 50 MINUTES (MORNING SESSION- 8.00-9.00A.M.)							
	TIME DIVIDED							
	8 Minutes	4 Minutes	4 Minutes	4 Minutes	4 Minutes	4 Minutes	6 Minutes	6 Minutes
Mon	Suryanamaskar	Padmasana	Sarbangasana	Padahastasana	Noukasana	Matsasana	Narisodhana	Vastrika Pranayama
Tues	Suryanamaskar	Padmasana	Sarbangasana	Padahastasana	Noukasana	Matsasana	Narisodhana	Vastrika Pranayama
Wed	Suryanamaskar	Padmasana	Sarbangasana	Padahastasana	Noukasana	Matsasana	Narisodhana	Vastrika Pranayama
Thurs	Suryanamaskar	Padmasana	Sarbangasana	Padahastasana	Noukasana	Matsasana	Narisodhana	Vastrika Pranayama
Fri	Suryanamaskar	Padmasana	Sarbangasana	Padahastasana	Noukasana	Matsasana	Narisodhana	Vastrika Pranayama

Table 2: Mean and stander Deviation of height and weight of the subject

Height (cm)		Weight (kg)	
pre	post	Pre	post
1.47±0.07	1.47±0.06	54.258±8.22	52.12±7.32

From the table-2 it was found that the mean and standard deviation of pre height of school girl are 1.42±0.07cm, post height of the school girls were 1.47±0.06cm, and the mean and standard deviation of pre weight of school girls were 54.52±8.22kg, post weight of school girls were 52.12±7.32kg.

Table-3: Mean, S.D, Mean Difference, Standard Error, and ‘t’- Value or Aerobic Fitness & Anaerobic Power Measurement of Sedentary School Girls

NAME OF THE VARIABLES	MEAN ± SD		MEAN DIFFERENCE	STANDARD ERROR	T- VALUE
	PRE-DATA	POST-DATA			
AEROBIC FITNESS (ml.kg-1.min-1)	38.52 ± 8.24	43.62 ±7.24	5.10	2.19	2.32
ANAEROBIC POWER	487.84 ±82.32	516.64 ±96.66	28.80	25.39	1.13

Table value of ‘t’ for at 0.05 level of confidence = *2.001

From table-3 It was found d that the mean and the standard deviation of aerobic capacity from the sedentary school girls in the pre and post intervention of training were 38.52±8.24(ml.kg-1.min₋₁) and 43.62±7.24(ml.kg-1.min-1) respectively. Figure -1 indicates the mean value of aerobic capacity of the sedentary schools girls. It was found that in case of aerobic capacity the significant difference was observed between the pre and post intervention condition.

From Table-3 it was observed that the mean and standard deviation of obtained data belonging to anaerobic power as, measured by MargariraKalaman Power Test of Sedentary school girls. The pre and post

intervention of training were 487.84±82.32(jule.sec-1) and 516.64±96 (jule.sec-10) respectively. Figure-2 indicates the mean value of aerobic capacity of sedentary school girls. It was found that in case of anaerobic fitness no significant difference was observed between the pre and post intervention condition.

On the basis of analysis of data the following results were obtains for the present project:

- (a) In aerobic capacity significant difference was found between the pre and post intervention condition of the sedentary school girls.

(b) No significant difference in anaerobic power was obtained between the pre and post intervention condition of the sedentary school girls.

Conclusion

Thus on the basis of the result it can be concluded that the yogic practices are effective for improving the aerobic capacity but not too much effective for improving anaerobic power.

Ethical Clearance: Nil

Source of Funding: Self

Conflict of Interest: Nil

Reference

1. Hannibal III NS, Plowman SA, Looney MA, Brandenburg J. Reliability and validity of low back strength/muscular endurance field tests in adolescents. *J PhyActand Health*. 2006 May;3(s2):S78-89.
2. Manley AF. Physical activity and health: A report of the Surgeon General. Diane Publishing; 1996.
3. Medbo JI, Tabata I. Relative importance of aerobic and anaerobic energy release during short-lasting exhausting bicycle exercise. *J App Physiol*. 1989 Nov 1;67(5):1881-6.
4. Haissaguerre M, Jaïs P, Shah DC, Takahashi A, Hocini M, Quiniou G, Garrigue S, Le Mouroux A, Le Métayer P, Clémenty J. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *New Eng J Med*. 1998 Sep 3;339(10):659-66.
5. Manley AF. Physical activity and health: A report of the Surgeon General. Diane Publishing; 1996.
6. Uddin R. A Critical Evaluation of the Organizational Structure, Administrative Frame-work and Facilities of Sports in Uttar Pradesh Jails (Doctoral dissertation, Aligarh Muslim University).

Effectiveness of Low Level Laser Therapy Versus Ultrasound Therapy with Plantar Fascia Stretching in Subjects with Plantar Fasciitis

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Abstract

AIM: To find the effectiveness of low level laser therapy versus ultrasound therapy with plantar fascia stretching in subjects with plantar fasciitis.

Materials and Method: Non equivalent quasi experimental study design was used in this study. Total of 30 subjects with plantar fasciitis were selected using non probability convenience sampling technique. 30 Subjects was divided into two groups by lot system. Group A received low level laser therapy and Group B received ultrasound therapy and for both the group plantar fascia stretching was given. The outcome measures are FAAM (foot ankle ability measure) and NPRS (numerical pain rating scale). Data collected and tabulated was statistically analysed.

Result: Statistical analysis of post-test, foot and ankle ability measure questionnaire (FAAM) and NPRS (numerical pain rating scale) revealed that there is statistically significant difference seen between Group A and Group B.

Conclusion: From the result, it has been concluded that low level laser therapy with plantar fascia stretching (Group A) is more effective than ultrasound therapy with plantar fascia stretching (Group B) in decreasing pain and improving the quality of life in subjects with plantar fasciitis.

Keywords: *Plantar fasciitis, low level laser therapy, ultrasound therapy.*

Introduction

The human foot is a strong and complex mechanical structure and terminal portion of the limb which bears weight and allows locomotion.¹ The plantar fascia is a dense, fibrous, connective tissue structure originating from the medial tuberosity of the calcaneus. It has three-medial, lateral and central portions.²

Plantar fasciitis is a degenerative condition resulting from compressive forces due to repeated trauma to plantar fascia making the foot's longitudinal arch of flat. Traction forces during the gait on support phase leading to inflammation results in fibrosis and degeneration. Plantar fasciitis is the common reason for heel pain for 80 percentage of cases. It affects most commonly people who are between 40 – 60 years of age.³

The exact etiology of plantar fasciitis still remains unclear but the risk factors which results in plantar fasciitis includes overuse of plantar fascia, exercises like ballet jumping activities, long distance running, long period of standing, obesity, pregnancy, military recruits, athletes. The patient usually complaints of pain over the medial side of plantar heel, usually when taking first few steps after waking up.⁴

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The common site of pain in plantar fasciitis is near to the origin of the central band of plantar Apo neurosis at the medial plantar tubercle of the calcaneus.⁵

The windlass mechanism explains these biomechanical stresses and factors. Plantar fasciitis forms the tie-rod that attaches from calcaneus to phalanges. Vertical forces from the weight of the body travel to medial longitudinal arch in downward direction through tibia and flattens the arch. Further, the ground reaction forces that travel in upward direction on the calcaneus and metatarsal heads, even more leads to flatten of arch as these forces fall anterior and posterior to the tibia. Plantar fascia prevent the collapse of arch by its tensile force and orientation⁶

Plantar fasciitis tends to improve in most cases regardless of the treatment selected. As a result conservative management is effective for nearly 90% of the patient. The conservative treatments used in management of plantar fasciitis vary widely and are dependent on physician specialty.¹

Methodology: The subjects were selected from the Saveetha physiotherapy, outpatient department of Saveetha medical college and hospital. 30 subjects with plantar fasciitis were selected based on the inclusion and exclusion criteria. Detailed procedure was explained to the subjects in the colloquial terms about the safety and simplicity of the procedure. Informed concern were given to those who were interested to participate in this study. Selected subjects were randomly assigned in to two groups 15 in each group by using lottery system. The outcome measure used in this study for pain is numerical pain rating scale(NPRS) and for the quality of life is foot and ankle ability measure questionnaire (FAAM) respectively. For all subjects’ pre and posttest values were calculated.

Procedure: Group A Were the subjects who received low level laser therapy along with plantar fascia stretch. Group B were the subjects who received ultrasound therapy along with plantar fascia stretch.

For group A Probe method (continuous) of low level laser therapy was used to treat the subjects. Safety precautions was taken to reduce the risk of exposure of laser light to the eyes. Low level laser therapy was given in painful area for 3 days/week for 2 weeks. The wave length used in the treatment is 830nm for 9 minutes. The irradiation area include 3 point over 3cm².

For group B Ultrasound therapy was given to the subjects in the frequency of 3 MHZ in the pulsed mode (1;4) for 8 minutes with the intensity of 0.5W/cm² for 2 weeks(3days/week).

For both the group plantar fascia stretching was givenwith the hold time for 20-30 seconds with the repetation of 10 times in the alternative days.

Results

The collected data was tabulated and analyzed using descriptive & inferential statistics. To all parameters mean and standard deviation (SD) was used. Paired t-test was used to analyse significant changes between pre and posttest measurements. Unpaired t test was used to analyse significant difference between the groups. P value <0.05 was considered as statistically significant.

Table 1 represents the FAAM Scale score for group A and B. The group A pre-test mean value is 39.93% (SD 7.93%) and post-test mean value is 66.87% (SD 7.30%).The group B pre-test mean value is 48.20% (SD 13.09%) and post-test mean value is 56.27% (SD 11.81%) .This shows that FAAM Scale score values are gradually increasing in the group A than group B, which is statistically significant.

Table 2 represents the NPRS score for group A and B. The group A pre-test mean value is 7.47cm (SD 1.19cm) and post-test mean value is 3.93cm (SD 0.80cm).The group B pre-test mean value is 6.27cm (SD 0.80cm) and post-test mean value is 5.53cm (SD 0.83) .This shows that NPRS score values are gradually decreasing in the group A than group B, which is statistically significant.

Table 1: Comparison of pre and post test values of FAAM scale for group A and B

FAAM Scale		MEAN	SD	t value	P value
Group A	PRE	39.93%	7.93%	38.8492	0.0001
	POST	66.87%	7.30%		
Group B	PRE	48.20%	13.09%	9.9896	0.0001
	POST	56.27%	11.83%		

Group 1: Comparison of pre and post test values of FAAM scale for group A and B

Table 2: Comparison of pre and post test values of NPRS scale for group A and B

NPRS Scale		MEAN	SD	t value	p value
Group A	PRE	7.47cm	1.19cm	14.9480	0.0001
	POST	3.93cm	0.80cm		
Group B	PRE	6.27cm	0.80cm	4.7845	0.0003
	POST	5.53cm	0.83cm		

Discussion

Plantar fascia is commonly a repetitive micro trauma overloaded injury of the attachment of plantar fascia at the inferior aspect of calcaneus.

The clinical presentation of plantar fasciitis include gradual insidious onset of heel pain. Pain and stiffness are worse in the morning(during first few steps) or after prolonged walking and increased by climbing stairs or doing raising up activity thus impairing the activity of daily life.

Conservative treatment for plantar fasciitis include ultrasound therapy, cryotherapy, low level laser therapy, medication (steroids), stretching, foot wear modification, manual therapy, splint, tapping and strapping.

This study compares the effectiveness of low level laser therapy and ultrasound therapy with plantar fascia stretching in subjects with plantar fasciitis in terms of pain and quality of life.

The subjects with age group of 30-60 years of both gender with plantar fasciitis were selected. 15 subjects in Group A were treated with low level laser therapy with plantar fascia stretching while 15 subjects in Group B were treated with ultrasound therapy with plantar fascia stretching.

The pre-test and post-test values of this study, revealed that there was a statistical difference (p<0.0005) in both the groups in terms of pain and quality of life, but there was more improvement in Group A than Group B.

WOLGIN M, et al stated that low level laser effects causes the stimulation of bodies own processes in healing tissue by light [12]. Phototherapy increases the both local and systemic micro circulation of the body thus it relieves pain and swelling [22]. The 2 major areas for which low level laser therapy is used is tissue healing and pain control. Laser therapy is used for pain relief in many conditions in both acute and long term (England 1998). [23] The laser therapy is found to be very effective

in various overuse tendinitis conditions. Laser has its effect on prostaglandin synthesis and thus it relieves inflammation. [24]. DR.ZANG said that 3 to 4 treatment are necessary for acute plantar fasciitis if treatment begins 6 to 8 weeks after the onset of symptoms.

Ultrasound has been utilized for pain through the ability of sound waves to introduce molecules of chemical substances through the skin by a process called phonophoresis [25]. Improvements in plantar fasciitis by the application of ultrasound therapy has been reported by Clarke and stenner (1976) [26]. The application of ultrasound therapy for pain relief, along with plantar fascia stretch is commonly indicated alternative therapy for plantar fasciitis [27]. The pulsed ultrasound is believed to have therapeutic benefits and can be applied to acute injuries [28]. The effects of ultrasound therapy are tissue relaxation, increase in local blood flow, scar tissue breakdown. By increasing the local blood flow level it reduces local swelling and inflammation. WATSON (2006) suggested that application of ultrasound to injured tissues, speed the rate of healing and enhance the quality of repair.

Plantar fascia stretching reduces the tightness in the plantar fascia. Plantar fascia stretching recreates the windlass mechanism by decreasing the micro trauma and inflammation. Plantar fascia stretching helps in reducing pain, improving function and gives overall satisfaction compared to standard Achilles tendon stretching exercises [13].

The post mean value in this study of quality of life [foot and ankle ability measure(FAAM)] and pain [numerical pain rating scale (NPRS)] score of Group A treated with low level laser therapy with plantar fascia stretching was 66.87 and 3.93 and Group B treated with ultrasound therapy with plantar fascia stretching was 56.27 and 5.33 at the end of 2 weeks.

Hence is has been proven that the recovery is earlier and faster in relieving pain and improving quality of life in Group A than Group B. Thus these statistical findings could be attributed to the fact that low level laser therapy with plantar fascia stretching works more statistically over ultrasound therapy with plantar fascia stretching

Conclusion

From the result, it has been concluded that low level laser therapy with plantar fascia stretching (Group A) is more effective than ultrasound therapy with plantar fascia

stretching (Group B) in reducing pain and improving quality of life in subjects with plantar fasciitis.

Ethical Clearance: Taken from Institutional Scientific Review Board

Conflict of Interest: Nil

Source of Funding: Self

Reference

1. Neufle,s., et al plantar fasciitis; evaluation and treatment . journal of the American academy of the orthopaedic surgery, 2008,16, 338-345.
2. Sbbrotzman, clinical orthopaedic rehabilitation: A team....., book.google.com[2017]
3. Renata gracile zanon, Adriana kundrat brasil, Marta Imamura- continuous ultrasound for chronic plantar fasciitis treatment (2006).
4. Ang Tee Lim, Choon How How, benedict Tan- management of plantar fasciitis in outpatient setting (2016).
5. Thomas G. MCpoil et al. heel pain- plantar fasciitis. Ortho sports phys ther. 2008:38(4): A1-A18.
6. Lori A. Bolgla; Terry R. Malone- plantar fasciitis and the windlass mechanism: a biomechanical link to clinical practice. Journal of athletic training 2004:39(1):77-82.
7. Nelson fong SooHOO, MD and caleb behrend, MD. Chapter 67- what is the best treatment for plantar fasciitis? 2009, pages 435-440
8. Yin MC, Ye J, Yao M, Cui XJ, Xia Y, Shen QX, Tong ZY, Wu XQ, Ma JM, Mo W (March2014). "Is Extracorporeal Shock Wave Therapy Clinical Efficacy for Relief of Chronic, Recalcitrant Plantar Fasciitis? A Systematic Review and Meta-Analysis of Randomized Placebo or Active-Treatment Controlled Trials". Arch Phys Med Rehabil. 95: 1585–1593. doi:10.1016/j. apmr.2014.01.033 .PMID 24662810 .
9. Tahririan MA, Motifard M, TahmasebiMN, Siavashi B (August 2012). "Plantar fasciitis" . J Res Med Sci. 17 (8): 799–804.PMC 3687890 . PMID 23798950
10. Lareau CR, Sawyer GA, Wang JH,DiGiovanni CW (June 2014). "Plantar andMedial Heel Pain: Diagnosis and Management". The Journal of the American Academy of Orthopaedic Surgeons. 22 (6): 372–80. doi:10.5435/JAAOS-22-06-372 .PMID 24860133
11. Brian Mccurdy. Study assesses laser treatment for plantar fasciitis. Journal of foot and ankle surgery. volume 28- issues 10- October 2015. Pages 14-17.
12. Dhia AK Jaddue M.B.Ch.B F.R.C.S (ED) Consultant Orthopedics Surgeon ** Ali. Sulaiman. M. Said Al-dulaimi M.B.Ch.B FICMS (ORTHO) Orthopedics Surgeon. Using of Laser Therapy in the Treatment of Patients With Plantar Fasciitis. Al- Kindy Col Med J 2008; Vol .4 (1): p72-76
13. Benedict f. digiovanni, plantar fascia-specific stretching exercise improves outcomes in patients with chronic plantar fasciitis, the journal of bone & joint surgery • jbjs.org volume 88-a • number 8 • august 2006
14. jan magnus bjordal, P.T., ph.D, "low level laser therapy in acute pain: a systematic review of possible mechanisms of action and clinical effects in randomized placebo – controlled trials". Photo medicine and laser surgery, volume 24, number 2, 2006, pg no:158-168.
15. Thomas G. MCpoil et al. heel pain- plantar fasciitis. Ortho sports phys ther. 2008:38(4): A1-A18.
16. alan "ultrasound treatment may be option for plantar fasciitis", health day, mar 1 2018.
17. Michael, H. slyton, "randomized controlled trail of intense therapeutic ultrasound for the treatment of chronic plantar fasciitis, journal of foot and ankle orthopaedics, oct 6 2016.
18. Hancock, C. l., Baker, R. T., & Sorenson, E. A. (2016).treatment of plantar fascia pain with joint mobilizations and positional release therapy: A case study. International journal of athletic therapy & training, 21(4), 23-29.
19. Aslihan ulusoy MD. Magnetic resonance imaging and clinical outcomes of laser therapy, ultrasound therapy, and extracorporeal shockwave therapy for treatment of plantar fasciitis: a randomized controlled trail. Volume 56, issues 4, july-august 2017, pages 762-767.
20. Cinar E, saxena S, uygur F. low level laser therapy in the management of plantar fasciitis: A randomized controlled trail. 2017 Dec 23. doi: 10.1007/s10103-017-2423-3.
21. jothi prasana K, A comparison of effect of low level laser therapy versus ultrasound therapy in patients with chronic plantar fasciitis, international journal of clinical science, (2018).

22. Samoilova KA, Zhevago NA, Petrishchev NN, et al. Role of nitric oxide in the visible light-induced rapid increase of human skin microcirculation at the local and systemic levels: II. Health volunteers. *Photomed. Laser surg* 26(5), 443-449(2008)
23. John Low and Ann Reed "electrotherapy explained principles and practice" 3rd edition 14th chapter, laser therapy pg no:356-375.
24. Jagmohan Singh, Ph.D "textbook of electrotherapy" 2nd edition pg no:226-236.
25. Joseph Khan "principles and practice of electrotherapy" 4th edition, 4th chapter, ultrasound pg no :49-68
26. John Low and Ann Reed "electrotherapy explained principles and practice" 2nd edition 6th chapter, therapeutic ultrasound, pg no:148-178.
27. Markus Vinicius Grecco, "1 year treatment follow up of plantar fasciitis: radial shockwaves vs. conventional physiotherapy", *Clinics*, 2013. pg no:1089-1095.
28. Paul Higgins "common clinical treatment of plantar fasciitis. A survey of physical therapists practising in the north east region", 2012.

Effect of Expiratory Training and Inspiratory Training with Lumbar Stabilization in Low Back Pain: A Randomized Controlled Trial

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Abstract

Background: Low back is the leading cause of work absence and activity limitation. It is often associated with faulty posture. Postural muscles have role in both postural control and respiration. Thus it is important to address breathing in treatment of low back pain.

Objective: The concept of breathing in low back pain is rarely translated into clinical practice. Thus, the present study will attempt to explore the evidence related to breathing and low back pain. On comparing the effect of expiratory training and inspiratory training with lumbar stabilization, the study will enlighten us whether expiratory or inspiratory training is more beneficial.

Method: The study is an RCT which included 36 subjects of the age group 20-50 years, assigned into three groups: group A (inspiratory training with lumbar stabilization), group B (expiratory training with lumbar stabilization) and group C (lumbar stabilization exercise). The intervention was performed every day in a week for 3 weeks. The outcome measures, VAS, Oswestry disability index (ODI), and stabilizer pressure biofeedback were measured at baseline and 3 weeks after the intervention.

Results: On comparing the outcome measures pre and post, all the three groups demonstrated clinically significant results, while group A produced statistically significant result in improving pain measured on VAS.

Conclusion: The study provides an affirmation for the effect of breathing in low back pain. The effectiveness of the interventions can be translated into clinical practice for the treatment of chronic mechanical low back pain.

Keywords: *Inspiratory training, expiratory training, lumbar stabilization.*

Introduction

Low back pain is one among the most pervasive medical problems, with a global point prevalence of

9.4%. GBD (global burden of disease) 2010 reported it to be first with reference to disability and sixth in overall burden. ¹ In Indian population, low back pain prevalence ranges from 6.2% to 92%.² Thus, it has been documented to be the most prevalent health dilemma affecting the day-to-day life and a major cause of absenteeism among employers all over the world which brings in extensive economic distress.

Low back pain is defined as pain that occurs between the 12th rib and gluteal fold.³ Low back pain can be acute (less than 4 weeks), sub-acute (4-12 weeks), and chronic (greater than 12 weeks).⁴ Chronic low back pain

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has been described to be the reason for sick leave and it has a slow and uncertain recovery rate.⁵ About 97% of the cases of back pain that arise from the spine structures like bone, discs, joints, ligaments, meninges, and nerves constitute mechanical low back pain.⁶

Core stability or trunk stability has been defined in terms of a coactivation of global and local muscles.⁷ According to Punjabi's hypothesis, spinal instability was defined as "a significant decrease in the capacity of the stabilizing system of the spine to maintain the intervertebral neutral zones within the physiological limits so that there is no neurological dysfunction, no major deformity, and no incapacitating pain". The stabilizing system of the spine comprises passive sub system (ligamentous system), active sub system comprising the muscles and tendons, and the neuronal control subsystem. This stabilization system has to work together in harmony so as to fulfil the stability needs of the spine. Lumbar stabilization exercise mainly focus on training the local muscle system (transversus abdominis and lumbar multifidus).⁸

Postural stabilizer muscles are found to do postural control and respiratory function, example transversus abdominis, diaphragm, and the muscles comprising the pelvic floor. These muscles have to function efficiently so as to maintain optimal posture and optimal respiration. Low back pain has been found to be associated with sub optimal respiration and sub optimal faulty posture. Also, diaphragm has an anatomic connection to the lumbar spine. Thus, it is important to address inspiratory muscle training while treating low back pain. Inspiratory muscle training has been found to enhance the lumbar proprioceptive signals which improves trunk stabilizing function of diaphragm.⁹

Maintenance of optimal zone of apposition (ZOA) of the diaphragm is one of the major concerns in both respiratory and postural demands. A smaller zone of apposition reduces the trans-diaphragmatic pressure. Also sub optimal ZOA diminish transversus abdominis muscle activity, which is a major respiratory and lumbar stabilizer muscle. Evidence suggests that expiratory training is more capable of improving the zone of apposition of the diaphragm.³

As this concept is rarely translated into clinical practice, the present study will attempt to explore the evidence related to breathing and low back pain. If the intervention is proved to be effective, it can be

implemented as a preventive measure in low back pain. As there is dearth of literature proving effectiveness of respiratory training in chronic mechanical low back pain, this study would enlighten us whether expiratory or inspiratory training is more beneficial.

Methodology

Study Design: The study is a randomized controlled trial conducted from May 2018 to April 2018 in the department of physiotherapy, in a tertiary hospital in Mangalore, India. After obtaining ethical clearance from the institutional ethics committee, participants with mechanical low back pain diagnosed by an orthopaedician were recruited. 36 subjects of the age group of 20-50 years, with the duration of symptoms for more than 12 weeks and VAS <5 were randomly allocated by block randomization with opaque sealed envelope into three groups: Group A (inspiratory training with lumbar stabilization exercise group), group B (expiratory training with lumbar stabilization exercise group) and group C (control group with lumbar stabilization exercise) with 12 in each group. Outcome measures, VAS scale, Oswestry disability index and stabilizer pressure biofeedback to assess pain, disability and core strength respectively were measured at the baseline and 3 weeks after the intervention by an assessor blinded to the intervention. Patients with any respiratory and cardiovascular pathology, with mental disorder, acute low back pain, tumour, fracture, radiating low back pain were excluded.

Procedure: Treatment was given for 3 weeks out of which, subjects did the intervention under the supervision of the therapist in the first week and it continued as a home for the subsequent 2 weeks, when telephone follow up was given. All the three groups received moist heat application for 10 minutes. Group A received inspiratory training (for 5 minutes) with lumbar stabilization exercise (for 25 minutes), group B received expiratory training (5 minutes) with lumbar stabilization (25 minutes) and group C received lumbar stabilization exercise (for 25 minutes) alone.

Group A (Inspiratory training with lumbar stabilization exercise): The participants of this group were given inspiratory training using respirometer along with lumbar stabilization exercise.

Inspiratory Training Using Respirometer: The patients were asked to hold the respirometer in an upright position, exhale normally and then place the lips tightly

around the mouth piece and was instructed to slowly inhale to raise the ball in the chamber to the set target.

- **Frequency** : 15 breaths per minute
- **Repetitions** : 3 sets
- **Rest period** : 1minute after each set
- **Treatment time**: 5 minutes

Group B (Expiratory training with lumbar stabilization exercise)

Expiratory Training Using Balloon And Ball:

Subjects has to lie in supine position facing the wall, placing the feet on the wall such that hip and knee are bend at an angle of 90 degree. A squeeze ball was kept between the knees and was instructed to press to engage inner thigh muscles. A balloon had been given in one hand and the other hand has to be raised above head. Now, the patient has to push down the heel of the foot so that the muscles of the back of thigh get engaged. This position had to be maintained throughout the exercise. Then the patient is instructed to keep balloon in the mouth and to inspire through nose and slowly exhale by blowing off into the balloon. Pause for almost 3 seconds with the tongue in resting position to prevent air outflow from balloon. Without pinching neck of balloon the subject has to inhale through the nose. Subjects were instructed to blow out slowly into the balloon so as to avoid any strain to the neck and cheeks.

- **Frequency** : 15 breaths per minute
- **hold time** : 2-3 seconds
- **Repetitions** : 3 sets
- **Rest period** : 1minute after each set
- **Treatment time**: 5 minutes

Group C (Lumbar stabilization exercise)

Lumbar stabilization exercise: It includes

Abdominal hollowing is performed in prone.

Abdominal hollowing in supine.

Abdominal hollowing in quadripod.

Bridging

- **Hold time**: 10seconds
- **Repetitions**: 3 sets of 10 repetitions each
- **Rest time**: 1minute after each set
- **Treatment time** : 25 minutes
- **Normal breathing**: 5 minutes

Statistical Analysis: The obtained data was evaluated using IBM SPSS software version 20.0. “One Way ANOVA with Post Hoc Tukey Test” was used for comparing the pre and post values of VAS, ODI and Stabilizer pressure biofeedback between the three groups. “Paired t- Test was used for within group analysis. The p-value assumed less than 0.005 was considered significant for the study.

Results

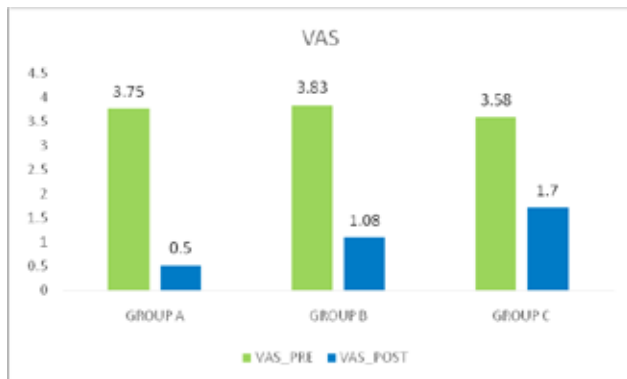
In the age distribution between the three groups, the mean age was 26 and a standard deviation of 8.728. The p value produced is 0.725, suggesting age is homogeneously distributed. While, gender is also homogeneously distributed with a p value of 0.430.

Even though all the three interventions were effective, analysing the pre post values of VAS, ODI and stabilizer pressure biofeedback between the three groups using One Way ANOVA and Posthoc Tukey test, GROUP A (Inspiratory training with lumbar stabilization exercise group) produced better results in reducing pain measured on VAS scale compared to all the other groups (Table 1). Posthoc comparison of VAS post between group A and C, produced a mean difference of 1.200 and a statistically significant p value of 0.0037. While, Posthoc comparison of VAS difference between group A and C, produced a mean difference of 1.450 with a statistically significant p value of 0.005.

Pre post comparison of outcome measures within the group using paired t test produced statistically significant mean difference in all the outcome measures with a p value of <0.001 (Graph 1, 2, and 3).

Table 1: Comparison of the outcome measures using post hoc tukey test

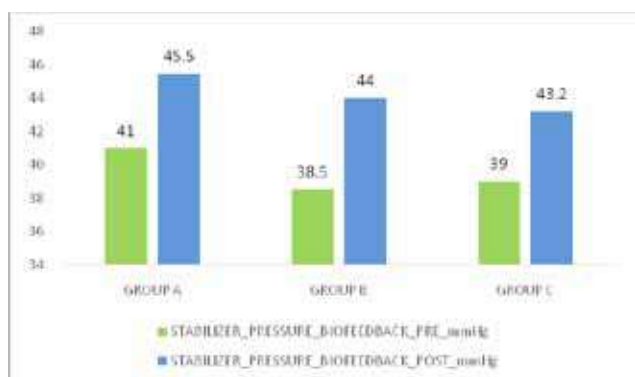
Dependent Variable	(I) group	(J) group	Mean Difference (I-J)	Std. Error	P VALUE
VAS_PRE	GROUP A	GROUP B	-0.083	0.186	0.895
		GROUP C	0.167	0.186	0.646
	GROUP B	GROUP C	0.25	0.186	0.381
VAS_POST	GROUP A	GROUP B	-0.583	0.44	0.392
		GROUP C	-1.200*	0.462	<u>0.037</u>
	GROUP B	GROUP C	-0.617	0.462	0.386
VAS DIFFERENCE	GROUP A	GROUP B	0.5	0.402	0.438
		GROUP C	1.450*	0.422	<u>0.005</u>
	GROUP B	GROUP C	0.95	0.422	0.078
ODI_PERCENTAGE_PRE	GROUP A	GROUP B	-3.18083	3.520943	0.642
		GROUP C	-6.5025	3.520943	0.17
	GROUP B	GROUP C	-3.32167	3.520943	0.617
ODI_PERCENTAGE_POST	GROUP A	GROUP B	-2.31583	2.533396	0.636
		GROUP C	-5.59933	2.657048	0.105
	GROUP B	GROUP C	-3.2835	2.657048	0.442
ODI PERCENTAGE DIFFERENCE	GROUP A	GROUP B	-0.865	2.442275	0.933
		GROUP C	0.4995	2.561479	0.979
	GROUP B	GROUP C	1.3645	2.561479	0.856
STABILIZER_PRESSURE_ BIOFEEDBACK_PRE_mmHg	GROUP A	GROUP B	2.5	1.273	0.137
		GROUP C	2	1.273	0.272
	GROUP B	GROUP C	-0.5	1.273	0.919
STABILIZER_PRESSURE_ BIOFEEDBACK_POST_mmHg	GROUP A	GROUP B	1.5	1.751	0.671
		GROUP C	2.3	1.837	0.432
	GROUP B	GROUP C	0.8	1.837	0.901
STABILIZER_PRESSURE_ BIOFEEDBACK_DIFFERENCE_ mmHg	GROUP A	GROUP B	-1	0.988	0.575
		GROUP C	0.7	1.036	0.779
	GROUP B	GROUP C	1.7	1.036	0.244



Graph 1: Pre post comparison of VAS using Paired T-Test



Graph 2: Pre post comparison of ODI using Paired T-Test



Graph 3: Pre post comparison of Stabilizer pressure biofeedback using Paired T- Test

ILLUSTRATIONS:



Figure 1: Providing expiratory training in 90-90 bridge with balloon and ball



Figure 2: Providing inspiratory training with respirometer

Discussion

The association of breathing and low back pain has been studied extensively. Diaphragm functions for respiration as well as stabilization of the spine. Evidence suggests that the coordinated function of breathing and spinal stabilization by core muscles is altered in low back pain.

Results of the study proved the effectiveness of the interventions by demonstrating statistically significant improvement in reducing pain, disability and enhancing core strength on analysing within each group

Expiratory training with ball and balloon in 90-90 bridge position demonstrated optimum ZOA (zone of apposition) of the diaphragm. This optimizes the intra-abdominal pressure essential for adequate spinal stiffness providing optimal spinal stability. As, low back pain is often associated with excessive lumbar lordosis, ideal ZOA also corrects this faulty posture. According to Boyle et al (2010) blowing out using a balloon enhances abdominal muscle activation, which is capable of opposing the diaphragm, further improving the ZOA of the diaphragm. Abdominal activation pulls the ribs inward hence relaxing the paraspinal muscles, which consequently diminish lumbar lordosis and back pain.³

Inspiratory muscle training enhance trunk stabilizing function of the diaphragm. Janssens et al (2013) had proposed that low back pain is associated with diaphragm fatigue.¹⁰ With inspiratory muscle training, diaphragm efficiency can be improved, which enhances the respiratory as well as trunk stabilizing function of the diaphragm.⁹ Pain gate theory (Mendell L M 2014) and enhancement in trunk proprioception following inspiratory muscle training (Janssens et al 2014) explains mechanism of statistically significant reduction in pain following inspiratory training.^{9, 12} According to Borghi Silvia et al (2008), by inspiratory muscle training, efficiency of diaphragm function is enhanced which improves oxygenation to the peripheral muscles along with the muscles surrounding the lumbar spine. Enhanced blood flow to the lumbar muscle spindle improves the proprioception which was previously overwhelmed by nociceptive input.^{11, 13} Hodges et al (2005) have proposed that, diaphragm training enhances intra abdominal pressure needed for optimum spinal stability.⁹ Thus, inspiratory muscle training enhances stability of the spine as well as reduces low back pain.

Lumbar stabilization exercise programme focuses mainly to achieve neutral zone, which is the part of normal physiological intervertebral motion. According to Punjabi(1992), this requires coordinates activation of the passive system (ligamentous system) and active systems (muscles and tendons) and neuronal control system. Ligaments provide passive support, muscles give active support, neural system receives information about the position and direction of movement and helps the muscles to contract and maintain stability by increasing the stiffness and reducing the size of neutral zone. This improves movement accuracy. Stabilization exercise program therefore focuses to improve movement accuracy thereby reducing low back pain.⁸

Conclusion

On completion of the study, it has been revealed that inspiratory training, expiratory training and lumbar stabilization exercises are effective in chronic mechanical low back pain. Whereas, inspiratory training proved to be superior in terms of improving pain. Limitations of the study included small sample size, no long term follow up. In future, the study could be done in radiating low back pain with long term follow and pulmonary function test can be checked to correlate breathing and low back pain

Conflict of Interest: The authors had declared that there is no conflict of interest

Source of Funding: Self

Ethical Clearence: The study has been approved by the institutional ethics committee

References

1. Hoy D, March L, Brooks P, Blyth F, Woolf A, Bain C, et al. The global burden of low back pain: estimates from the Global Burden of Disease 2010 study. *Ann Rheum Dis.* 2014;73(6):968-974.
2. Bindra S, Sinha AG, Benjamin AI. Epidemiology of low back pain in Indian population: A review. *International journal of basic and applied medical sciences.* 2015;5(1):166-79.
3. Boyle L K, Olinik J, Lewis C. The value of blowing up a balloon. *N Am J Sports Phys Ther.* Sep 2010;5(3):179-188.
4. Cooper G. Lower Back Pain: An Overview of the Most Common Causes. *Non-Operative Treatment of the Lumbar Spine.* 2015.
5. Leo AS, Irani A, Sharma S, Borade NG. Forced Expiratory Volume in the first second [FEV1] in patients with chronic low back pain. *Journal of Research in Medical and Dental Science.* 2017;5(1):27-32.
6. Chien JJ, Bajwa ZH. What is mechanical back pain and how best to treat it?. *Current pain and headache reports.* 2008;12(6):406-11.
7. Imai A, Kaneoka K, Okubo Y, Shiina I, Tatsumura M, Izumi S et al. Trunk Muscle Activity During Lumbar Stabilization Exercises on Both a Stable and Unstable Surface. *J Orthop Sports Phys Ther.* 2010;40(6):369-375.
8. A Luque-Suarez, E. Diaz-Mohedo, I. Medina-Porqueres, Ponce-Garcia. Stabilization exercise for the management of Low Back Pain, Low Back Pain. *InTech.* 2012.
9. Janssens L, McConnell AK, Pijnenburg M, Claeys K, Goossens N, Lysens R, et al. Inspiratory Muscle Training Affects Proprioceptive Use and Low Back Pain. *Med. Sci Sports Exerc.* 2015;47(1):12-19.
10. Janssens L, Brumagne S, McConnell AK, Hermans G, Troosters T, Gayan-Ramirez G. Greater diaphragm fatigability in patients with recurrent low back pain. *Respir Physiol Neurobiol.* 2013;188(2):119-23.
11. Janssens L, Pijnenburg M, Claeys K, McConnell AK, Troosters T, Brumagne S. Postural strategy and back muscle oxygenation during inspiratory muscle loading. *Med Sci Sport Exerc.* 2013;45(7):1355-62.
12. Borghi-Silva A, Oliveira CC, Carrascosa C, et al. Respiratory muscle unloading improves leg muscle oxygenation during exercise in patients with COPD. *Thorax.* 2008;63(10):910-5.
13. Mehling WE, Hamel KA, Acree M, Byl N, Hecht FM. Randomized, controlled trial of breath therapy for patients with chronic low-back pain. *Altern Ther Health Med.* 2005;11(4):44-52.

Influence of Self-Efficacy on Student Engagement of Senior Secondary School Students

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Abstract

Context: The present study examined to investigate the influence of self-efficacy on student engagement of Senior Secondary School students. The respondents were students from senior secondary school of Jammu and Kashmir. A Sample of 400 senior Secondary School Students (200 boys and 200 girls) were selected from Jammu and Kashmir by employing simple random sampling. T-test, correlations and regression were employed to analyze the data. The study indicated that (a) there exists significant difference between senior Secondary School boys and girls with their self-efficacy (b) there exists Significant Difference Between Private and Government senior Secondary school Students with their self-efficacy (c) there exists Significant Difference Between senior Secondary School Boys And Girls with their student engagement (d) there exists significant difference between private and government senior Secondary school Students with their student engagement. It revealed that significant relationship was found between self-efficacy and student engagement of senior secondary school students. It also found the self-efficacy had significant influence on student engagement of senior Secondary School Students.

Keywords: *Self-efficacy, Student Engagement, Senior Secondary School students.*

Introduction

Self-efficacy refers to a man's conviction that they can proficiently completed at an allocated levels in a specific academic part of information. A man's trust in their ability to make, executes, and guides execution with the ultimate objective to deal with an issue or accomplish an endeavor at an appointed level of capacity and aptitude. Students who are sure about their capacity to execute, to sort out and manage with their basic reasoning or activity execution at an allocated levels of fitness is showing high self-efficacy. Self-efficacy is by and large viewed as a multidimensional develops separated over different spaces of working. Self-efficacy

is grounded in principle by¹. As per Self-Efficacy assumption, Self-Efficacy is a "person's trust in their capacity to compose and execute a given strategy to take care of an issue or achieve an assignment". As indicated by² self- efficacy alludes to people's feelings that they can effectively perform given errands at assigned levels. Self- efficacy is the conviction about person's assessed capacity to play out a given task. Self- Efficacy contains convictions individuals have about their capacity to achieve specific results.³ It is noticed that self-efficacy is the certainty a man has in realizing a particular result. Self-efficacy as persons' confidence about their abilities to make appointed levels of execution that actions affect over events that impact their lives. As shown by him, it chooses how people feel, think, and conscious themselves and carry on.⁴ Self- efficacy suggested proposes that Academic Self- efficacy can change in quality as a component of undertaking trouble. Two general classes of academic hope convictions have been assumed. Understanding the distinction between these two types of hope convictions is very important

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as people can trust that a specific conduct will deliver a specific (result desire), yet may not trust they can play out that conduct (efficacy desire)". Found that there exists a positive correlation between Mental Health of senior secondary school Boys and girls with their Life Skills and Self-Efficacy.⁵ results found that significant relationship was found between academic performance of senior secondary school students with their self-efficacy and social support.⁶

Student Engagement: The idea of student engagement has progressively increased the consideration throughout the most recent decade. It comprehensively alludes to Students' Engagement in actions that gave up to their knowledge accomplishments and their sense of belongings with their educational network. It additionally included actions other than those straightforwardly identified with course work, for example, non necessary companion learning exercises and administration exercises, for example, positions of authority in student tutoring or study group assistance. Found that there exists significant correlation among social support and student engagement of Secondary School Students.⁷ Also, engagement is how much students are engage in their learning actions and their commitment is emphatically connected to a large group of preferred results, include student satisfaction and determinations. This definition infers the utilization of three interrelated criteria to evaluate Student engagement levels namely:

Emotional Engagement: refers to the connections among students and their teachers, schoolmates and school. This has likewise been called 'recognizable proof' with school and learning rehearses. Students are engaged in when they feel incorporated into the school and feel a passionate security with the school, its teachers and their companions.

Cognitive Engagement: It can be understand as a student's psychological importance in their own knowledge. At the point when a student is cognitively engage in, student believe, spotlight on accomplishing objectives, are stretchy in their endeavor and familiarize you to dissatisfaction. This is unique in relation to high achievement a student who is performing great may at present be disengaged whether they are wandering and not inspired to endeavor themselves more than is vital to obtain by.

Behavioral Engagement: refers to students'

involvement in classroom activities and in learning. This includes holding fast to behavior rules, leaving to exercises as necessary and reaching at classes on time. Essentially, Behavioral Engagement refers to the educational performances that are critical for high students' implementation, which may include cooperation and communication with companions. Moreover, it covers students' investment in various elements of school life, e.g., school community activity and extracurricular actions.

The present study is intended to find out how Student Engagement is related to Self-efficacy. Movements like universlization of elementary education as a fundamental right have improved the quality and quantity of school education in India. Kashmir, being a role model, has better education system as compared to other states. Self-efficacy has a significant task in influencing students' academic Success and Student engagement. Many teachers complain that student's are giving less important to their academic activities, because they were not able to cope up effectively with academic success. Improved Self-efficacy may help to increases Student engagement. In this study investigators try to find out whether Self-efficacy had any significant influence on Student engagement.

Objectives:

1. To compare the difference of self-efficacy of senior secondary school students on the based on gender.
2. To compare the difference of student engagement of senior secondary school students on based on gender.
3. To find out the relationship between self-efficacy and student engagement of senior secondary school students.
4. To find out the influence of self-efficacy on student engagement of senior secondary school students.

Hypotheses:

1. There exists no significant difference of self-efficacy of senior secondary school students on the basis of Gender.
2. There exists no significant difference of Student engagement of senior secondary school students on the basis of Gender.
3. There exists no significant relationship between Self-efficacy and Student engagement of senior

secondary school students.

- There exists no significant influence of self-efficacy on Student engagement of senior Secondary School Students.

Methodology: Descriptive Survey Method was used. Data was collected from Senior Secondary School students of Jammu & Kashmir, by employing simple Random Sampling technique. The sample consists of 400 senior secondary school Students.

Instruments:

1. Self-Efficacy Scale: this scale was developed by Bhatnagar and Mathure. Self-Efficacy is the confidence that one can successfully complete in a given circumstance. Self-Efficacy Scale plans to study the dimension of self-efficacy in any age group over 14 years. It comprises of 22 items, managing eight factors. Reliability co-efficient of the scale was estimated by test-retest and found 0.79 to 0.86.

2. Student Engagement Scale: This scale was developed by Dogan (2014) and was adopted in Indian context. The scale is a 5-point Likert Scale consisting of 22 items and 3 sub-dimensions (cognitive, emotional, and behavioral engagement). The final set of statements was checked for internal consistency using SPSS-22 version. The Cronbach’s alpha for the final set of statements was found out to be .765

Procedure: Initially the investigators randomly identified various secondary schools and contacted the authorities of the secondary school personally. The purpose, objectives and relevance of the study were explained to the head of the institution. Then, the tools were directed to the participant after giving necessary instructions to them. Reassurance was given to each that the information collected from them would be used only for research identity and purpose would not to be disclosed. The scoring was done as per the manual and entered the data in to a spread sheet for further Statistical Analysis by using t-test, correlation and Regression to analyze the data.

Results and Discussions

Table 1: There exists no significant difference of self-efficacy of senior secondary school students on the basis of Gender.

	Gender	N	Mean	S.D	t- value	Levels of significance
Self-efficacy	Boys	200	88.03	4.40	6.33	Significant
	Girls	200	84.91	4.96		

According to the above table reflects that the mean scores of boys and girls of senior secondary school students is 88.03 and 84.91 respectively. The S.D for boys and girls Senior Secondary School Students is 4.40 and 4.96 respectively. Further, the t-value is 6.33 which is significant at 0.05 level. So, that there exist significant difference between Senior Secondary school girls and boys in their self-efficacy.

Further it is evident from the table that mean score

(88.03) of boys’ Senior Secondary School Students was greater than (84.91) of girls Senior Secondary School Students. So, it can be interpreted that boys’ Senior Secondary School Students had higher self-efficacy than girls’ senior secondary school students.

According to the above results, it confirmed that the hypothesis no. 1, “there exists no significant difference of Self-efficacy of Senior Secondary School Students on the basis of gender” is thus rejected.

Table 2: There exists no significant difference of Student engagement of senior secondary school students on the basis of Gender.

	Gender	N	Mean	S.D	t-value	Levels of significance
Student engagement	Boys	200	90.98	4.18	7.51	Significant
	Girls	200	88.06	3.49		

According to the above table reflects that the mean scores girls and boys of Senior Secondary School Students are 90.98 and 88.06 respectively. The S.D for girls and boys Senior Secondary School Students is 4.18 and 3.49 respectively. Further, the t-value is 7.51 which are significant at 0.05 levels.. So, that there exist Significant Difference Between Senior Secondary School Girls and Boys in their Student engagement.

Further it is obvious from the table that Mean score (90.98) of Boys Senior Secondary School Students

was greater than (88.06) of Girls Senior Secondary School Students. So, it can be interpreted that Boys Senior Secondary School Students had higher Student engagement than Girls Senior Secondary School Students.

According to the above results, it can be confirmed that hypotheses no 2 i.e. “there exists no significant difference of Student engagement of Senior Secondary School Students on the basis of gender” is thus rejected.

Table 3: there exists no significant relationship between self-efficacy and student engagement.

		Student engagement	Self-efficacy
Student engagement	Pearson’s Correlation	1	.316**
	(sig.2 tailed)		.000
	N	400	400
Self-efficacy	Pearson’s Correlation	.316**	1
	(sig. 2 tailed)	.000	
	N	400	400

**correlation is significant at 0.01 levels of significance (2-tailed).

According to the above table it can be seen that Self-efficacy significantly correlated with Student engagement. It is observed that there exists a significant relationship between Self-efficacy and Student engagement of Senior Secondary School Students. From the above table it reflects that coefficient of correlation between Self-efficacy and Student engagement of senior secondary school students is .316 that is significant at 0.01 level of significance. This indicated that there exists a significant relationship between Self-efficacy and Student engagement of Senior Secondary School Students. It also shows that Self-efficacy had significant Influence on Student engagement of Senior Secondary School Students.

Therefore hypothesis 3, namely “there exists no significant relationship between Self-efficacy and Student engagement” stands rejected.

Thus self-efficacy increased student engagement. Self-efficacy plays an essential position in determining student engagement. Students’ who have possessed high self-efficacy are very much more engaged in their studies. It is same as in the case that Student engagement

and that those who have high self-efficacy show more Cognitive, Behavioral and Emotional engagement. Manikandan and Neethu(2018) supported our study and found that Student engagement is significantly related to academic Stress and Self-efficacy.

There exists No Significant Influence of Self-Efficacy on Student Engagement.

Table 4: Model Summary for Regression Analysis

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.316*	.100	.098	3.899

According to above table shows the correlation coefficient of Self-efficacy and Student engagement of adolescents. The coefficient of correlation is .316* and its square is 0.100 Regression suggests that predictive variables i.e. Self-efficacy can explain 1.0% variance of the criterion variable (Student engagement).

In Order to study the influence of self-efficacy on student engagement ANOVA has been applied on the influence of self-efficacy on student engagement.

Table 5: Summary Of Anova By Regression

Model	Sum of square	df	Mean of square	F	Sig
Regression	673.494	1	673.494	44.304	.000*
Residual	6050.203	398	15.202		
Total	6723.698	399			

According to the above table shows that the results of ANOVA of self-efficacy on student engagement. It is clear that acquired F-value is (44.304) which are statistically significant at 0.01 level of significance which

shows the statistically significant Relationship Between self-efficacy and Student engagement. The predictive variable (Self-efficacy) can influence the criterion variable (Student engagement). The above findings revealed that Self-efficacy has significant influence on Student engagement. So there exists significant influence of Self-efficacy on Student engagement. Therefore, regression analysis is allowed and feasible.

Therefore hypothesis 4, namely “there exists be no significant influence of Self-efficacy on Student engagement” stands rejected.

Table 6: Summary of Coefficient Of Regression

Model	Unstandardized Coefficient		Standardizes Coefficient	t	Sig.		
	B	Std. Error	Beta				
(Constant) elf-efficacy	66.734	.263	3.422	.040	.316	19.503**	.000
						6.656*	.000

According the above table with B=.263 and t=6.656 which is significant at 0.05 level of significance. It implies that Self-efficacy plays an important role in predicting Student engagement. So, it can be revealed that Self-efficacy had significant Influence on Student engagement. The regression equation for predicting student engagement by the predictor variable i.e. Self-efficacy. Therefore, the regression equation formulated from these two variables is given below:

$$\text{Student engagement} = 66.734 + .263 \times \text{Self-efficacy}$$

Conclusions

The study presented the following conclusions:

- Based on the result analysis it found that there exist significant difference between senior secondary school Boys’ and Girls’ in their self-efficacy. Boys of senior secondary school students had higher self-efficacy than girls of Senior Secondary School Students.
- There exist significant Difference Between Private and Government senior secondary school students in their Self-efficacy. Government Senior Secondary School Students had higher Self-efficacy than Private senior secondary school Students.
- There exists Significant Difference Between Senior secondary school Girls and Boys in their Student

engagement. Boys had higher Student engagement than Girls.

- There exists significant difference between in Student engagement among Senior secondary school students on the basis of Type of School. Government Senior Secondary School Students had higher than Private Senior Secondary School Students.
- Self-efficacy had significant Influence on Student engagement. There exists significant influence of Self-efficacy on student engagement.
- There exists a Significant relationship between self-efficacy and Student engagement of Senior secondary school students. It also shows that Self-efficacy had significant Influence on Student engagement of Senior Secondary School Students.

Implications of the Study: The findings revealed that self-efficacy is significantly correlated with Student engagement; this also has some suggestion. Since self-Efficacy alludes to an individuals’ opinion of their capability to arrange and achieve the plan of activity essential to bring about prearranged sorts of engagement and worried about the estimation of what one can achieve with the aptitudes one presently achieves. It suggests that students who are Self-efficacious will in general produce and test elective strategies of activities when they don’t at first make progress. This implies that

students ought to be positive to create, have or develop efficacy disposition. This is essential in light of the fact that it could fill up in as a defense that may support the students up regardless of their experience to be engaged. If students are given tasks that are challenging but not too difficult and they experience success upon completion of these tasks that Self-efficacy to learn may increase. As Self-efficacy to learn increases, so will interest, value, and utility. A strategy such as this one would be very useful for teachers to implement. Teachers can organize and design their instructions to have a constructive result on students' self-efficacy to learn which would lead to improved Student engagement and improved learning.

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References

1. Bandura A. Self-efficacy: toward a unifying theory of behavioural change. *Psychological review*. 1977 Mar; 84(2):191.

2. Schunk DH. Self-efficacy and academic motivation. *Educational psychologist*. 1991 Jun 1;26(3-4):-207-31.
3. Pajares F, Britner SL, Valiante G. Relation between achievement goals and self-beliefs of middle school students in writing and science. *Contemporary educational psychology*. 2000 Oct 1;25(4):406-22.
4. Eccles JS, Wigfield A. Motivational beliefs, values, and goals. *Annual review of psychology*. 2002 Feb;53(1):109-32.
5. Bashir, L, Abdullah, B. Mental health among senior secondary school students in relation to life skills and self-efficacy. *RESEARCH REVIEW International Journal of Multidisciplinary*, 2018 Sep 3(9).
6. Abdullah, B. & Singh, K. Academic Performance of Senior Secondary School Students In Relation to their Self-Efficacy and Social Support. *American International Journal of Research in Humanities, Arts and Social Sciences*. 2019 April; 26(1): 09-12.
7. Abdullah, B. & Singh, K. Social Support as Predictor of Student Engagement among Secondary School Students. *International Journal of Innovative Technology and Exploring Engineering*. 2019 May; 8(7).

Ruptured Bicornuate Uterus Mimicking Ectopic Pregnancy: A Case Report

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Abstract

Introduction: Congenital malformations of uterus occur due to abnormal formation, fusion or resorption of mullerian ducts during fetal life. A normal uterus is formed by fusion of two mullerian ducts which starts at 10th week and uterine development is completed by 20th week. If the two mullerian ducts fail to fuse it results in separate uterine horns also known as Bicornuate uterus.

Presentation of Case: We are presenting a case of 24 year old primigravida presented to us at 15th weeks of gestation who was having amenorrhoea for 3 months and 26 days along with gaseous distention of abdomen and lower abdomen pain for 6-7 days. She again underwent an abdominal ultrasonography at a different centre and it was suggestive of ?abdominal pregnancy. She underwent an abdominal ultrasonography again after 2 weeks of this where she was diagnosed as abdominal pregnancy with minimal as cites. To take further advice she presented to us the next day with both the reports. An assessment of ectopic pregnancy was made, she was counselled and consent for lapratomy was taken. At surgery a gravid bicornuate uterus with pregnancy in left cornua was found. Tubes and ovaries were normal. The conceptus ruptured the left uterine wall and the omentum was found adhered to the uterus. Omentum was ligated. The ruptured left horn was removed at its junction to right horn. Product of conceptus was taken out, pelvis was drained of blood and uterus and abdomen were closed in layers after achieving complete hemostasis.

Discussion: Our patient had ultrasonographic diagnosis of abdominal pregnancy at 15th week so an emergency laparotomy was done to save patients life. On laparotomy bicornuate uterus with ruptured pregnancy in left horn was found. Blood, fluid replacement therapy and exploratory laparotomy followed by repair of uterus and drainage of pelvic blood was necessary to save patients life.

Conclusion: This case highlights the fact that a bicornuate uterine pregnancy can mimic an ectopic pregnancy and the two should be differentiated.

Keywords: *Bicornuate uterus, Ectopic pregnancy.*

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Introduction

Congenital uterine malformations result from abnormal formation, fusion or resorption of mullerian ducts during fetal life^[1]. Columbo et al was the first person to report and describe a case of vaginal a genesis in 16th century^[2]. Development of genital tract begins as mullerian ducts also known as paramesonephric

ducts, forms lateral to each mesonephros. These ducts grow downwards and join in midline. Uterus is formed by fusion of these two ducts by 10th week. After that, cellular proliferation at the upper portion forms the pyriform shape of uterus. At the same time desolution of cells at lower pole forms the uterine cavity. Uterine development is completed by 20th week. If the two mullerian ducts fail to fuse it results in separate uterine horns of varying degree. Bicornuate uterus is a common defect which occurs due to lack of fusion of fundus of two hemi uteri, however there is only one cervix and vagina. This defect can lead to various obstetrical outcome like miscarriage, malpresentation and premature delivery^[3]. The prevalence of congenital uterine malformations ranges from 0.1% to 10%^[4] Diagnostic modalities include hysterosalpingography, magnetic resonance imaging and 3 dimensional ultrasonography. Since bicornuate uterine pregnancy is difficult to diagnose, mimicks ectopic pregnancy and is associated with complications^[5] we report a case of bicornuate uterus with pregnancy in one cornua which mimicked ectopic pregnancy on ultrasonography. Confirmation was done by laparotomy. Pregnancy had ruptured the uterus leading to peritoneal adhesions, so it has to be terminated. The uterine and abdominal walls were closed after achieving complete hemostasis.

Case Report: A 24 years old female presented to us with amenorrhoea for 3 months and 26 days along with gaseous distention of abdomen and lower abdomen pain for 6-7 days. There is no history of bleeding per vaginum or medication intake. Obstetric history was g1 p0a0l0. Her appearance was slightly pale and was comfortable. Height was 162cm and weight was 49 kgs. Pulse rate was 102/min, blood pressure was 106/58 mm of mercury in right arm supine position. Respiratory rate was 18/min. Head to toe examination was within normal limits except slight distension of lower abdomen. Abdomen was soft and tender in left lumbar are and right iliac fossa. Fundal height was of 18 week pregnancy. On per vaginal examination was insignificant hemoglobin was 10 gm/decilitre other blood indices were within normal limits.

Before coming to us she underwent an abdominal ultrasonography at a different centre which revealed a normal pregnancy of 15.1 weeks in lower abdomen and it was suggestive of? abdominal pregnancy. She

underwent an abdominal ultrasonography again after 2 weeks of this where she was diagnosed as abdominal pregnancy with minimal ascites. To take further advice she presented to us the next day with both the reports. An assessment of ectopic pregnancy was made, She was counselled and consent for lapratomy was taken. At surgery (fig 1) a gravid bicornuate uterus with pregnancy in left cornua was found. Tubes and ovaries were normal. The concept us had ruptured the uterine wall through an opening in superior lateral region (left uterine horn) with continuous bleeding from the edges. Omentum was found adhered to the uterus. Omentum was ligated, left horn was removed, product of conceptus was taken out and sent for histopathological examination. Pelvis was drained of blood and uterus and abdomen were closed in layers after achieving complete hemostasis. Two units of packed cells were also transfused. The patient was stable after operation, post-operative period was uneventful and she was discharged in a healthy condition on fourth post-operative day.



Fig. 1: picture showing gravid bicornuate uterus with pregnancy in left cornua



Fig. 2:

Fig. 1 and Fig. 2 showing two horns of the uterus which were seen at the time of laparotomy.

Discussion

Congenital uterine malformations are common and most of the time asymptomatic. Women with uterine abnormalities have poor reproductive outcome and lower pregnancy rates as compared to women with normal uterus. Uterine anomalies are associated with complications like miscarriage, malpresentation and premature delivery and a need for caesarean section^[6]. Our case was a previously unbooked and primi gravid case whose uterine anomaly was found after laparotomy which was done for suspected ectopic pregnancy. The pregnancy led to the rupture of uterus and formation of peritoneal adhesions. Ultimately the pregnancy has to be terminated. Nwosu and co-workers^[7] reported a case of a 28 year old women in which the pregnancy in one horn of bicornuate uterus led to rupture of pregnancy. In this case one horn of uterus was removed and she was able to carry out subsequent pregnancies to term. SqnLdr Amit Suri, Lt Col L Satija^[8] reported two cases in which one the case was of a 27 years old nulliparous woman who underwent artificial insemination, at 6 weeks presented

with bleeding per vaginum, ultrasound showed a healthy gestational sac with a live foetus. Because of recurrent bleeding afterwards ultrasound was done again which revealed two gestational sacs-one in each horn of a previously undetected bicornuate uterus. This case ultimately delivered a healthy baby. While in our case since pregnancy had ruptured the uterus we had to terminate the pregnancy. This case also highlighted the importance of careful ultrasonographical monitoring of pregnancy and bicornuate uterine pregnancy leading to misdiagnosis. LD Aliyu and MK Abdullahi^[9] reported a case of a 26 year old women with an obstetric history of G₆P₅₊₀ (3 alive). Ultrasound showed empty uterus with mass in right adenexa. Laparotomy was done suspecting ectopic pregnancy, bicornuate uterus was revealed with intact pregnancy. Spontaneous abortion occurred shortly after discharge. Since she had previous pregnancies without complications, this case revealed that even with bicornuate uterus successful pregnancy without complications can be attained, however our case had complication even in her first pregnancy. Reddy Ravikanth^[10] reported a case of 32 years old women with repeated complications during pregnancy. During first pregnancy it was IUGR baby, during second it was breech presentation with oligohydramnios with IUGR and in third pregnancy she underwent ultrasound which showed 10 week fetus implanted in left cornua of uterus, this pregnancy was also lost at 14 weeks. This case highlighted the complications of congenital anomalies of uterus as in our case and also that recurrent complications in a pregnancy can be due to malformations of uterus and clinician should think in this direction too.

Although bicornuate uterine pregnancy is not that rare, it draws sufficient interest. however it is not necessary that a women with bicornuate uterus can not have normal pregnancies but such women are at higher risk of developing complications like rupture of uterus, IUGR, Oligohydramnios, Malpresentationetc. Ultrasound in experienced hands is a good tool to diagnose uterine malformations but interpretations are operator dependent. Such pregnancies should be managed with extra care. It is necessary for obstetricians to create a patient awareness regarding this condition and its possible outcomes. It is also necessary to make prenatal diagnosis to provide proper care.

Conclusion

We reported this case as to highlight the fact that if uterine anomaly is present, uterine rupture can occur

in early pregnancy. Obstetricians should be aware of this condition and its life threatening potential. Early sonography should be done but it must not be completely trusted upon as it might mislead the diagnosis of ruptured bicornuate uterus as ectopic pregnancy.

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References

1. Moore KL, Persaud TVN, Torchia MG. The Urogenital System. Before We Are Born: Essential of Embryology and Birth Defects. 7th edn. Philadelphia: Saunders/Elsevier; 2008. pp. 162–189.
2. Steinmetz GP. Formation of artificial vagina. West J Surg. 1940. 48:169-3.
3. Williams Obstetrics 24th Ed. 2014 page 37 and 41
4. Hua M, Odibo AO, Longman RE. Congenital uterine anomalies and adverse pregnancy outcomes. Am J Obstet- Gynaecol. 2011;1(5):205–558.
5. Agrawal R, Agrawal K. Pregnancy in bicornuate uterus mimics “Ectopic”. J Obstet Gynaecol India Vol. 60, No. 5 : September/October 2010 pg 436-437.
6. Green LK, Harris RE. Uterine anomalies; frequency of diagnosis, and obstetric complications. 1976;47(4):427-8.
7. Nwosu B, Ogboaja JO, Obi-Nwosu A. Spontaneous rupture of the gravid horn of bicornuate uterus at term. Nig Med J. 2010;5(4):184–185.
8. SqnLdr Amit Suri, Lt Col L Satija. Bicornuate uterus with bilateral pregnancy presenting as threatened abortion a report on two cases. Med J Armed Forces India. 2000 Jul; 56(3): 233–234.
9. BICORNUATE UTERUS MIMICKING ECTOPIC PREGNANCY - A case report LD Aliyu and MK Abdullahi. J West Afr Coll Surg. 2012 Jan-Mar; 2(1): 84–90.
10. Bicornuate Uterus with Pregnancy. Reddy Ravikanth. Journal of Basic and Clinical Reproductive Sciences • July-December 2017 • Vol 6 • Issue 2:150

Patient Satisfaction in a Dental Hospital with Respect to Clinician Expertise

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Abstract

Aim: To compare the level of patient satisfaction in a dental hospital with respect to clinician expertise.

Objective: To assess the patient satisfaction in a dental hospital and compare the patient satisfaction between those who were treated by undergraduates, fourth year undergraduates and Compulsory Rotational Interns (CRI) based on the clinician's speed of treatment, explanation and caring and cleanliness.

Background: Patient satisfaction is regarded as an important outcome of care and is one of the major factors that contribute to better patient compliance and consequently to improved clinical outcomes. Measuring patient satisfaction allows for evaluation of health systems, particularly comparisons between different models of care delivery.

Rationale: As teaching facilities, dental school clinics must constantly strive to find a balance between meeting the needs of the patient and meeting the needs of the student, all the while knowing that patients and their satisfaction are critical to the education of our students.

Materials and Method: This study was conducted among the patients undergoing treatment in Saveetha Dental Hospital, Chennai. Feedback was collected from 1500 patients of which 500 were treated by third years, 500 were treated by final years and 500 were treated by CRI (Compulsory Rotational Internship) and the satisfaction level of patient was assessed based on the speed of the procedure, explanation of the procedure, empathy and cleanliness on a scale of 0-10 and the average score was compared among third year undergraduates, fourth year undergraduates and CRI. Statistical analysis was done by SPSS software using Anova and Post-Hoc test.

Results: Overall, the satisfaction score of patients treated by interns were higher in all the categories followed by final years and third years. Interns were significantly better than third years and final years in terms of explanation and cleanliness. But, there was no statistically significant difference between 3rd years, fourth years and interns in terms of speed of treatment.

Conclusion: From this study, it can be concluded that as the level of expertise increases the level of patient satisfaction increases.

Keywords: *satisfaction, cleanliness, explanation, caring, speed of treatment.*

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Introduction

Patient satisfaction in dental care is an important aspect of the quality of care that influences the future utilisation of the service. It is regarded as an important

outcome of care and is one of the major factors that contribute to better patient compliance and consequently to improved clinical outcomes. Today, health care is being transformed from a provider centred approach to a patient centred approach in which satisfaction of the patients' needs is part of the definition of quality. A major issue for careful monitoring is recognition of the complex relationship between patients' views of the health care system and their health and illness behaviour.^[1,2] Dentist-patient interactions during a consultation, including cognitive and emotional aspects, have been demonstrated to affect patient compliance with clinical advice and follow-up visit. Patient satisfaction with care is a useful measure that evaluates care, including the quality of care and provider-patient relationships. It has been demonstrated that patient satisfaction is a multidimensional concept. Some dimensions of dental care that have been identified are technical or aspects of care related to the process of diagnosis and treatment; interpersonal; accessibility/availability; financial access; efficacy/outcomes; continuity of care; facilities; and general or attitudes about overall care.^[3,4] Patient satisfaction measures the process of care, broadly defined as the professional activities associated with providing care which allows for evaluation of health systems, particularly comparisons between different models of care delivery.^[5, 6]

The most important aspects considered with regards to dental treatment in this study is explanation about the procedure which involves clinical examination and proper diagnosis followed by explaining about the treatment options and the procedure. The next aspect is caring, where the patient needs to be assured about the safety of the procedure and should be explained about the adverse effects if the patient does not undergo the treatment. The final aspect is cleanliness, which is an important aspect as it is what represents the patient's perception about the doctor. Clean working setup is essential with proper sterilised instruments.

In a dental college, the students undergo training in pre-clinical labs during their first and second year and enter the clinics during third year. Students undergo training in clinics during third year, final year and internship. During their clinical posting, students provide various dental treatments to patients under the concerned specialists supervision

As teaching facility, dental school clinics must constantly strive to find a balance between meeting the

needs of the patient and meeting the needs of the student, all the while knowing that patients and their satisfaction are critical to the education of the students. Also, dental school clinics play a prominent role in promoting oral health care. Furthermore, in a dental school setting, the focus on meeting requirements for graduating students must be balanced with patients' satisfaction. Though both care providers and patients benefit from their interaction, patient satisfaction must be prioritised.^[7]

Although there are many studies showing satisfaction level of patients pertaining to various aspects in medical field, not many studies are available that determine the patient satisfaction in relation to the clinician expertise. Hence, this study aims in determining the patient satisfaction with respect to clinician expertise ie whether there is any difference in patient satisfaction between those who treated by third year undergraduates, fin

Materials and Method

This study was approved by the Scientific Research Board of Saveetha Dental college. This study was conducted in Saveetha Dental College, Chennai. Feedback is generally collected from all the patients undergoing treatment in Saveetha Dental college. This study consisted of three groups- interns (group 1), final years (group 2) and third years (group 3). Data was collected from the feedback note. 1500 feedbacks were collected of which 500 each belonged to patients who had undergone treatment from third years, final years and interns. The feedback form had three categories- speed of treatment, explanation and caring, cleanliness which were scored on a scale of 10 by the patients. Once the treatment is completed, the patients are asked about their overall experience, if they were satisfied with their treatment or if they faced any difficulties. Mean value was calculated for all the categories and statistical value was determined using Anova and post hoc test.

Results

The mean value of speed of treatment in group 1, 2 and 3 are as follows- 8.862±4.09, 8.674±0.70 and 8.594±0.85. The mean value of explanation and caring in group 1, 2 and 3 are as follows- 8.77±0.72, 8.764±0.79 and 8.61±0.73. The mean value of cleanliness in group 1, 2 and 3 are as follows- 8.73±0.74, 8.65±0.73 and 8.60±0.82. Table 1

The p value of group 1 and 2 in terms of speed of treatment was 0.445, 0.985 in terms of explanation and

caring and 0.210 in terms of cleanliness. The p value of group 2 and 3 in terms of speed of treatment was 0.863, 0.005 in terms of explanation and caring and 0.585 in terms of cleanliness. The p value of group 3 and 1 in terms of speed of treatment was 0.194, 0.003 in terms of explanation and caring and 0.021 in terms of cleanliness. Table 2, 3.

Table 1: Mean value of patient satisfaction

GROUPS	SPEED OF TREATMENT	EXPLANATION AND CARING	CLEANLINESS
	MEAN STDEV	MEAN STDEV	MEAN STDEV
INTERNS (1)	8.862±4.09	8.77±0.72	8.73±0.74
FINAL YEARS (2)	8.674±0.70	8.764±0.79	8.65±0.73
THIRD YEARS (3)	8.594±0.85	8.61±0.73	8.60±0.82

Table 2: Comparison between groups

GROUPS	SPEED OF TREATMENT	EXPLANATION AND CARING	CLEANLINESS
	P VALUE	P VALUE	P VALUE
1 AND 2	0.445	0.985	0.21
2 AND 3	0.863	0.005	0.585
3 AND 1	0.194	0.003	0.021

Table 3: Post hoc test

SPEED OF TREATMENT			Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
	(I) group	(J) group				Lower Bound	Upper Bound
	1	2	.188	.155	.445	-.18	.55
	3	.268	.155	.194	-.10	.63	
2	1	-.188	.155	.445	-.55	.18	
	3	.080	.155	.863	-.28	.44	
3	1	-.268	.155	.194	-.63	.10	
	2	-.080	.155	.863	-.44	.28	
EXPLANATION AND CARING			Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
	(I) group	(J) group				Lower Bound	Upper Bound
	1	2	.008	.048	.985	-.10	.12
		3	.156*	.048	.003	.04	.27
	2	1	-.008	.048	.985	-.12	.10
		3	.148*	.048	.005	.04	.26
	3	1	-.156*	.048	.003	-.27	-.04
	2	-.148*	.048	.005	-.26	-.04	
CLEANLINESS			Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
	(I) group	(J) group				Lower Bound	Upper Bound
	1	2	.082	.049	.210	-.03	.20
		3	.130*	.049	.021	.02	.24
	2	1	-.082	.049	.210	-.20	.03
		3	.048	.049	.585	-.07	.16
	3	1	-.130*	.049	.021	-.24	-.02
	2	-.048	.049	.585	-.16	.07	

Discussion

The result of this study shows that, overall the patient satisfaction is good as the grade is above eight for all the groups in all the three aspects. Overall, the patient satisfaction in terms of speed of treatment, explanation and caring and cleanliness was higher in interns followed by fourth years and then third years. There was no significant difference in relation to speed of treatment. There was significant difference between groups 2 and 3 ($p=0.005$), and groups 3 and 1 ($p=0.003$) in terms of explanation and caring. There was significant difference between groups 1 and 3 ($p=0.021$) in terms of cleanliness.

A study conducted in Ohio state compared the patient satisfaction between ohio state university dental clinics and ohio state university dental students. Dental satisfaction questionnaire (DSQ) was used for this study and the only items of the DSQ that were significantly different were people are usually kept waiting a long time when they are at the OSU dental clinic ($p=0.02$) and OSU dental students are able to relieve or cure most dental problems that people have ($p=0.02$). A possible reason for the longer patient waiting times was that there was a learning curve that first year for all involved— clinic staff, students, and patients. This learning curve resulted in patients being kept waiting longer than before.^[8] When compared with our study, the waiting time and speed of treatment was not a factor affecting the patient satisfaction in all the three groups irrespective of their year of study.

A study in Greece recorded the patient's perception and expectations regarding quality of dental care. It was found out that empathy was the most important aspect that needed to be fulfilled followed by assurance, responsiveness and reliability. There was a large quality gap regarding responsiveness, empathy and reliability reflecting the need to improve quality of dental health care. The examined patients considered that they were not sufficiently informed about oral diseases^[9] which is similar in our study. The level of explanation and caring was higher in interns and final years and there was a significant difference between final years and third years, third years and interns.

A study in Ajman university recorded the patient satisfaction level based on their reason for visit and educational qualification of the patient. The major reason for admission (80.0%) was relief of pain. A high

proportion of the patients (83.0%) visited the dentist only when they had a problem, just 7.4% came twice a year. The largest category for treatment received (23.0%) was operative treatment, followed by endodontic treatment (19.3%). There was a statistically significant association between the level of education and the dental satisfaction scale. The most highly educated patients were the least satisfied with the treatment provided. Patients who visited the clinic for pain relief were significantly more satisfied than those who visited the clinic for routine care ($P < 0.01$). The dental satisfaction levels were also significantly higher among patients who visited the clinic only when they had problems ($P < 0.05$).^[10]

Another study showed the relationship between patient satisfaction and ethnicity. Black patients tended to be the least satisfied; Hispanic patients were only moderately satisfied when compared to non-Hispanic patients.^[11]

According to a study conducted in turkey, the type of health insurance was the most significant predictor of patient satisfaction and time spent waiting seems to be the main reason for patient dissatisfaction in dental outpatient clinic in Turkish state hospitals.^[12]

Conclusion:

The overall score of all the three groups were above average. There was a significant difference between final years and third years in terms of explanation and caring and interns and third years in terms of cleanliness. From this study, we can conclude that with experience, explanation about the treatment and cleanliness improves as they gain more confidence.

1. **Conflict of Interest:** Authors have no conflict of interest
2. **Source of Funding:** Nil
3. **Ethical Clearance:** Nil, Questionnaire study

References

1. Hashim R. Patient satisfaction with dental services at Ajman University, United Arab Emirates. *East Mediterr Health J* 2005;11:913-21.
2. Schouten BC, Hoogstraten J, Eijkman M. Patient participation during dental consultations: The influence of patient's characteristics and dentists' behaviour. *Community Dent Oral Epidemiol* 2003;31:368-77.

3. Davies AR, Ware JE. Measuring patient satisfaction with dental care. *Soc Sci Med* 1981;15A:751-60.
4. Davies AR, Ware JE, Jr. Development of a dental satisfaction questionnaire for the health insurance experiment. Santa Monica, CA: The Rand Corporation, 1982.
5. Donabedian A. Evaluating the quality of medical care. *Milbank Memorial Fund Quarterly* 1966;44:166-203.
6. Donabedian A. The definition of quality and approaches to its assessment: explorations in quality assessment and monitoring. Volume I. Ann Arbor, MI: Health Administration Press, 1980.
7. Mascarenhas AK. Patient satisfaction with the comprehensive care model of dental care delivery. *Journal of Dental Education*. 2001 Nov 1;65(11):1266-71.
8. Mascarenhas AK. Patient satisfaction with the comprehensive care model of dental care delivery. *Journal of Dental Education*. 2001 Nov 1;65(11):1266-71.
9. Karydis A, Komboli M, Pannis V. Expectation and perception of Greek patients regarding the quality of dental health care: 2001; 13: 409-416. *Int J for Qua in Health Care*.
10. Hashim R. Patient satisfaction with dental services at Ajman University, United Arab Emirates.
11. Handelman SL, Fan-Hsu J, Proskin HM. Patient satisfaction in four types of dental practice. *Journal of the American Dental Association*, 1990, 121(5):624-30.
12. Sur H, Hayran O, Yildirim C, Mumcu G. Patient satisfaction in dental outpatient clinics in Turkey. *Croatian medical journal*. 2004 Oct 1;45(5):651-4.

Psychological Effects of Trauma to Anterior Teeth

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Abstract

Context: Dental trauma has a very distressing experience on physical, emotional and psychological aspects of the patient. The aim of the study was to determine the psychological effects of anterior dental trauma on patients.

A questionnaire study was carried out to know the psychological aspects of trauma to anterior teeth based on the Oral Health Impact Profile (OHIP-14) index. It is regarded as the most comprehensive tool for measuring Oral Health Related Quality of Life. This study concentrated only on psychological discomfort and psychological disability. Each item was scored on a five-point scale ranging from “never” (coded 0) to “very often” (coded 4).

The statistical significance of the scores thus obtained and the mean levels of the severity scores between genders and age groups were calculated using the statistical chi-square test. In our study psychological effects to anterior teeth trauma was most observed in the age group of 18-25. Interestingly when the observation was monitored across genders, we observed large psychological effect in females when compared to male gender.

Keywords: Anterior dental trauma, psychological effects, OHIP index.

Introduction

Health is described “a complete state of physical, mental, and social well-being of an individual and not just mere absence of disease” (WHO, 1948). This concept of health embraces the bio-psychosocial model of health into which physical functioning, symptoms, emotional and social well-being are holistically incorporated (Kleinman, 1988). Hence health related researchers have rightly focused on health as a multi-dimensional construct.^[1]

Oral Health Related Quality of Life (OHRQoL) forms an integral part of general health and well-being and is recognized by the WHO as an important segment of the Global Oral Health Program (WHO, 2003).^[2] It is imperative to evaluate the extent to which the oral diseases impacts on ones normal functioning and psychology.^[3]

In the field of dentistry, OHRQoL address four dimensions: pain and discomfort; functional aspects concerning the ability to chew and swallow food without difficulty, speaking and pronunciation; appearance and self-esteem; and social aspects reflecting social interaction with others.^[4]

So it is fair to qualify that oral health affects various aspects of social life, including social interaction, self-esteem, school and job related performance, specifically when the issues related to anterior dental trauma are involved. Incidents arising from physical fight, traffic

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accident and sporting injuries contributes the major cause of anterior dental trauma.^[5]

Dental trauma is usually a pain filled experience for most people which can impair oro-facial function, negatively affecting growth, aesthetics and occlusion.^[6] Unlike a chronic condition, severe dental trauma causes immediate and unexpected pain. The obvious economic cost apart, it can trigger a series of socio-economic consequences affecting the quality of life and possibly lead to the absence from college or work, disturbances during sleep and changes in the normal daily schedule. This could be further compounded by the stress patients may experience as a result of unhelpful behaviour by their peers, society and family members. The impact is quite significant when anterior dental trauma is involved, which is what this study tries to document via Oral Health Impact Profile(OHIP-14) survey.

Since anterior dental trauma is often caused by accidents that cause life-threatening injuries, limb fractures or concussion, emergency care prioritizes on more important issues. As a consequence of this delay, sometimes it becomes impossible to provide timely treatment that would have otherwise allowed the affected front tooth to be saved.^[7]

Dental trauma frequently affects the upper central incisors, most likely because of their position in the mouth and also having less of a protection in comparison with the other teeth. Consequently the position and appearance of the anterior teeth have very important psychological and social impacts on the quality of life of the patient. When injuries to incisors produce pain, poor aesthetics/disfigurement or other psychological effects, patient may avoid smiling or laughing and this can affect their social relationships. So overall this has a very distressing experience on physical, emotional, and

psychological levels of the patient which is a matter of great concern.^[8,9,10]

OHIP-14 index assesses seven dimensions of impacts of oral conditions on one’s quality of life including functional limitation, physical pain, psychological discomfort, physical disability, psychological disability, social disability and handicap.^[11] This is widely regarded as the most comprehensive assessment for measuring OHRQoL.

The aim of the study was to determine the psychological effects of anterior dental trauma on patients and to assess the impact of these injuries on the quality of life based on OHIP-14 index.

Materials and Method

The study was conducted in the Department of Conservative Dentistry & Endodontics, AB SMIDS, Karnataka, India. Ethical clearance was obtained from Nitte (Deemed to be University), Cert. No: ABSM/EC07/2019.

The total numbers of subjects were 256 based on approximately 20% incidence of anterior tooth fractures. Patients in the age group of 18 and above with anterior tooth trauma were included in the study. Participation was voluntary, anonymous and started off with patients consent.

Study was carried out to know the psychological aspects of trauma to anterior teeth based on the OHIP-14 index, specifically w.r.t psychological discomfort and disability. Each item was scored on a five-point scale ranging from “never” (coded 0) to “very often” (coded 4).^[1,2,10,12]

Findings: 1. Gender Comparison:

Table 1: Psychological discomfort scores

		Psychological discomfort scores					Total	
		Never	Hardly ever	Occasionally	Fairly Often	Very Often		
Gender	Male	Count	5	18	112	22	1	158
		% within gender	3.2%	11.4%	70.9%	13.9%	0.6%	100.0%
	Female	Count	2	1	8	75	12	98
		% within gender	2.0%	1.0%	8.2%	76.5%	12.2%	100.0%
Total		Count	7	19	120	97	13	256
		% within gender	2.7%	7.4%	46.9%	37.9%	5.1%	100.0%

Chi-Square- 13.438 P= 0.001 sig

Table 2: Psychological disability scores

		Psychological disability scores					Total	
		Never	Hardly ever	Occasionally	Fairly Often	Very Often		
Gender	Male	Count	0	128	21	5	4	158
		% within gender	0.0%	81.0%	13.3%	3.2%	2.5%	100.0%
	Female	Count	6	15	51	18	8	98
		% within gender	6.1%	15.3%	52.0%	18.4%	8.2%	100.0%
Total		Count	6	143	72	23	12	256
		% within gender	2.3%	55.9%	28.1%	9.0%	4.7%	100.0%

Chi-Square=108.365 P= 0.001 sig

2. Age comparison

Table 3: Psychological discomfort scores

		Psychological discomfort scores					Total	
		Never	Hardly ever	Occasionally	Fairly Often	Very Often		
Age	18-25	Count	14	12	20	90	2	138
		% within age	10.1%	8.7%	14.5%	65.2%	1.4%	100.0%
	25-35	Count	0	1	50	34	1	86
		% within age	0.0%	1.2%	58.1%	39.5%	1.2%	100.0%
	35-45	Count	9	12	10	1	0	32
		% within age	28.1%	37.5%	31.2%	3.1%	0.0%	100.0%
Total		Count	23	25	80	125	3	256
		% within age	9.0%	9.8%	31.2%	48.8%	1.2%	100.0%

Chi-Square=108.433 p=0.001

Table 4: Psychological disability scores

		psychological disability scores					Total	
		Never	Hardly ever	Occasionally	Fairly Often	Very Often		
Age	18-25	Count	2	6	14	88	28	138
		% within age	1.6%	4.7%	10.9%	63.8%	21.9%	100.0%
	25-35	Count	1	10	42	23	10	86
		% within age	1.2%	11.6%	48.8%	26.7%	11.6%	100.0%
	35-45	Count	2	9	11	8	2	32
		% within age	6.2%	28.1%	34.4%	25.0%	6.2%	100.0%
Total		Count	5	25	67	119	40	256
		% within age	1.9%	9.7%	26.1%	46.4%	15.6%	100.0%

Chi-Square=67.451 p=0.001

The OHIP-14 data were captured and details were entered into SPSS tool (v.16; IBM Corp, Somers, NY) for further analysis. The dependent variables were based on the responses to the OHIP-14 were made on a five-point ordinal scale ranging from “never” coded as “0”, “hardly ever” coded “1”, “occasionally” coded “2”, “fairly often” coded “3”, to “very often” coded “4”.

The statistical significance of the scores and the mean levels of the severity scores between genders and age groups were calculated using the statistical chi-square test.

Above Table: Captures the percentage distribution of patients responses across the two dimensions namely

psychological discomfort and psychological disability for the scale ranging from “never” to “very often” ($p=0.001$).

In Table:1, which is related to psychological discomfort scores related to breakdown w.r.t gender, around 70.9% of the male individuals experienced “occasional” psychological discomfort compared to 76.5% impact of “fairly often” in females ($p=0.001$).

In Table:2, which is related to psychological disability scores related to breakdown w.r.t gender, around 81% of the male individuals experienced “hardly ever” psychological disability compared to 52% impact of “occasional” in females ($p=0.001$).

In Table:3, which is related to psychological discomfort scores related to breakdown w.r.t age, around 48.8% of the individuals experienced the impacts of “fairly often”. Largest contribution to this came from the age group of 18-25 with 90 individuals out of 138(65.2%) experiencing this impact ($p=0.001$).

In Table:4, which is related to psychological disability scores related to breakdown w.r.t age, around 46.4% of the individuals experienced the impacts of “fairly often”. Largest contribution to this came from the age group of 18-25 with 88 individuals out of 138 (63.8%) experiencing this impact ($p=0.001$).

Age group 18-25 showed higher scores in the psychological disability and discomfort dimension. The comparison across genders showcased a similar significantly higher uptick for women in the psychological dimensions.

Discussion

Psychological trauma occurs as a consequence of an overwhelming amount of stress experienced that exceeds one’s ability to cope or integrate the emotions involved with that experience. Effects of the trauma varies according to one’s subjective experiences. So, not all who experience a traumatic event will become traumatized psychologically.

Traumatic injuries constitute painful and distressing event with multilevel consequences for patient and their families. Despite being confined in a small body region as is the oral cavity, dental trauma constitutes a relatively common finding in population-based studies. Andersson noted that although the oral region comprises 1 percent of the total body area, oral injuries account for almost 5

percent of all injuries and for a higher proportion among early adults.

Among these anterior dental trauma forms an important and visible part of human anatomy. These are characterized as major public health problems due to their high prevalence and serious aesthetic and functional consequences. Such trauma can significantly disrupt patients’ normal functioning and impact dramatically on the quality of life.

Since anterior dental trauma is often caused by accidents that cause life-threatening injuries, limb fractures or concussion, emergency care prioritizes initially on more critical issues. As a consequence of this delay, sometimes it becomes impossible to provide timely treatment that would have otherwise allowed the affected front tooth to be saved.^[8]

The psychological and social impact of dental trauma is widely recognized as having consequences that can affect emotional balance, social contact and also well-being of the patient. There is an evidence of increasing necessity to use indices for measuring the impact of oral health on the quality of life. OHIP-14 index has been the flag bearer in this regard and is thus used for this study.

OHIP-14 index is used to measure patient’s perceptions of the social impact of oral disorders on their general well-being. It provides a comprehensive system of measurement for dimensions related to discomfort, self-reported dysfunction and related disability arising from oral conditions.^[12]

According to Lockeret al., OHIP-14 is a patient-centred assessment. It gives a greater weight to behavioural and psychological outcomes and is found to be better at detecting psychosocial impacts among individuals. Hence it also satisfies the main criteria for the measurement of OHRQoL.

The study outcome captured in above set of tables show cases the percentage distribution of responses across age and gender respectively for the two psychological dimensions for category scale ranging from “never” to “very often” as captured in the OHIP-14 index. The purpose of this paper was to review the impact of anterior dental trauma on psychological discomfort and psychological disability attributes across various age categories and gender respectively.

Psychological effects dimension based on age criteria: When this psychological effect dimension

was reviewed based on age criteria, it was observed that lowest measured age group of 18-25 had the most psychological impact at 65.2% with the issue tapering down with age.

The younger age group with little maturity has higher psychological impact than the older more mature groups post 25 years of age. Severity of the issue could be higher among lower age groups, since usually nature of accidents occurs from sports or accidents involving rash driving of youngsters.

Psychological impacts of dental trauma for this age group may be severe so aesthetic considerations should not be neglected. It is found to be one of the important considerations of the age group 18-25. Usually dental conditions are the most severe among health issues in early stages of adulthood, however as one age, other health considerations dominate including life threatening ones. It is quite likely as a result of this, older age groups manage the situation in a better way resulting in reduction of psychological discomfort as compared to younger generation.

Equally important is the fact that younger age group usually is just about starting to become independent financially. Hence this is a in-between phase wherein they are largely still reliant on the family for financial support. As a result may neglect the dental treatment at the appropriate time and the effects become severe later on.

Psychological effects dimension based on gender:

Interestingly when the observation is monitored across gender, we observe large discomfort in females in comparison with male gender.

Aesthetic dimension forms a key part for female gender, considerations encompass:

1. Beauty affected hence social impact
2. Societal pressure of friends, family, peers and social media like Facebook, Instagram etc.

It is quite likely this impact would be a lot lower among lower income groups as day to day survival is more important compared to other factors.

There are general attributes which adds to the psychological impact and which usually cuts across gender and ages:

1. Affect by presence of blood and visible nature of the dental trauma.

2. Loss of “hours of schooling/work” with economic consequences. Being able to take time from school/work for these procedures might become cumbersome if the dental clinics are not located at comfortable points.
3. Perception of work peers, friends and family members.

Additionally visit to dental emergency can trigger dental anxiety/fear responses among first time visitors. Hence calming effect of dental surgeon, explanation of the procedures in an easy way and anon-hospital like environment goes a long way in helping the patient settle down and reduce the psychological impact.

The data presented in this study provide a insight into patients’ feelings and should be considered essential when evaluating further treatment options. In addition to the prognosis and outcomes, clinicians should consider patients’ preferences and perceptions as well as the influence each therapy may have on their quality of life both short-term and long-term.

Health psychologists have recognized that behavioural assets such as resilience, social connectedness and optimism have a direct correlation with an individual’s quality of life and how well one is able to cope with health conditions.^[1]

Conclusion

In our study psychological discomfort to anterior teeth trauma was most observed in the age group of 18-25. Interestingly when the observation is monitored across genders, we observe large discomfort in females in comparison with male gender.

The study covered suburban areas of Dakshina Kannada district, further studies need to be carried out for a larger population set. Irrespective of age and gender, psychological impact if not handled appropriately could have a life-long impact and affect the general well-being of the patient.

This study will help to create need based and critical psychological adjunct services which can be incorporated into various community-based projects, with the basic idea of integrating dental health with overall well-being and quality of life of the patient.

Communication and positive reinforcement method is most effective way in reducing the psychological impact and should be considered a valuable investment.

This is aptly highlighted by Andersson in his editorial: “empathy for our trauma patients is the common denominator.” It helps to build a trusting relationship and plays a key role in relieving the distress experienced by the patient.

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References

1. Oral health-related quality of life: what, why, how, and future implications, Sischo L, Broder HL, J Dent Res 2011, 90:1264–1270.
2. What do measures of ‘oral health-related quality of life’ measure?, Locker D, Allen FP, Community Dent Oral Epidemiol 2007, 35:401–411.
3. Quality of life measured by OHIP-14 and GOHAI in elderly people from Bialystok, north-east Poland, Ewa Rodakowska, Karolina Mierzyńska, Joanna Bagińska and Jacek Jamiołkowski.
4. Slade GD. Assessment of oral health-related quality of life. In: Inglehart MR, Bagramian RA, editors. Oral Health-Related Quality of Life. Chicago, IL: Quintessence; 2002. pp. 66–79.
5. Andersson L. Trauma in a global health perspective. Dent Traumatol 2008;24:267
6. Intrusion injuries of primary incisors. Part I: Review and management, Diab M, elBadrawy HE, Quintessence Int 2000; 31(5): 327-34.[PMID: 11203943]
7. Review of recommendations for the management of dental trauma presented in first-aid textbooks and manuals, Emerich K, Gazda E, Dent Traumatol 2010; 26: 212–6.
8. Traumatic oral vs.non-oral injuries, Peterson EE, Anderson L, Sorensen S, Swedish Dent J. 1997;21:55.
9. Textbook and Color Atlas of Traumatic Injuries to the Teeth, Andreasen JO, Andreasen FM, 3rd ed. Copenhagen: Munksgaard; 1994.
10. Prevalence of fractured incisal teeth among children in Harris County, Alonge OK, Narendran S, Williamson DD, Texas. Dent Traumatol. 2001;17:218–21.
11. Development and evaluation of the Oral Health Impact Profile, Slade GD, Spencer AJ, Community Dent Health 1994, 11:3–11.
12. Assessment of oral health related quality of life. Health Qual Life Outcomes, Allen PF, 2003, 1:40.

Physical Characteristics and Somato Type of Trained Badminton Players

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Abstract

Context: The aim of this study was to analyze the relationship among somato type characteristics and physical training of young male and female Badminton players. A total of 30 players (15 males and 15 females), who represented Kerala in national level competitions, were evaluated with the sex as a factor. Different body measurements were recorded following the guidelines proposed by the ISAK such as body mass, height, skinfold thicknesses at different sites (biceps, triceps, subscapular, supraspinale and medial calf), girths (arm relaxed, thigh, and calf) and breadths (bicipicondylarhumerus and femur). In addition to anthropometrical analysis, body composition and somato type of the participants had been assessed. A t- test for independent samples was performed to examine the statistical differences between sex groups and a Pearson's coefficient was applied to evaluate the correlation between variables. An endomorph-ectomorph somatotype characteristics was observed for the entire group. Analysis, taking into account the sex factor, revealed an endomorph-mesomorph somatotype for the males and an endomorph-ectomorph somatotype for the females. Data corresponding to body composition contrasted by sex showed higher body fat percentage for the female group than the males. Within the tested age interval range, body fat content in female players was higher than the male counterparts. Although these differences might be the consequence of a normal growth, it was advisable to integrate educational and nutritional strategies in order to maintain an optimum body fat content. Training procedure must be considered to improve the body type for the specific sports event.

Keywords: Somato type, Badminton, Body mass, Height, Skinfold thickness.

Introduction

Badminton is an individual asymmetric sport, in which hits are required with great speed and power.¹ Technical actions that take place during the game are unilateral at the trunk and upper extremities level. Thus the dominant side of the player goes into action repeatedly and exclusively.² It is an acyclic sport in which work and rest time periods are continuously alternated.³ Also, the intensity developed during the match makes it mixed activity, taking into account the energetic metabolism.

It is a game characterized by consecutive series of fast and powerful hits against a lightweight ball. This has an alternating demand of aerobic-anaerobic requirement, caused by short and intermittent exercise and efforts with incomplete recoveries.⁴ Moreover, the dominant arm is totally involved with different positions that link the racket-arm to develop techniques of this sport.⁵ The most important physical capacities of the players are endurance and velocity, due to short time high intensity periods under anaerobic metabolism that characterize the match: Players need velocity training while the capacity to face match duration mainly depends of endurance training.⁶ However, strength, coordination and flexibility may also have a key role in this sport. It is evident that the physical training is an important factor to reach sport success; several studies demonstrated that, at the same training level, the best performances are obtained by

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athletes with more compatible anatomic conditions.⁷ Since 1940 numerous studies on body composition influenced the development of somatotyping and, in the last 20 years, many studies had defined the somatotype profile of athletes in different sports. Research interest in anthropometric characteristics and body composition of the players of different sports had been developed during the last decades.⁸ Different studies supported the requirement of specific anthropometric characteristics which determine the suitability of the player for best performance in that specific game.⁹

Statement of the Problem: The main objectives of the present study was to explore the possible role of training in 10-20 years aged male and female right handed Badminton players.

The objectives of the present study were aimed at following points:

1. To compare the effects of similar type of training in male & female Badminton players in similar age ranges.
2. How body type of the players can be improved by improving the physical training method?
3. Whether the body type of the both male and female Badminton players affect their performances.

Methodology: Subjects in the present study male right handed Badminton players (n=14) who were trained for 2 to 8 years with an average age of 13.29(±1.86) years and female right handed Badminton players (n=15) who were trained for 4 to 12 years with an average age of 13.93(±3.13) years participated as subjects. Individual NFHS (National Standard of Living Index) and SCAT (Sports Competition Anxiety Test) were carried out in each subject. Participants of this study were from different places of Kerala with participation experiences at national level competitions. All the players were involved in regular scheduled training programs of 30 min free hand exercises followed by 90 to 120 min game practice with full efforts intermittently for 6 days per week. All the participants were students and do not participate in any other recreational game.

Administration of Test: Anthropometric measurements were done on same day for each subject in same session to avoid technical error. Level 1 Anthropometrists accredited by International Society for the Advancement of Kinanthropometry (ISAK) was involved in the measurements. Method described in the

ISAK manual were followed. Stature was measured with an Anthropometric Rod up to 1 mm and body mass was measured with an electronic weighing machine. Skinfold thicknesses were measured with a Slim guide skinfold caliper (CESCORF). Anthropometric tape and sliding caliper (CESCORF) were used to measure circumferences and bone diameter respectively.

Somatotype Heath: Carter method was followed for somatotype rating. The following equations were used for calculating somatotype. Endomorphy = $-0.7182 + 0.1451 \times \Sigma SF - 0.00068 \times \Sigma SF^2 + 0.0000014 \times \Sigma SF^3$ where ΣSF = (sum of triceps, subscapular and supraspinale skinfolds) multiplied by (170.18/height in cm). Mesomorphy = $0.858 \times \text{humerus breadth} + 0.601 \times \text{femur breadth} + 0.188 \times \text{corrected arm girth} + 0.161 \times \text{corrected calf girth} - \text{height} \times 0.131 + 4.5$. Three different equations are used to calculate ectomorphy according to the height-weight ratio (HWR): If HWR is greater than or equal to 40.75 then, Ectomorphy = $0.732 \times \text{HWR} - 28.58$. If HWR is less than 40.75 and greater than 38.25 then, Ectomorphy = $0.463 \times \text{HWR} - 17.63$. If HWR is equal to or less than 38.25 then, Ectomorphy = 0.1. 3.4. Body Fat % Durnin and Womersley technique was followed for body density. Body fat% was derived from the equation of Brozek et al.

Physical Performances Flexibility tests (lower back & hamstring flexibility, ankle flexibility, trunk & neck flexibility, shoulder flexibility & elastic leg strength) were performed & agility of the players of both groups was also measured.

Statistical Analysis: Mean values & Standard Deviation of each mentioned parameters of both sexes were calculated. The unpaired two tail T-test was done to compare each of the parameters of the both genders, Probability of error due to random sampling was rejected at the level of $p < 0.05$. The correlation (r) is done for all parameters with Body height (cm), Body weight (kg), Fat percentage (%), Hand span of both hands (cm), Arm girth (cm), Calf girth (cm), Biepicondylar humerus circumference (cm), Biepicondylar femur circumference (cm), Chest circumference (cm), Waist circumference (cm), Hip circumference (cm), Mid thigh circumference (cm) & Upper thigh circumference (cm). by Pearson's Correlation Coefficient (r).

Normal Results and Discussions: The mean value, standard deviation and level of significance of Height (cm), Weight (kg), Body Fat %, Total fat content

(kg), Lean body mass (kg), Lower back & Hamstring flexibility (cm), Ankle flexibility (cm), Trunk & Neck flexibility (cm), Shoulder flexibility (cm), Elastic leg strength (cm), Agility (sec), Hand span of both hands (cm), Handgrip strength of both hands (kg), Arm girth (cm), Calf girth (cm), Biepicondylarhumerus circumference (cm), Biepicondylar femur circumference (cm), Chest circumference (cm), Waist circumference (cm), Hip circumference (cm), Mid thigh circumference (cm) & Upper thigh circumference (cm) of male (n=14) & female (n=15) trained Badminton players, the correlation values & level of significance of Height (cm), Weight (kg), Hand span (cm), Arm girth (cm), Calf girth (cm), Biepicondylarhumerus circumference (mm), Biepicondylar femur circumference (mm), Chest circumference (cm), Waist circumference (cm), Hip circumference (cm), Mid thigh circumference (cm) & Upper thigh circumference (cm) of both male & female trained Badminton are represented. No statistically significant differences were observed in male and female trained right handed Badminton players in Height (cm), Weight (kg), Lower back & Hamstring flexibility (cm), Ankle flexibility (cm), Trunk & Neck flexibility (cm), Shoulder flexibility (cm), Agility (sec), Hand span of both hands (cm), Handgrip strength of both hands (kg), Arm girth (cm), Calf girth (cm), Chest circumference (cm), Waist circumference (cm), Hip circumference (cm), Mid thigh circumference (cm) & Upper thigh circumference (cm) (Table 1). Body fat percentage and total fat content is significantly higher in female than their male counterparts (Table 1), but lean body mass was much higher in male than female players and it was statistically significant. Elastic leg strength was found to be higher in male players than female players and it was statistically significant. Shoulder flexibility of male players were significantly higher than the female players at $p < 0.05$ level. Both biepicondylarhumerus breadth and biepicondylar femur breadth were slightly higher in male Badminton players than their female counterparts and they were statistically significant.

Discussion on Findings: The variable samples were based on 10 anthropometric parameters needed to determine somatotype characteristics using the Carter and Heath method [18]. The growth and development differences among the participants of these age group (10 -20 year) were very significant to compare them directly through anthropometric measurements, but when determining the somatotype using the Carter and Heath method [18], the only relevant interrelation was between 10 anthropometric parameters and chronological age.

That fact nullified the age difference and enabled further comparisons. Fifty percent male subjects belonged to the group dominated by the endomorphic component, but in case of female subjects sixty seven percent had endomorphic component. The group with an accentuated influence of the endomorphic somatotype component but also a highly emphasised mesomorphic component was characterised by high levels of subcutaneous fat tissue. It included endomorphs, the majority of whom had an accentuated mesomorphic component (mesomorphic endomorphs), followed by those with a balance of the two components (mesomorphic-endomorphic); there were also a few ectomorphs with an accentuated endomorphic component. The 21% of the male population and none of the female population belong to the group dominated by mesomorphic somatotype component. This group comprised subjects with high numerical values for the mesomorphic components compared to the other two somatotype components (endomorphic and ectomorphic). Based on the values of those two less emphasised components, it was possible to further divide the subjects of this group into those dominated by the endomorphic component of the mesomorphic somatotype (endomorphic mesomorphs), those dominated by the ectomorphic component (ectomorphic mesomorphs), and those with a balance of the two components (balanced mesomorphs). The 29% of the males and 33% of the females belong to the group predominant ectomorphs dominated by the ectomorphic somatotype component. The values of the other two components (endomorphic and mesomorphic) were much less emphasised and subdivide this group into two ectomorphic subtypes (mesomorphic ectomorphs and balanced ectomorphs). It seemed to be obvious that a mesomorphic predominance could play a decisive role in any sport, including Badminton. Indeed, several investigations carried out on Badminton players demonstrated a superior muscular development in lower extremities. But in our study it was found that only 21% of the males and none of the females were mesomorphic. In a structurally complex game such as Badminton, competitive success is primarily a result of the quality and degree of technical and tactical knowledge. Accordingly, the differences in the competitive success of the young Badminton players are mostly the result of differing levels of technical as well as tactical skills. Those differences are much more salient at this competitive level than among top senior players where a high level of technical/tactical knowledge can be assumed. Although the existence of suitable morphological features certainly represents an

advantage and plays a role in achieving competitive success (especially among top players), in a technically complex game.

Discussion on Hypotheses: Badminton, it is just one of many factors that influence competitive success. At this age, a player's basic anthropometric characteristics and body constitution is an important factor but far from crucial factor in achieving top competitive results. The predominance of a physique dominated by the mesomorphic and ectomorphic somatotype components only reveals the potential advantage of these types of body constitution in increasing the likelihood of success, but it is not a decisive factor that directly influences competitive success among young Badminton players. Average body fat percentage and average total fat content (kg) were significantly higher in female players as the female players possessed a high quantity of subcutaneous fat. On the other hand average lean body mass (kg) of the male players was significantly higher than their female counterparts as the quantity of subcutaneous fat for the males were comparatively low. Average elastic leg flexibility of the male players was significantly higher than the female, so the leg flexibility of the male players was better than the female players. Average biepicondylarhumerus and biepicondylar femur breadths were found significantly ($p < 0.05$) higher in male than female as the bone breadth of the males were high.

Conclusions

In the present study male and female trained Badminton players were analyzed in different ways, like height, weight, body composition, anthropometric parameters, flexibility, elastic leg strength, hand span, handgrip strength and agility. All values were correlated with each other to assess the differences between male and female Badminton players in their musculoskeletal fitness and body type. High correlation values were found between arm girth, calf girth, biepicondylarhumerus breadth, biepicondylar femur breadth, chest circumference, waist circumference, hip circumference, mid thigh circumference and upper thigh circumference in both genders. It was found that there were only 21 % of the males and none of the female players were mesomorphic. But mesomorphy was essential for the improvement of performance in Badminton players. It could be concluded that the physical training procedure might not be specific to the event's demand. Musculoskeletal development

of the players did not specify the Badminton event. Endomorphy had been found in both male and female players. Thus the muscle content of the players must be enhanced by improving the event specific physical training and by prescribing proper diet to the players. It is advisable to integrate educational and nutritional strategies in order to maintain an adequate body fat content.

Ethical Clearance: Nil

Source of Funding: Self

Conflict of Interest: Nil

References

- [1] Chin M, Wong A, So R, Siu O, Steininger K, Lo D. Sport specific fitness testing of elite badminton players. *Brit j sports med.* 1995 Sep 1;29(3):153-7.
- [2] Krøner K, Schmidt S, Nielsen A, Yde J, Jakobsen B, Møller M, Jensen J. Badminton injuries. *Brit j sports med.* 1990 Sep 1;24(3):169-72.
- [3] Hughes M. Physiological demands of training in elite badminton players. *Sciand racket sports.* 1995:32-7.
- [4] Callow N, Hardy L, Hall C. The effects of a motivational general-mastery imagery intervention on the sport confidence of high-level badminton players. *Res Quar Exerc and Sport.* 2001 Dec 1;72(4):389-400.
- [5] Phomsoupha M, Laffaye G. The science of badminton: game characteristics, anthropometry, physiology, visual fitness and biomechanics. *Sports med.* 2015 Apr 1;45(4):473-95.
- [6] Reilly T, Bangsbo J, Franks A. Anthropometric and physiological predispositions for elite soccer. *J Sports Sci.* 2000:669-683.
- [7] Ackland T, Ong K, Kerr D, Ridge B. Morphological characteristics of Olympic sprint canoe and kayak paddlers. *J Sci and med sports,* 2003;6(3): 285-294.
- [8] Gualdi R, Zaccagni, L. Somatotype, role and performance in elite volleyball players. *J Sports Med and Phy Fit.* 2001. 41 (2):256-262.
- [9] Siders, W. Relationships among swimming performance, body composition and somatotype in competitive collegiate swimmers. *J Sports Med and Phy Fit,* 1993; 33 (2):166-171.

Health Care Services Under Consumer Protection Laws of Union Territories of Jammu and Kashmir: A Socio-Legal Mapping

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Abstract

Context: Ever since the passing of the *Jammu & Kashmir Consumer Protection Act, 1987*, the doctor-patient's relationship came under critical scrutiny, controversy and litigation. The inadequacy of consumer protection laws results in unavoidable contingency, spiralling cost shifting and inordinate health care complexities. It examines health care services as a matter of consumer rights under *Consumer Protection Act, 1986*, *Jammu and Kashmir Consumer Protection Act, 1987* and *Consumer Protection Act, 2019*. It makes consumers to navigate between hope and despair for access to health care. The paper is driven to analytical study of inadequacy of consumer laws in dealing effectively deficiency of medical service, insufficiency of health care services, lack of medical professionalism and negligence in Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Srinagar by encompassing a legislative survey of consumer laws in inculcating Consumer Right Awareness (CRA) and toning of structural governance of grievance redressal mechanism. The gap between the precept and practice of consumer justice and compensation in health care services is identified for adoption of a robust infrastructural and schematic revamping.

Keywords: *Health Care Services, Consumer Right Awareness, Grievance Redressal Mechanism, Consumer Justice and Compensation.*

Introduction

The health care facilities to the people of the erstwhile state of Jammu and Kashmir (J & K) is marred by constraints of financial resources, difficult topography and terrain, poor road connectivity, low presence of private sector, low accessibility and affordability by under-privileged segments of the population. There has been a gradual decay in the health services of J & K over the last three decades. The state is under shadows of infectious diseases like tuberculosis, RTI, UTI diarrhoea disease.¹ There is growing shadow of chronic diseases like hypertension, coronary artery disease, cancers, and

diabetes. Factually speaking there are 3,807 health care institutions in the state which is considered the highest number of hospitals in the country. The annual budget for the health sector in J & K is Rs. 2,423-crore. The per capita spending under plan, non-plan and centrally sponsored schemes is estimated at Rs. 1,931 crore.² According to the *State's Economic Survey Report, 2017*, there were 4,433 government health institutions in J & K at the primary, secondary and tertiary levels with 6,674 doctors.³ The paper examines the efficacy of *J & K Consumer Protection Act, 1987* to give effect to *Consumer Protection Act, 1986* to take care of consumer right awareness among patients for robust health care services in two Union Territories of J & K under *Jammu and Kashmir Reorganisation Act, 2019*.

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Materials and Method

The material and method applied for the study include analytical method of legal research by

undertaking the legislative survey and scrutiny of consumer laws at central and state levels. These laws are studied under Parsonian Effecttheory in the context of health care services.⁴ The comparative consumer law study of *Consumer Protection Act, 1986*, *J & K Consumer Protection Act, 1987* and *Consumer Protection Act, 2019* is based on established canons of statutory interpretation. The material and method partakes an empirical framework of SKIMS, Srinagar a premier medical institution in J & K state. The case study is based on Consumer Right Awareness (CRA) under four major parameters which include consumer right awareness, redressal against medical negligence, and recourse to deficiency of medical service and compensation and consumer justice.

Findings: It is important to note that the both *Consumer Protection Act, 1986*, *J & K Consumer Protection Act, 1987* and *Consumer Protection Act, 2019* are public welfare legislation and has been designed to avoid procedural technicalities, delays, and requirement of court fees to protect consumers availing medical facilities and health care services.⁵ It contains three-tier consumer disputes redressal system at the District, State and National levels along with Central Consumer Appellate Authority (CCAA) including right to health and environment.⁶

Central Consumer Protection Act, 1986: The *Consumer Protection Act, 1986* forms the basis of *J & K Consumer Protection Act, 1987* therefore a perusal of this law in brief is imperative. The Act seeks to promote and protect the interest of consumers against deficiencies and defects in goods or services.⁷ It also seeks to secure the rights of a consumer against unfair trade practices, which may be practiced by manufacturers and traders. The Act applies to all goods and services unless specifically exempted by the Union Government and covers all sectors, whether private, public, or cooperative. It ordains simple, speedy and inexpensive machinery for redressal of consumer's grievances, the marketing of goods and services to consumers, as well as the relationships, transactions and agreements between the consumers and the producers, suppliers, distributors, importers, retailers, service providers and intermediaries of those goods and services.⁸ The application of *Consumer Protection Act, 1986* to health services derives life breath and sustenance from Supreme Court ruling in *Indian Medical Association v. V.P. Shantha*.⁹ In this case the question raised was whether the treatment provided by medical practitioners to their patients would

constitute "service" under the meaning of the Act and whether patients would be treated as 'consumers' under the same *Consumer Protection Act, 1986*. The court noted that the issues arising in the complaints against medical negligence can be speedily disposed of by the procedure being followed by consumer disputes redressal agencies. Thus the *Consumer Protection Act, 1986* is pioneering law in protection of consumer from the standpoint of health, environment and consumer justice.¹⁰

J & K Consumer Protection Act, 1987: The *J & K Consumer Protection Act, 1987* aims to provide effective safeguards to the consumers against defective goods, deficient services and unfair trade practices. The Act provides speedy redressal to consumer complainants by setting up of a District Consumer Redressal Forum and State Commission having jurisdiction to claim of Rs. 10 lakhs and Rs. 30 lakhs respectively. The State Commission will be vested with appropriate appellate and revisional powers. It shall apply to all goods and services except those which are specially exempted by notification by the state government did not specifically exempted health care services provided by government hospitals. It seems profitable to refer section 2(1) (0) as under:

"Service" means service of any description which is made available to potential users and includes the provision of facilities in connection with banking, financing, insurance, transport, processing, supply of electrical or other energy, board or lodging or both, entertainment, amusement or the purveying news or other information, under a contract of personal service.

The necessary penal and punitive provisions have been incorporated for effective redressal of unfair trade practices, defect in the goods, and deficiency of services. The Consumer Commissions are authorized to impose penalties on trader or person against whom complaint is made if he fails to comply with the order of the redressal agency.

J & K Government Doctors (Relaxation of Restrictions on Private Practice) Rules, 1987: It will be appropriate to see the application of *J & K Consumer Protection Act, 1987* and *J & K Government Doctors (Relaxation of Restrictions on Private Practice) Rules, 1987* in holistic perspective in regard to doctor patient relationship and health care services. This is also important to see this law in the context of penalty or punishment may involve imprisonment for a period

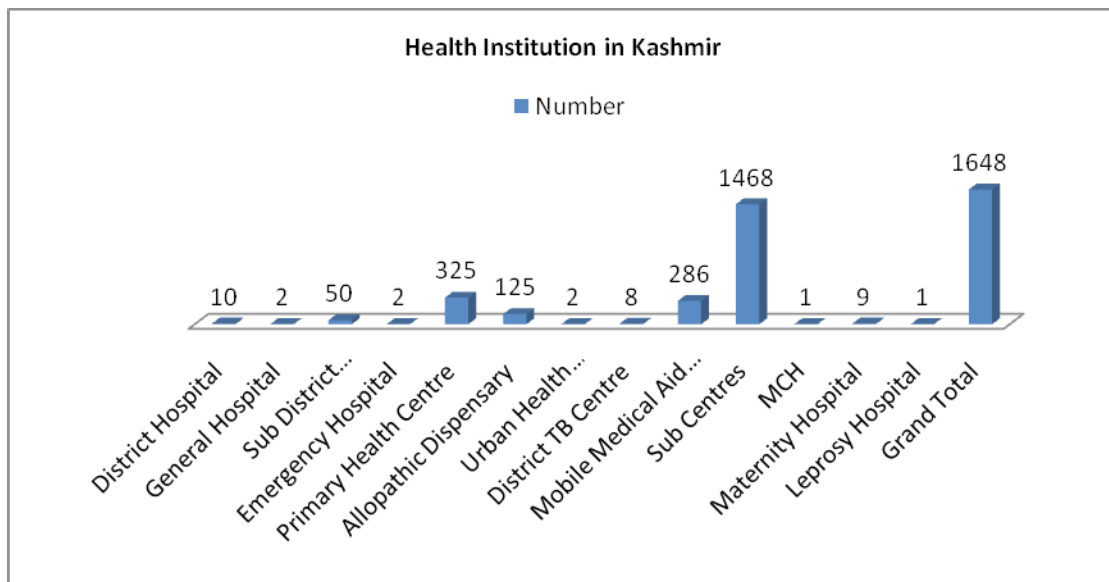
not more than 3 years or a fine or both. The complaint mechanism by a consumer voluntary organization, registered society, company and state government will also be scrutinised in pragmatic discourse. Therefore, it is also worthwhile to inquire the synergy of both legislations from the lens of the executive and judicial attitude towards disciplining doctors and foster health care services to patient *vis-a-vis* banning private practice. The J & K High Court in *Dr. Ashutosh Gupta v. State of J & K*,¹¹ while hearing petition for quashing of Government Order No. 43/HME of 2013 dated 17.01.2013 regarding of banning of private practice by doctors of government medical college, associated hospitals and dental colleges upheld the impugned order of the Government. In *Sukesh Chander Khajuriav. State of J & K*,¹² the J & K High Court dismissed the writ petition regarding validity of J

& K Government Doctors (Relaxation of Restrictions on Private Practice) Rules, 1987.

Discussions

The study of health care services under consumer protection laws of J & K health institutions is an empirical study of SKIMS with 900 bedded tertiary care hospital and undergraduate medical college with intake capacity of 100 students. According to survey there are total 1648 health institutions in J & K State.¹³

Selection of Area of Study: SKIMS being premier medical institution in India, it provides additional services including prevention, treatment, rehabilitation, obstetrics, substance abuse, health education, and screening for cancers and other diseases.¹⁴



The case study of SKIMS is based on four major parameters *viz*; consumer right awareness,¹⁵ redressal against medical negligence, recourse to deficiency of medical service and compensation and consumer justice under the *J & K Consumer Protection Act, 1987* and *J & K Government Doctors (Relaxation of Restrictions on Private Practice) Rules, 1987*. Located in Soura area of Srinagar, this is the largest medical Institute under *Sher-i-Kashmir Institute of Medical Sciences, (Grant of Degrees) Act, 1983*.¹⁶ The *J & K Consumer Protection Act, 1987* is not applicable to government hospitals because of free medical care services to patients. But the medical services rendered by doctors and hospitals falls within the ambit of a “service” as defined in Section 2(1) (o) of the Act.

Consumer Right Awareness & Health Care Services: By this analogy persons who are rendered free service are “beneficiaries” and as such come within the definition of “consumer” under Section 2(1) (d) of the Act. Similarly the deficiency of service is spelt out under Section 2(1) (g) which covers diagnostic, surgical and therapeutic service.¹⁷ A sample survey of 100 patients admitted to SKIMS was conducted regarding consumer right awareness to healthcare.¹⁸ The following table and chart-1 shows the nature and depth of consumer right awareness among randomised number of patients is in and out patient department. The simple question regarding the legal literacy of consumer law and redressal agencies were put to these patients.

Table 1: CRA & Health Care Services

Patients	Respondents	Yes	%age	No	%age	Indifferent	%age
In Patients	50	10	20	35	70	05	10
Out Patients	50	12	24	34	68	04	08
Total	100	22	88	79	79	09	09

Source: Field work

The above table clearly shows that 22% respondents have knowledge about consumer law or redressal agencies while as 79% respondents said that no they were not having any knowledge about consumer laws however 9% respondent didn't said anything about the information of consumer laws. The legal literacy about

the complaint mechanism for the deficiency in medical services is also in abysmally low. When we asked patients about the deficiency of medical services gives rise to grievance redressal at appropriate consumer forum almost 2/3 respondents feign ignorance about it.

Table II: CPA & Grievance Redressal Mechanism

Patients	Respondents	Yes	%age	No	%age	Indifferent	%age
In Patients	50	10	20	35	70	05	10
Out Patients	50	11	22	34	68	05	10
Total	100	21	21	69	69	10	10

Source: Field Work

The medical negligence on as the part of health care provider is frequent in J & K that is why the patient affected by medical negligence have faint idea about the complaint mechanism as victims. The Table II shows that 21% respondents have knowledge about complaints

in consumer forums. on the basis of data received from respondents 69% respondents said that they were not aware about the concept of complaints in consumer forums, however 10% respondents didn't say anything about the complaints in consumer forums.

Table III: CPA & Medical Negligence

Patients	Respondents	Yes	%age	No	%age	Indifferent	%age
In Patients	50	10	20	34	68	06	12
Out Patients	50	13	26	32	64	05	10
Total	100	23	23	66	66	11	11

Source: Field Work

The Comptroller and Auditor General (CAG) of India has reported that 'even the emergency medicine department has been found to be not fully equipped to deal with cases of road traffic accidents having multiple organ injuries including orthopedic injuries.' This is also pathetic to note that ambulances meant for patients have been found mis-utilized to the extent of 40 to 47 per cent during 2008-12.¹⁹

Health Care & Medical Negligence: The knowledge regarding negligence in health care services reveals that 23% respondents were aware about the complaints mechanism. The ordinary prudence about medical negligence depicts that 66% respondents don't have knowledge about grievance redressal and 11% remain indifferent to liability of doctors and hospital authorities.

Table IV: Health Care Services & Medical Negligence

Patients	Respondents	Yes	%age	No	%age	Indifferent	%age
In Patients	50	11	22	36	72	03	06
Out Patients	50	10	20	35	70	05	10
Total	100	21	21	71	71	08	08

Source: Field Work

Compensation & Consumer Justice: the compensation incase of medical negligence to the patients and their kith and kin also represent empathitic and ignorance. The patient interviewed regarding their response to compensation in case of medical negligence reveals that 21% respondents show that they have

knowledge about penal provisions against doctors.²⁰ Still majority of patients to the tune of 71% said that they were not having any information related penal provisions whereas 8% are either ignorant or indifferent didn't say anything about penal action can be initiated in case of medical negligence on part of hospital and doctor.

Table V: Compensation & Consumer Justice

Patients	Respondents	Yes	%age	No	%age	Indifferent	%age
In Patients	50	08	16	38	76	04	08
Out Patients	50	09	18	36	72	05	10
Total	100	17	17	74	74	09	09

Source: Field Work

The apex court ruling has played seminal role in curbing medical malpractice and making compensation an integral part of consumer justice that 17% respondents have knowledge about compensation given by consumer forums and 74% said that they were not having any information related compensation related consumer forums however 09% respondents didn't say anything about compensation provided by consumer courts. This places the consumer justice in a conundrum especially in the aftermath of Supreme Court decision.

Conclusion

The analysis of health care services under consumer laws of erstwhile J & K state now Union Territories of J & K under *Jammu and Kashmir Reorganisation Act, 2019* reveals that health status of the people has not been able to keep pace with the national targets. The state has a considerable segment of population living below poverty line, inadequacy of healthcare and burden of disease in an environmentally benign setting.²⁰ The *J & K Consumer Protection Act, 1987* has not achieved consumer right awareness and assertiveness in realisation health care services. The health services and disease

overburden needs proper regulation. This becomes more important in the wake of unrest of decades has worsened the health status of people especially of population living below poverty line. The only salacious aspect is to note that the purpose and object with which the *J & K Consumer Protection Act, 1987* has been passed has substantially achieved in the ambit of patient's rights notably compensatory justice. But the SKIMS have been found inadequately equipped to deal with accidents and trauma prevention and gross mis-utilisation of ambulance services despite rich infrastructure. The most significant and equally multifaceted as well complex service in the field of consumer grievances is that of medical malpractice and the doctors of SKIMS and other government hospitals of state need to be more circumspect and careful towards medical services to patients to enlarge the realm of consumer justice, access to health and compensatory jurisprudence.

Conflict of Interest: No

Source of Funding: self

Ethical clearance: No

References

- (1) World Health Organization. The World Health Reports 2002. Reducing Risk, Promoting Healthy Life: World Health Organization; 2002.
- (2) GOI. National Health Policy - 2002. Department of Health, Ministry of Health and Family Welfare. Govt of India: New Delhi; 2002.
- (3) Economy Survey, 2017. [Internet]. [Cited on 2014 Sept 15]. Available from: <http://ecostatjk.nic.in/Economic%20Survey%202017.pdf>
- (4) Parson, Talcott. Action Theory and the Human Condition: Free Press. New York; 1978.
- (5) Nomani, M.Z.M. Public Interest Litigation Movement and Consumer Protection in India: In: A. R. Kidwai, Ed. New Directions in Higher Education in India. Viva Books: New Delhi; 2014. p. 152-165.
- (6) Nomani, M.Z.M. Right To Health: A Socio- Legal Perspective. 56 Uppal Publications. New Delhi; 2004.
- (7) The Consumer Protection Act, 1986. (Act 68 of 1986). Government of India: [Internet]. Available from: http://ncdrc.nic.in/1_1.htm
- (8) Pilgaokar Anil. Doctors and Consumer Protection Act: 1986; Edinburgh Medical and Surgical Journal. 1845; p. 63-176.
- (9) Indian Medical Association v. V.P. Shantha, [AIR 1996 SC 550].
- (10) Nomani, M.Z.M. 'Climate Change, Environment Sustainability and Consumer Justice: IV [7 & 8] International Journal of Environmental Consumerism, 2009; p. 52-63.
- (11) Dr. Ashutosh Gupta v. State of J & K, Jammu [SWP No 326 of 2013].
- (12) SukeshChander Khajuria v. State of J & K,[SWP No. 407/1992 vide judgment dated 14.02.1994].
- (13) Department of health and medical education Jammu & Kashmir: [Internet]. [Cited on 2019 July 05]. Available from: <http://jkhealth.org/new2017/govorder.php#>
- (14) Sher-i-Kashmir Institute of Medical Sciences: [Internet]. Available from: https://en.wikipedia.org/wiki/Sher-i-Kashmir_Institute_of_Medical_Sciences
- (15) Nomani, M.Z.M. & Azvar Khan. Consumer Right Awareness and Its Enforcement in Rural and Urban Areas of Muzaffarnagar and Saharanpur District of U.P [Ph.D. Thesis] A.M.U. Aligarh; 2006.
- (16) Sher-i-Kashmir Institute of Medical Sciences: (Grant of Degrees) Act, 1983 (Act of 12 of 1983). [Internet]. [Cited 2019 July 05]. Available from: <http://www.bareactslive.com/JK/JK297.HTM>
- (17) Jammu and Kashmir Consumer Protection Act; 1987: (Act No.16 of 1987) (Dated 29.8.1987). [Internet]. Available from: <http://www.bareactslive.com/JK/JK056.HTM>
- (18) Nomani, M.Z.M. et.al., Consumer Right Awareness & Development of Rural Marketing Strategies in Shamli District of Uttar Pradesh: An Empirical Mapping. in Babita Agarwal Ed. Role of Rural Consumer Awareness in Development of Rural Marketing Strategies, Managlam Publisher & Distributors, Delhi; 2013. p. 79-93.
- (19) Kashmir's dream hospital has seen 12,860 deaths in last 5 years: CAG. The Hindu [Internet]. Available from: <https://www.thehindu.com/news/national/other-states/kashmirs-dream-hospital-has-seen-12860-deaths-in-last-5-years-cag/article4585689.ece>.
- (20) Sharma Anand. VibhakarMansotra, Sourabh Shastri. An Exploratory Analysis of Public Healthcare Data: A Case Study of Jammu & Kashmir State: Asian Journal of Computer and Information Systems. Volume 03, Issue 05, December 2015.

Platelet Rich Fibrin (PRF): Revolutionary Boon to Dentistry

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Abstract

Context: With time, the treatment protocol changes and currently there is a new school of treatment called accelerated orthodontics wherein the goal is to shorten the time needed to align the teeth.

Platelets are one of the initiators both in the soft and hard tissue wound healing processes. They contain growth factors such as the platelet derived growth factor, transforming growth factor, Endothelial growth factor, and others. Platelet-rich fibrin (PRF) is a natural biomaterial with favourable results in orthodontics and other specialities with minimal risk.

The following article attempts to summarise the relevant literature regarding benefits of PRF over PRP, focusing on its preparation, advantages and disadvantages of using it in clinical scenarios in medicine and dentistry, due to its minimally invasive technique and low risks.

Keywords: Platelet-rich fibrin, Platelet-rich plasma, Platelet derived growth factors, Leukocyte platelet rich fibrin, Orthodontic tooth movement, Platelet concentrate,

Introduction

With time, the treatment protocol changes and currently there is a new school of treatment called accelerated orthodontics wherein the goal is to shorten the time needed to align the teeth. Increased duration of treatment poses various risks like pain, caries, white spot lesions, external root resorption etc.

Numerous options have been put forth to accelerate orthodontics such as:

1. Drugs
2. Surgeries
3. Non-surgical methods (PRP, PRF)

Platelet-rich plasma (PRP) is an autologous concentration of human platelets in a small volume of plasma which releases a cocktail of growth factors. PRP is first generation platelet concentrate. However, using it also presents risk because bovine thrombin, which is used to handle PRP, may generate antibodies to factors V, XI, and thrombin that could cause coagulopathies¹.

Platelet-rich fibrin (PRF) is a natural fibrin-based biomaterial prepared from an anticoagulant-free blood harvest without any artificial biochemical modification (no bovine thrombin is required) that allows obtaining fibrin membranes enriched with platelets and growth factors.

Platelets: Platelets are produced from bone marrow cells called megakaryocytes and contain cytoplasmic granules with platelet-specific and non-platelet-specific proteins (fibrinogen, fibronectin etc.). These dense granules have high concentration of calcium, ADP, ATP and serotonin. However, activation of platelets to achieve the healing and repair process is aided by leukocytes².

Matras research in 1970 has led to the extensive use of fibrin glues³.

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In 1997, Whitman et al were the first to use PRP in oral surgical procedures and concluded that it enhanced the osteoprogenitor cells in bone⁴.

Choukroun et al⁵ first used PRFin 2001 which was derived from human blood and contained blood cells including platelets, B- and T-lymphocytes, monocytes, stem cells and growth factors.

Classification: Dohan et al proposed a classification in 2009 and categorized the products on 2 key parameters:

- The presence of a cell content (mostly leukocytes)
- The fibrin architecture.

This separation defined four main families to regroup the products⁶.

1. Pure Platelet-Rich Plasma (P-PRP) Or Leukocyte-Poor Platelet-Rich Plasma: These products are preparations without leukocytes and form a low density fibrin network after activation. Mostly used as a liquid solution or in an activated gel form.

Preparation:

- **Plasmaphoresis:** This was the first method of producing platelet concentrates for topical use. It uses a cell separator that employs a differential ultracentrifugation in which platelets, leucocytes and RBCs are first separated from the PPP, which can then be re-infused to the patient. Optical reader detects the first buffy elements in the serum, that are automatically collected into a separate bag as the platelet concentrate (PRP), when it detects elements of RBCs, platelet collection is interrupted and RBCs, mixed with leucocytes and some residual platelets, are directed towards a third separate collection bag before eventual re-infusion. But the final PRP always contains residual RBCs and leucocytes and this protocol is cumbersome and labour-intensive.

- **Anitua's PRGF (Manual protocol):** Anitua in 1999 described PRGF (Plasma rich in growth factors) wherein venous blood is collected and centrifuged in several small tubes to obtain three typical layers: RBCs, 'buffy coat' and acellular plasma⁷.

The upper half of the acellular plasma is called plasma poor in growth factors (PPGF) and is discarded by careful pipetting. The remaining plasma is termed PRGF and is collected with a pipette. Following this, fibrin polymerization is induced by a 10% calcium chloride

solution which leads to formation of an unstable PRGF gel after 15-20 min that has to be used immediately. This method is inexpensive but lacks reproducibility⁸.

2. Leukocyte and Platelet Rich Plasma (L-PRP):

They were developed with an objective of using platelet which are easy to harvest and does not require transfusion laboratory work.

Preparation:

- **Manual Method:** There are mainly two protocols Curasan (Germany)⁹ and Friudent-Schutze (Austria)¹⁰. The first centrifugation step which separates the blood components into three layers is the same as P-PRP. The PPP and buffy coat layers are collected in another tube and are subjected to a second centrifugation step at high speed, which separates the sample again into its components. PRP concentrate obtained is composed of high quantity of platelets, leucocytes and circulating fibrinogen, but it also contains residual RBCs. The concentrate is applied with bovine thrombin and calcium chloride.

- **Automated protocols:** Systems like PCCS (Platelet Concentrate Collection System) by 3I and Smart PReP by Harvest Corp (USA) have been developed. In the PCCS method, citrated whole blood is transferred into the first compartment and centrifuged to obtain the three layers. Then, using a tubular opening and air pressure, PPP and buffy coat are transferred to the second chamber and centrifuged again but for a longer period. Finally, using the same air pressure system, most of the PPP layer is transferred back into the first compartment and discarded^{11,12}.

The SmartPReP protocol is a multifunctional system, designed to automatically transfer the upper layers (PPP and buffy coat) into the second chamber based on variations in weight and centrifugation speed.

3. Pure Platelet-Rich Fibrin (P-PRF) Or Leukocyte-Poor Platelet-Rich Fibrin: They are preparations without leukocytes and with a high-density fibrin network, exist only in gel form and cannot be injected.

Preparation:

- The only one product commercially available is known as Fibrinet PRFM (Platelet-Rich Fibrin Matrix) kit by Cascade Medical (USA). Small amount of blood is drawn into a collection tube, which has trisodium

citrate as an anticoagulant and separator gel, which is centrifuged for six minutes at high speed. The three typical layers are obtained out of which buffy coat and PPP are easily transferred to a second tube containing CaCl_2 wherein clotting process is triggered and the tube is immediately centrifuged for 15 min leading to formation of a stable PRFM clot. It is claimed to be natural concentrate due to the absence of bovine thrombin¹¹.

4. Leukocyte- And Platelet-Rich Fibrin (L-PRF): Choukroun's Prf: Choukroun's PRF protocol was developed in France⁵. It can be considered as second-generation platelet concentrate because it is natural without any anticoagulants.

Preparation:

- Venous blood is collected in glass tubes and centrifuged at low speed. In the absence of anticoagulants, platelet activation and fibrin polymerization are triggered immediately and three layers are formed: the RBC base layer, acellular plasma top layer and a PRF clot in the middle. The PRF clot forms a strong 3-D fibrin matrix with most of the platelets and leucocytes harvested from the blood. When pressed between two gauzes, the PRF clot becomes a strong membrane which has been used in ENT and Maxillofacial Surgeries etc.
- This method is easy and allows the production of a high quantity of L-PRF clot at low cost.

Biological Activity:

- In vitro activity of L-PRF membrane and P-PRP gel were compared by evaluating the slow release of growth factors and matrix molecules^{13,14}. Both the preparations demonstrated slow release of three key growth factors Transforming Growth Factor $\beta 1$ (TGF $\beta 1$), Platelet-Derived Growth Factor AB (PDGF-AB) and Vascular Endothelial Growth Factor (VEGF) along with matrix proteins and Thrombospondin 1 (TSP1) at an interval of 20 min, 1hr, 4hr, 24hr, 72hr, 120hr and 168hr.
- Dohan et al reported that L- PRF membrane remained intact for 7 days and released a large quantity of growth factors continuously¹⁵. On the contrary, the P-PRP gel released most of its growth factors in the first hours and got completely dissolved in the medium after 3 days.

- These studies concluded that PRF families undergo natural polymerization with release of intrinsic growth factors whereas PRP gel families demonstrate artificially provoked polymerization with extrinsic growth factors leading to their immediate release and destruction.

Clinical Applications:

In Dentistry:

- The L-PRF is mostly used in oral and maxillofacial surgery as L-PRF clots and it presents a volume and shape easy to combine with most surgical techniques, as filling and interposition healing biomaterial or as protection healing membrane.
- In periodontal bone defects to achieve reduction in probing depth and filling of radiographic defect¹⁶.
- Reduction of osteitis in surgical sites of the third molars¹⁷.
- As an adjunct to palatal wound healing after harvesting a free gingival graft¹⁸.
- In multiple extraction cases to preserve the alveolar ridge height¹⁹.
- Bone regeneration around implants, inside the alveolar defect¹⁹.

General:

- Reconstruction of large bone defects post cancer surgery²⁰.
- Membrane form is used in otological surgeries²¹.

Orthodontics:

- L-PRF has been used in PAOO (Periodontally Accelerated Osteogenic Orthodontics). Combining it with traditional bone grafts potentially accelerates wound healing and reduces post-surgical pain, inflammation, infection without interfering with tooth movement or post-orthodontic stability²².
- A randomized control trial was conducted to study the effect of autologous leukocyte platelet rich fibrin on the rate of orthodontic tooth movement that concluded the rate of movement was higher in the experimental group to that of the control group²³.
- Effects of PRP on the rate of orthodontic tooth movement have been investigated in six skeletally mature male mongrel dogs that showed maxillary tooth movement to be significantly faster on the

experimental side compared to the control side (mean of 15.60mm versus 9.46mm)²⁴.

- Effects of different concentrations of PRP on alveolar bone density and orthodontic tooth movement shows that injection of both moderate and high concentrations of PRP might accelerate orthodontic tooth movement by decreasing alveolar bone density on para-dental tissues by enhancing osteoclastic activity in a transient way²⁵.
- PRP and alveolar bone grafting done in cleft patients revealed bone grafts with the use of PRP showed significantly more bone density up to 6-months post-surgery and pain and swelling persisted for longer period in control group²⁶.

Clinical trials are being conducted to test the efficacy of i-PRF (injectable platelet rich fibrin). i-PRF provides an edge in accelerating treatment with PRF being superior to PRP and the injectable form making it a lesser invasive procedure²⁷.

Conclusion

The application of different forms of PRF is becoming well established in many fields of both medicine and dentistry. On one hand, its use in implant dentistry and oral surgery may seem obvious, but on the other side its use is still being anticipated in orthodontics. The clinical efficacy of this rapidly evolving area will need to be carefully watched as laboratory based studies are undertaken in clinical practice. Clinical studies have been done already, these are often limited to small numbers of patients and this may, for the time being, limit its widespread use. Further studies should involve well planned randomised controlled trials investigating not only the potential benefits of PRF but also any potential risks or complications.

Ethical Clearance: Ethical committee gave a waiver as it is a review article.

Source of Funding: Self

Conflict of Interest: Nil

References

1. Kiran NK, Mukunda KS and Tilak Raj TN. Platelet concentrates: A promising innovation in dentistry. *J Dent Sci Res* 2011;2:50-61.
2. Dohan DM, Choukroun J, Diss A, Dohan SL, Dohan AJ, Mouhyi J and Gogly B. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part II: platelet-related biologic features. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2006;101:e45-50.
3. Matras H. Die Wirkungen verschiedener Fibrinpräparate auf Kontinuitätsstrennungen der Rattenhaut. *Osterr Z Stomatol.* 1970;67:338-359.
3. Whitmann DH, Berry RL and Green DM. Platelet gel: an alternative to fibrin glue with applications in oral and maxillofacial surgery. *J Oral Maxillofac Surg* 1997;55:1294-1299.
4. Choukroun J, Adda F, Schoeffler C and Vervelle A. Une opportunité en parodontologie: le PRF. *Implantodontie* 2000;42:55-62.
5. Dohan Ehrenfest DM, Rasmusson L, Albrektsson T. Classification of platelet concentrates: from pure platelet-rich plasma (P-PRP) to leucocyte- and platelet-rich fibrin (L-PRF). *Trends Biotechnol.* 2009;27:158-167.
6. Anitua, E. Plasma rich in growth factors: preliminary results of use in the preparation of future sites for implants. *Int. J. Oral Maxillofac. Implants* 1999;14:529-535.
7. Anitua E., Sánchez M., Orive G. and Andía I. The potential impact of the preparation rich in growth factors (PRGF) in different medical fields. *Biomaterials.* 2007;28:4551-456.
8. Weibrich, Gernot & Kleis, Wilfried & Hafner, Gerd & Hitzler, Walter & Wagner, Wilfried. Comparison of platelet, leukocyte, and growth factor levels in point-of-care platelet-enriched plasma, prepared using a modified Curasan kit, with preparations received from a local blood bank. *Clinical oral implants research.* 2003;14:357-362
9. Weibrich, Gernot & Kleis, Wilfried & Buch, Richard & Hitzler, Walter & Hafner, Gerd. The Harvest Smart PRP/PTM system versus the Frident-Schutze platelet-rich plasma kit. *Clin. Oral Implants Res* 2003;14:233-239
10. Leitner, Gerda & Gruber, Reinhard & Neumüller, Josef & Wagner, A & Kloimstein, P & Höcker et al. Platelet content and growth factor release in platelet-rich plasma: a comparison of four different systems. *Vox Sang.* 2006;91:135-139
11. Weibrich, Gernot & Kleis, Wilfried & Hitzler, Walter & Hafner, Gerd. Comparison of the platelet concentrate collection system with the plasma-rich-in-growth-factors kit to produce platelet-rich

- plasma: a technical report. *Int. J. Oral Maxillofac. Implants* 2005;20:118–123
12. David M. Dohan Ehrenfest, Tomasz Bielecki, Ryo Jimbo, Giovanni Barbe, Marco Del Corso, Francesco Inchingolo et al. Do the Fibrin Architecture and Leukocyte Content Influence the Growth Factor Release of Platelet Concentrates? An Evidence-based Answer Comparing a Pure Platelet-Rich Plasma (P-PRP) Gel and a Leukocyte- and Platelet-Rich Fibrin (L-PRF)”, *Current Pharmaceutical Biotechnology*. 2012;13: 1145.
 13. Zumstein MA, Bielecki T, Dohan Ehrenfest DM. The Future of Platelet Concentrates in Sports Medicine: Platelet-Rich Plasma, Platelet-Rich Fibrin, and the Impact of Scaffolds and Cells on the Long-term Delivery of Growth Factors. *Operative Techniques in Sports Medicine*. 2011;19:190-197.
 14. Dohan Ehrenfest DM, de Peppo GM, Doglioli P, Sammartino G. Slow release of growth factors and thrombospondin-1 in Choukroun’s platelet-rich fibrin (PRF): a gold standard to achieve for all surgical platelet con-centrates technologies. *Growth Factors*. 2009;27:63-69.
 15. Chang YC and Zhao JH. Effects of platelet-rich fibrin on human periodontal ligament fibroblasts and application for periodontal infrabony defects. *Aust Dent J* 2011;56: 365-371.
 16. Hoaglin DR and Lines GK. Prevention of localized osteitis in mandibular third-molar sites using platelet-rich fibrin. *Int J Dent* 2013; 2013:875380.
 17. Kulkarni MR, Thomas BS, Varghese JM and Bhat GS. Platelet-rich fibrin as an adjunct to palatal wound healing after harvesting a free gingival graft: A case series. *J Indian Soc Periodontol* 2014;18:399-402.
 18. Simonpieri A, Del Corso M, Vervelle A, Jimbo R, Inchingolo F, Sammartino G and Dohan Ehrenfest DM. Current knowledge and perspectives for the use of platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) in oral and maxillofacial surgery part 2: Bone graft, implant and reconstructive surgery. *Curr Pharm Biotechnol* 2012;13:1231-1256.
 19. Reyes M, Montero S, Cifuentes J and Zarzar E. Extraction technique and surgical use of the plasma rich in growth factors (P.R.G.F.): Update. *Rev Dent Chile* 2002;93:25-28.
 20. Choukroun JI, Braccini F, Diss A, Giordano G, Doglioli P and Dohan DM. Influence of platelet rich fibrin (PRF) on proliferation of human pre-adipocytes and tympanic keratinocytes: A new opportunity in facial lipostucture (Coleman’s technique) and tympanoplasty. *Rev Laryngol Otol Rhinol (Bord)* 2007;128:27-32.
 21. Muñoz F, Jiménez C, Espinoza D, Vervelle A, Beugnet J, Haidar Z. Use of leukocyte and platelet-rich fibrin (L-PRF) in periodontally accelerated osteogenic orthodontics (PAOO): Clinical effects on edema and pain. *J Clin Exp Dent*. 2016;8:119-24.
 22. Tehranchi A, Behnia H, Pourdanesh F, Behnia P, Pinto N, Younessian F. The effect of autologous leukocyte platelet rich fibrin on the rate of orthodontic tooth movement: A prospective randomized clinical trial. *Eur J Dent*. 2018;12:350–357.
 23. Rashid A, ElSharaby FA, Nassef EM, Mehanni S, Mostafa YA. Effect of platelet-rich plasma on orthodontic tooth movement in dogs. *Orthod Craniofac Res*. 2017;20:102-110.
 24. Güleç A, Bakkalbasi BC, Cumbul A, Uslu U, Alec B, Yarat A. Effects of local platelet-rich plasma injection on the rate of orthodontic tooth movement in a rat model: A histomorphometric study. *Am J Orthod Dentofacial Orthop*. 2017;151:92-104.
 25. Gupta C, Mehrotra D, Mohammad S, Khanna V, Singh GK, Singh G, et al. Alveolar bone graft with platelet rich plasma in cleft alveolus. *J Oral Biol Craniofac Res*. 2013;3:3-8.
 26. ClinicalTrial.org [Internet]. Efficacy of Injectable Platelet Rich Fibrin (i-PRF) in Enhancing Bone Quality [updated 2019 July 18]. Available from: <https://clinicaltrials.gov/ct2/show/NCT03399760>

Compliance of the Cigarettes and Other Tobacco Products Act (Cotpa) 2003: A Baseline Survey in Vijayapura District of North Karnataka

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Abstract

Introduction: According to WHO, tobacco use is considered a single most preventable cause of death. According to Global Adult Tobacco Survey 2009-10, almost 1 in every 2 adult males and 1 in 5 adult females use tobacco in some form in India. In 2003, the Government of India enacted comprehensive legislation for tobacco control called the Cigarettes and Other Tobacco Products (Prohibition of Advertisement and Regulation of Trade and Commerce, Production, Supply and Distribution) Act (COTPA). The purpose of the COTPA Act is fulfilled only when the community takes participation in its strict implementation.

Objectives: To measure the level of compliance to COTPA-2003 in Vijayapura district of North Karnataka.

Method: A cross sectional survey was planned to assess the implementation of COTPA 2003 in Vijayapura district by using structured Interview method for a period of two months. Around 250 places were assessed in five taluka head quarters each of the district by using proforma based on the regulations given in Section 4, 5, 6a, 6b, 7,8,9 of COTPA 2003.

Results: Implementation level found in the district was 30% for section-4, 84% for section-5, 92% for section-6a, for 64% section-6b and 99% for section-7, 8, 9.

Conclusions: COTPA includes measures that are intended to protect residents from exposure to secondhand smoke, to significantly restrict tobacco advertising and to eliminate easy access to tobacco products by youth. The COTPA-2003 implementation in all the taluka headquarters of district is found less as expected. The reason may be less awareness regarding the act & the punishment followed after violation.

Keywords: COTPA, Compliance, Section, Tobacco, Regulation.

Introduction

According to World Health Organization, tobacco use is considered a single most preventable cause of

death.¹ Tobacco use kills one-third to one half of all lifetime users prematurely. Tobacco-related illnesses account for 1 in 10 adult deaths worldwide, and if current trends continue, one billion people are estimated to die from tobacco use in the 21st century.^{2,3}

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India is the third largest producer of tobacco worldwide and ranks second in total tobacco products consumption. According to Global Adult Tobacco Survey 2009-10, almost 1 in every 2 adult males and 1 in 5 adult females use tobacco in some form in India. Smokers are not the only ones sickened and killed

by tobacco; scientific evidences have unequivocally established that exposure to second hand smoke is as harmful as active smoking and causes death, disease and disability.³

Considering the harmful effects of tobacco, the WHO in 2003 negotiated the world's first public health treaty called "The Framework Convention on Tobacco Control" (FCTC), which mandates governments of all nations to take specific steps to reduce tobacco use. Article 8 of the FCTC binds governments to protect their citizens from exposure to tobacco smoke and requires them to adopt and implement effective legislative, executive, administrative and/or other measures for this purpose.⁴

In 2003, the Government of India enacted comprehensive legislation for tobacco control called the Cigarettes and Other Tobacco Products (Prohibition of Advertisement and Regulation of Trade and Commerce, Production, Supply and Distribution) Act (hereafter referred to as COTPA) – which prohibits smoking in public places and requires display of 'No smoking' signage with proper specifications at conspicuous points.⁵

Provisions under the Act prohibits smoking of tobacco in public places (Section-4), Advertisement of tobacco products including cigarettes is prohibited (Section-5), Tobacco products cannot be sold to person below the age of 18years (Section-6a) and in places within 100 meters radius from the outer boundary of an institution of education (Section-6b), Tobacco products must be sold, supplied or distributed in a package which shall contain an appropriate pictorial warning, its nicotine and tar contents (Section-7,8,9).⁶

Mere enactment of legislation is not enough to stop smoking in public places and it requires strong enforcement to ensure compliance to the law by the public. So the study was planned to know the extent of adherence to the regulations of Law by the community.

Methodology: A cross sectional survey was conducted to measure the level of compliance to COTPA-2003 in public places, at Points of sale, in Educational institutions and with regards to other regulations of Act in the Vijayapura district situated in North part Karnataka state in India in February & March 2019.

With 95% confidence level and margin of error of

±3%, a sample size of 1067 places allowed the study to determine the compliance of COPTA in all talukas of Vijayapura district. After round off the figure, recruitment target was set at 1080 places (216 places per taluka head quarters – that includes Public places, Point of sale & educational institutes together) Sample size was calculated by using the formula: $n = \frac{z^2 p(1-p)}{d^2}$ Where Z= z statistic at 5% level of significance, d is margin of error and p is anticipated prevalence rate (50%).

The study was conducted in head quarters of all talukas present in the Vijayapura district. The district contains five talukas namely Vijayapura, Indi, Sindagi, BasavanBagewadi&Muddebihal. By keeping the main Bus stand as central point the team moved in all directions (preferably main roads) till the desired sample is covered for all the sections. If the desired sample is not achieved, next main roads or crowded places like markets were surveyed by using the checklist. Educational institute present on the way of survey were included and those which are situated in faraway places were visited by using private vehicle till desired sample was achieved. Purpose of the survey was explained at educational institutions & at point of sale before collection of information.

Study Units:

Section 4: Public places means any place to which the public have access and includes auditoriums, movie theatres, hospitals, public transport (aircraft, buses, trains, metros, monorails, taxis,) and their related facilities (bus stands/stations, railway stations), restaurants, hotels, bars, amusement centres, offices (government and private), libraries, courts, post offices, markets, shopping malls, canteens, refreshment rooms, banquet halls, coffee houses, educational institutions and parks.

Section 5: Points of sale where tobacco products are sold in each taluka headquarters were selected to observe the advertisement of tobacco products.

Section 6a: The points of sale where tobacco products are sold in each taluka headquarters were considered.

Section 6b: Educational Institutions is a place including any school/college/institution where education is imparted by an appropriate authority. The educational institutions present in taluka headquarters

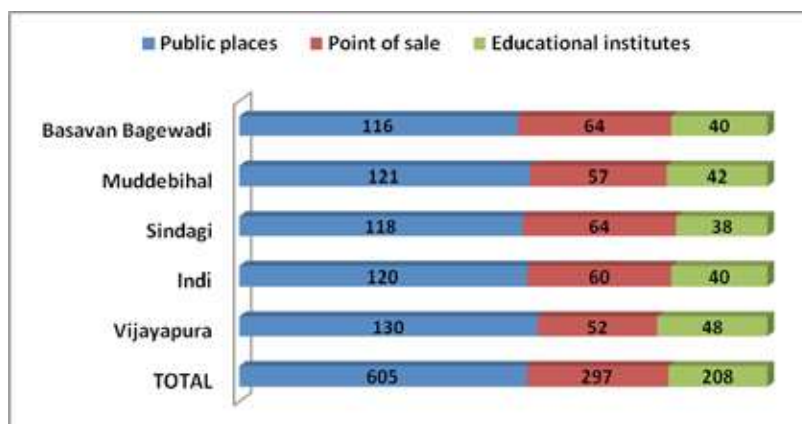
were considered for the study.

Section 7, 8, 9: The Packaged tobacco products were observed in each points of sale (POS) as identified under section 5 & 6a.

Statistical analysis of the information collected were summarized descriptively and presented diagrammatically.

Observations: Total around 240 to 250 visits were done to assess the compliance of COTPA-2003 in each taluka head quartersof Vijayapura district. Following were the observation made during the visits,

Figure 1: Taluka Wise Distribution of Visits Made During the Survey.



Nearly equal numbers of places were visited during the survey in all the taluka headquarters as shown in figure I.

Table 1: Compliance to COTPA-2003 regulations in Vijayapura district

COTPA-2003	Regulations	Number	%
Section-4	People found smoking during visit	127	21
	‘NO SMOKING’ warning board NOT displayed according to the guidelines	423	70
	Smoking aids were present	17	03
	Used cigarettes / bidis found	42	07
Section-5	Tobacco product advertisement in POS- present	48	16
	Promotion of any brand name of tobacco product	14	05
Section-6a	Sale of tobacco to minors observed	17	06
	Sale of tobacco by minors observed	03	01
	Shopkeeper asking age of purchaser of tobacco products	00	00
	Tobacco products are easily visible	240	80
	Display of ‘prohibition of sell of Tobacco products to minors’ present	23	08
Section-6b	Sale of Tobacco products within 100 yards present	74	36
	Information regarding section 6b displayed	33	16
	Display NOT according to the guidelines	190	91
Section-7,8,9	Health warning present		100%
	Nicotine content, Mentioned		00%
	Health warning get damaged, while opening		55%
	Helpline number to quit tobacco mentioned		100%

About 70% public places not found following the rule of displaying **NOSMOKING** board according to the guidelines but among those who displayed only 12% were according to the guidelines. Among the boards of ‘NO SMOKING’ displayed in public places majority were in language Kannada (65%) followed by English (27%) and Hindi (08%). In few places smoking aids (3%) were present, which facilitates smoking in public places whereas in

7% of places used smoking buds were found during the visit.

Violation of Section-4 of COTPA is observed in public places with respect to open smoking in eating (13%) & accommodation facility (9%) followed by working places (10%) during the visits. Out of 30% public places where 'NO SMOKING' board was displayed, majority were eating (30) & accommodation facility (27%).

The violation of section-5 regarding displaying of advertisement of tobacco products was observed in 16% of Point of Sale and all of them were belonging to print type; illuminated & non-illuminated forms. Brand which is most commonly seen advertising is 'GOLD FLAKE' cigarette.

The sale of tobacco products was seen in Grocery shops also (19%) next to shops selling similar type products (65%). Sale of tobacco to minors (section-5) was observed in around 6% of point of sales during the visit whereas the shopkeeper was found not enquiring the age in any of the cases or in general also. In few shops (6%) of Vijayapura taluka, selling of tobacco by minors was found on observation but they were not accepting their age as less than 18 years during interview.

Awareness regarding asking the age of purchasers during selling tobacco by shopkeeper was found around 41% whereas displaying warning according to section-6a of COTPA was found only in 8% of point of sales. In 80% of point of sales, there was open exhibition of tobacco products, which was very easily visible and found attractive to the purchasers particularly adolescent age groups.

Sale of tobacco products was found in surrounding area of 36% of educational institutes and they were situated on an average 50 meters distance from them. Very less number of educational institutes (16%) followed the rule of displaying No Tobacco sale near the school premises & among them who followed around 50% was according to the guidelines of Section-6a of COTPA.

Display of health warning both textual & pictorial was found on all the tobacco products as per the guidelines of Section 7, 8, 9 of COTPA. Most common health warning present was 'Tobacco causes cancer' then 'Tobacco causes painful death'. No tobacco products mentioned Nicotine content on the packets whereas

Helpline number to quit tobacco was mentioned in all the products including local made.

Discussion

Present study found compliance to the regulations of COTPA-2003 in the district was 30% for section-4, 84% for section-5, 92% for section-6a, for 64% section-6b and 99.9% for section-7,8,9.

Similar studies were conducted by Tripathy et al.⁷ who found a mere 23% compliance of Section 4 of COTPA at a tertiary health-care institution in a smoke-free city of India. In study done by Goel et al.⁸ found very high compliance rate of 92.3% for Section-4 of COTPA in a district of North India.

The COTPA Sections 4 and 5 violation was 134 (67%) and 94 (47%), respectively. A total of 124 (62%) of the educational institutions had tobacco vendors within 100 yards, and only 30 (15%) had signboard for the prohibition of tobacco use. Around 14 tobacco vendors had bidis without proper pictorial warning with them which violated Section 7 of COTPA.⁹

Among the 100 Educational Institutes surveyed (53 government, 47 private), tobacco products were sold at 43 outlets within a radius of 100 yards of 27 EIs. No outlet had a display board prohibiting sale of tobacco products to minors. One outlet sold tobacco products to minors during the period of observation, but sale of tobacco products by minors was not observed. Only 38% of EIs displayed board prohibiting tobacco sales; private EIs were significantly less likely to display signs prohibiting tobacco sales than government EIs.¹⁰

Signage indicating ban on smoking was seen at 71.9% places. Active smoking was absent at 77.2% places. About 25% shops around the institutes were found selling tobacco products. Signage displaying ban on sale within 100m of educational institution and sale to minors was not observed at any shop. Tobacco product vendor was seen around 80% of educational buildings. Tobacco free institution signage was seen at 60% of educational premises.¹¹

The study found moderate to low compliance to the provisions of COTPA regarding the ban on sale of tobacco products, to and by the minors, and around educational institutions. Tobacco products were easily accessible to minors in 57.7% of tobacco shops. The mandatory signages under Section-6(b) of COTPA

were not displayed in less than half of the educational institutions. In nearly one fifth, tobacco products were being sold in and around 100yards of institute's boundary.⁸

Conclusion

COTPA includes measures that are intended to protect residents from exposure to secondhand smoke, to significantly restrict tobacco advertising and to eliminate easy access to tobacco products by youth. The Cigarette & Other Tobacco Products Act 2003 implementation in all the taluka headquarters of Vijayapura district is found less as expected. The main reason found behind this is low awareness regarding the act. Public places are the places where the crowd of the area stays most, is more susceptible for the side effects of second hand smoking if the Act is not effectively implemented. The educational institutes contain the more vulnerable groups of the community i.e. adolescent who are very easy targets for the tobacco sellers who are not following the guidelines of the act.

Recommendations: Increase the awareness regarding side effects of tobacco use and Second hand smoking among the population. Create awareness among the population regarding the rules & regulations of COTPA-2003. Regular inspection of the facilities followed by strict enforcement of law by the authorities on those who violate it. License of the point of sale should be held in suspension or canceled if the guidelines are not followed.

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Conflict of Interest: Nil.

Ethical Clearance: Taken from the Institutional Ethics Committee

References

1. World Health Organization. WHO Report on the Global Tobacco Epidemic, 2008: The MPOWER Package. Geneva: World Health Organization; 2008.
2. <http://www.searo.who.int/thailand/factsheets/fs0028/en/>
3. Gauravi A. Mishra, Sharmila A. Pimple, Surendra S. Shastri. An overview of the tobacco problem in India. *Indian J Med Paediatr Oncol.* 2012 Jul-Sep; 33(3): 139–145.
4. https://www.who.int/tobacco/framework/WHO_FCTC_english.pdf
5. Goel S, Ravindra K, Singh RJ, Sharma D. Effective smoke-free policies in achieving a high level of compliance with smoke-free law: Experiences from a district of North India. *Tob Control* 2014;23:2914.
6. The Cigarettes and Other Tobacco Products (Prohibition of Advertisement and regulation of Trade and Commerce, Production, Supply and Distribution) Act, 2003; An Act enacted by the Parliament of Republic of India by Notification in the Official Gazette (Act 32 of 2003). Available from: <https://nhm.gov.in/index4.php?lang=1&level=0&linkid=459&lid=692>
7. Tripathy JP, Goel S, Patro BK. Compliance monitoring of prohibition of smoking (under section-4 of COTPA) at a tertiary health-care institution in a smoke-free city of India. *Lung India* 2013;30:312-5.
8. Goel S, Kumar R, Lal P, Singh RJ. How effective is tobacco control enforcement to protect minors: Results from subnational surveys across four districts in India. *Int J Non-CommunDis* 2016;1(3):116-21.
9. Khargekar NC, Debnath A, Khargekar NR, Shetty P, Khargekar V. Compliance of cigarettes and other tobacco products act among tobacco vendors, educational institutions and public places in Bengaluru City. *Indian J Med Paediatr Oncol* 2018;39:463-6.
10. Rajesh Yadav, LeimapokpamSwasticharan, and Renu Garg. Compliance of Specific Provisions of Tobacco Control Law around Educational Institutions in Delhi, India. *Int J Prev Med* 2017;8:62.
11. Thakur A et al. Assessment of compliance to the COTPA 2003 legislation in tertiary healthcare institutes of Shimla: a smoke free city in India. *Int J Community Med Public Health.* 2019 Mar;6(3):1229-1234.

One Year Clinical Evaluation of Different Bulk Fill Restorative Resins in Class-I Restorations

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Abstract

Context: The aim of this study is to compare the one year clinical performance of three bulk fill restorative materials in posterior class I occlusal restorations. 20 patients received three class I with one of three bulkfill restorative resins. Sonicfill, Tetric Evoceram and Filtek bulkfill. All restorations were evaluated at baseline, at three, six, nine months, and one year after placement. Two calibrated examiners other than the operator were evaluated each restoration. Modified USPHS criteria was used to evaluate the restorations. The results were statistically insignificant. More studies need to be carried out and for a long period of time.

Keywords: Resin based composites, bulkfill composites, clinical performance.

Introduction

With the increasing awareness among the patients there is a rise in the demand for aesthetic restorative materials even for the posterior teeth. So dental composites, have been an obvious choice for restorative material. But, the conventional layering or incremental technique used in dental composites is cumbersome and time consuming. This has led to the innovation of a new class of resin based composite (RBC) materials. They are an attempt to speed up the restoration process by enabling up to 4 or 5 mm thick increments (bulk fill) to

be cured in one step, thus skipping the time consuming layering process.¹

The main concern while using the bulk fill composites is potentially increased polymerization shrinkage stress at the tooth material interface.² The physical mismatch between the shrinkage prone restorative material and the stiffer tooth structure could result in micro leakage, marginal staining and post-operative sensitivity. This could lead to compromise in the physical and mechanical properties of the restoratives having a detrimental effect on their clinical performance.^{3,4}

The aim of this study was to compare the one year clinical performance of three bulk fill restorative materials in posterior class I occlusal restorations.

Method & Material

Selection Criteria: Twenty three patients with ages ranging from 18 to 30 years and having at least three class I carious lesions were included in the study. The approval for this clinical study was obtained from

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The Ethical committee, Maharshi Markandeshwar University, Ambala.

For the inclusion in the study the tooth to be restored were vital without pulpal or periodontal disease with at least one neighboring tooth present and an existing occlusal contact. The specific exclusion criteria included patients with poor oral hygiene, pulpal or periodontal disease, pain and preoperative sensitivity, serious health problems, heavy bruxism, known allergy to the substances used in the study. The patients were informed about the procedure and asked to sign the informed consent before the clinical procedures.

Restorative Procedure: All operative procedures were performed by same operator. Before starting with the cavity preparation bitewing radiographs were taken to evaluate the extent of caries. Class I cavity were prepared using a diamond abrasives with a high speed hand piece. The cavity design was restricted to eliminate carious tissues only. The grouping will be based on the resin based composites used. The details about these composites is summarized in table 2.

Group.1: Teeth restored with Sonic Fill bulk fill resin based composite. (Kerr Corporation)

Group.2: Teeth restored with Tetric Evoceram bulk fill resin based composite. (IvoclarVivadent, Inc.)

Group.3: Teeth restored with Filtek Bulkfill posterior restorative resin based composite.(3M ESPE, St. Paul, USA))

A standardised procedure was followed for etching and bonding for all the cavity preparation in all the three groups. Following which restorative resins were placed in bulk with help of filling instruments, additionally the dispensing gun was used for Filtek bulkfill and for placing the sonic fill bulkfill composite, sonic fill hand piece was used. It vibrated at 5 – 6 kHz, ejection force ranges between 0 to 170 N. After placement of composite, curing was done for 40 seconds. Then finishing was accomplished using finishing burs as per the protocol.

Clinical Evaluation: The restorations were evaluated by two calibrated examiners at Baseline (1 week after restoration), 3 months, 6months, 9 months and 1 year using mirrors and probes following the Modified USPHS (US Public Health Service)criteria described by Cvar and Ryge . The post operative

evaluation was done by tactile method using probe and stream of compressed air for 5 seconds. The restorations were examined and labelled as Alpha (highest score of clinical acceptability), Bravo, Charlie and Delta to indicate the degree of clinical acceptability at every visit

Alpha: Perfect

Bravo: not perfect, but clinically acceptable

Charlie: restoration requires replacement

Delta: failure

Any discrepancy in evaluation between the two evaluators was immediately resolved at chair side. The three restorative materials for each criteria were compared using Chi-square test, Kruskal – wallis test at a significance level of 0.05.

Results

A total of 69 restorations were placed in 23 patients. There were three types of restoration in each patient. The recall rate was 100% at one year period.

The result of this study are summarized in tables (1-6). This presents the data for anatomic form, secondary caries, color match, retention, marginal adaptation, marginal discoloration, surface texture.

All the restorations were scored as alpha for **anatomic form** at the baseline. After one year one sonicfill restoration received a Bravo. There were no significant different among the restorative groups in terms of anatomic form.

In terms of **secondary caries**, all the teeth scored alpha. At the end of one year there were no loss of restorations, a 100% retention rate was recorded for all three restorative materials.

There were no significant differences among the restorative groups in terms of color match. Tetric evoceram shows all alpha scores at the end of one year. Sonic fill and Filtek restorations received one bravo score.

In the **marginal adaptation**, filtek bulkfill received the highest numbers of Bravo scores at the end of one year. Sonicfill received two bravo scores, but none of the restoration of tetric evoceram received a bravo score. There were no statistical differences among the restorations.

In terms of **marginal discoloration**, only one restoration from sonicfill and one from filtek bulkfill received bravo scores, whereas all restorations from tetric evoceram received alpha at the end of one year. No significant differences were observed in surface texture between the restorative materials. The results for intragroup comparison between baseline and each evaluation period were statistically insignificant. (P>0.05).

Table 1: Baseline Parameters

	Group I	Group II	Group III
Color match A	23/23	23/23	23/23
Secondary caries A	23/23	23/23	23/23
Surface roughness A	23/23	23/23	23/23
Marginal adaptation A	23/23	23/23	23/23
Retention A	23/23	23/23	23/23
Anatomic form A	23/23	23/23	23/23
Sensitivity A	23/20		
Sensitivity B	23/2	23/23	23/23
Sensitivity C	23/1		
Marginal staining A	23/23	23/23	23/23

Table 2: Parameters after Three months

	Group I	Group II	Group III
Color match A	23/23	23/23	23/23
Secondary caries A	23/23	23/23	23/23
Surface roughness A	23/23	23/23	23/23
Marginal adaptation A	23/22	23/23	23/23
Marginal adaptation B	23/1		
Retention A	23/23	23/23	23/23
Anatomic form A	23/22	23/23	23/23
Anatomic form B	23/1		
Sensitivity A	23/22	23/23	23/22
Sensitivity B	23/1		23/1
Marginal staining A	23/23	23/23	23/23

Table 3: Parameters after Six months

	Group I	Group II	Group III
Color match A	23/23	23/23	23/23
Secondary caries A	23/23	23/23	23/23
Surface roughness A	23/23	23/23	23/23
Marginal adaptation A	23/21	23/23	23/23
Marginal adaptation B	23/2		
Retention A	23/23	23/23	23/23
Anatomic form A	23/22	23/23	23/23
Anatomic form B	23/1		
Sensitivity A			23/21
Sensitivity B	23/23	23/23	23/1
Sensitivity C			23/1
Marginal staining A	23/23	23/23	23/23

With regard to **post-operative sensitivity**, one from sonicfill at the baseline, one from filtek bulkfill at the 6 month period scored charlie. Tetric evoceram showed excellent results that is all alpha score at the end of one year. There were no statistically significant differences among the restorations in terms of post-operative Sensitivity.

Table 4: Parameters after Nine months

	Group I	Group II	Group III
Color Match A	23/22		23/22
Color Match B	23/1	23/23	23/1
Secondary caries A	23/23	23/23	23/23
Surface roughness A	23/23	23/23	23/23
Marginal adaptation A	23/22	23/23	23/22
Marginal adaptation B	23/1		23/1
Retention A	23/23	23/23	23/23
Anatomic form A	23/22	23/23	23/23
Anatomic form B	23/1		
Sensitivity A			
Sensitivity B	23/23	23/23	23/23
Marginal Staining A	23/22	23/23	23/23
Marginal Staining B	23/1		

Table 5: Parameters after One year

	Group I	Group II	Group III
Color match A	23/22	23/22	23/21
Color match B	23/1	23/1	23/2
Secondary caries A	23/23	23/23	23/23
Surface roughness A			23/22
Surface roughness B	23/23	23/23	23/1
Marginal adaptation A	23/21	23/20	23/19
Marginal adaptation B	23/2	23/3	23/4
Retention A	23/23	23/23	23/23
Anatomic form A	23/22	23/23	23/23
Anatomic form B	23/1		
Sensitivity A	23/23	23/22	23/22
Sensitivity B		23/1	23/1
Marginal staining A	23/22	23/22	23/22
Marginal staining B	23/1	23/1	23/1

Discussion

The present study showed that all of the 3 tested materials are suitable and acceptable for restorations involving occlusal surfaces. Moreover, the bulk-fill technology has obvious advantages: 1) fewer voids may be present in the mass of the material, since all of it is placed at one time; 2) the technique would be faster than placing numerous increments if curing times were identical; 3) It may be easier than numerous increments.⁵

The reason for selecting patients with a minimum of three carious lesions, was so that all the three restoratives used in the study received similar oral environmental conditions.

Tetric Evo Ceram Bulk Fill (Ivoclar Vivadent) is a nanohybrid composite and contains in its composition an inhibitor of sensitivity to light and thus provides prolonged time for modeling of filling, an inhibitor of shrinkage stress in order to achieve optimal marginal seal, and Ivocerin, polymerization photoinitiator allowing curing of 4 mm layers of material.⁶

Filtek Bulk Fill posterior restorative (3M ESPE), a low-viscosity, visible-light activated flowable material for filling with bulk-fill technique, is manufactured in four shades (each of which may be polymerized in 4 mm increments according to international ISO standards).⁶

Oscillation energy has been proposed in as a new method to pack resin composite. The principle of this technique assumes that vibration lowers the viscosity of the resin, allowing the material to flow and easily adapt to the cavity walls in a similar way as a flowable resin composite.^{1,4}

Shrinkage stress compensation mechanism in SonicFill system is obtained using a resin having low shrinkage properties and high filler content (84%).⁶ The Sonicfill system composite used in this study is a combination of flowable and universal composites. As sonic energy is applied through the hand piece, the modifier causes the viscosity to drop (up to 87%), increasing the flowability of the composite. When the sonic energy is stopped, the composite returns to a more viscous, non-slumping state.^{5,7} A study found that ultrasonic packing technique resulted in better but not statistically significant different interfacial adaptation values compared to application without ultrasonics of condensable composites.^{4,8}

In this study, Modified USPHS (US Public Health Service) criteria described by Cvar and Ryge has been used. In terms of color match one restorative from all the 3 groups received bravo scores at the end of one year and group 1 and group 3 at the end of 9 months.

In terms of marginal adaptation three restoration from sonic fill and tetric evoceram and five from filtek received Bravo scores at the end of one year. The marginal adaptation is influenced mainly by the polymerization shrinkage of resin composite and the

adhesive type, so both factors might have influenced the clinical results of this study.

A study conducted by Mirosław orłowski et al showed that a higher marginal integrity and lower penetration of dye in fillings inserted using a sonic-activation condensing device was shown when compared with manual condensation. Statistically significant better marginal integrity of Sonic Fill, and Filtek Bulk Fill (compared to the composite Tetric Evo Ceram Bulk Fill), may be due to their flow consistency during application.^{6,7}

Bulk-fill composite materials evaluated in the study by Bowski M. et al seem to meet satisfactorily the requirements of this type of materials in terms of marginal adaptation. The dye penetration test showed no microleakage for high percentage (73.33–93.33%) of tested restorations. Bulk-fill composites are more translucent than other restorations, which allow the light to get to much deeper layers.⁶

Post operative sensitivity is one of the most common complaints of patients with posterior resin restorative in this study. The cavities with class I resin composite restoration were more prone to marginal failure and post operative sensitivity due to of higher cavity configuration factor (C=5).^{5,6} . In the present study tetric evoceram showed least post operative sensitivity.

It is most important to note that the modulus of elasticity is lower in the bulk-fill RBCs than in the nanohybrid and microhybrid RBCs. A material with a low modulus of elasticity, particularly when placed in load-bearing areas, will result in a higher deformability under masticatory stresses. This will cause, as a final consequence, catastrophic failures¹. An exception is Tetric EvoCeram Bulk Fill, which shows moderate values for the modulus of elasticity, albeit having a high filler content. It must, however, be considered that Tetric Evo Ceram Bulk Fill also contains prepolymerized fillers, which is included in the total filler amount. Thus, the inorganic filler content, which in effect increases the modulus of elasticity, is consistently lower.¹ This could be the reason for the better performance of tetric evoceram, though not statistically significant, could be clinically significant.

Further clinical studies addressing different cavity types and longer duration should be conducted.

Conclusion

All the three bulkfill restorative resins showed similar clinical results statistically. Tetric evo-ceram showed a better performance in terms of marginal adaptation and sensitivity, which could be clinically significant and contribute to the clinicians while selecting restorative materials.

Conflicts of Interest: The authors declare that there is no conflict of interest regarding the publication of this paper.

Source of Funding: Self

Ethical Clearance: Ethical clearance has been taken from Institutional Ethical Committee

References

1. Ilie N, Bucuta S, Draenert M. Bulk fill resin based composites: An invitro assessment of their mechanical performance. *Oper Dent.* 2013; 38(6): 618-625.
2. Van Dijken JW . Durability of resin composite restoration in high C- factor cavities: A 12 year followup. *J Dent.* 2010; 38(6): 469-474.
3. Joseph Sabbagh, Sonic Fill TM System: a clinical approach. *Clinical article* 2012.
4. Sara Mohamed Hany et al, Evaluation of Adaptation of Resin composite restorations packed using ultrasonic vibration techniques A systematic review. *Indian Journal of Science and Technology .* 2016 may; 9(18).
5. Atabek Didem et al. Comparitive mechanical properties of bulkfill resins. *Open Journal of composite materials.* 2014;4:117-121.
6. Miroslaw etal, Evaluation of marginal integrity of four bulk-fill composite materials; invitro study. *The scientific World Journal,* 2015
7. Yazici AR, Ustunkol I, Ozgunaltay G, Dayangac B. Three year clinical evaluation of different restorative resins in class I restorations. *Oper Dent.* 2014;39(3): 248-255.
8. Mahmoud SH, El-Embaby AE and AbdAllah AM. Clinical performance of ormocer, nanofilled and nanoceramic resin composites in class I and class II restorations: A three year evaluation. *Oper Dent.* 2014;39(1): 32-42.
9. Baracco B, Perdigao J, Cabrera E, Ceballos L. Two year clinical performance of a low shrinkage composite in posterior restorations. *Oper Dent.* 2013;38(6): 591-600.
10. Baracco B, Perdigao J, Cabrera E, Ceballos L. Clinical evaluation of a low shrinkage composite in posterior restorations: one year results. *Oper Dent.* 2012; 37(2): 117-129.
11. Kiremitic A, Aplalan T, Gurgan S. Six year clinical evaluation of packable composite restorations. *Oper Dent.* 2009;34(1):11-17.
12. Dresch W, Volpato S, Gomes JC, Ribeiro NR, Reis A, Loguercio AD. Clinical evaluation of a nanofilled composite in posterior teeth: 12 month results. *Oper Dent.* 2006; 31(4): 409-417.
13. Abdel-Karim UM, El- Eraky M, Etman WM. Three year clinical evaluation of two nano hybrid giomer restorative composites. *Tanta Dental Journal* 11 (2014) 213-222.
14. Van Dijken JW, Pallesen U. A randomized controlled three year evaluation of “bulk-filled” posterior resin restorations based on stress decreasing resin technology. *Dent Mater* 2014 Sep; 30(9):e245-51.
15. Gaintantzopoulou MD, Gopinath VK, Zinelis S. Evaluation of cavity wall adaptation of bulk esthetic materials to restore class II cavities in primary molars. *Clin Oral Investig.* 2017 May;21(4):1063-1070.
16. Pfeifer CS. Polymer-Based Direct Filling Materials. *Dent Clin North Am* 2017 Oct;61(4):733-750.
17. Colak H, Tokay U, Uzgur R, Hamidi MM, Ercan E. A prospective, randomized, double-blind clinical trial of one nano-hybrid and one high-viscosity bulk-fill composite restorative systems in class II cavities: 12 months results. *Niger J Clin Pract.* 2017 Jul;20(7):822-831.
18. Fugolin APP, Pfeifer CS . New Resins for Dental Composites. *J Dent Res.* 2017 Sep; 96(10):1085-1091.
19. Van Dijken JW¹, Pallesen U². Posterior bulk-filled resin composite restorations: A 5-year randomized controlled clinical study. *J Dent.* 2016 Aug; 51:29-35.
20. Van Dijken JW, Pallesen U. Randomized 3-year clinical evaluation of Class I and II posterior resin restorations placed with a bulk-fill resin composite and a one-step self-etching adhesive. *J Adhes Dent.* 2015 Feb;17(1):81-8.

21. Yazici AR, Antonson SA, Kutuk ZB, Ergin E. Thirty-Six-Month Clinical Comparison of Bulk Fill and Nanofill Composite Restorations Oper Dent. 2017 Sep/Oct;42(5):478-485.
22. Bayraktar Y, Ercan E, Hamidi MM, Colak H. One year clinical evaluation of different types of bulkfill composites. J Investig Clin Dent 2017 May ; 8(2).
23. Atabek D, Aktas N, Sakaryali D, Bani M. Twoyear clinical performance of sonic – resin placement system in posterior restorations. Quintessence Int 2017; 48(9): 743-751.
24. Van Dijken JW, Pallesen U. Bulk fill posterior resin restorations based on stree-decreasing resin technology – a randomized controlled 6- year evaluation. Eur J Oral Sci 2017 Aug; 125(4): 303-309.

Lower Extremity Perfusion among Patient with Type 2 Diabetes Mellitus in a Tertiary Care Hospital, Kochi

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Abstract

Introduction: Diabetes as one of Non-communicable diseases has consumed a large share of money, material, time and human resources of health systems. Now, due to advancement in lifestyle and industrial process, prevalence of diabetes and its associated complications have been raised. Among these complications, diabetic foot considered as a common complication of diabetes.

Method: The present study was a quantitative quasi experimental two group pretest posttest design. The study was done at Amrita Hospital, Kochi. The main objective of the study was to evaluate the effectiveness of Burger Allen exercise on level of lower extremity perfusion among patients with type 2 Diabetes Mellitus. Totally 100 samples were taken in which 50 are in experimental and 50 in control group using convenience sampling technique.

Results: In the present study, majority were males with the average age among experimental group were 55.30 +- 4.58, 36(72%) and 55.30+- 4.58, 34 (68%) in the control group. The study result showed that mean and standard deviation of ABPI score among both groups on Day 1(0.07±0.01), day 2 (0.05±0.02) and day 3(0.19±0.01). There was statistical significance with the p value <0.01. There was also significant difference between the groups and within the groups in ABPI scores in 3 days among patients with type 2 DM which is significant at <0.05.

Conclusion: In the light of present study result, it depicted that the Buerger Allen exercise improve lower extremity perfusion among patient with type 2 diabetes mellitus.

Keywords: Buerger Allen exercise, Lower extremity perfusion, Type 2 diabetes mellitus.

Introduction

Diabetic mellitus is a group of metabolic disease in which defects in insulin secretion or action result in elevated blood glucose (hyperglycemia). In 2017, The WHO global report on diabetes demonstrates that the number of adults living with diabetes is 422 million adults. 1.6 million deaths are directly attributed to

diabetes each year. Type 2 DM accounts for around 90% of all diabetes worldwide.¹ Reports of type 2 diabetes in children have increased globally. Diabetes currently affects more than 62 million Indians, which is more than 7.1% of adult population. The average age of onset is 42 years. Nearly 1 million Indians die due to diabetes every year. Kerala is known as diabetes capital of India as prevalence of diabetes is high 20% which is double the national average of 8%. As compared the prevalence in Thiruvananthapuram was 17%, in Hyderabad and New Delhi 15%, in Nagpur 4% and in Dibrugarh 3%.²

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Diabetic foot complication is a major cause of disability, reduced quality of life, prolonged

hospitalization, financial loss, lower limb amputation and mortality rate.^{3,4} People with diabetes develop foot ulcers because of neuropathy, vascular insufficiency and impaired wound healing.⁵ Nearly 90% of diabetes related lower limb amputations were preceded by foot ulcers.⁶ The value of these exercises had frequently been emphasized by Allen, many medical experts considered them as important adjuvant treatment and postoperative care for circulatory disturbances in the extremities.^{7,8} The exercises involve the individual lying flat in bed with the legs elevated at 45 degrees until blanching occurs or for a maximum of 2 minutes. The patient then sits at the edge of the bed with the feet hanging down. Further exercises include dorsiflex, plantar flex, then inward and outward movement of the feet, followed by flexing and extending of the toes for 2 minutes. Finally the individual lies supine with the feet covered with a warm blanket lasting 5 minutes. The whole cycle is repeated 3 to 6 times each session, and the complete sequence is repeated 2- 4 times a day.⁹

The ankle brachial pressure index is a simple non-invasive and inexpensive diagnostic tool of choice for diagnosing peripheral artery disease in diabetic patients. The ABPI is the ratio of the systolic blood pressure in the angle to the systolic blood pressure in the arm. It is an objective indicator of arterial disease that allows the examiner to quantify the degree of stenosis. Doing exercise will help the patient to improve the vascularization and at the same time it will help to improve the wound healing process.

People with long standing Diabetes mellitus develop complication of PAD, which leads to grave complications like gangrene in the lower limbs. The most common symptom is muscle pain in the lower limbs on exercise. In diabetes, pain perception may be blunted by the presence of peripheral neuropathy. Therefore, a patient with diabetes is more likely to present with an ischemic ulcer or gangrene. The use of ankle-brachial-pressure index in the clinic and bedside provide a measure of blood flow to the ankle. This could help early detection, initiate early therapy and may thus reduce the risk of critical limb ischemia and limb loss.

Buerger Allen Exercise is one of the intervention to stimulate the development of collateral circulation in the legs. Primary care providers should focus on prevention by early recognition and prevention of PAD to those at increased risk. An awareness of diagnostic and treatment strategies will enable primary care provide

providers to educate patients. This will help to improve both concordance with treatment and disease outcome. Considering the above factors and review of literature, the investigator felt that all patients with diabetes mellitus should do the

Buerger Allen Exercise to improve lower extremity perfusion.

Methodology: The present study was a quantitative quasi experimental two group pretest posttest design. The study was done at Amrita Hospital, Kochi. The main objective of the study was to evaluate the effectiveness of Burger Allen exercise on level of lower extremity perfusion among patients with type 2 Diabetes Mellitus.

Selection Method of the Study Participants: The study included all patients between 45-60 years with Type 2 Diabetes Mellitus and whose ABPI score was 0.9 -0.4. The sample size was obtained using Master software based on previous article conducted by John J and Rathiga R on effectiveness of Buerger Allen Exercise to improve the lower extremity perfusion among patients with type 2 diabetes mellitus with -80% power, 95% Confidence interval minimum sample size 10 in each group. Totally 100 samples were taken in which 50 are in experimental and 50 in control group using convenience sampling technique. The study excluded patients who are unconscious, disoriented, critically ill, on anti-coagulant therapy, on treatment of deep vein thrombosis and also who are not willing to participate. The ABPI score was obtained by dividing the highest ankle systolic pressure to the highest brachial systolic pressure. After obtaining written informed consent, the ABPI was measured in each subjects and those subjects whose ABPI score was between 0.9 to 0.4 had been given the Buerger Allen Exercise for 12-13 minutes on three days. On the third day again the ankle brachial pressure index was calculated. Ethical clearance had been obtained from the Thesis review committee of AIMS and research Committee of Amrita College of Nursing.

Software Used for Data Entry, Compilation and Statistical Analysis: Microsoft Excel spread sheet was used for data entry and data analysis was done using the SPSS 20.0 version. In this study the quantitative data were expressed in terms of descriptive statistics. Paired t-test had been used for comparing statistical significant to compare the pre- test and post-test scores of ankle brachial pressure index among Type 2 Diabetic

Mellitus patients. Chi-Square test was used to find out the association between ABPI score and selected demographic variables.

Ethical Consideration: The project has been approved by the ethics committee of the institution. Informed consent was obtained from the participants before initiating the study.

Results

In the study, the average age of experimental group is 55.30 +/- 4.58. 36 (72%) were males, almost 45 (90%)

had education up to secondary level, 32 (64%) subjects were employed, 23 (46%) were doing sedentary and moderate work each, 46 (92%) were non-vegetarian diet, 29 (58%) had no ill habits and 33 (66%) had type 2 DM for more than 11 years. Whereas in the control group, the average age is 55.30 +/- 4.58, 34 (68%) were males, 41 (82%) had education up to secondary level, 26 (52%) were unemployed, 31 (62%) were moderate workers, almost 45 (90%) were following non-vegetarian diet, 34 (68%) had no ill habits.

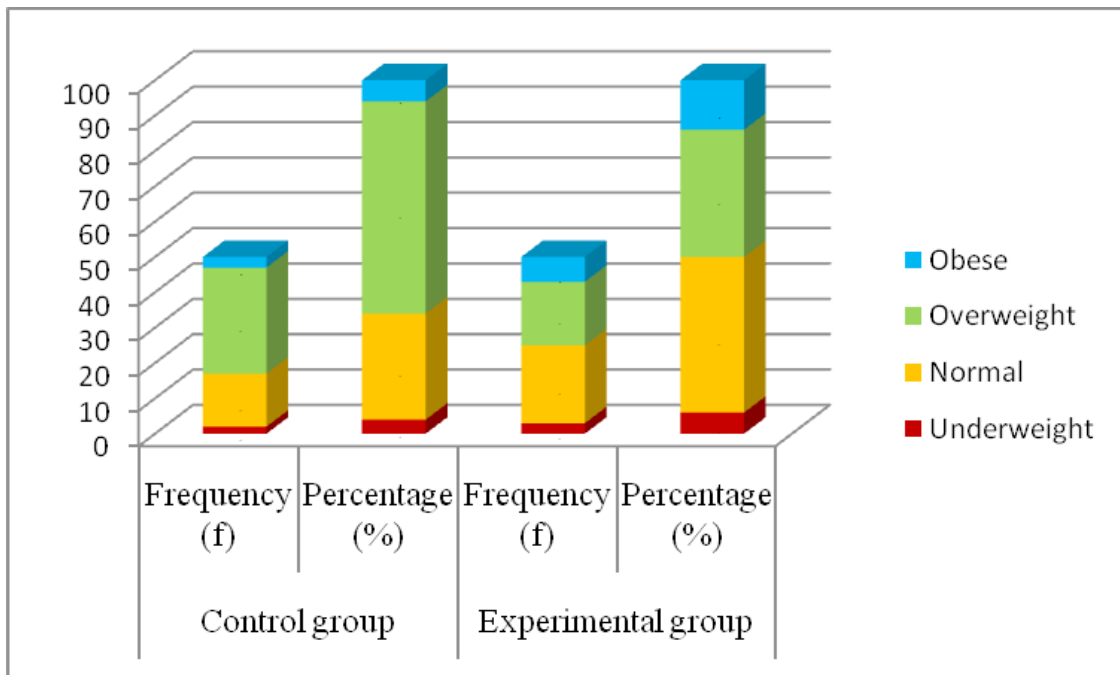


Figure 1: Frequency and percentages distribution of BMI among patients with Diabetes mellitus in control and experimental group.

In the present study, the result shows that BMI category in control group were 2(4%) underweight, 15(30%) normal, 30(60%) overweight and 3(6%) obese. In experimental group, 18(36%) were overweight and 7(14%) were obese.

Table 1: Comparison of mean, median and standard deviation of clinical variables among patients with diabetes mellitus in control and experimental group. N=100

Group	Clinical parameters	Mean	Median	Standard deviation (SD)
Control group	Height	159.24	158	6.14
	Weight	64.96	65	9.95
	BMI	25.56	25.8	3.10
Experimental group	Height	159.24	160	5.17
	Weight	64.48	60	11.71
	BMI	25.42	24.69	4.33

The above table shows that among the control group the mean and standard deviation of height, weight and BMI is (159.24± 6.14), (64.96± 9.95) and (25.56± 3.10) respectively. In the experimental group the mean and standard deviation of height, weight and BMI is (159.24± 5.17), (64.48± 11.71) and (25.42± 4.33) respectively.

Table 2: Mean and standard deviation of Ankle brachial pressure index among control and experimental group. N=100

ABPI Score	Mean	Standard Deviation	F	p- value
Day 1	0.07	0.01	4.44	0.00**
Day 2	0.05	0.02	2.88	0.01*
Day 3	0.19	0.01	0.60	0.00**

Data present in the table shows that mean and standard deviation of ABPI score among both groups on Day 1 (0.07±0.01), day 2 (0.05±0.02) and day 3(0.19±0.01). There was statistical significance with the p value <0.01.

Table 3: Comparison of ABPI scores among patient with diabetes mellitus in between and within the control and experimental groups. N=100

Variables	Days		Mean	Sum of square	df	F	p-value
ABPI score	Day 1	Between groups	0.135	0.13	1	45.55	0.000*
		Within groups	0.003	0.29	98		
	Day 2	Between groups	0.064	0.06	1	6.68	0.01*
		Within groups	0.009	0.93	98		
	Day 3	Between groups	0.984	0.98	1	349.92	0.000*
		Within groups	0.003	0.27	98		

The table 3 depicts the significant difference between the groups and within the groups in ABPI scores in 3 days among patients with type 2 DM which is significant at <0.05. There was no association between the demographic variables and the ABPI score

Discussion

Diabetes is a complex metabolic disease. A Non pharmacological natural approach is needed to overcome that problem. Burger’s Allen exercise is a simple, which is easy to do, have no notable side effects and most acceptable one to reduce Diabetes mellitus.

In the present study, the average age of experimental group is 55.30 +- 4.58. 36 (72%) were males, almost 45 (90%) had education up to secondary level, 32 (64%) subjects were employed, 23 (46%) were doing sedentary and moderate work each, 46 (92%) were non- vegetarian diet, 29 (58%) had no ill habits and 33 (66%) had type2 DM for more than 11 years. Whereas in the control group, the average age is 55.30+- 4.58, 34 (68%) were males, 41 (82%) had education upto secondary level, 26 (52%) were unemployed, 31 (62%) were moderate workers, almost 45 (90%) were following non vegetarian diet, 34

(68%) had no ill habits.

Another study conducted by M. Vijayarathi (2013) on effectiveness of buergerallen exercise on wound healing process among the diabetic foot ulcer patients admitted in diabetology department which results showed that in considering the age wise distribution, 36.7 % of subjects were in 50 to 60 years of age, in the experimental group. In the control group 33.3 % of subjects were more than 60 years of age. In the sex wise distribution, females were high in both experimental and control group as 80.0% and 83.3%.In Experimental group majority was educated up to primary education 50.0 % (15) and in Control group 63.3% (19) equally educated up to primary education and High School. When considering the type of family most of them belong to nuclear family in both the groups. In both the groups when considering the education status most of the subjects had only primary education.¹⁰

The present study shows that 30 (60%) subjects are overweight in control group whereas in the experimental group most of the subjects 22 (44%) have normal BMI.

Leelavathi. M (2015) conducted a study on

effectiveness buerger'sallen exercise on improving lower extremity perfusion among patients with diabetes mellitus which inferred that most of the patients with diabetes mellitus had B.M.I. of 25-29 (43.3%, 43.3%). Increased BMI was associated with increased prevalence of diabetes mellitus. An increase in body fat is generally associated with increased risk of metabolic diseases such as type II diabetes mellitus.¹¹

Data present in the table shows that mean and standard deviation of ABPI score among both groups on Day 1(0.07±0.01), day 2 (0.05±0.02) and day 3(0.19±0.01). There was statistical significance with the p value <0.01.

Dr. Aruna S, Thenmozhi P (2015) conducted a study on effectiveness of allenbuerger exercise in preventing peripheral arterial disease among people with type 2diabetes mellitus.Experimental Research Design with 30 samples in experimental group and 30 samples in control group were selected by using random sampling technique at Kuthambakkam village. The findings of the study revealed that there is a significant improvement in Ankle-Brachial index Score in preventing peripheral arterial disease among people with Diabetes Mellitus in experimental group after receiving Allen Buerger exercise at the level of P<0.05. Independent t test revealed that there is significant difference between the experimental group and control group in preventing peripheral arterial disease among people with Diabetes Mellitus at the level of P<0.05.¹²

Anju Kumari, Kanika Rai, Vinay Kumari, Dr Jyoti Sarin conducted a study on effectiveness of buergerallen exercise on foot perfusion among patients with diabetes mellitus showed that (50%) patients were suffering from comorbid illness in which 56.6% were suffering from hypertension, 8/30 (26.6%) were suffering from Chronic Kidney Disease (CKD), 1/30 (3.33%) was suffering from CVA, 04/30 (13.3%) were suffering from CAD, and 30/60 (50%) of patients were not suffering from any comorbid illness.¹³

In the present study, the significant difference between the groups and within the groups in ABPI scores in 3 days among patients with type 2 DM which is significant at <0.05.

Jemcy John and A Rathinga conducted a research study showed a significant improvement in the lower extremity perfusion after the Buerger Allen exercise. Data depicts that the mean post- test ankle brachial index

score was higher than the mean pre-test ankle brachial index score. The calculated t value was greater than the table value. The computed t value shows that there was a significant difference between the two mean ankle brachial index score.¹⁴

Mellisha MS conducted a study on effectiveness of buergerallen exercise on lower extremity perfusion and pain among patients with type 2 diabetes mellitus showed that in the experimental group, the mean score of level of lower extremity pain was reduced from 4.33 to 1.30. The reduction of pain was statistically significant difference at 1% level of significance (p=0.001). The mean score of level of lower extremity perfusion was increased from 44.50 to 52 and it showed a statistically significant difference at 1% level of significance (p=0.001).¹⁵

The above finding clearly indicates that the Buergerallen exercise was found to be an effective on lower extremity perfusion among patients with type 2 Diabetic Mellitus.

Conclusion

The study concluded that the study participants got benefited by Allen Buerger exercise in preventing Peripheral Arterial Disease among patients with type 2 Diabetic Mellitus. Nurses plays a significant role in preventing Peripheral Arterial Disease there by reducing the risk of amputation and restore normal function of the extremity by encouraging them to do the exercise which will help to improve the quality of life. It also suggests that Buerger's exercises could be an alternative procedure on improving peripheral circulation.

Conflict of Interest: There is no conflict of interest for the study.

Source of Interest: Not a funded study.

References

1. World Health Organization (WHO). Diabetes fact sheet 2017 [internet]. Geneva: WHO; 2017. Available from: www.who.int/diabetes/en/
2. Mohan V, Sandeep S, Deepa R, Shah B, Varghese C. Epidemiology of type 2 diabetes: Indian scenario. Indian J Med Res. Mar 2007;125(3):217-230. Available from: <http://admin.indiaenvironmentportal.org.in/files/file/type%20%20diabetes.pdf>
3. Boulton A J M, Vileikyte L, Ragnarson-Tennvall

- G Apelqvist J. The Global Burden of Diabetic Foot Disease. 2005;366: 1719-24.
Available from: [http://dx.doi.org/10.1016/S0140-6736\(05\)67698-2](http://dx.doi.org/10.1016/S0140-6736(05)67698-2)
4. Health Promotion and Administration, Ministry of Health and Welfare Diabetes; 2014. Available from: <http://www.hpa.gov.tw/BHPNet/Web/HealthTopic/Topic.aspx?id=201409290001>
 5. Harrington C, Zagari M, Corea J, Klitenic, J. A Cost Analysis of Diabetic Lower-Extremity Ulcers. *Diabetes Care*. 2000; 23: 1333-38.
Available from: <https://pdfs.semanticscholar.org/4aab/50a2b2131b8ac45e11d575c0fed6814ac712.pdf>
 6. Alvarsson A, Sandgren B, Wendel C, Alvarsson M, Brismar, K. A Retrospective Analysis of Amputation Rates in Diabetic Patients: Can Lower Extremity Amputations Be Further Prevented? *Cardiovascular Diabetology*.2012; 11:1-11.
Available from:<http://dx.doi.org/10.1186/1475-2840-11-18>
 7. Bernheim A R, London I M. Arteriosclerosis and ThromboangiitisObliterans. *JAMA*.1937;108: 2102-09.
Available from:<http://dx.doi.org/10.1001/jama.1937.02780250016005>
 8. Edwards L, Crisenberry H. Vascular Disorders of the Extremities: A Discussion of Nursing Care. *American JournalofNursing*.1938;38:13-17.
Available from: <http://dx.doi.org/10.2307/3414247>
 9. Bottomley J M. The Insensitive Foot. In: Timothy, L.K., John, O.B. and Michael, L.M., Eds., *Geriatric Rehabilitation Manual*, Churchill Livingstone, Edinburgh. 2007;2:333-43.
Available from:<http://dx.doi.org/10.1016/B978-0-443-10233-2.50058-4>
 10. Vijayarathi. Buerger Allen Exercise for Type 2 Diabetes Mellitus foot ulcer patients. *International Journal of Innovative Research in Science*. 2014;3(12):2319-8753 Available from: http://repository-tnmgrmu.ac.in/9541/1/300116314vijaya_barathi.pdf
 11. Leelavathi M. Effectiveness of buerger'sallen exercise on improving the lower extremity perfusion among patients with Diabetes Mellitus admitted at Apollo Hospitals. The Tamil Nadu Dr. M.G.R University; 2018.
Available from: <http://repository-tnmgrmu.ac.in/1937/1/3001128leelavathim.pdf>
 12. S Aruna, Thenmozhi P. Effectiveness of allenbuerger exercise in preventing peripheral arterial disease among people with type 2 diabetes mellitus. *International Journal of Pharma and Bio Sciences*. 2015;6(2):966-70.
Available from: https://www.researchgate.net/publication/283021440_Effectiveness_of_allen_buerger_exercise_in_preventing_peripheral_arterial_disease_among_people_with_type_II_diabetes_mellitus
 13. Kumari A, Rai K, Kumari V et.al. A study to assess the effectiveness of Buerger Allen exercise on foot perfusion among patients with diabetes mellitus admitted in selected hospital of Ambala, Haryana. *Int J Health Sci Res*. 2019; 9(1):112-119.
Available from:http://www.ijhsr.org/IJHSR_Vol.9_Issue.1_Jan2019/18.pdf
 14. John J, Rathiga A. Effectiveness of Buerger Allen Exercise to improve the lower extremity perfusion among patients with Type 2 Diabetes Mellitus. *International journal of current research and academic review*.2015 April; 3(4):358-66.
Available from: <http://www.ijcrar.com/vol-3-4/Jemcy%20John%20and%20A.Rathiga.pdf>
 15. Mellisha MS. Effectiveness of Buerger Allen Exercise on Lower Extremity Perfusion and Pain among Patients with Type 2 Diabetes Mellitus in Selected Hospitals in Chennai. *International Journal of Science and Research (IJSR)*. 2016;5(7):1822-6.
Available from: <https://pdfs.semanticscholar.org/0b1a/2a1a06a4b05c0983fa3a782c1ed8548ab273.pdf>

Child Abuse: An Empirical Study Emphasizing on Child Health in Present Indian Socio-Economic Situation

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Abstract

Context: Child abuse is often neglected in the society. However, it should not be overlooked as this problem might become a major problem in the long run. Due to the hush-hush nature of this problem in the society, it is slowly creeping in as social stigma amongst the people which restricts the problem from being addressed directly. The main objective of the paper is to identify the health related factors of Child Abuse in present Indian socio-economic situation. The results of the study show that Child abuse is a growing peril in the Indian society and it must be addressed as soon as possible. Less research has been done in this field and there is a need to explore the various options in order to mitigate it. Adjusted odd ratios (OR) was used for the analysis of the data.

Keywords: Child Abuse, Child Health, Indian Socio-economic Situation, Adjusted odd ratios (OR)

Introduction

Child abuse, particularly sexual abuse, is often associated with the girls, however, it must be noticed that boys are also affected by this as much as the girls. Under these perilous circumstances wherein the children are exploited in an inhumane manner, some of the large epidemics like malaria, tuberculosis, HIV, etc. have adolescents fall under the highest risk group especially in the low income countries as they are subjected to large amount of stress by imbibing them into a background

which is rich in violence, gender inequalities, health inequalities and low life expectancy (Fang, et al., 2016)³. This is especially so as these children are seen as commodities rather than human beings who are in need of nurturing and they are not kept under optimally hygienic conditions. This nurturing is proactively provided by the parents and guardians of the children and they are the best persons who can prevent child abuse by properly looking after their children (Gallo, et al., 2017)⁴.

Literature Review: Lots of research has been done on the kinds of abuse committed against children. 44.4 per cent of the Indian population comprises of children below the age of 18 years and amongst this, half of the population are not provided with the most basic amenities required for surviving, that is, nutrition, health and basic education and from this we can say that these deficiencies make the children more vulnerable against the evil called child abuse (Carson, et al., 2014)². Other factors that can be responsible for the increase in the rate of child abuse are insufficient income, domestic

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violence, low socioeconomic status, other stresses like various socio-demographic factors, parental separation, illnesses, low maternal schooling, absence of mother's partner, parental death, maternal smoking, poor maternal mental health, unemployment, etc. (Metzler, et al., 2017)⁷. The various consequences of Child abuse can be broadly classified as physical and psychological (Malhotra & Biswas, 2006)⁶. A study has revealed that mothers, having intellectual disability run an increased risk of developing mental health problems, alcohol and drug addiction belonging from lower economic strata and their children have a higher prevalence rate of suffering from violence induced injuries and abuse in the long run (Wickstrom, et al., 2017)¹⁰. As a result, it is imperative that childhood abuse cases are detected as early as possible in order to lessen the adverse effects in the long term and as well as the short term and this can be made possible by developing an accurate screening process in the emergency departments of hospitals wherein the majority of the cases are first reported (Louwers, et al., 2014)⁵. A study was carried out in Saudi Arabia amongst the dental practitioners regarding the knowledge about Child abuse and neglect and it was found out that a majority of them (59 per cent) had experienced such a case in their career, however, only 10 per cent of the respondents reported the case for their lack of certainty about the diagnosis, the fear of reprisal from the family or their uncertainty over how to manage the case as only

20.9 per cent of them were knowledgeable about child protection policies (Mogaddam, et al., 2016)⁹. There has been instances when sexual abuse reaches its extremity as in the case of single perpetrator or multiple perpetrator rape, it was seen that alcohol was used as a common weapon against girls mostly at parties and as a result the girls had a hard time remembering the events leading up to their trauma and these victims require help in order to diagnose these physical findings, provide therapy for trauma, treatment of the Sexually Infected Diseases if infected and finally care and support. Thus, detecting child sexual abuse becomes notoriously difficult for investigative as well as for treatment purpose (Mitchell, et al., 2017)⁸.

Socio-Geographical Context: India is a country with a population of about 1.2 billion and is rich in culture. India is the third largest democracy in the world and is a significant global player. Overall annual growth is expected to grow at an annual rate of 7.0 per cent for the fiscal year 17/18. It is roughly estimated that 10 per cent of the world's street children reside in India and the causes for this unusual development ranges from the fact that their parents hail from joint families who are illiterate to that of the children having to experience intra-familial physical abuse (Bonfim, et al., 2015)¹. Following table describes the demographic profile of the respondents (Table 1).

Table 1: Demographic Profile of the Respondents

Serial No.	Variables	Participants included in the analysis	Participants included in the analysis %
1.	Gender	N=193	N = 193
	Male	102	52.85
	Female	91	47.15
2.	Age of the Children	N = 193	N = 193
	10 to 14 years	92	47.67
	14 to 18 years	73	37.82
	More than 18 years	28	14.51
3.	Family income	N = 193	N = 193
	Less than Rs. 2000	92	47.67
	Rs. 2000 to Rs. 4000	26	13.47
	Rs. 4000 to Rs. 6000	58	30.05
	More than Rs. 6000	17	8.81
4.	Education of the Child	N = 193	N = 193
	Pursuing Primary Education	58	30.05
	Pursuing Secondary Education	07	3.63
	Not pursuing education	128	66.32
5.	Employment of the Child	N = 193	N = 193
	Employed	90	46.63
	Unemployed	103	53.37

Research Methodology: Here, our research model has been established with the help of both primary and secondary data. The primary data was collected from the parents and other various identified eye-witness of these issues where children had been abused. The target population were from the guardians of the street children, the caregivers or caretakers of the children belonging from the low economic background, the hawkers found in the busy market areas of major cities and also from the railway stations, bus stops, market areas who have working children, the shopkeepers who employ children for doing menial jobs, guardians of the children who do not live with their parents for earning a livelihood, etc. and the caretakers of the children found to be residing in the slums. For this study, samples were taken through convenience sampling technique only from these caregivers and caretakers and occasionally

from the parents of those children who were capable of providing the complete data (N=193).

Analysis and Results: Each of the situational factors faced by children were taken and evaluated separately. Each affirmative answer would fetch one point (Yes=1 & No=0) for each of the situational factors. Thus, the total score can vary from 0 (no issues experienced) to 5 (all the issues experienced) for each respondent. The prevalence of each of these factors was also analyzed. Multinomial logistic regression was used to calculate the odds ratio (OR) and their respective 95% confidence intervals (95% CI) for the associations between the factors and their score which was generated. The OR was also calculated based on the kind of inter-relationships between the various types of factors. The analytical part of the study was carried out with the help of SPSS-21 and Microsoft Excel.

Table 2: Adjusted odd ratios (OR) and 95% confidence interval for pair wise relationships between different factors (N= 193).

Factors	Health Related Factors OR (95% CI)	Physical Abuse Related Factors OR (95% CI)	Education Related Factors OR (95% CI)	Income Related Factors OR (95% CI)	Family Related Factors OR (95% CI)
Health Related Factors		1.5 (0.5,2.6)**	2.9 (1.8, 3.7)*	4.3 (2, 6.7)*	1.6 (1.1, 2.2)
Physical Abuse Related Factors	1.5 (0.5,2.6)**		1.2 (0.2, 2.3)**	2.4 (1.6,3.3)**	1.9 (1.6,2.3)**
Education Related Factors	2.9 (1.8, 3.7)*	1.2 (0.2, 2.3)**		4.7 (3.5, 6)*	1.1 (0.7, 1.6)
Income Related Factors	4.3 (2, 6.7)*	2.4 (1.6,3.3)**	4.7 (3.5, 6)*		0.7 (0.3, 1.2)*
Family Related Factors	1.6 (1.1, 2.2)	1.9 (1.6,2.3)**	1.1 (0.7, 1.6)	0.7 (0.3, 1.2)*	

Adjusted for gender, age, family income, child education, child employment, area profile, * p-value <0.01 ** p-value < 0.05, Collected by the Researcher during the course of the Study

Table-2 shows the associations between the pairs of each of the factors experienced by the respondents. Five factors were taken for the mapping of the associations between the factors. These factors were Health Related factors, Physical Abuse Related Factors, Education Related Factors, Income Related Factors and Family Related Factors. p-value showcases the percentage of error. Both positive and negative associations have been showcased. Table-2 also shows the associations between the pairs of each of the issues experienced by

the respondents adjusted for the various demographic variables were gender, age, family income, child education and child employment. Strongest associations were seen between the Family Related Factors and Physical Abuse Related Factors. Highest positive associations were seen between Education Related factors and Health related factors and Income Related factors and Education Related factors. It was seen that a child experiencing undesirable situations due to Income Related factors were having 4.7 times higher incidences

of being affected by Education Related factors and vice versa. Similarly, a child experiencing adverse scenario due to Income Related factors was having 4.3 times higher incidences of experiencing Health related factors and vice versa. Negative associations could be found between Education Related factors and Health related factors and also between Educations related factors and Physical Abuse Related factors.

Discussion and Findings: Physical Abuse Related factors include intra familial physical abuse, domestic violence and Intimate Parental Violence. Intimate partner violence can be often found co-occurring with child abuse and it has a negative influence on the child. Also, it is clear that Intimate Partner Violence negatively influences the Overall Development of the Child. Furthermore, the families having low socio-economic status are more prone to physical abuse as well as neglect and neighborhood characteristics like housing instability, poverty, substance abuse, childcare burden, immigrant concentration, residential density, social impoverishment, etc., adversely affects the occurrence of Child maltreatment. Education is one of the most important aspects of the advancement of the civilization and it does have a major implication on the cause of child abuse. Education Related Factors include illiteracy, low maternal schooling, and higher rate of school dropouts and low levels of cognitive functioning. In reality, the rapid spread of Child sexual abuse in India is a complex mixture of socio-ecological, individual and situational factors of which factors such as lack of education and poverty are not only exclusive to the Indian context. Several factors like low family income, low maternal schooling, absence of the mother's partner, etc., are associated with a higher risk occurrence of Adverse child Experiences which further poses a negative effect on the overall child development by hampering their physical as well as their mental well-being. Family Related factors were seen as the most important factor related to child abuse in this study. Family Related Factors include neglect, housing instability, childcare burden, residential density, single parent's households and parental death under accidental circumstances. Poor living conditions and other issues can lead to child abuse which may develop various health related situations for the children as revealed from the inter-relationship between family related factors and health related factors. It was found out from the current study that housing instability and other family factors like childcare burden and neglect can be causal factors for domestic violence

and other intra family physical abuse. The emotional burden on the parents can result in this which might further deteriorate the emotional growth and stability of the children. Income related factors include poverty and poor employability. There is a relationship between the income related factors and the health related factors as poverty situations lead a child to live a unhealthy lifestyle wherein basic amenities are not provided to them. It was seen that there is a strong co-relationship between insufficient incomes in the family with that of child maltreatment. Neglect and Housing instability can cause the children to develop certain habits which are not good for the physical as well as the emotional development of the children such as substance abuse, alcohol addiction, etc.

Managerial Implications: It is pretty evident that special care must be ensured so that the younger generation can feel safe in the Indian environment. This will motivate them to build a future for themselves in India itself and will prove a milestone in developing the country. The government needs to come up with certain laws and regulations to restrain this societal epidemic as much as possible. Otherwise, this will spiral forward drastically and then it will be very difficult to restrain it. The future of the nation is dependent on the youth. Thus, the youth should be provided with such an environment which will make them feel safe.

Conclusion

Child abuse is shaping itself into an epidemic and spreading to the various parts of India. It is becoming a growing nuisance in India. This problem must not be put aside. It must be addressed immediately and steps should be taken to control it to a certain extent. In order for the authorities to take certain steps, at first, it would be of great importance if the factors responsible for this crisis are found out. As discussed in the paper, there are a multitude of factors that are responsible for this societal disease; however, these factors can be closely monitored so that these kinds of activities can be prevented before they are caused. This will ultimately result to be of benefit to the society and humanity as a whole. The purpose of this study was to figure out the root cause of this evil polluting our society in present Indian socio-economic scenario and to find out the ways of removing this from its very root.

Ethical Clearance: Ethical approval for this study has been taken from selected Municipal Authorities from

selected states in India for executing the data collection process smoothly. Also respondents have been assured for keeping complete confidentiality of their responses regarding our research topic.

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Conflict of Interest: Nil

References

1. Bonfim CB, Santos DN, Barreto LM. The association of intra-familial violence against children with symptoms of atopic and non-atopic asthma: A cross sectional study in Salvador, Brazil. *Child Abuse and Neglect*. 2015;50(1): 244-253.
2. Carson DK, Foster JM, Tripathi N. Sexual Abuse of Children and Youth in India: An Anthropological Perspective. *The Oriental Anthropologist*. 2014;14(2). 149-170.
3. Fang L, Chuang D, Lee Y. Adverse Childhood Experiences, gender and HIV risk behaviours: Results from a population-based sample. *Preventive Medicine Reports*. 2016; 4(1):113-120.
4. Gallo EAG, Loret De Mola C, Wehrmeister F, Goncalves H, Kieling C, Murray J. Childhood maltreatment preceding depressive disorder at age 18 years: A prospective Brazilian birth cohort study. *Child Abuse and Neglect*. 2017; 217(1): 218-224.
5. Louwers ECFM, Korfage IJ, Affourtit MJ, Ruige M, Van den Elzen APM, De Koning HJ, Moll HA. Accuracy of a screening instrument to identify potential child abuse in emergency departments. *Child Abuse and Neglect*. 2014; 38(1): 1275-1281.
6. Malhotra S, Biswas P. Behavioral and Psychological Assessment of Child Sexual Abuse in Clinical Practice. *International Journal of Behavioural and Consultation Therapy*. 2006; 2(1): 17-28.
7. Metzler M, Merrick MT, Klevens J, Ports KA. Adverse Childhood Experiences and life opportunities: Shifting the narrative. *Child Abuse and Neglect*. 2017; 72(1): 141-149.
8. Mitchell K, Moynihan M, Pitcher C, Francis A, English A, Saewyc E. Rethinking research on sexual exploitation of boys: Methodological challenges and recommendations to optimize future knowledge generation. *Child Abuse and Neglect*. 2017; 66(1):142-151.
9. Mogaddam M, Kamal I, Merdad L, Alamoudi N. Knowledge, attitudes, and behaviours of dentists regarding child physical abuse in Jeddah, Saudi Arabia. *Child Abuse and Neglect*. 2016; 54(1):43-56.
10. Wickstrom M, Hoglund B, Larsson M, Lundgren M. Increased risk for mental illness, injuries, and violence in children born to mothers with intellectual disability: A register study in Sweden during 1999-2012. *Child Abuse and Neglect*. 2017; 65(1): 124-131.

A Glimpse of Manual Scavenging in India

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Abstract

Context: Across India, manual scavenging and its allied forms — the manual cleaning of dry latrines, sewers, manholes and septic tanks, abstraction of debris from sewage canals and any interaction with excreta — are openly prevalent, defined as a “cultural vocation”. “In India, every five days, a manual scavenger dies in a sewer, septic tank or a manhole,” the report verbally expressed. However, its scope was constrained as its primary source of data was statistics from NCSK, which has disarrayed information organised arbitrarily. The few key features of the Act Prohibits the expression or maintenance of insanitary toilets, Prohibits the engagement or employment of anyone as a manual scavenger, Violations could result in a years’ imprisonment or a fine of INR 50,000 or both. The press Information Bureau, Government of India, Ministry of Social Justice and Empowerment has verbally expressed that a Task Force was constituted for carrying out a National Survey of manual scavengers in 2018 in 170 identified districts of 18 states. The right technology is considered as one of the solution to eradicate this scourge. In spite of that, the social and gender issues should be abolished by educating pupil about this ill.

Keywords: manual scavengers, manholes, insanitary latrines, health issues

Introduction

Across India, manual scavenging and its allied forms — the manual cleaning of dry latrines, sewers, manholes and septic tanks, abstraction of debris from sewage canals and any interaction with excreta — are openly prevalent, defined as a “cultural vocation” annexed to a few make-believe lower castes — Hindu Dalits, a few Dalit Muslims and some converted Dalit Christians. In India, this affair is hazardous, unsafe, unsanitary, degraded and above all, illicitly proscribed by Parliament a few years ago. The level of susceptibility increases as we peregrinate from rural to urban areas. However,

reports designate that these days; there is incremented fatality in rural India, as well.¹

The data from the National Commission for SafaiKarmacharis (NCSK) revealed appalling facts on the pattern of the deaths of manual scavengers from January 2017 to September 2018 and were widely shared by media houses and convivial media users. “In India, every five days, a manual scavenger dies in a sewer, septic tank or a manhole,” the report verbally expressed. However, its scope was constrained as its primary source of data was statistics from NCSK, which has disarrayed information organised arbitrarily.

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Manual Scavenger at work--- A bitter truth of reality

The two major Acts have been since 1993 by Parliament to ban and control manual scavenging. One of the Act passed by Narsimha Rao Government in 1993 created a history in the legislation banning manual scavenging altogether and aimed at rehabilitation of scavengers followed by passing of another Act in 2013 by UPA II after it was reported that manual scavenging still persists despite a slow progress.²

According to the India census of 2011, there are more than 2.6 million dry latrines in the country. Along with that toilets with human excreta flushed in drains is 13, 14,652 and 7, 94,390 dry latrines are cleaned manually. It has as well been identified that seventy three percent of these are in rural areas and twenty seven in urban areas.

The few key features of the Act are

Prohibits the expression or maintenance of insanitary toilets

Prohibits the engagement or employment of anyone as a manual scavenger

Violations could result in a years' imprisonment or a fine of INR 50,000 or both

Prohibits a person from being engaged or employed for hazardous cleaning of a sewer or a septic tank³

Offences under Act are cognizable and non-bailable calls for a survey of manual of scavengers in urban and rural areas within a time limit framework. While the Act is encouraging in that it focuses on the duty of official to ensure its implementation, it does not outline administrative measures beyond conduct rules that can be imposed if officials do not implement the Act.

The mundane accidents include falls/slips fire or explosion, oxygen depletion, heat stress, drowning, asphyxiation arising from gas, gas poisoning, vapour and entrapment by free flowing solids. Amongst these hazardous gases etc are facilely overlooked or neglected leading to earnest casualties.⁴

Definition: Manual scavenging refers to the unsafe and manual removal of raw (fresh and untreated) human excreta from buckets or other containers that are used as toilets or from the pits of simple pit latrines.

According to the Indian Law, 1993, Manual scavengers means a person engaged or employed at the commencement of this Act or any time thereafter, by an individual or a local authority or an agency or a contractor for manually cleaning carrying, disposing of or otherwise handling in any manner, human excreta in an insanitary latrine or in an open drain or pit into which the human excreta from the insanitary latrines is disposed of, or railway track or in such other spaces or premises, as the central government or a state government may notify, before the excreta fully decomposes in such manner as may be prescribed, and the expression 'manual scavenging' shall be construed accordingly.⁵

The prohibition of Employment of Manual Scavengers and their Rehabilitation Act, 2013, defines a manual scavenger as an individual employed by a local authority or agency for manually cleaning, carrying and disposing of human excreta from insanitary latrines.²

Categories of Sanitation Workers: A caste predicated and hereditary vocation, which is bequeathed, as a legacy from one generation to the next; "manual scavenging" has been an age-old routine for this community, which is untouched by technological advancement in sanitary practices.

i. **Sewer Cleaners:** These cleaners are involved in unblocking and cleaning of the permissive wastewater drains. The work is need based (pluvial season) and infrequently for preventive maintenance. The sewer gas is a complex amalgamation of toxic and non toxic flatulency engendered and accumulated in sewage system by the decomposition of organic home or industrial waste.

ii. **Latrine Cleaners:** They are involved in cleaning the process of evacuating dry/single-pit latrines preferably in rural areas. The process involves daily amassment and convey/evacuating of faecal matter.

iii. **Faecal Sludge Handling:** The scavengers muddled in faecal sludge by emptying, collecting and transporting human waste from septic tanks. The work is carried out on demand. The frequency of de-sludging ranges from six months to 10 years.

India does not even have categorical licit provisions cognate to the management of faecal sludge, additionally called septage in municipal parlance, albeit a number of laws cover sanitation accommodations and environmental regulations.⁶

iv. **Railway Cleaners:** These employees clean the human excreta i.e. remains of a train that has ended its journey, leftover food, packets and paper boxes from the track as well as cleaning of the railway toilets. All these activities are carried out several times a day. These workers are employed by private contractors to whom the India Railways has outsourced. Most of the time when the water doesn't get the job done or the drains get clogged, the cleaners have to scoop up the excreta with ply boards using their bare hands without any precautions.⁷

v. **Treatment Plant Workers:** Treatment plant workers maintain and operate sewage and faecal sludge treatment plants on a quotidian footing. Workers are mostly in urban areas spread across India – working in the 527 STPs/FSTPs.⁸

vi. **Community and Public Toilet Cleaners:** These workers are engaged in maintaining the public toilets on daily basis. The workers belong to the rural and urban areas of slums and public convenience shelters. The task of these cleaners (halalkhors) is still the same as of colonial era.⁹

Statistics on Manual Scavengers in India: According to the findings of the socio-economic and caste census, 2011, the Ministry of Rural Development (Government of India) has revealed that that a paramount number of manual scavengers were analyzed in the state of Maharashtra followed by Madhya Pradesh at second position. The other states in the line of higher number are Jammu and Kashmir, Karnataka, Tripura, Punjab, Uttar Pradesh, Daman and Diu, Bihar. The census has as well acknowledged that Tamil Nadu, Kerala, Goa, Andhra Pradesh, Telangana, Gujrat, Assam and Manipur have no manual scavengers. These statistics are based on the number of households in the states. This survey communicates that India has 18.06 lakh manual scavengers in the country.¹⁰

The press Information Bureau, Government of India, Ministry of Social Justice and Empowerment has verbally expressed that a Task Force was constituted for carrying out a National Survey of manual scavengers in 2018 in 170 identified districts of 18 states. The national Survey concluded in 163 of the 170 identified districts. A total of 50,644 persons registered themselves in the survey camps. It was claimed that 20,596 persons have been accepted after identification with subsequent verification as manual scavengers. Data of the identified manual scavengers is being digitized in National Safaikaramcharis Finance and Development Corporation. Besides that the data of remaining 11,757 manual scavengers were digitized upto October 2018. Onetime cash assistance has been relinquished to 8438 identified manual scavengers.¹¹

Schemes Available for Manual Scavengers: The National SafaiKaramcharis Finance and Development Corporation (A Government of India undertaking the Ministry of Social Justice and Empowerment) introduced Self Employment Scheme for Rehabilitation of Manual Scavengers (SRMS) and their dependents in alternative occupations by 2009. According to the updated number announced by States/UTs, 1.18 lakh manual scavengers and their dependents in 18 States/UTs were determined. One from each family of the identified manual scavenger is eligible for receiving cash assistance of Rs. 40000 immediately after their identification. The beneficiary is sanctioned to withdraw an amount of Rs. 7000 maximum in monthly instalments.

The quantum of loan upto a maximum cost of Rs. 10 lacs is permissible under this scheme and a sum of Rs. 15 lacs in case of sanitation related projects such as vaccum loader, suction machine with vehicle, garbage disposal vehicle etc. which are immensely compatible for target group with high success rate and income. The moratorium period is of two years. The repayment mode is of five years including the period of moratorium for the projects upto five years.¹²

Beneficiaries can as well avail the facility of subsequent loan from banks, if needed without capital and interest subsidy.

The training is administered to the beneficiaries for gaining new skills and entrepreneurship capabilities. The training is being provided by govt. agencies/Institutions along with the reputed specialized training agencies. The training is given as per their level of education and aptitude.¹²

Remedies: The solution, it seems, is a public-private partnership. Collaboration would work best because it would ravage the mafia of private cleaners, making them accountable

It was also found that some scavengers have endeavoured to challenge their social and economic status by transmuting their jobs. But determinately, they have to return to their pristine profession because of a social boycott and the lack of foothold from both private and governmental agencies. The law and order machinery has additionally proved inefficient.

Eradication of manual scavenging needs to be worked out on war footing. A mission for total eradication of manual scavenging and rehabilitation of manual scavengers needs to be set up and implemented by the government.

The right technology is considered as one of the solution to eradicate this scourge. In spite of that, the social and gender issues should be abolished by educating pupil about this ill.

The sewage handlers come across with multiple health issues such as respiratory and skin diseases, anaemia, jaundice, carbon monoxide poisoning and sometimes leads to death. The health issues should be taken care by the agency and safety equipments to be provided before handling. Vaccination against hepatitis A, E-Coli, Rotovirus, Norovirus must be administered to these workers to avoid deaths at young age of their life.

The construction of toilets under Swachh Bharat Mission on a large-scale was built under single pit toilets but the cleaning of these excreta is carried out by manual scavengers. Therefore, a technology based structure should be introduced to dispose of waste and reduce the figures of manual scavengers.

Ethical Clearance: Nil

Source of Funding: Self

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References

1. SwaroopKanthi, India's Manual Scavengers: Ugly truths of unsanitary sanitation work an open secret; law needs better enforcement, Firstpost, 2019
2. Mishra Neeraj, Manual Scavenging: Lies, Damned Lies and Numbers, Indian Legal Stories that Count, 2019
3. United Nations of India, Breaking Free: Rehabilitating Manual Scavengers, 2013, <https://in.one.un.org/page/breaking-free-rehabilitating-manual-scavengers>
4. MitraArun, Manual Scavenging in India, Daily Excelsior Newspaper, 2019
5. The Employment of Manual Scavengers and Construction of Dry latrines (Prohibition) Act 1993, Ministry of Housing and Urban Poverty Alleviation, Govt. of India
6. Rohilla Suresh, Luther Bhitush, etal, Urban shit: where does it all go, Down to Earth, 2016
7. Roy Sidhartha, The not-so-swachh life of the Railways' cleaners, The Hindu, 2016, <https://www.thehindu.com/news/national/The-not-so-swachh-life-of-the-Railways%E2%80%99-cleaners/article14623426.ece>
8. BakshiAnahitaa, The Nine Kinds of Manual Scavenging in India, The Wire, 2018, <https://thewire.in/labour/manual-scavenging-sanitation-workers>
9. DarokarShailesh Kumar, Manual Scavengers: A blind Spot in Urban Development Discourse, Engage, 2018;53: 22 <https://www.epw.in/engage/article/manual-scavengers-blind-spot-urban-development-discourse>
10. India-18.06 lakh manual scavengers, Maharashtra tops manual scavenging ststes# WTF news, Kractivist.org,2017, <https://kractivist.org/india-18-06-lakh-manual-scavengers-maharashtra-tops-manual-scavenging-states-wtfnews>
11. GehlotThaawarchand, Government is keen to eradicate Press Information Bureau, Government of India, Ministry of Social Justice & Empowerment, 2018, <http://pib.nic.in/newsite/PrintRelease.aspx?relid=184118>
12. National SafaiKaramcharis Finance & Development Corporation, (A Government of India undertaking under the Ministry of Social Justice & Empowerment), <https://nskfdc.nic.in/en/content/revised-srms/self-employment-scheme-rehabilitation-manual-scavengers-srms>

Knowledge of Primary School Teachers Regarding Learning Disorders among Children at Schools of Satara District

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Abstract

Introduction: “Learning disorder is a general term that refers to a group of disorders manifested by difficulty in the acquisition and use of listening, speaking, reading, writing, & mathematical abilities. These disorders are inherent to the person supposed to be because of central nervous system malfunction.

Most students who undergo from learning disorders will not be recognized before standard 3-4 of primary school since their teachers don't have adequate knowledge about learning disorder. Teachers are the child's first contact person in school and the perfect person to find out a learning difficulty. Unluckily, most either pay no attention to the problem or blame it on the child's personality.²

Methodology: The study was designed in the form of non-experimental descriptive type. Study comprised of 316 primary school teachers from conveniently selected schools at Satara district.

Result: Majority of the teachers was belongs to 41 to 58 age groups 203(64.24%), 199(62.97%) were females, 277(87.65) were Hindu, 301(95.25%) teachers was married, 214(67.72%) teachers were having educational qualification of D.Ed., 243(78.89%) teachers was having above 11 years of experience. 166(52.26%) of the subject had poor knowledge, 146(46.20%) teachers had average knowledge & 04(1.26%) had good knowledge.

Conclusion: Present study showed the need for intensive training of primary school teachers on learning disorders.

Keywords: Knowledge, Learning Disorders, Primary School Teachers, Primary School, children.

Introduction

“Learning disorder is a general term that refers to a group of disorders manifested by difficulty in the acquisition and use of listening, speaking, reading, writing, & mathematical abilities. These disorders are inherent to the person supposed to be because of central nervous system malfunction¹. The 4th version of Diagnostic and Statistical Manual (DSM-IV) refers these

disabilities as learning disorders rather than academic skills disorders and mentioned under the section called “disorders first diagnosed in infancy, childhood or adolescence.²

Most students who undergo from learning disorders will not be recognized before standard 3-4 of primary school since their teachers don't have adequate knowledge about learning disorder³.

Students who are suffering from learning disorders are very prone to get common social and emotional disorders and will have low motivation and incomplete learning from their lessons. Some time they are showing difficult behaviors also. It is supposed that, this problem is always probable to appear in students and if teachers

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can't identify this problem, students are labeled: lazy, irresponsible, with no interest and motivation.⁴

Students suffering from learning disorders may become so disturbed with their academic performance in school they may feel like failure want to leave school or may develop behavior problems so learning disorders should be identified as early as possible during school years.

Teachers are the child's first contact person in school and the perfect person to find out a learning difficulty. Unluckily, most either pay no attention to the problem or blame it on the child's personality. Today our goal is all children's must learn in the school irrespective of their psychological and intellectual characteristics.

Due to difference in cognitive abilities of students, teaching should be based on teacher's knowledge means teachers should think about these learning disorders in students while teaching in class & finally, the best teaching- learning method should be selected.⁵

Lack of awareness about learning disorders is one of the major reasons for not identifying great talent in school children. Therefore, there is a need to create consciousness about the problem among teachers. Teachers should be given proper training to identify children with learning disorders so, easily they can find out these problems at school level.⁶

Methodology: The study was designed in the form of one group pre-test, post-test, design. With the objective of assessing the knowledge of primary school teachers regarding learning disorders among children. The study was conducted in selected schools of 11 talukas of satara district. The sample for the present study comprised of 316 primary school teachers from conveniently selected schools. For data collection, tool was used which consisted of two sections: Section I: Demographic data of primary school teachers. Section II Structured Knowledge Questionnaire related to learning disorders consist 30 questions. One mark was given to each correct answer & zero mark for incorrect answer.

A prior written permission was obtained from district education officer. After self-introduction, nature and objectives of study was explained to the participants to obtain maximum cooperation. Anonymity and confidentiality were assured to them. Written Consent was obtained from the participants and they were made comfortable.

Result

The data collected were analyzed according to the plan for data analysis which includes both descriptive and inferential statistics. Objective of the study was to assess the knowledge of primary school teachers regarding learning disorders among children.

Table 1: Description of demographic characteristics of teachers(N =316)

Demographic Variable	Frequency	Percentage
Age in Years		
20-40	114	36.07
41-58	202	63.92
Sex		
Male	113	35.75
Female	203	64.24
Religion		
Hindu	278	87.97
Muslim	38	12.02
Marital status		
Married	301	95.25
Un married	15	4.74
Educational status:		
D.Ed	215	68.03
B.Ed	97	30.69
M.Ed	4	1.26
Year of experience		
1 to 10yrs	73	23.10
Above 11	243	78.69
Tranning program attended related to learning disorders		
Yes	51	16.13
No	265	83.86
Previous Knowledge		
Yes	30	9.49
No	286	90.50
Residence area		
Urban	120	37.97
Rural	196	62.02

Distribution of demographic variable showed that majority of the teachers was belongs to 41 to 58 age groups 203(64.24%),199(62.97%) were females, 277(87.65) were Hindu, 301(95.25%) teachers was married, 214(67.72%) teachers were having educational qualification of D.Ed., 243(78.89%) teachers was having above 11 years of experience, 265(83.86%) teachers

were not attended any kind of training program related to learning disorders, 283 (89.55) teachers were not having previous knowledge related to learning disorders, 196(62.02%) teachers were residing in urban area.

Table 2: Assessment of pre test Knowledge of teachers regarding learning disorders. N=316

Sr.No.	Knowledge score	Pretest	
		Number	Percent
1.	Poor (0-10)	166	52.53
2.	Average (11-20)	146	46.20
3.	Good (21-30)	04	1.26

In above mentioned table represents total knowledge score of subject regarding knowledge of learning disorders in pre test 166(52.26%) of the subject had poor knowledge, 146(46.20%) teachers had average knowledge & 04(1.26%) had good knowledge.

Discussion

In present study 166(52.26%) of the subject had poor knowledge, 146(46.20%) teachers had average knowledge & 04(1.26%) had good knowledge. This study supported by study done by Karande S, Mehta V, S Ghimire 9, Dr. Neena Sawhneya 10, Syed Arifa, Nsreen A 11 & Poorna Shukla 12, Kulkarni M⁷. Other study done by Basim Ali C. T & *et.*⁸

In general, primary school teachers have very little knowledge about learning disorders. This may be due to the lack of teacher training programs related to learning disorders. Also, teachers are not interested for any further training that focuses on how to teach the children with learning disorders. The educational authorities should provide ongoing in-service training for teachers about teaching learners with special needs at school levels.⁹

Recommendation:

- Similar study can be conducted in a large group to generalize the study findings.
- Comparative study can be done between urban and rural areas.
- A study can be conducted in term of knowledge, attitude and practice of alternative learning method among school teachers of children with learning disabilities.

Conclusion

Present study showed the need for training of primary school teachers on Learning disorders it will help them to easily identify the student at early stage so, further Complications can be prevented.

Limitations: Due to time constraints, convenient sampling was adopted for data collection; and data are limited to Satara district, hence the findings cannot be generalized.

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Conflict of Interest: None.

Source of Funding: None.

Ethical Clearance: Institutional ethical clearance was obtained prior to study

Reference

- National Joint Committee on Learning Disabilities (NJCLD) Fact Sheet Available at http://www.Idonline.org/pdfs/njclld/njclld_factsheet_Nov2016.pdf
- Dele Pilliteli "Care of the Growing Family" 3rd Edition, Little Browns Company, Toronto, (1987) P: 162.
- Nsreen A. Alahmadi 1 & Mogeda El Sayed El Keshky. Assessing Primary School Teachers' Knowledge of Specific Learning Disabilities in the Kingdom of Saudi Arabia. Journal of Educational and Developmental Psychology. 2019 Vol. 9 (1); 2019 P.9-14
- Lyon, G.R. Learning Disabilities. Special education for students With Disabilities. The future of children USA. sage publications, . 2016; 10(6): p16-18.
- Keivan, Kakabaranea, Aliakbar Arjmandnia b, Gholam Ali Afrooz c. The study of awareness and capability of primary school teachers in identifying students with learning disability in the province of Kermanshah. Procedia - Social and Behavioral Sciences 2012 Vol. 46(6). 2615 –2619.
- Urie Bronfenbrenner and Stephen J. Ceci. Nature-Nurture Reconceptualized in Developmental Perspective: A Bioecological Model. Psychological Review 1994, Vol. 101. (4): 568-586.

7. Karande S, Mehta V, Kulkarni M. Impact of an education program on parental knowledge of specific learning disability. *Indian J Med Sci.* 2007; Vol. 61 (7):398-406.
8. Basim Ali C. T., Fysal N., Akhila Thasneem A. Assessment of knowledge level on learning disability among primary school teachers. *International Journal of Contemporary Pediatrics.* 2019. Vol 6(2):410-416
9. Sasmita Ghimire. Knowledge of Primary School Teacher Regarding Learning Disabilities in School Children. *Journal of Nobel Medical College.* 2017:6(10):29-35.
10. Sawhney Neena & Bansal Sneha. Metacognitive awareness of undergraduate students in relation to their academic achievement. *International Journal of Indian psychology.* 2015 1(8), 107-114.
11. Syed Arifa, Syed Shahid Siraj. A descriptive study to assess the knowledge and attitude of primary school teachers regarding learning disabilities. *Journal of Pediatrics and Nursing Science.* 2019; 2(1):19-32
12. Poorna Shukla, Gaurav Agrawal. Awareness of Learning Disabilities among Teachers of Primary Schools *Online Journal of Multidisciplinary Research (OJMR)* 2015, 1(1), 33-38

Efficacy of Cognitive Behaviour Therapy and SSRI in Treatment of Conversion Disorder

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Abstract

Context: Current understanding of the phenomenon of conversion disorder implicates some role of the unconscious in the pathophysiology of this condition. It is therefore less likely to respond to treatment when the manifestations of the conversion are confronted directly as a unitary method of therapy. Many patients who experience a conversion disorder are unable to understand this inner conflict, which is perhaps occurring on an unconscious level. They may achieve resolution of the conflict, as well as their physical symptoms, once they are gently made aware of this connection. Once the patient is aware of this, the psychological currency of the symptom loses value, and the symptom may be allowed to improve. Efficacy of Cognitive Behaviour Therapy and SSRI in treatment of Conversion Disorder reveals that CBT combined with SSRI would be more efficacious to reduce the symptoms severity than SSRI alone for conversion disorder patients.

Keywords: Conversion Disorder, Cognitive Behaviour Therapy, Selective Serotonin Reuptake Inhibitor, Psychosocial Dysfunction.

Introduction

In Conversion disorder patients come with their symptoms such as numbness, paralysis, or seizures, where no medically evident explanations found^[1]. Mostly these complications rise in reaction to problems which patient faces in their daily life. Both, ICD-10 as well as DSM-V (APA, 2013) considered that conversion is a psychiatric disorder^{[2][3]}. According to ICD-10 “conversion” is usually useful to some complaints; it suggests that the unlikely distress, produced by the complications and clashes which the patient is not able to resolve, gets changed into the signs. According to ICD-10, dissociative (or conversion) disorders is an incomplete or comprehensive loss of the usual actions associated with the recalls of the past, consciousness of self, awareness of surroundings and controlled body

activities. Usually, an important amount of controlled awareness on the recalls and senses can be chose for instant care and for the actions that has to be approved.

However, these complaints previously classified as “conversion hysteria”, now, the term “hysteria” is seems to be avoided.

Diagnostic Criteria: Conversion symptoms, also described as pseudo-neurological symptoms, are abnormalities or deficits in voluntary motor or sensory function that are medically unexplained. Some of the most common pseudo-neurological symptoms are pseudo-seizures, pseudo-paralysis and psychogenic movement disorders. According to DSM-IV, conversion disorder is characterized by the presence of one or more pseudo-neurological symptoms that are distressing and/or disruptive and are associated with psychological stressor(s) or conflict(s). Also, the symptoms cannot be intentionally produced or feigned^[8]. The onset and course of conversion disorder often take the form of an acute episode. Symptoms may remit within a few weeks of an initial episode and they may recur in the

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future. Some research indicates that a brief duration of symptoms prior to treatment is associated a better prognosis [9][10][11].

The aetiology of conversion disorder was always controversial. According to some researchers sexual categories, mental distress, family clashes, economical status, home stress, social surroundings are some of the important factors which plays an important role^[12]. It was proved that the onset of this disorder in mid to late age range is due to the parental dysfunction and family psychopathology in younger age. The prevalence is highest in rural areas, uneducated and in the lesser socioeconomic classes

Treatment of Conversion Disorder: Although treating conversion disorder by psychoanalytic and behavioural method were emphasized in recent years with growing interest in using Cognitive Behavioural Therapy (CBT) in clinics worldwide, the efficacy of the method is found considerable. CBT has been declared as a successful treatment for the conditions grouped under the somatoform disorders, currently known as Somatic Symptom and Related Disorders. Randomized controlled clinical trials found that conversion disorder can be successfully treated with CBT which included the modification of catastrophic cognitions and inappropriate behaviours. A study conducted showed CBT to be effective in treating conversion disorder^{[13][14]}.

Studies report improvement with selective serotonin reuptake inhibitors (SSRIs), beta-blockers, analgesics, and benzodiazepines^[15]. An open trial of antidepressants in patients with psychogenic movement disorder and recent or current depression also showed that class of medications to be effective in reducing conversion symptoms^[16]. An ongoing randomized controlled study is evaluating the effectiveness of sertraline for patients with nonepileptic seizures and comorbid depression and anxiety^[17].

Demographic and Clinical Characteristics: The demographic characteristics of conversion disorder have not been investigated extensively. Nevertheless, there is some evidence that conversion disorder is more common among women^{[6][18]}, non-whites and individuals from lower socioeconomic classes^[19]. Co-morbid psychiatric distress in patients with pseudo-neurological symptoms is high; it has been estimated that 30% to 90% of patients seeking treatment for pseudo-neurological symptoms also meet criteria for at least one other psychiatric

disorder, typically somatoform disorders, affective disorders, anxiety disorders, or personality disorders^[20]. A co-morbid personality disorder diagnosis has been found to indicate poor prognosis of conversion disorder^[21].

Psychosocial Dysfunction: Dysfunctions in conversion disorder patients refer to lowering of functioning irrespective of whether an adjustment is made with the circumstances or not, whether it is of permanent nature or not and whether it can be corrected in the treatment or not. Hence, after remission of the disease, the different level of dysfunction is a psychological concept, which is concerned with the present functioning of the individual at a particular point of time in comparison to particular reference point in the person's life, without changing one with adjustment, without categorizing it as permanent or temporary and without creating a personal view on curability. All the five areas of dysfunctions (i.e., social, personal, familial, vocational, and cognitive) are intrinsically correlated with each other to such an extent that a particular area cannot be advocated by excluding another area, but the cognitive dysfunction is the predominant area on which other functioning are mostly dependent^{[22][23]}.

Hypothesis:

- 1) There would be a significant difference on symptoms severity at Pre-post treatment level after SSRI in conversion disorder patients.
- 2) There would be a significant difference on symptoms severity at Pre-post level after CBT combined with SSRI in conversion disorder patients.
- 3) CBT combined with SSRI would be more efficacious than SSRI alone to reduce the symptoms severity of conversion disorder patients.
- 4) SSRI alone would be more efficacious than CBT combined with SSRI to reduce the symptoms severity of conversion disorder patients.

Methodology: To achieve the objectives of the study an appropriate design and methodology is an important step in any research. A research design encompasses the methodology and procedures employed to conduct scientific research.

Aim: of this study was to study the Efficacy of Cognitive Behaviour Therapy and SSRI in treatment of conversion disorder. Description of methodology is as following:

Design: Quasi- experimental research design.

Sampling: sample consisted of conversion diagnosed patients. A sample of 30 females (20-40 years) patients with conversion disorder selected from Lady Harding medical college hospital, Delhi. Patients suffering with any co-morbid disorder and with any serious physical illness were excluded from the study.

Measures:

Dysfunction Analysis Questionnaire (DAQ): (Pershad et al., 1985): The DAQ (Pershad et al., 1985) developed at PGIMER, Chandigarh, primarily for the measurement of the dysfunction in various areas of persons with psychiatric illnesses. This scale has 50 items grouped under 5 areas, viz., social, vocational, personal, family and cognitive. Each area which the scale assesses has 10 items and each item has 5 alternative answers indicating the same, better or worse level of functioning compared with the premorbid level of functioning. Rating of 1 indicates better than premorbid level of functioning and rating of 4 indicates rapid deterioration of functioning. Some items may not be applicable to a particular patient. This scale is used to assess various psychosocial dysfunctions of an individual. This scale has highly satisfied test-retest and split half reliabilities that ranged from 0.77 to 0.97.

Procedure: To conduct the present study, ethical considerations were taken care of. Official permission was sought from the administration of the selected departments for the data collection. Subject information sheet was given to the patient in his language to explain the research. The patient consent form was given to the participants to take permission for using data for research. The questionnaires were given to the participants to be filled by themselves. The duration of administration was of 10-15 minutes. After this, SSRI alone and cognitive behaviour therapy combined with SSRI treatment was planned for the patients by the trained professional. The 12-sessions of CBT sessions were considered to help patients disturb behavioural, physiological, and emotional reactions that happened at the time of onset of illness along with sertraline 50 mg. Patients were re-examined with Dysfunction Analysis Questionnaire to examine the result and effectiveness of the treatment.

Results Analysis

The study was designed to examine the DAQ scores in the individual patient in all five domains of DAQ. The

study subjects were divided into two groups 15 patients in SSRI group and 15 patients in CBT combined with SSRI. Thus, in all 30 patients were recruited for this study.

Analysis of Treatment Effectiveness: Mean of Pre-Post treatment assessment of patient dysfunction level were compared by using *t*. test to see the difference between symptoms severities of conversion disorder after SSRI. Obtained result is mentioned below.

Table 1: Dysfunction level (Pre-post) of Conversion disorder after SSRI

Variable	Pre-Treatment Mean (S.D.)	Post-Treatment Mean (S.D.)	t. (d.f.=14)
Dysfunctioning level	66.6 (5.44)	51.2 (5.54)	14.3**

Note: ***p*<.01

The above results shows the pre-treatment mean score (M=66.6) and standard deviation (S.D. =5.44) of the dysfunctional level. As well as, the post-treatment mean score (M=51.2) and standard deviation (S.D. =5.54). Comparison between both the mean shows significant difference on dysfunction (*t*. =14.3, *p*<.01) which means that the symptoms severities of pre-post level of conversion disorder after SSRI is reduced.

Mean of Pre-Post treatment assessment of patient dysfunction level were compared by using *t*. test to see the difference between symptoms severities of conversion disorder after CBT combined with SSRI. Obtained result is mentioned below.

Table 2: Symptom severity (Pre-post) of Conversion disorder after CBT combined with SSRI

Variable	Pre-Treatment Mean(S.D.)	Post-Treatment Mean (S.D.)	t. (d.f.=14)
Dysfunctioning level	72.1 (7.3)	44.1 (7.89)	15.31**

Note: ***p*<.01

The above results shows the pre-treatment score of (M=72.1) and standard deviation (S.D=7.3) As well as, the post-treatment score (M=44.1) and standard deviation (S.D=7.89) of CBT combined with SSRI. Comparison between both the mean shows significant difference on dysfunction level (*t*. =15.31, *p*<0.1). The symptoms severities of pre-post level of conversion

disorder after SSRI are reduced.

To know whether all treatment combinations have produces similar reduction in symptom severity of conversion disorder, post treatment mean difference between different treatments combinations are calculated by using paired sample t-test. Obtained result is given in table no. 3

Table 3: Post treatment mean comparison between different treatment combinations

SSRI M (SD)	SSRI and CBT M (SD)	t.	Significance
51.26	44.13	2.70	.01
(5.54)	7.89		

Note **p<.01

As mentioned in table no. 3, paired sample t-test revealed that there is significant difference between the post treatment mean scores of conversion disorder patients treated by SSRI only, patients treated with combination of SSRI and Cognitive behaviour therapy ($t.= 2.70, P<.01$).

Above results shows that SSRI when combine with CBT found to be more effective than SSRI alone because when dysfunction level decreases the condition and symptoms of patient improves.

Discussion

Diagnosis and treatment of conversion disorder was controversial throughout the history of psychiatry. Even the form of its diagnosis sited on the basis of psychogenic model. In recent times, many researchers focused to determine the doubt related to aetiology and causal factors.

The most important cause for the diagnosis of disorder is a distortion or lack in neurological functioning without any organic injury. Conversion disorder is showed with pseudo-neurological symptoms in both classifications that must be well-known from true medical findings. In the past, hysteria was supposed as female disease. According to Early Egyptian physicians it was recognised as the symptoms of hysteria specifically related to women.

Psychosocial causes related to conversion disorders are reflected as conflicts in interpersonal relationship and social communication. As a result, it appear in avoidance from obligation, expression of emotion, symbolize a

feeling or belief. Females were well thought-out as lesser then male and had no right to express their feeling as well as emotions willingly; so they were more likely to to develop hysterical symptoms. In Sub-continent, these let go thoughts are still prevailing. Personality features along with social, cultural and ethnic background may contribute in development of conversion disorder.

There is inadequate data on the treatment of conversion disorder or of pain disorder to make any conclusion. An evaluation of the empirical research on CBT for somatoform disorders suggests that in some respects it mirrors the literature on evaluating the efficacy of psychotherapy literature with various mental disorders. CBT has been shown to be superior to various control conditions, especially waiting lists or standard medical treatment. Effect sizes are respectable, relative to other medical or quasi-medical interventions.

According to some researches Selective serotonin reuptake inhibitors (SSRIs) may be helpful for somatization or dissociation. A pilot randomized controlled trial of sertraline in 38 patients with PNES revealed a 59.3% seizure reduction in the combined CBT and drug arm compared to the conventional treatment group. Neuroleptics and propranolol may be employed for severe dissociative disorders.

In this study, it was found that CBT combined with SSRI was proved to be more effective to improve the dysfunctions of conversion disorder patients whereas SSRI alone was not found to be that effective.

Conclusion

Most patients with functional Conversion Disorder will require an integrated multidisciplinary approach to treatment. The diagnosing clinician should communicate with the treating physical therapist and/or mental health clinician, and everyone should agree on the treatment plan. Other established health care providers should be informed of the functional Conversion Disorder diagnosis, as patients may present with other physical symptoms of uncertain origin, and there should be agreement on the message among all providers and minimization of unnecessary treatments. Functional Conversion Disorder are truly at the intersection of Conversion and psychiatry: patients present with neurological symptoms that are a manifestation of a neuropsychiatric disorder. Dualistic thinking is not helpful for these patients, as neurological symptoms and emotional functioning need to be viewed as influencing

each other. Integration of care is needed for this patient group.

Hence, according to this study CBT when combined with SSRI proved to be effective for conversion disorder patients

Conflict of Interest: Nil

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Ethical Clearance: Taken from SGT, University Ethical Committee.

Reference

- [1]. Sadock VA. Synopsis of psychiatry behavioral Sciences/clinical psychiatry. Translate by Rafiei H, Sobhaniyan KH. Tehran: Arjmand. 2007;2:135-82.
- [2]. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5®). American Psychiatric Pub; 2013 May 22.
- [3]. World Health Organization. The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines. Geneva: World Health Organization; 1992.
- [4]. Wengrat B. Theater of disorder: Patients, doctors, and the construction of illness. Oxford University Press; 2001 Oct 4.
- [5]. Singh SP, Lee AS. Conversion disorders in Nottingham: alive, but not kicking. *Journal of psychosomatic research*. 1997 Oct 1;43(4):425-30.
- [6]. Deveci A, Taskin O, Dinc G, Yilmaz H, Demet MM, Erbay-Dundar P, Kaya E, Ozmen E. Prevalence of pseudoneurologic conversion disorder in an urban community in Manisa, Turkey. *Social psychiatry and psychiatric epidemiology*. 2007 Nov 1;42(11):857-64.
- [7]. Owens C, Dein S. Conversion disorder: the modern hysteria. *Advances in Psychiatric Treatment*. 2006 Mar;12(2):152-7.
- [8]. American Psychiatric Association. APA (1994). Diagnostic and statistical manual of mental disorders. 1996;4.
- [9]. Crimlisk HL, Bhatia K, Cope H, David A, Marsden CD, Ron MA. Slater revisited: 6 year follow up study of patients with medically unexplained motor symptoms. *Bmj*. 1998 Feb 14;316(7131):582-6.
- [10]. Hafeiz HB. Hysterical conversion: a prognostic study. *The British Journal of Psychiatry*. 1980 Jun;136(6):548-51.
- [11]. Grattan-Smith P, Fairley M, Procopis P. Clinical features of conversion disorder. *Archives of Disease in Childhood*. 1988 Apr 1;63(4):408-14.
- [12]. Carter RB. On the pathology and treatment of hysteria. J. Churchill; 1853.
- [13]. LaFrance Jr WC, Devinsky O. The treatment of nonepileptic seizures: historical perspectives and future directions. *Epilepsia*. 2004 Jun;45:15-21.
- [14]. Voon V, Lang AE. Antidepressant treatment outcomes of psychogenic movement disorder. *The Journal of clinical psychiatry*. 2005 Dec.
- [15]. LaFrance Jr WC, Barry JJ. Update on treatments of psychological nonepileptic seizures. *Epilepsy & Behavior*. 2005 Nov 1;7(3):364-74.
- [16]. Faravelli C, Salvatori S, Galassi F, Aiazzi L, Drei C, Cabras P. Epidemiology of somatoform disorders: a community survey in Florence. *Social psychiatry and psychiatric epidemiology*. 1997 Jan 1;32(1):24-9.
- [17]. Folks DG, Ford CV, Regan WM. Conversion symptoms in a general hospital. *Psychosomatics*. 1984 Apr 1;25(4):285-95.
- [18]. Binzer M, Andersen PM, Kullgren G. Clinical characteristics of patients with motor disability due to conversion disorder: a prospective control group study. *Journal of Neurology, Neurosurgery & Psychiatry*. 1997 Jul 1;63(1):83-8.
- [19]. Mace CJ, Trimble MR. Ten-year prognosis of conversion disorder. *The British Journal of Psychiatry*. 1996 Sep;169(3):282-8.
- [20]. Chadda RK. Social support and psychosocial dysfunction in depression. *Indian J Psychiatry* 1995;37:119-23.
- [21]. Verma SK, Pershad D. Measurement of change in psychosocial functioning following illness and therapeutic intervention. *Indian J Clin Psychol* 1989;16:64-7.
- [22]. Nicholson TR. Studies in Conversion Disorder: Testing the Psychological Model and Freudian Theories.
- [23]. Furqan Nusair, M.B.B.S., Nathan Franck, B.A., Rafael Klein-Cloud, A.B.(2017) Conversion Disorder With Conceptual and Treatment Challenges 19 Apr 2017 <https://doi.org/10.1176/appi.ajp-rj.2016.110708>.

- [24].Brigitte Khoury* and Joumana Ammar,(2014)” Cognitive behavioral therapy for treatment of primary care patients presenting with psychological disorders” 2014 Mar 31. doi: 10.3402/ljm.v9.24186.
- [25].Vyskocilova J, Prasko J, Sipek J,” Cognitive behavioral therapy in pharmaco-resistant obsessive-compulsive disorder” 2 December 2015.
- [26].Verdurmen MJH, Videler AC, Kamperman AM, Khasho D, van der Feltz-Cornelis CM,” Cognitive behavioral therapy for somatic symptom disorders in later life: a prospective comparative explorative pilot study in two clinical populations” 1 September 2017 Volume 2017:13 Pages 2331—2339

In Vitro Study of Constitutive and Inducible Clindamycin Resistance in *Staphylococcus Aureus* with Reference to Methicillin Resistant *Staphylococcus Aureus*: Experience From Tertiary Care Hospital in Punjab

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Abstract

Background: Serious infections due to methicillin resistant *Staphylococcus aureus* (MRSA) have become a major clinical challenge. Globally Macrolide-lincosamide streptogramin B family of antibiotics are commonly used to treat such infections as an alternative to vancomycin. The study was to conducted to find out the presence of inducible clindamycin resistance among *Staphylococcus aureus* and their association with methicillin resistance.

Method: The study conducted over one year (Jan 2016 - Dec 2016) in microbiology department of Guru Gobind Singh Medical College, Faridkot . Two hundred fifteen *S.aureus* isolates were included in the study. Methicillin resistance was detected by cefoxitin (30µg) disc diffusion method and inducible clindamycin resistance by erythromycin and clindamycin disc approximation test (D-Test).

Results: Of the 215 clinical isolates of *S.aureus*, 140 (65.11%) were MRSA. Erythromycin and clindamycin resistance was seen in 79.06%(170/215) and 49.30% (106/215) respectively. Resistance to erythromycin and clindamycin were higher in MRSA than MSSA (erythromycin resistance:100%v s 22.5% and Clindamycin resistance:70.1% vs 10.6%). Both iMLSB and cMLSBphenotypes are predominant in MRSA.

Conclusion: Detection of MRSA in our study shows the need to improve health care practices and to formulate new infection control policies to control MRSA infections. Inducible and constitutive resistance is comparatively higher in our study in MRSA .So It is necessary to perform D-test for detection of inducible clindamycin resistance among MRSA in routine antibiotic sensitivity testing so that therapeutic failures can be avoided.

Keywords: *Staphylococcus aureus*, MRSA, Inducible Clindamycin resistance, D-test

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Introduction

Antimicrobial resistance in *Staphylococcus aureus* has become an ever-increasing problem. Methicillin resistant *S. aureus* (MRSA) which are often multiply resistant to other classes of antibiotics in addition to β-lactams, with increasingly high resistance to macrolides (erythromycin, clarithromycin) and lincosamides (clindamycin, lincomycin) leaving very

few therapeutic options⁽¹⁾. Newer antibiotics like vancomycin, linezolid and quinupristin-delfopristin have been advocated in treatment of such resistant isolates. Recent reports of resistance to these antibiotics raise real concerns about difficulties in therapy. The macrolide-lincosamide-streptogramin B (MLS_B) family of antibiotics is commonly used in the treatment of staphylococcal infections. However, widespread use of MLS_B antibiotics has led to an increase in number of staphylococcal strains acquiring resistance to MLS_B antibiotics.⁽²⁾ Clindamycin, a lincosamide, represents an attractive option for treatment erythromycin resistant *Staphylococcus aureus* both in methicillin-resistant and susceptible staphylococcal infections, especially skin and soft tissue infections, for various reasons: available in both oral and intravenous formulations; excellent tissue penetration; less costly; inhibits productions of certain toxins and virulence factors in staphylococci⁽³⁾. However, possible presence of inducible clindamycin resistance among staphylococcal isolates is a major concern in use of clindamycin.⁽⁴⁾

Macrolide resistance arises either by an efflux mechanism or by target modification, the later resulting into resistance not only to macrolide but also to lincosamides and group B streptogramins⁽⁵⁾. An *erm* gene encodes methylation of the 23S rRNA- binding site that is shared by these drugs. Phenotypically, such resistance can be constitutive (MLS_{Bc} phenotype) or inducible (MLS_{Bi} phenotype)⁽⁶⁾. It is also possible for mutations to occur spontaneously that will transform MLS_{Bi} strains to MLS_{Bc} phenotype without the presence of a macrolide inducer, a concern being that this change might occur in the midst of therapy⁽⁷⁾.

S. aureus isolates with constitutive resistance show resistance to erythromycin and clindamycin on in-vitro testing, whereas isolates with inducible resistance show resistance to erythromycin but appear sensitive to clindamycin on disc diffusion testing. Inducible clindamycin resistance in staphylococci can be detected by D test⁽⁸⁾. For erythromycin-resistant isolates, D test can help to determine whether clindamycin could be used as a therapeutic option. This study was undertaken to determine prevalence of inducible and constitutive clindamycin resistance among clinical *S. aureus* isolates and to study their association with MRSA.

Material and Method

This prospective study conducted over one year

(January 2016 to December, 2016). A total of 215 *Staphylococcus aureus* (Catalase positive, coagulase positive)⁽⁹⁾ were isolated from various clinical specimens like pus, blood, urine and catheter tips and drains. Methicillin resistance was detected by cefoxitin disc (30µg). The isolates which yielded zone diameter of <22mm around cefoxitin reported as MRSA.⁽⁸⁾

The erythromycin resistant strains were subjected to D –Test as per CLSI guidelines. Briefly, erythromycin (15µg) disc was placed at a distance of 15mm (edge to edge) from clindamycin (2µg) disc on a Mueller Hinton agar plate previously inoculated with 0.5 McFarland bacterial suspension. Following overnight incubation at 37°C, flattening of zone (D-shaped) around clindamycin in the area between the two discs, indicated inducible clindamycin resistance.⁽¹⁰⁾

Three different phenotypes were appreciated after testing and interpreted as follows:

- 1. MS Phenotype:** Staphylococcal isolates exhibiting resistance to erythromycin (zone size ≤13mm) while sensitive to clindamycin (zone size ≥21mm) and giving circular zone of inhibition around clindamycin.
- 2. Inducible MLS_B Phenotype:** Staphylococcal isolates showing resistance to erythromycin (zone size ≤13mm) while being sensitive to clindamycin (zone size ≥21mm) and giving D shaped zone of inhibition around clindamycin with flattening towards erythromycin disc were labeled as having this phenotype .
- 3. Constitutive MLS_B Phenotype:** This phenotype was labeled for those Staphylococcal isolates which showed resistance to both erythromycin (zone size ≤13mm) and clindamycin (zone size ≤14mm) with circular shape of zone of inhibition if any around clindamycin.

Results

Of 215 *S.aureus* isolates 65.11% (140/215) were MRSA and 34.89% (75/215) were MSSA. Erythromycin and clindamycin resistance was seen in 79.06% (170/215) and 49.30% (106/215) isolates respectively. In this study erythromycin resistance (100%vs22.5%) and clindamycin resistance (70%vs10.6%) both were significantly higher in MRSA than among MSSA (p value=0.000). Similarly, constitutive as well inducible clindamycin resistance phenotypes were significantly

higher in MRSA (53% and 16.42%) than among MSSA (7.5% and 2.6%). In this study prevalence of iMLSB among *S.aureus* was found to be 13.48%.

Table1: Clindamycin susceptibility patterns among MRSA and MSSA

Phenotype	MRSA N=140	MSSA N=75
E-S, Cl-S	Nil	45(60%)
E-R, CL-S (iMLSB)	23(16.42%)	6(8%)
E-R, Cl-R (cMLSB)	75(53%)	2(2.6%)
E-R, Cl-S (MS Phenotype)	42(30.17%)	22(29.33%)

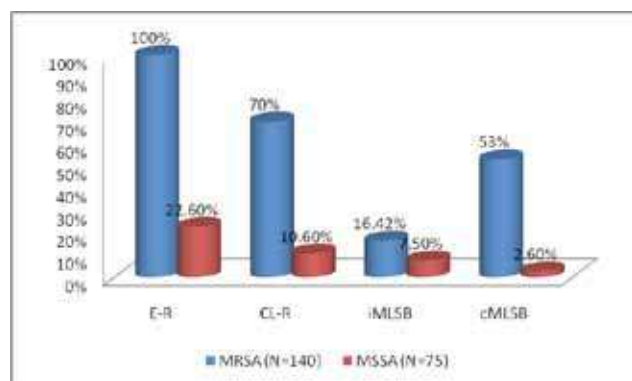


Fig 1: Comparison of erythromycin, clindamycin, iMLSB and cMLSB resistance among MRSA and MSSA

Table 2: Clindamycin susceptibility pattern among erythromycin resistant isolates: N=170

	MRSA	MSSA	TOTAL
iMLSB	23 (13.52%)	6 (3.5%)	29 (17.02%)
cMLSB	75 (44.11%)	2 (1.1%)	77 (45.21%)
MS phenotype	42 (24.70%)	22 (12.94%)	64 (37.64%)

Discussion

Improper infection prevention practices in hospital, indiscriminate use of antibiotics and hospitalization in ICUs has contributed to emergence of MRSA. Macrolide-Lincosamide-sterptograminB family of antibiotic are commonly used to treat MRSA infections. In the present study constitutive resistance to clindamycin was observed in 53% which is almost similar to the findings of Adhikari *et al*⁽¹¹⁾ but much higher than the studies of Baiuet *al*⁽¹²⁾, Koppada *et al*⁽²⁾ and Sahet *al*⁽¹⁾. The reason for this could be selective pressure because of wide spread use of erythromycin and clindamycin for the treatment of even minor staphylococcal infections. Molecular studies have shown that some SCCmec elements on MRSA

carry transposon Tn554 which contains the *ermA* gene mediating MLS resistance resulting in higher rate of resistance to MLS antimicrobial agents⁽¹³⁾.

Inducible clindamycin resistance was found to be 16.42% in our study which is similar to that reported by Ansari *et al*.⁽¹¹⁾ and Govindan *et al*⁽¹⁴⁾. However higher iMLSB resistance of 37.5% from another study from India⁽¹⁵⁾ and 91% from Japan⁽¹⁶⁾ has also been reported.

In the present study, 30.17% of MRSA among the erythromycin resistant isolates were MS phenotype (E-R, Clin-S). This means that clindamycin could be used as a treatment option only for 30.17% of MRSA which are erythromycin resistant. So, there are only 30.17% chances of clinical efficacy of clindamycin while treating erythromycin resistant MRSA infections as an alternative to vancomycin. These findings further emphasize the need of performing D- test in routine to avoid clinical failure while using clindamycin as an alternative to anti-MRSA antibiotics like vancomycin and linezolid. Regular surveillance of hospital associated infections, monitoring of antibiotic sensitivity pattern of MRSA and formulation of definite antibiotic policies may be helpful in reducing the incidence of MRSA infections. This will guide clinicians to choose appropriate antibiotics to treat such infections without causing treatment failures.

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Ethical Clearance: The study in the article is sub part of the thesis. Ethical clearance of thesis is attached here:

References

- Sah P, Khanal R, Lamichhane P, Upadhaya S, Lamsal A, Pahwa VK. Inducible and constitutive clindamycin resistance in *Staphylococcus aureus*: an experience from Western Nepal. *Int J Biomed Res.* 2015;6(5):316–9.
- Koppada R, Meeniga S, Anke G. Inducible Clindamycin Resistance among *Staphylococcus Aureus* Isolated From Various Clinical Samples with Special Reference to MRSA. *Sch J Appl Med Sci.* 2015;3(6D):2374–80.
- Stevens DL, Gibbons AE, Bergstrom R, Winn V. The Eagle effect revisited: efficacy of clindamycin, erythromycin, and penicillin in the

- treatment of streptococcal myositis. *J Infect Dis.* 1988;158(1):23–8.
4. Panagea S, Perry JD, Gould FK. Should clindamycin be used as treatment of patients with infections caused by erythromycin-resistant staphylococci? *J Antimicrob Chemother.* 1999;44(4):581–2.
 5. Leclercq R. Mechanisms of resistance to macrolides and lincosamides: nature of the resistance elements and their clinical implications. *Clin Infect Dis [Internet].* 2002;34(4):482–92.
 6. Weisblum B. Erythromycin resistance by ribosome modification. Vol. 39, *Antimicrobial Agents and Chemotherapy.* American Society for Microbiology; 1995. p. 577–85.
 7. Lewis JS, Jorgensen JH. Inducible clindamycin resistance in Staphylococci: should clinicians and microbiologists be concerned? *Clin Infect Dis [Internet].* 2005;40(2):280–5.
 8. Clinical & Laboratory Standards Institute: CLSI Guidelines - Performance Standards for Antimicrobial Susceptibility Testing. 2018; Available from: https://clsi.org/media/1469/m100s27_sample.pdf
 9. Baird D. Staphylococcus: cluster forming gram positive cocci. In: Mackie and McCartney practical medical microbiology. Churchill Livingstone New York, NY, USA; 1996. p. 245–61.
 10. Tekin A, Dal T, Deveci O, Tekin R, Atmaca S, Dayan S. Assessment of methicillin and clindamycin resistance patterns in Staphylococcus aureus isolated from a tertiary hospital in Turkey. *Infez Med.* 2013;21(2):111–6.
 11. Adhikari RP, Shrestha S, Barakoti A, Amatya R. Inducible clindamycin and methicillin resistant Staphylococcus aureus in a tertiary care hospital, Kathmandu, Nepal. *BMC Infect Dis.* 2017;17(1):483.
 12. Baiu SH, Al-Abdli NE. Inducible Clindamycin Resistance in Methicillin Resistant Staphylococcus aureus. *Am J Infect Dis Microbiol.* 2016;4(1):25–7.
 13. Blair JMA, Webber MA, Baylay AJ, Ogbolu DO, Piddock LJ V. Molecular mechanisms of antibiotic resistance. *Nat Rev Microbiol.* 2014;13(1):42–51.
 14. Govindan S, Mohammed CA, Bairy I. Inducible Clindamycin Resistance Among the Staphylococcus aureus Colonizing the Anterior Nares of School Children of Udupi Taluk. *Nepal J Epidemiol.* 2014;4(1):337–40.
 15. Lall M, Sahni AK. Prevalence of inducible clindamycin resistance in Staphylococcus aureus isolated from clinical samples. *Med J Armed Forces India.* 2014;70(1):43–7.
 16. Shoji K, Shinjoh M, Horikoshi Y, Tang J, Watanabe Y, Sugita K, et al. High rate of inducible clindamycin resistance in Staphylococcus aureus isolates--a multicenter study in Tokyo, Japan. *J Infect Chemother.* 2015;21(2):81–3.

A Study of Gender Based Knowledge Level on Risk and Cause of Obesity among Management Students of Urban, Rural, Semi Urban Areas of East Midnapore District

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Abstract

Context: Obesity is becoming a huge burden for our society, it causes premature death and impairment of health some times for life long as it calls many diseases. The obesity is preventable. Awareness on obesity is a key of success of controlling that, but unfortunately our society is not showing aware of it. In this study we are trying to find out the knowledge level on risk and causes of obesity among different genders by using independent samples t test and to see the difference of knowledge level (both causes and risk of obesity) among rural, semi urban and urban, we have done ANOVA. We have used SPSS, 17th version. Total 138 students from those areas are included in the study. The study shows overall knowledge score is poor and there is gender inequality existing in semi urban and rural areas in respect of knowledge. Also the study showed knowledge level on obesity is statistically different among urban, rural and semi urban areas.

Keyword: Obesity, urban, rural, semi urban, society, awareness, gender inequality.

Introduction

Obesity is a metabolic disorders and it causes diseases like cardio vascular disease, diabetes, some cancer and many more (Schmidt, 2011)¹⁴ and it is now a major cause of disability and pre mature death. Number of obesity increases about 50% during 1980 to 2013. The western life styles are assimilated by developing countries; rapid urbanization, fast and sedentary lifestyle, consumption of junk foods, and many unhealthy practice are the cause obesity (Gothankar, 2011)⁶. Health promotion is generally concentrated on the health education, and health knowledge (Chaponniere, 2013)³. Study shows the adult people who are lacking the formal education

are more likely to have poor health (Lui C K, 2014)⁹. The Indian women are more involved in the household work which in turn to be sedentary life (Saikia, 2009)¹³. Not only urban areas but also rural women are slowly affected by unhealthy life style, the situation is worse as rural people are having poor educational background (Deying, 2011)⁵. Though few researchers showed that the urban girls are more prone to be obese than that of rural girls as the life style of urban and rural girl differs significantly (Hallal, 2006)⁷, but now the rural life is slowly getting affected by modern life. The rural people is having poor health knowledge (Qiuzhuang, 2007)¹². A study shows the rural women have higher total cholesterol level than rural male. Life style changed frequently in case of young population which is in most of the cases unhealthy. It is also seen that decrease physical activities, more time spending in television, engage in the social networking site are one of the major causes of obesity (Vohra, 2011)¹⁷. India is having gender discrimination in terms of education, health and even nutrition; in this regard education can play a vital role in it (Chaudhary, 1995)⁴. Few studies have made to

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assess the impact of obesity in the rural areas. Though the prevalence rate of obesity is more in case of urban areas than that of rural areas (Brahmbhatt, 2012)² but obesity is persistent in the both the areas. Study in the rural areas is becoming essential, as the rural areas are slowly influenced by modern life style (Shetty, 2002)¹⁵ also poor level of awareness is existing (Ade, 2014)¹. Desired level of awareness of obesity is still confined to those populations who are adhering with the health care field (Nyaruhucha, 2003)¹¹. As there are few number of researches have done to show the difference of knowledge level on obesity among students of urban, rural and semi urban areas so it is necessary to do such research, also as many study showed there is existing level of gender inequality among students so it is became necessary to included in the study. So the objective of the study is

1. To see whether there is existence of any differences of knowledge level on risk and causes of obesity among the college goers from urban, rural and semi urban areas.
2. To see whether there is existence of gender inequality in respect of knowledge level on risk and causes of obesity among the college goers from urban, rural and semi urban areas.

Materials and Method

A cross sectional study has carried out in three different private management colleges located in East Midnapore. The Undergraduate students of the college, who are studying management, are included in the study and they are aged between 18 to 22 years. An informed consent is taken from the students and only those who are interested, are included in the study. Purpose of the study is also informed to the student before conducting the study. The study was also approved by the ethics committee. A questionnaire was developed which comprises two segments – first segment comprises 10 questions which are to assess the knowledge level of causes of obesity and second segment comprises 10 questions which are to assess the knowledge of risk associated with obesity or health hazard associated with obesity. Students are divided into three segments according to their locality – urban, rural and semi urban. From each segments 60 students were randomly selected. So total 180 students were included in the study, but 22 of them are rejected as they gave incomplete answer so at the end 43 students from urban, 44 students from semi urban and 52 from rural i.e. total 139 students are

included in the study. To see the difference of knowledge level of risk and the causes of obesity among the students from urban areas, rural areas and the semi urban areas as well as the students of different gender, ANOVA and independent samples t test have run by the use of SPSS 17th version.

Results

Table 1: Characteristics of the respondents

According to Gender		
	Frequency	Percentage
Male	65	47.10%
Female	73	52.89%
According to Locality		
	Frequency	Percentage
Urban	42	30.43%
Rural	52	37.68%
Semi Urban	44	31.88%

The above table shows the distribution of the respondents by the gender. 65 i.e. 47.10% are male and 73 i.e. 52.89% of them are Female. The table is also showing the distribution of the respondents by their residence. 42 i.e. 30.43% of them are from Urban areas, 52 i.e. 37.68% of them are from Rural areas and 44 i.e. 31.88% of them are from Semi Urban areas. The knowledge level towards the risk and causes of obesity are collected and plotted in the SPSS and one way ANOVA performed and it gives the output below

Table 2: The Descriptive analysis

Knowledge level of Risk of Obesity		
	N	Mean
Rural Areas	52	21.38
Semi Urban Areas	44	25.75
Urban Areas	43	26.28
Total	139	24.47
Knowledge level of Causes of obesity		
	N	Mean
Rural Areas	52	23.73
Semi Urban Areas	44	29.82
Urban Areas	43	30.93
Total	139	28.15

From the above chart it can be concluded that the mean of knowledge level of risk of obesity in people of urban areas (26.28) followed by Semi Urban areas (25.75) and lastly the rural areas (21.38). Apart from that the mean of knowledge level of causes of obesity in

people of urban areas (30.93) followed by Semi Urban areas (29.82) and the Rural areas (23.73).The existing knowledge level of risk and causes of obesity is different

in urban, rural and semi urban areas are collected and plotted in the SPSS and one way ANOVA was performed and it gives the output below

Table 3: ANOVA table

Knowledge level of Risk of Obesity					
	Sum of Squares	Df	Mean Square	F	Significance
Between Groups	702.849	2	351.424	41.444	< .001
Within Groups	1153.209	136	8.479		
Total	1856.058	138			

Knowledge level of Causes of Obesity					
	Sum of Squares	Df	Mean Square	F	Significance
Between Groups	1460.591	2	730.296	48.601	< .001
Within Groups	2043.567	136	15.026		
Total	3504.158	138			

From the first ANOVA table, it can be concluded that there is significant differences existing among Students from rural, urban and semi urban areas on existing level of knowledge of risk of obesity. $F(2, 136) = 41.444$, and the P value is less than .001, also from the second ANOVA table it can be concluded that there are significant differences persisting among Students from rural, urban and semi urban areas on existing level of knowledge of causes of obesity. $F(2, 136) = 48.601$ and the P value is less than .001.

Table 4: Multiple comparisons for knowledge level of risk of Obesity

Areas 1	Area 2	Significance
Rural	Semi Urban	< .001
	Urban	< .001
Semi Urban	Rural	< .001
	Urban	.601
Urban	Rural	< .001
	Semi Urban	.601

Table 5: Multiple comparisons for knowledge level of causes of Obesity

Areas 1	Area 2	Significance
Rural	Semi Urban	< .001
	Urban	< .001
Semi Urban	Rural	< .001
	Urban	.346
Urban	Rural	< .001
	Semi Urban	.346

The Games Howell method reveals that significant differences among Rural - Semi Urban, Rural-Urban and Semi Urban – rural are existing in respect to level of knowledge on risk of obesity. In case of rural - semi urban, rural-urban the p value is less than .001 but in case of semi urban – urban, no significant differences is found, p value is .601. Another comparison reveals - there are significant differences existing between Rural-Semi Urban, Rural-Urban and Semi Urban-rural in respect to level of knowledge on causes of obesity. In case of rural - semi urban, rural - urban the p value is less than .001 but in case of semi urban – urban there is no significant differences between them. The p value is .346.

Table 6: 2 tailed sample t test to see to see the gender and area wise knowledge gap

Urban Area					
Causes of Obesity		P value	Risk of Obesity		P value
Male	Female		Male	Female	
30.38	31.45	.196	26.19	26.36	.856
Rural Area					
Causes of Obesity		P value	Risk of Obesity		P value
Male	Female		Male	Female	
27.34	20.86	< .001	24.21	19.13	<.001
Semi Urban Area					
Causes of Obesity		P value	Risk of Obesity		P value
Male	Female		Male	Female	
32.90	26.72	< .001	27.18	24.31	<.001

The above table shows there is no gender inequality existing in case of urban students in terms of knowledge level of causes and risk of obesity, as the p value is .196 and .856 respectively, but in case of both the rural and semi urban areas the knowledge level of causes and risk associated with obesity is statistically different among genders. In both the cases the p value is less than .001.

Discussion

The overall level of knowledge score on risk and causes of obesity is poor among urban, rural and semi urban students, same types of research result was shown by Nyaruhucha¹¹ in the year 2003. Among them urban have scored highest followed by semi urban and lastly rural students. Same kinds of results can be found in many studies including Iloh⁸ in the year 2011. The ANOVA analysis reveals that the students of urban and semi urban have statistically same level of knowledge score on causes and risks of obesity. In case of rural – semi urban and rural – urban the difference is statistically significant. That means the knowledge level on obesity of rural people is poorest. The study also has some other perspective i.e. gender. In case of urban area the knowledge level on risk and causes of obesity is same in both the gender i.e. difference of knowledge levels on obesity in both male urban and female urban have statistically insignificant. The p value is .196 and .856 respectively, but in case of both the genders of semi urban and rural the difference is huge and the differences are statistically significant and P value in both the cases is less than .001., same kind of results can be seen in research paper published by Mugo¹⁰ in the year 2016. So there is gender inequality existing in case of rural and semi urban students in respect of knowledge level on risk and causes of obesity but it is not true in case of urban students. The study suggests an extensive awareness program on obesity is needed and same kind of suggestion is given by Tiwari¹⁶ in the year 1998. Urban areas are well communicated with health care facilities and the people are more aware of many health problems but unfortunately it is not true in case of rural and semi urban areas. In those areas gender inequality can be seen too in terms of health awareness but it is not true in case of urban areas.

Implication: The study reveals two different and important aspects, first one is showing that knowledge regarding risk and causes of obesity is poorest among rural population and secondly the knowledge level regarding obesity differs in both the genders of rural

population. Rural girls have poorer knowledge level on obesity than rural boys. It is not true in case of urban or semi urban population. So a clear discrimination can be seen in rural population in respect of existing knowledge level of obesity among two genders. So series of extensive surveys and continuous health educational programs are required to be conducted for the purpose of enhancement of knowledge level on health among rural girls. Also as the knowledge level of obesity is also poor in other groups they are also included in those programs too.

Conclusion

The study shows that the college goers are not satisfactorily aware of the risk and causes of obesity, also there is gender inequality existing in semi urban and rural areas in respect of level of knowledge on obesity. Also the study reveals though the urban and semi urban people have almost same level of knowledge on obesity but in case of rural people the knowledge level is poorest. So there is need of improvement of awareness among students of different areas, especially among rural people. Apart from that as there is existence of gender inequality among students of semi urban and rural areas so special emphasis on the implementation of process for up gradation of knowledge level among girl of those areas are needed.

Ethical Clearance: We got ethical clearance from Vice Chairman of different private colleges of Purba Midnapore district. Also the researchers have explained the purpose of the research and each respondent was assured by the researchers to maintain complete confidentiality.

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Conflict of Interest: Nil

Reference

1. Ade Anju, Chethana K V, Mane Abhay, Hiremath S G. Non-communicable diseases: Awareness of risk factors and lifestyle among rural adolescents. International Journal of Biol Medical Research 2014; 5(1):3769-377.
2. Brahmhatt KR, Oza UN. Obesity among adolescents of Ahmadabad city, Gujarat, India-a community based cross-sectional study. Int J Biol Med Res 2012; 3(2):1554-7.
3. Chaponniere P A, Cherup S M, Lodge L J.

- Measuring the impact of health education modules in Cameroon, West Africa. *Transcult Nurs* 2013; 24(3):254-62.
4. Chaudhary P D. Girl Child and Gender Bias. *Social Change* 1995; 25(2 & 3):84-93.
 5. Deying L, Haiyun Y. The western rural areas the main problems of the basic medical and health resources allocation and the countermeasure analysis. *Western Econ Manage* 2011; (04):28. 30-62.
 6. Gothankar J S. Prevalence of obesity and its associated comorbidities amongst adults. *National Journal of Community Medicine* 2011; 2(2):221-24.
 7. Hallal PC, Victora CG, Azevedo MR, Wells JC. Adolescent physical activity and health: a systematic review. *Sports Med* 2006; 36(12):1019-30.
 8. Iloh G, Amadi AN, Awankwo BO, et al. (2011). Obesity in Adult Nigerians: A study of its pattern and common primary co-morbidities in a rural mission General Hospital in Imo state South-eastern Nigeria. *Nigerian Journal of Clinical Practice*. 2011; 14(2): 212-218. DOI: 10.4103/1119-3077.84019
 9. Lui C K, Chung P J, Wallace S P, Aneshensel C S. Social status attainment during the transition to adulthood. *J Youth Adolesc* 2014; 43(7):1134-50.
 10. Mugo A. Obesity among Women in Rural Kenya: Knowledge, Beliefs, and Perceptions 2016.
 11. Nyaruhucha C N M, Achen J H, Msuya J M, Shayo N B, Kulwa K B M. Prevalence and Awareness of Obesity Among People of Different Age Groups in Educational Institutions in Morogoro, Tanzania. *East African Medical Journal* 2003; 80(2): 68-72.
 12. Qiuzhuang W. The status of rural health education present situation and practical countermeasures. *J Pract Med Tech* 2007; 14(12):1643-4.
 13. Saikia N, Singh A. Does type of household affect maternal health? Evidence from India. *J Biosoc Sci* 2009; 41:329-353.
 14. Schmidt MI, Duncan BB, Azevedo e Silva G, Menezes AM, Monteiro CA, Barreto SM, et al. Chronic non-communicable diseases in Brazil: burden and current challenges. *The Lancet* 2011; 377(9781):1949-6. DOI [https://doi.org/ 10.1016/S0140-6736\(11\)60135-9](https://doi.org/10.1016/S0140-6736(11)60135-9).
 15. Shetty PS. Nutrition transition in India. *Public Health Nutr* 2002; 5(1A):175-82. DOI: 10.1079/PHN2001291.
 16. Tiwari R, Wagh VV, Babar VY. Obesity: As rural females perceive it. *Indian J Med Sci* 1998; 52:248-52. Retrieved from https://www.researchgate.net/publication/13438798_Obesity_as_rural_females_perceive_it
 17. Vohra R, Bhardwaj P, Srivastava J P, Srivastava S, Vohra A. Overweight and obesity among school-going children of Lucknow city. *J Family Community Med* 2011; 18:59-62.

Prevalence of Dengue Fever in India along with its Prevention and Treatment By Herbal Medicine

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Abstract

Background: Dengue viruses are the causative organism of dengue fever (DF) and dengue hemorrhagic fever (DHF). Dengue virus belongs to family Flaviviridae. Dengue virus has four serotypes (DENV-1, DENV-2, DENV-3 and DENV-4) that spread by the bite of infected *Aedes Aegypti* mosquitoes. In Ayurvedic perspectives, Dengue fever comes under the group of Abhishangaja Jvara. Dengue fever can be controlled and prevented by the number of herbal drugs which is free from any side effects. Main aim of this article is to elaborate the dengue fever and its incidence in India along with review herbal drugs which is effective in prevention and treatment of dengue fever.

Materials and Method: This review work was carried out by using a widespread and planned data mining approach. To achieve significant literature author uses the key words “dengue fever” “dengue fever in India” and “herbal medicine for Dengue fever” searched in Google Scholar, web of science, Science direct, Scopus, Medline and PubMed Central journal literature.

Results: Seven publications were included in the final selection after systematic analysis.

Conclusion: Dengue is endemic in more than 128 countries; about half of the world’s populations are at risk for infection. It is suggested that herbal plants could be used for prevention and treatment of dengue fever as potential anti-DENV agents and increasing the platelet (PLT) count, white blood cells (WBC) etc. Some herbal extracts have ovicidal activity against *Ae. Aegypti*.

Keywords: *Dengue fever, India, Herbal drugs, Abhishangaja Jvara.*

Introduction

Dengue fever and dengue hemorrhagic fever (DHF) are caused by infection due to any of the four serotypes

of dengue viruses (DENV-1, DENV-2, DENV-3 and DENV-4)^{1,2}. *Aedes aegypti* mosquito transmits the infection which breeds in clean water.³ *Aedes albopictus* is another important competent vectors for dengue virus in India⁴. According to the World Health Organization (WHO) guideline 1997, dengue patients can be categorized into three categories including dengue fever, dengue hemorrhagic fever, and dengue shock syndrome.

Dengue hemorrhagic fevers (DHF) and dengue shock syndromes (DSS) are serious clinical manifestation of the dengue infection. Over the last 30 years, there has been increase in the frequency of dengue fever (DF), DHF and DSS and their epidemics. Dengue fever is also known

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as break bone fever because of severe body and joint pains is main feature along with fever. The pathogenesis of DHF/DSS is not clear. It has been observed that sequential infection with any two of the four serotypes of dengue virus result in DHF/DSS in an endemic area.⁵ In Ayurvedic perspectives, Dengue fever comes under the group of *Abhishangaja Jvara* predominantly *Pittaja* in pathological ground. The complications of this disease represent *Raktaja* and *Sannipataja Jvara*.

Dengue infection has become endemics in most of the South East Asian countries including India. In the last one decade several minor or major outbreaks have been reported from various parts of India⁶. Dengue hemorrhagic fever was first epidemic in 1954 in Philippines country after that quickly spread in another part of world because Dengue virus is transported from one place to another by infected travelers. It is estimated that during an outbreak of DHF, about 150-200 mild to silent infections occur in community for each case of DSS seen in hospital⁷. The first major epidemics of Dengue hemorrhagic fever in India is 1996 that involve mainly areas around Delhi and Lucknow and then it spread to all over the country. Delhi and other parts of North India experienced many number of cases of Dengue fever in 2003 and 2006. Mortality rate of this disease is more common in young child as compared to adults. In India during the period between 1996–2015, dengue cases reported more than 5 times due to increase global warming unplanned urbanization, changes in environmental factors, host–pathogen interactions and population immunological factors⁸. Now, Dengue is endemic in more than 128 countries, about half of the world's populations are at risk for infection and up to 50 million cases of dengue estimated each year⁹. In India monsoon usually starts in July and ends in September–October, this is common season for dengue fever also.

Main endemic state for dengue in India is Assam, Bihar, Uttarakhand, Jharkhand, and Orissa. India experienced the highest dengue incidence in 2012 (about 41 per million population), 2013 (61 per million population) and 2014 (32 per million population).¹⁰

Dengue fever is spread by bites of *Aedes aegypti* or *Aedes albopictus* mosquitoes and these mosquitoes bite mostly during day time. In India this disease is commonly occurs during rainy season and immediately afterwards (July to October). If a person suffering from Dengue fever then Dengue virus is present in their blood. When *Aedes* mosquito bites dengue fever patients, then dengue virus enters into their body. The virus undergoes advance development in the body of the mosquito and when virus containing mosquito bites a normal human being, the virus is injected into the normal person's body and develop symptoms of dengue fever.¹¹

The clinical manifestation of dengue virus infection varies from asymptomatic to severe life-threatening illness in the form of DHF/DSS. Most dengue infections in young children are mild and indistinguishable from other common cause is usually characterized by fever with chills, flushed face, headache, retro-orbital pain, bony and muscle pain, maculopapular skin rash and epistaxis.¹² The entire period of Classical Dengue fever lasts for about 5-7 days and after that symptoms subside. Some patients of dengue infections have varying degree of mucosal and cutaneous bleed with some degree of thrombocytopenia. Patients falling in this category may be seen in significant number in epidemics.¹³⁻¹⁴⁻¹⁵

Grading of severity of Dengue hemorrhagic fever (DHF): On the basis of clinical features DHF is classified into four grades of severity, wherein grades III and IV are considered to be DSS.

Grading	Clinical features
Grade-I	Fever accompanied by non-specific symptoms and only hemorrhagic manifestation is a positive tourniquet test.
Grade-II	In addition to the manifestation in grade I there may be spontaneous bleeding. But there is no hypotension.
Grade-III	Circulatory failure manifested by a rapid weak pulse and narrowing of pulse pressure (<20 mm Hg) or hypotension with presence of cold clammy skin and restlessness.
Grade-IV	Profound shock with undetectable blood pressure or peripheral pulses.

In mild and moderate condition of disease, supportive treatment is advised with either oral or intravenous rehydration¹⁶ but for severe cases blood transfusion is indicated¹⁷. Aside from eliminating

the mosquitoes, many researcher work for develop a vaccine and medicine that target the virus. World Health Organization mentions that about 70–80% of the world populations depend on non conventional medicines

mainly of herbal medicine for their healthcare. In modern medicine there are no particular medicines or antiviral or any vaccine to cure the dengue fever but you advised to rest and drink plenty of water. In this situation, many people are turning to some herbal medicines to control this dreaded disease.

The main aim of this review article is to review systematically the published research pertaining to dengue fever and use of medicinal plants in the management of dengue fever by using the PubMed and other database. Findings described in the literature, showed that it is hypothesized an antiviral activity against DENV of some medicinal plants.

Methodology: This review work was carried out by using a wide-ranging and organized data mining approach. To achieve significant literature author uses the key words “dengue fever in India” and “plants, herbal medicine for Dengue fever, Antiviral effect, Ayurveda” were parallel searched in Google Scholar, web of science, Science direct, Scopus, Medline and PubMed Central journal literature.

Inclusion criteria were literature sources such as peer reviewed journal articles, UGC care list journal, conference/ seminar proceedings book, refereed books and abstracts.

Herbal medicine used in prevention and treatment of Dengue fever: There are no specific antiviral drugs for dengue fever in any system of medicine; however, maintaining proper fluid balance and analgesics are important line of treatment. In this article author reviewed various plants and their preparations which have been reported for treatment of dengue and guideline given by CCRAS (*Central Council for Research in Ayurvedic Sciences*) for clinical management of Dengue. Various herbal formulations have also been tried and used in dengue fever and simultaneously been scientifically validated and documented by modern researchers.

- A. Many researches showed *C. papaya* is very effective in human against dengue infection. In one study showed that *C. papaya* leaf juice have significant role in increase the platelet counts in the dengue virus infected patients within 24 h of treatment.¹⁸
- B. Another study showed that *C. papaya* leaf extract (CPL) have role in preventing the condition of thrombocytopenia by increase effect of Arachidonate 12-lipoxygenase and Platelet-Activating Factor

Receptor gene which responsible for platelet production.¹⁹⁻²⁰

- C. Leaves extract of Neem (*Azadirachta indica*) is effective *in vitro* and *in vivo* action against dengue virus type-2 showed positive effect in reduction of virus.²¹⁻²²
- D. leave decoction of Tulsi (*Ocimum sanctum*) is effective in prevention and treatment of Dengue fever.²³
- E. Stem decoction of Guduchi (*Tinospora cordifolia*) is effective in prevention of Dengue fever.²⁴
- F. Whole plant of Patha (*Cissampelos pareira*) extract is effective *in vitro* and *in vivo* conditions and found effective against all four serotypes of Dengue fever.²⁵
- G. The herbal extracts had clinical evidence that using oil of Neem (*Azadirachta indica*) and Karanj (*Pongamia glabra*) showed 100% egg mortality against *Aedes* mosquito by ovicidal activity. While leaves of *Limonia acidissima* exhibited 83.2% ovicidal activity.²⁶
- H. CCRAS also advice a combination of herbal drugs which is effective in Dengue fever that is 2 gram *Shunthi* (Dry Ginger) powder twice daily with infusion prepared by adding 5 gram (one teaspoonful) of *Guduchi* (*Giloye*) powder in 100 ml (1/2 glass) of boiled water. Dose for children between 6 to 12 years of age will be half and for children below 6 years will be one fourth. One teaspoon of honey can be added to the infusion.
- I. Guduchi ghana Vati, Amritadi Kwath and Tulsi Swarasaare effective in Dengue fever.
- J. Green coconut water may be given in suitable quantity for maintain hydration and electrolyte.

Conclusion

Dengue fever is caused by four dengue virus (DENV) serotypes and this is transmitted by *Aedes aegypti* (*Ae. aegypti*) and *Aedes albopictus* mosquitoes. Dengue is a mosquito-borne viral infection. Dengue fever comes under the group of *Abhishangaja Jvara* predominantly *Pittaja* in pathological ground. The complications of this disease represent *Raktaja* and *Sannipataja Jvara*. The global incidence of dengue has grown dramatically in last 50 years to about half of the world's population is now at risk due unplanned

urbanization, changes in environmental factors. In India during the period between 1996–2015, dengue cases reported more than 5 times. In modern medicine there are no particular medicines or antiviral or any vaccine to cure the dengue fever but you advised to rest and drink plenty of water. In this situation, many people are turning to some herbal medicines to control this dreaded disease. Now herbal medicines have been considered as an important option for prevention and treatment of dengue fever. Very limited number of plants show efficacy against dengue virus. Aqueous extract of Neem leaves which have Azadirachtin compound have action against replication of dengue virus type-2 (DENV-2). *C. papaya* leaf extract (CPLE) have potential activity against DF by increasing the platelet (PLT) count, white blood cells (WBC) and neutrophils (NEUT). Tea, which is prepared by using *Ocimum sanctum* boiled leaves, acts as a preventive medicament against DF. Herbal extracts of Neem (*Azadirachta indica*) and Karanj (*Pongamia glabra*) showedovicidal activity against *Ae. Aegypti*. CCRAS also advice a combination of Shunthi (Dry Ginger) powder and Guduchi (*Giloye*) powder which is effective in Dengue fever.

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References

1. Normile D. Surprising new dengue virus throws a spanner in disease control efforts. *Tropical medical Science*. 2013;342(6157):415–415.
2. Benelli G. Green synthesized nanoparticles in the fight against mosquito-borne diseases and cancer—a brief review. *Enzyme Microbial Technology* 2016; 1(95): 58-68
3. Global strategy for dengue prevention and control 2012–2020. Geneva (Switzerland): World Health Organization; 2012. Part 3.3: Sustainable vector control. p. 14-16.
4. Gubler DJ. Dengue and dengue hemorrhagic fever. *Clinical Microbiology Rev* 1998; 11: 480–496.
5. Halstead SB. Dengue hemorrhagic fever In: *Handbook of viral and Rickettsial Hemorrhagic fever*. Gear JHS (Edition). Boca Raton, Florida CRC press 1988.85-94.
6. Lall R, Dhandha V. Dengue hemorrhagic fever and dengue shock syndrome in India. *Natl Med J India* 1996;9:20-23
7. Anonymous, clinical diagnosis, in: *Dengue hemorrhagic fever, diagnosis, treatment, prevention and control*; II edition, Geneva, world health organization 1997:pp12-23
8. Whitehorn J, Farrar J. Dengue. *Br Med Bull*. 2010;95(1):161–173.
9. Lam SK, Burke D, Gubler D et al. Call for a World Dengue Day. *Lancet* 2012; 379: 411–412.
10. Srinivasa Rao Mutheneni, Andrew P Morse, Cyril Caminade, and Suryanaryana Murty Upadhyayula: Dengue burden in India: recent trends and importance of climatic parameters; *Emerg Microbes Infect*. 2017 Aug; 6(8): e70.
11. Kuldeep Singh, Md. Zeeshan, Vaseem A. Ansari, Zeeshan Ahmad, Paramdeep Bagga and Pragati Shakya: Prevention and control of dengue by herbal remedies; *Journal of Chemical and Pharmaceutical Research*, 2016, 8(3):708-713.
12. Singh M: Diagnosis and management of dengue infections in children. *Indian Journal practice of pediatrics* 1999,1:161-165.
13. Moreau J, Rosen L, Squgrain J, Lagraulet J. An epidemic of dengue on Tahiti, associated with hemorrhagic manifestations. *Am J Tropical Medicine Hygiene* 1973;22:237-241.
14. Pande JN, Kabra SK. Dengue hemorrhagic fever and dengue shock syndrome. *Natl Medical Journal India* 1996;9:256-258.
15. Sumarmo HW, Jahja E, Guber DJ, Subaryono W, Soremsem K: Clinical observation on virologically confirmed fatal dengue infection in Jakarta. *Bull WHO* 1983,61:693-701.
16. Wright S, Jack M. Tropical medicine (chapter 21) In: Knoop KJ, Stack LB, Storrow AB, Thurman RJ, editors. *Atlas of emergency medicine*. 3rd ed. New York (NY): McGraw-Hill Professional; 2009. pp. 649-687.
17. Dengue: guidelines for diagnosis, treatment, prevention and control. Geneva (Switzerland): World Health Organization; 2009. Part 2.3: Recommendations for treatment. p. 32-53.
18. Kala C.P. Leaf juice of *Carica papaya* L.: a remedy of dengue fever. *Med Aromatic Plants*. 2012;1:109.
19. Kasture P.N., Nagabhushan K.H., Kumar A. A multi-centric, double-blind, placebo-controlled, randomized, prospective study to evaluate the

- efficacy and safety of *Carica papaya* leaf extract, as empirical therapy for thrombocytopenia associated with dengue fever. *J Assoc Physicians India*. 2016; 64:15-20.
20. Singh PK, Rawat P. Evolving herbal formulations in management of dengue fever. *J Ayurveda Integrated Medicine* 2017; 8(3): 207-210.
 21. Parida MM, Upadhyay C, Pandya G, Jana AM. Inhibitory potential of neem (*Azadirachta indica* Juss) leaves on dengue virus type-2 replication. *J Ethnopharmacol* 2002; 79(2): 273-278
 22. Parida M.M., Upadhyay C., Pandya G., Jana A.M. Inhibitory potential of Neem (*Azadirachta indica*. Juss) leaves on dengue virus type-2 replication. *J Ethnopharmacol*. 2002;79(2):273-278.
 23. Mohan L., Amberkar M.V., Kumari M. *Ocimum sanctum* Linn (Tulsi) - An overview. *Int J Pharm Science Rev Res*. 2011;7(1):51-53.
 24. Sharma S.D., Sahu K., Chandrol G.K., Jain P.K., Sharma V. Ethnobotanical survey of five villages of Durg District of Chhattisgarh, (India) *Int J Adv Res Biological Sci*. 2016;3(10):104-110.
 25. Sood R., Raut R., Tyagi P., Pareek P.K., Barman T.K., Singhal S. *Cissampelos pareira* Linn: natural source of potent antiviral activity against all four dengue virus serotypes. *PLoS Negl Trop Dis*. 2015;9(12).
 26. Benelli G. Plant-borne ovicides in the fight against mosquito vectors of medical and veterinary importance: A systematic review. *Parasitol Res* 2015; 114(9): 3201-3212.

Influence of Cardiorespiratory Fitness Protocol on Physical Function Performance in Geriatric Patients Undergoing Long Term Physiotherapy Treatment

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Abstract

Background: The study aimed to find the effect of Structured Cardiorespiratory fitness protocol on Physical Function Performance in geriatric patients undergoing long term physiotherapy treatment.

Method: An Experimental Study was conducted among 45 Geriatric patients undergoing more than 2 month Physiotherapy treatment. The intervention were carried out daily for 6 weeks. All Patients received Structured Cardiorespiratory fitness Protocol. The interpretation of the study was done on the basis of comparing pre-test and post-test assessment of Peak Expiratory Flow Rate (PEFR), Respiratory Rate, Borg scale.

Result: pre and post-test Comparison result, respiratory rate (13.6 ± 1.42 and 13.8 ± 1.25 ; $p=0.026$) and PEFR (168.67 ± 48.97 and 171.11 ± 49.55 ; $p=0.02$) were found to be statistically significant and Borg scale were found to be extremely significant (15.73 ± 1.42 and 15.02 ± 0.23 ; $p < 0.0001$).

Conclusion: A Structured Cardiorespiratory fitness protocol was improved the physical function performance in geriatric patient undergoing long term physiotherapy treatment.

Keywords: *Cardiorespiratory fitness; Geriatric Patients; Physical Function; Structured protocol*

Introduction

A consequence of aging is a degeneration in many physiological variable, with the most important being, sarcopenia and the subsequent loss of muscle strength.^[1] Aging is associated with a decrease in lung function and respiratory muscle strength declining at a rate of 8 to 15% per decade of life after 50 year of age.^[2, 3] The deficit in respiratory muscle strength affects physical

performance leading to diminish in exercise tolerance, deterioration of gait, and decrease of quality of life with advancing age.^[4] The reduction of respiratory muscle function in the elderly thus make this population more vulnerable to disease and disability.^[5]

The respiratory muscle show a decrease in type II fibers with age, with a subsequent reduction in maximal respiratory pressures, maximal inspiratory and expiratory, which reflects the integrated function of all of the respiratory muscles.^[6-8] These reductions associated with aging occur after 50 years of age and can interfere with coughing efficiency. These changes can also facilitate the occurrence of pathological processes, such as the accumulation of bronchial secretions and respiratory infections, which can interfere with the activities of daily living in elderly individuals.^[9]

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Both static and dynamic measures of lung function gradually deteriorate with age. Decreased elastic recoil capacity results in decreased vital capacity, reduced peak expiratory flow etc. With ageing results reduced alveolar support, increased rigidity of the rib cage, weakness of the respiratory muscles. Loss of efficient breathing is particularly noted with exercises with common complaints like shortness of breath while walking upstairs. The work of breathing increases as there is increase in the intensity of exercise. The older people hyperventilate for the same oxygen in comparison with young population.^[10]

Cardiorespiratory fitness is the ability of circulatory and respiratory systems to provide oxygen to skeletal muscle, and thereby ability of the skeletal muscle to utilize the oxygen during prolonged moderate to vigorous physical activity.^[11]

Physical function is defined as the ability to perform the basic actions essential for independence and carrying out complex activities.^[12]

Physical fitness is the ability to carry out daily activities with strength and vigilance, without getting tired and with adequate energy to enjoy leisure-time pursuits and to compete with unanticipated emergencies.^[13] It is a mixture of skill-related, health-related and physiologic components. Skilled components include agility, balance, co-ordination, speed, power and reaction time. Health components include cardio-respiratory endurance, muscular endurance, muscular strength, body composition and flexibility.^[14] Geriatric population show various cardiorespiratory changes like;

Cardio-Vascular System: Degeneration of the heart muscle takes place, leaving room for fat and calcium deposits, Heart rate decreases and becomes more irregular but resting heart rate does not change much, Stroke volume decreases due to decreased myocardial contractility, The ageing heart is often in capable of increasing cardiac output during maximum exercise.

Respiratory System: In geriatric patient, lungs are only 56% efficient and maximum oxygen in take during exercise is only 40% when compared to a 30 year old person, Total lung capacity decreases, residual volume increases, and ventilatory capacity decreases, Forced expiratory volume (FEV₁) decreases, Altered pulmonary gas exchange: oxygen tension falls with age at a rate of 4mm Hg/decade. PO₂ is 75 at the age of 70, which

is the 90 at 20 years, Decreased ciliary action to clear secretions, Strength of respiratory muscle decreases, Chest wall becomes rigid results in increased work of breathing.

The respiratory system is a vital route for gaining the elements essential to sustain life. Physical work capacity is declined with aging for multiple reasons. For example, structural and functional changes of the heart and blood vessels become more visible with advancing age. In general, aerobic work capacity is declined as with combined effects of lowered maximum target heart rate, reduced myocardial contraction, and consequently, stroke volume, in addition to reduce maximum oxygen consumption.^[15] The reduction in maximum oxygen consumption noted with aging, however, is not exclusively caused by the altered physiologic functions, but also the physical deconditioning associated with increasing sedentary lifestyle.^[16] Decreased alveolar capacity to diffuse air combine to reduce different parameters of ventilatory lung function, such as vital capacity, maximum voluntary ventilation, and forced expiratory capacity.^[17,18] In a geriatric Population average respiratory rate is 12 – 28 breaths/min.^[19] older adults have decreased sensation of dyspnea and diminished ventilatory response to hypoxia and hypercapnia, making them more vulnerable to ventilatory failure during high demand states and possible poor outcomes.^[20]

Method

An approval for the Study was obtained from the Protocol committee and institutional Ethical committee of KIMSDU. Patients who fulfilled the inclusion and Exclusion Criteria were Informed consent was taken from each of the Patient prior to Participation. Instruction was given to the Patients about techniques performed. A total of 45 patients was treated. All Patients received Structured Cardiorespiratory fitness Protocol. Pre and post-test assessment was taken by using PEFr, Respiratory Rate and Borg scale to assess the patients. A total 45 patients both male and female Geriatric Patients Undergoing more than 2 month Physiotherapy treatment were included in the study. They were aged between 65-70 years, Patient who did not having previous history of cardiac surgery, Patient who are at least able to walk with Stick. Exclusion criteria were Patient who taken Physiotherapy treatment in last 6 month for improving Pulmonary functions, Patient who using Inhaler, Patient with Neurological or Psychiatric conditions.

Table 1: Structured Cardiorespiratory Fitness protocol

Cardio respiratory Fitness Protocol	
Exercises	Dosage
week 1	
1. Inspiratory Diaphragmatic Breathing Exercise. ^[21-23]	Combined Diaphragmatic breathing and Pursed lip breathing exercise given for 15 min at each session. 1 session daily.
2. Expiratory Pursed lip breathing exercise. ^[21, 23-24]	
week 2 – 3	
Continue above all exercises.	
1. Respiratory Muscle Training. ^[25-26]	Using Incentive respiratory spirometer For 15 min at each Session 1 session daily.
2. Balloon Blowing Exercise. ^[27]	Exs performed tow times at maximum Balloon blowing Over one min. The Exs Given One session daily.
3. Straw Breathing Exercise. ^[28]	Exs is performed five min breath only Through straw. Exs is repeat three times to complete one set. Exs given 1 session daily.
week 4 – 6	
Continue above all exercises.	
1. Treadmill exercise Training. ^[29]	All Exs given 15 min at each session. 1 session daily.
2. Static Cycling. ^[30]	
3. Walking. ^[31]	
4. Stair Climbing. ^[31]	

Results

Primary Outcome used for the result were Respiratory rate, Borg Scale and PEFR.

Gender Distribution:

Table 2: Gender Distributions.

Gender	Frequency	Percentage
Male	23	51%
Female	22	49%
Total	45	100%

Respiratory Rate: In this study there was significant difference in respiratory rate.

Borg Scale: In this study there was extremely significant difference in respiratory rate.

Peifr: In this study there was significant difference in respiratory rate.

Table 3: mean and SD of outcome measures

Parameters	Pre test	Post test	t value	p value
Respiratory rate	13.6 ± 1.42	13.8 ± 1.25	2.29	0.0267
Borg Scale	15.73 ± 1.42	15.02 ± 0.23	5.48	<0.0001
PEFR	168.67 ± 48.97	171.11 ± 49.55	2.41	0.02

Discussion

In Geriatric Population Cardiorespiratory Changes occur like Decreased lung Function, Lung Capacity, and Strength of respiratory muscle and it affects the normal physical function of the geriatric patients. This Study “Influence of Cardiorespiratory Fitness Protocol on Physical Function Performance in geriatric Patients Undergoing long term Physiotherapy treatment.” Was conducted to find the effect of structured exercises protocol on geriatric patients undergoing long term physiotherapy treatment. If Cardiorespiratory Fitness improved it will directly improve the physical function among geriatric patients.

The Aim of the Study were to find the effect of Structured Cardiorespiratory fitness protocol on physical function performance in geriatric patients undergoing long term physiotherapy treatment.

The study was conducted with 45 patients. Prior consent was taken from them. The interventions were carried out daily for 6 weeks. The outcome measures for this study were PEFR, Respiratory Rate, and Borg Scale.

The patient in Structured Cardiorespiratory fitness Protocol received Breathing Exercises, Respiratory muscle training, Balloon Blowing Exercise, Straw Breathing Exercises, Treadmill exercise training, Static cycling, walking and Stair climbing.

Patil P. et al.^[32] Effect of Abdominal Muscle Exercises on Peak Expiratory Flow Rate in Post-Menopausal Women. This study concluded that abdominal muscle exercise had significant improved clinically and statistically on PEFR in post-menopausal women.

Raquel RB. Britto et al.^[33] Effect of the aging process on respiratory function. The identification on breathing patterns in healthy elderly individuals and changes in the respiratory system related to the normal aging process is important to detect and prevent respiratory dysfunction.

Bret D. et al.^[34] Physiology considerations in the Geriatric patient. Respiratory changes with age related development of osteoporosis results in a reduction of height of the thoracic vertebrae causing further restriction. Reduction of respiratory muscle mass may contribute to a decrease in the force produced by the respiratory muscle activity.^[35,36]

Sarawat J. et al.^[24] Effects of Pursed-Lip breathing exercise Using windmill toy on lung function and respiratory Muscle Strength in the Elderly. Aging results in decline in lung function and reduction of respiratory muscle strength.

Sonia UM. Et al.^[37] Effectiveness of shoulder and Thoracic Mobility Exercises on Chest Expansion and Dyspnoea in Moderate chronic obstructive pulmonary disease patient. This study concluded that shoulder and thoracic mobility exercises were more effective in improving chest expansion and reducing dyspnoea in COPD patients.

$J_{IN} - S_{EOP} K_{IM}$ et al.^[27] Effect of balloon blowing exercise on lung function of young adult smokers. A study was done to clarify lung capacity when a balloon blowing exercise was used to increase Patients lung function. Balloon blowing exercise improves the physical functions in geriatric patients.

The result of this study showed that there was significant improved physical function in geriatric patients after 6 weeks of intervention. Within the group comparison was done by applying 'Wilcoxon rank sum test' to pre and post training values of same group for all outcome measures. Respiratory Rate Post training there was significant improvement ($p = 0.0267$), Borg scale Post training there was extremely significant improvement ($p < 0.0001$), PEFR Post training there was significant improvement ($p = 0.02$) noted in geriatric

patients undergoing long term physiotherapy treatment.

Therefor result of the present study showed that the structured cardiorespiratory fitness protocol was improved the physical function performance in geriatric patients undergoing long term physiotherapy treatment.

Conclusion

On the basis of the result of our study, It was concluded that the structured cardiorespiratory fitness protocol was improved the physical function performance in geriatric patients undergoing long term physiotherapy treatment.

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References

1. Watsford ML, Murphy AJ. The effects of ageing on respiratory muscle function and performance in older adults. *J Sci Med Sport* 2007; 10:36-44.
2. Lalley PM. The aging respiratory system- Pulmonary structure, function and neural control. *Respir Physiol Neurobiol* 2013; 187: 199-210.
3. De Albuquerque IM, Rossoni CS, Cardoso DM, Paiva DN, Fregonezi G. Effects of short inspiratory muscle training on inspiratory muscle strength and functional capacity in physically active elderly: a quasi-experimental study. *Eur J Physiother* 2013; 15: 11-7.
4. Buchman AS, Boyle PA, Leurgans SE, Evans DA, Bennett DA. Pulmonary Function, Muscle strength, and incident mobility disability in elders. *Proc Am Thorac Soc* 2009; 6: 581-7.
5. Visser M, Schaap LA. Consequences of sarcopenia. *Clin Geriatr Med* 2011; 27: 387-99.
6. Tolep K, Higgins N, Muza S, et al. Comparison of

- diaphragm strength between healthy elderly adults and young men. *Am J Respir Crit care Med.* 1995; 152(2): 677-82.
7. Nikolic ME, Rejeski WJ, Blair SN, Duncan PW, Judge JO, King AC et al. Physical activity and public health in older adults: recommendation from the American college of sports medicine and the American heart association. *Med. Sci. Sports Exerc.* 2007; 39(8):1435-45.
 8. Green M, Road J, Sieck Gc, Similowski T. Test of Respiratory Muscle Strength. *Am J Respir Crit Care Med.* 2002; 166(4): 528-547.
 9. Freitas Fs, Ibiapina CC, Alvim CG, et al. Relationship between cough strength and functional level in a group of elderly individuals. *Rev Bras Fisioter.* 2010; 14(6): 470-76.
 10. Waqar Naqvi's text book of Physiotherapy in Community health and Rehabilitation; 1st ed, 5 – 21.
 11. American college of sports medicine. ACM'S guidelines for exercise testing and prescription. 9th ed. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins Health; 2014.
 12. Painter P, Stewart AL, Carey S. Physical Functioning: definitions, measurement and expectations. *Adv Ren Replace Ther.* 1999 Apr; 6(2):110-23.
 13. Caspersen, C.J., Powell, K.E. and Christenson, G.M. Physical Activity, Exercise, and Physical Fitness: Definitions and Distinctions for Health-Related Research. 1985
 14. W.R. Thompson, ed. Baltimore, MD: Lippincott Williams & Wilkins, American College of Sports Medicine. Exercise prescription for other clinical populations. In: ACSM's Guidelines for Exercise Testing and Prescription (7th ed.), 2010. pp.62,81-89
 15. Steven R, Kristjan T, et al, Rehabilitation of the Geriatric Orthopaedic Patient. *Clinical orthopaedics and related research.* 1995 July; 316: 80-92.
 16. Astrand P, Rodahl K: Textbook of work physiology. Physiological Bases of Exercise. Physical performance, Ed 3. New York, McGraw Hill 1986; 295 – 353.
 17. Higgins MW, Keller JB: Seven measures of ventilatory lung function. *Am Rev Respir Dis* 1973; 108:258-272.
 18. Keltz H: Pulmonary Function and Disease in the Aging. In Williams TF (ed). *Rehabilitation in the Aging.* New York, Raven Press 1984; 14 – 15.
 19. Rodríguez – Molinero A, Narvaiza L, et al, Normal Respiratory Rate and Peripheral Blood Oxygen Saturation in the Elderly Population. *Journal of the American Geriatric Society.* 61(12): 2238-40.
 20. Gulshan Sharma, James Goodwin. Effect of aging on respiratory system physiology and immunology. *Clinical intervention in aging* 2006;1(3).
 21. KyoChul S, Park Seung Hwan, Kwangyong P; The effect of inspiratory diaphragm breathing exercise and expiratory pursed-lip breathing exercise on chronic stroke patient's respiratory muscle activation. *J. Phys. Ther.Sci* 2017;29:465-469.
 22. Seo K, Park SH, Park K: Effect of diaphragm respiration exercise on pulmonary function of male smokers in their twenties. *J Phys Ther Sci,* 2015, 27:2313-2315.
 23. Seo KC, Lee HM, Kim HA: The effects of combination of inspiratory diaphragm exercise and expiratory pursed lip breathing exercise on pulmonary functions of stroke patients. *J phys Ther Sci,* 2013, 25:241-244.
 24. Sarawut Jansang, Timothy Mickleborough, Daroonwan Suksom; Effect of pursed-lip breathing exercise using windmill Toy on Lung Function and Respiratory muscle strength in the elderly. *J Med Assoc Thai* 2016; 99 (9): 1046-51.
 25. Lllia N.D.F. Lima, Guilherme A.F. Fregonezi, et al., Obstructive practice of incentive spirometry in stroke patients. *Brazilian journal of physical therapy* 2017; 21(1):24-29.
 26. Chang-Yong kim, Jung-Sun Lee, Hyeong-Dong Kim, In seob kim; Effects of the combination of respiratory muscle training and abdominal drawing-in maneuver on respiratory muscle activity in patients with post-stroke hemiplegia: a pilot randomized controlled trial. 2015
 27. Jin Seop Kim, Yeon- Seop Lee; Effect of a Balloon-Blowing Exercise on lung Function of young Adult Smokers. *J. Phys. Ther. Sci.* 2012; 24:531-534.
 28. Martin M, Deborah Roth, Andrea Liss, Richard P., Response to Symptom induction exercises in Panic disorder. *Behaviour Research and Therapy* 44(2006) 85-98.
 29. Horacio pineda, Francois hass, Kenneth; Treadmill exercise Training in Chronic obstructive pulmonary

- disease. Arch phys med Rehabil vol.67, March 1986.
30. Eliane A, Ana Belen, Pedro Jose, et al., What is the most effective exercise protocol to improve cardiovascular fitness in overweigh and obese subjects? Journal of sports and Health Science 6 (2017) 454-461.
 31. Leena Hakola; Cardiorespiratory fitness and physical activity in older adults, A population-based study in men and Women University of eastern Finland, faculty of health Sciences. Publication of the University of Eastern Finland. Dissertation in Health Sciences 276. 2015.73.
 32. Patil P, Sagar J; Effect of Abdominal Muscle Exercise on Peak Expiratory Flow Rate in Post-Menopausal Women. IOSR-JDMS. March, 2017; 16(3): 70-74.
 33. Raquel RB, Camila CZ, et al.; Effect of the aging process on respiratory function. Gerontology 2009; 55 (5), 505-510.
 34. Bret D. Alvis, Christopher G. Hughes; Physiology Considerations in the geriatric patient. Anesthesiol Clin 2015 September; 33(3): 447-456.
 35. Sprung J, Gajic O, Warner DO. Review article: Age Related alterations in respiratory function-anesthetic considerations. Canadian journal of anaesthesia=journal Canadian d'anesthesie.2006; 53: 1244-57.
 36. Sharma G, Goodwin J. Effect of aging on respiratory system physiology and immunology. Clinical interventions in aging. 2006; 1: 253-60.
 37. Sonia UM, T. Poovishnu Devi, Vaishali KJ. Effectiveness of shoulder and thoracic mobility Exercises on chest Expansion and Dyspnoea in Moderate Chronic Obstructive Pulmonary Disease Patients. Int J Physiother Res 2017; 5(2): 1960-65.

Efficacy of Tele-Rehabilitation for the Management of Physical Impairments of the Children with Cerebral Palsy in the Inclusive Educational Settings: A Protocol for a Systematic Review

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Abstract

Introduction: Cerebral palsy (CP) elucidates a group of permanent disorders of movement and posture disorders caused by non-progressive damage to developing brain with a prevalence rate of about 2-2.5 per 1000 live births in the world. Despite the effectiveness of tele-rehabilitation in various physical ailments, there is a paucity of the literature of tele-rehabilitation for CP in inclusive educational settings. Therefore, the aim of the present review is to identify the efficacy of tele-rehabilitation in limiting down and managing these physical impairments of CP children in educational settings.

Method and Analysis: This protocol for a systematic review is based on principles of the preferred reporting items for systematic reviews & meta-analysis protocols (PRISMA-P). Published literature in the English language on the efficacy of tele-rehabilitation in improving physical impairment among CP children between ages 3-18 years will be included in the review. The *electronic databases such as PubMed, Scopus, Pedro, EMBASE, and MEDLINE (Ovid)* will be used for literature search between 2000 to 2018 years. The *Rev Man 5.3 software* will be used to extract the data. Down and Black critical appraisal checklist will be employed to evaluate the risk of bias. The guidelines for grading of Recommendations, Assessment, Development, and Evaluation (GRADE) will be used to assess the quality of research evidence.

Ethics & dissemination: This review does not inculcate the collection of primary data, so no ethical approval is required for the study. Findings of the review will be disseminated through peer-reviewed publication and conference presentation. Criteria for the review were set a priori and the present protocol got registration from PROSPERO (International Prospective Register of Ongoing Systematic Review) with ID: 42019130555.

Keywords: *Tele-rehabilitation, Information and communication technology, inclusive education setting, videoconferencing and physiotherapy.*

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Introduction

Cerebral palsy (CP) is a group of non-progressive permanent movement and posture disorders caused by damage to developing the brain.³ Globally, the prevalence of the CP is 2 to 2.5 per 1000 live births,

whereas the prevalence is much higher as 2-10 /1000 lives in developing countries with a clinical presentation of cerebrocortical and sub-cortical injury occurring in the very first year of life of child.⁴ Since the CP requires long-term care and support for both CP children and their parents, the governments are committed to improve access to quality rehabilitation services and policies to reduce the discrimination, enhance access and inclusion in the society. The revised persons with disability act, 2016 clarifies that children with CP should not be denied for admission in a normal school as CP is the main disabling condition.^{5,6} Being a heterogeneous group of disorder, children with CP experience various barriers and challenges in various activities due to deficient motor skills, altered muscle tone, poor balance, low cardiovascular endurance, postural deviations and poor hand functions as compared with normal children in an inclusive educational setting.^{7,8} There is a paradigm shift in the focus of integrating the educational needs of CP children into the mainstream of education under the inclusive setting. In such settings, CP children often require help and assistance not only from parents and healthcare professionals but also from teachers and special educators for managing the physical impairments.⁹ However, the management of physical impairments is not being addressed sufficiently in such inclusive setup due to lack of skills and resources especially for children studying in remote and rural areas.

The management of physical impairments of these children should be given high priority for enhancing learning and to achieve desired educational goals. The teachers and special educators should ensure the good positioning and posture of CP to maximize the physical efficiency in writing and reading process.⁷ In an inclusive education setting, these teachers or special educators should be trained on fundamental management of physical impairments as a supportive service for improving muscular strength and mobility that may be incorporated into existing training programs delivered either via workshops.⁸ This might assist these CP children in participating in mainstream schools activities with the guidance of physiotherapists emphasizing effective management of mobility, gross and fine motors skills.^{10,11} However, CP children in an inclusive educational setting in rural and remote areas are unable to get physiotherapy services as these services are not available in those areas.

Tele-rehabilitation (TR) refers to the delivery of rehabilitation services via information and

communication technology (ICT) services as a subset which includes assessment, treatment, and monitoring.¹² Literature reports that TR has been used for delivering speciality rehabilitation services by the various allied health professionals such as a physiotherapist, occupational therapist and speech therapist in clinics, schools or community settings.¹³ TR covers a range of orthopaedics and neurological pathologies like traumatic brain injuries, spinal cord injuries, joint replacement, Parkinson's disease, Cerebral palsy and Multiple sclerosis.¹⁴

Despite the strong evidence of TR, authenticating that TR can improve the activity limitations of various physical disorders; there exist paucity of literature on the role of TR for CP children in educational settings. Further, there is yet no review published revealing the efficacy of TR in improving the physical impairments among CP children in inclusive school settings. Therefore, the objective of the present review is to identify the efficacy of TR in the management of physical impairments of CP children in educational settings.

Method and Analyses

Study Design: This protocol for a systematic review is based on principles of the preferred reporting items for systematic reviews and meta-analysis protocols (PRISMA-P).¹

Study Registration: Criteria for the review were set a priori and the present protocol got the registration from PROSPERO (International Prospective Register of Ongoing Systematic Review, CRD UK) with ID: 42019130555.

Eligibility Criterion:

Types of Study: All the randomized controlled trials, quasi-randomized trials, case-control studies, cohort studies, case series & case studies, published and unpublished conference papers on inclusive tele-rehabilitation for cerebral palsy children in educational settings published between years 2000 to 2018 in the English language will be included. Articles other than English language and animal studies will be excluded.

Participants: CP children of any category/type as participants with a mean sample age between 3 -18 years will be included in the study. CP children with other associated problems such as hearing impairment, visual impairment, epilepsy and mental retardation will be included in the study.

Types of Interventions: Children receiving therapeutic services (tele-physiotherapy, tele-occupational therapy, tele-speech therapy or tele-rehabilitation) via information and communication technology to improve the physical impairment of children with CP for any duration or intensity and frequency in school settings will be considered. Studies which reveal the interventions targeting upper and lower extremities and reporting gross or fine motor skills with activities of daily living (ADLs) will be included. The interventions via face-to-face method in a school setting will be excluded.

Comparisons or Control: The comparator of interest of the present study are no therapy, usual care, computer or video games, table games, conventional physiotherapy, and other exercise programs will be included in the study.

Outcome Measures: The outcome of interest will be TR feasibility, improvement in physical impairment and educational outcome within different levels of ICF models will be included.¹⁵ Keeping in mind the possibility of TR and its effectiveness, following areas of the outcome will be applied revealing feasibility, cost-effectiveness, social and psychological aspects, child-related outcome within all levels of ICF models. All results will be reported in the form of both quantitative and qualitative.

Search strategies for the identification of data source: The electronic databases; PubMed (<https://www.ncbi.nlm.nih.gov/pubmed>), SCOPUS (<https://www.scopus.com>), PEDro (<https://www.pedro.org.au>) and EMBASE (<https://www.embase.com>), Ovid MEDLINE (<http://www.ovid.com/product-details.901.html>) will be employed for literature search. The published literature in English language reporting information and communication technology based rehabilitation/physiotherapy will be included. Using MESH term including “Tele-rehabilitation or tele-physiotherapy, tele-therapy, and technology-based rehabilitation, tele-occupational therapy and tele-exercise” for the management of CP in inclusive educational settings will be used for the search. The reference section of each article will be reviewed for relevant more studies on the proposed topics. From each search database, the searches will be exported into Mendeley (<https://www.mendeley.com>) to make a consolidated file of all the studies.

Screening of Studies: The duplicity of literature

will be rectified using the duplicate find function in Mendeley referencing. Further, the searched article's title and abstract will be evaluated for the eligibility based on the inclusion and exclusion criteria by PAHWA, a reviewer. These articles again will be counter checked by the other three reviewers (MANI, SHARMA, and SINGH). The final full articles will be received from two independent reviewers. Inter-rater agreements between the reviewers will be addressed in any phase of review. The difference of opinion between the reviewers shall be resolved through discussion in consent with another independent reviewer.

Data Extraction: Rev Man 5.3 software will be used to extract data from the included studies. To enhance the consistency between reviewers (PAHWA, MANI, SINGH & SHARMA), a data extraction form will be screened as a pilot study before starting the data collection. Two reviewers of the study will extract the data independently. During the data extraction, any disparity found between the authors will be rectified by the conversation with the fourth author, when needed.

Multiple records of single inquiry research subject area will be searched by comparing author name, interventions, sample sizes and outcome files of concerning eligible records. The data of study details (Author, year, country and funding), study design, sample characteristics, intervention characteristics, comparator, outcome measures, ICF domain, therapeutic and educational impact, and conclusion will be extracted. The data extracted will be summarised in tables and figures.

Risk of bias in Individual Research: Down and Black critical appraisal checklist will be employed to evaluate the quality of study for included quantitative research studies. It comprises of 27 questions items across five constructs that include study quality, external validity, study biases (in intervention and outcome), confounding and selection bias and power of the study.¹⁶ Risk of bias of included qualitative studies will be assessed by JBI Critical appraisal checklist having 10 questions in Yes/No form.¹⁷ Risk of bias for all the final included eligible studies will be assessed by two independent reviewers (PAHWA and MANI) without blinding. Results across the studies will be presented graphically. In case of the existence of substantial difference in risk of bias of included studies, results will be synthesized separately for studies which are at higher and lower risk of prejudice.

Strategy for Data Synthesis: For homogeneous studies in terms of interventions and outcomes, a meta-analysis will be carried out by using strata V.14 to make consistency, size, and direction of feasible effects of available sufficient data. In case, the study showing poor established thresholds results for meaningful change of a given measure, the effect size (ES) thresholds as advised by Kohen¹⁸ will be used revealing as trivial values ($ES < 0.20$), small values ($ES = 0.20 - 0.50$) and moderate values ($ES = 0.50 - 0.80$), indicating under or overestimation of magnitude of intervention-related change with course of time.¹⁹ In situations where the meta-analysis is not possible due to substantial heterogeneity, a narrative synthesis of the findings from the included studies will be carried out and the heterogeneity will be quantified using the I^2 statistics. This summary with related quality of evidence for each outcome will be synthesized to reveal the effectiveness of TR for children with CP in inclusive educational settings.

Quality of Evidence: The guidelines for grading of Recommendations, Assessment, Development, and Evaluation (GRADE) will be used to assess the quality of research evidence of included studies.²⁰

Discussion

To the extent of our knowledge, this will be the first systematic review to investigate the efficacy of TR for the management of physical impairments in children with CP in inclusive educational settings. Previous studies reported that tele-rehabilitation could improve the physical impairment and activity limitation for CP,²¹ and other neurological disabilities.²² Furthermore, it has been noticed that CP children taking participation in activities shown significant improvement in performance indicating the need for rehabilitation and intervention programs in inclusive education settings.²³ The TR based skill practice and continuous delivery of rehabilitation services may give promising results to promote motor skills improvements in CP children. TR in educational settings has the potential for delivering training the special teachers for the management of disabilities in improving educational goals for CP children.²⁴ Each school under an inclusive educational setting should have access for a novel TR services to bring the physiotherapy, occupational therapy, and speech therapy services in their school premise via ICT. However, there is a scarcity of evidence on the feasibility and efficacy of TR in an educational settings.¹⁴

Considering the poor availability of rehabilitation services in rural areas, it is imperative to analyze the role of TR in managing physical impairments of CP children in educational settings. The result of this study will provide the evidence regarding frequency, time and mode of delivery of TR services which are effective in managing the physical impairments in cerebral palsy child and will, in turn, inform the development of TR-based program for educational settings.

Ethics and Dissemination: The current research does not require primary data collection, so there is no ethical approval requirement. The author will disseminate the results by publishing them in the peer-reviewed journal & through the presentation at the conference. The findings will be recorded for systematic reviews and meta-analysis according to the latest edition of preferred reporting items (PRISMA).¹

Protocol Amendments: Any change in systematic review protocol will be documented with the date along with the description of that changes with proper justifications.

Conflict of Interest: The authors state no conflict of interest to declare regarding the study.

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References

1. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. 2015; 1–9.
2. Schünemann HJ, Knottnerus A, Tugwell P, et al. GRADE guidelines: A new series of articles in the Journal of Clinical Epidemiology. J Clin Epidemiol. Epub ahead of print 2010. DOI: 10.1016/j.jclinepi.2010.09.011.
3. Bax M, Goldstein M, Rosenbaum P, et al. Proposed definition and classification of cerebral palsy, April 2005. Dev Med Child Neurol 2005; 47: 571–576.
4. Jan MMS. Cerebral Palsy: Comprehensive Review and Update. Ann Saudi Med 2006; 26: 123–132.
5. Ministry of Law and Justice. The Rights of Persons with Disability Act. Gov India 2016; 1–35.
6. Dubey M. The Right of Children to Free and

- Compulsory Education Act, 2009. Soc Change 2010; 40: 1–13.
7. Group W bank. Toolkit for Master Trainers in Preparing Teachers for Inclusive Education for Children with Special Needs- Module 3: Including Children with Cerebral Palsy. 2014.
 8. Eshphan W, King'ori, Philip G, Mwangi PMM. Teachers' Preparedness in Identification of Cerebral Palsy Among Learners In Special Schools in Nyahururu Sub-County, Laikipia County, Kenya. *Int J Adv Res Educ Technol* 2015; 2: 23–27.
 9. Rézio GS, Formiga CKMR. Inclusion of children with cerebral palsy in basic education. *Fisioter e Pesqui* 2014; 21: 40–46.
 10. Crombie S. The physical management of children with cerebral palsy attending mainstream primary school. *Open Grey*.
 11. S. C. Exploring the physical management of children with cerebral palsy in the mainstream primary school setting. *Dev Med Child Neurol*.
 12. Brennan D, Tindall L, Theodoros D, et al. A Blueprint for Telerehabilitation Guidelines. *Int J Telerehabilitation* 2010; 2: 31–34.
 13. Crutchley S, Campbell M. TeleSpeech Therapy Pilot Project: Stakeholder Satisfaction. *Int J Telerehabilitation* 2010; 2: 23–30.
 14. Criss MJ. School-based telerehabilitation in occupational therapy: using telerehabilitation technologies to promote improvements in student performance. *Int J telerehabilitation* 2013; 5: 39–46.
 15. WHO. World Health Organization-Towards a Common Language for Functioning, Disability and Health: ICF -The International Classification of Functioning, Disability and Health. 2002.
 16. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. 1998; 377–384.
 17. JBI, The Joanna Briggs Institute Critical Appraisal tool 2017. Checklist for Systematic Reviews and Research Syntheses. *Crit Apprais Checkl Syst Rev Res Synth*.
 18. Cohen L. Statistical power analysis for behavioral sciences (revised ed.). Acad Press (New York).
 19. Middel B, Van Sonderen E. Statistical significant change versus relevant or important change in (quasi) experimental design: some conceptual and methodological problems in estimating magnitude of intervention-related change in health services research. *Int J Integr Care*; 2. Epub ahead of print 2002. DOI: 10.5334/ijic.65.
 20. Guyatt GH, Oxman AD, Tugwell P, et al. Grade Series - Guest Editors, Sharon Straus And Sasha Shepperd Grade guidelines: A new series of articles in the Journal of Clinical Epidemiology. 2011; 64: 380–382.
 21. Golomb MR, Barkat-Masih M, Rabin B, et al. Eleven months of home virtual reality telerehabilitation - Lessons learned. 2009 Virtual Rehabil Int Conf VR 2009 2009; 23–28.
 22. Hailey D, Roine R, Ohinmaa A, et al. The status of telerehabilitation in neurological applications. *J Telemed Telecare*. Epub ahead of print 2013. DOI: 10.1177/1357633X13501775.
 23. Schenker R, Coster WJ, Parush S. Neuroimpairments, activity performance, and participation in children with cerebral palsy mainstreamed in elementary schools. *Dev Med Child Neurol*. Epub ahead of print 2005. DOI: 10.1017/S0012162205001714.
 24. Benham S, Gibbs V. Exploration of the Effects of Telerehabilitation in a School-Based Setting for At-Risk Youth. *Int J Telerehabilitation* 2017; 9: 39–46.

Emotional Flanker Compatibility in Patients with Non-Demented Parkinson's Disease and Healthy Ageing

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Abstract

Context: Parkinson's disease (PD) is a neurodegenerative disease caused by degeneration of the dopamine-synthesizing cells of the mesostriatal-mesocortical neuronal pathway, which affects motor pathway in basal ganglia (BG). Neuropsychological studies showed that degeneration of dopamine neuroreceptor also affects nigrostriatal and mesocortical limbic system which is associated with emotional processing in PD. However, very few studies have identified deficit in selective attention in patients with PD patients except in patients with PD-MCI (PD-Mild Cognitive Impairment) or PD-D (PD-Dementia). Thus, the present study examined the effect of emotion on attentional processing in PD and matched control. Emotional flanker task was designed by using pictures selected from the International Affective Picture System (IAPS) based on their normative valence ratings. Results revealed that attentional processing of emotional images were slower in PD patients in comparison to matched healthy control.

Keywords: attention, emotion, Parkinson.

Introduction

Parkinson's disease (PD) is a neurodegenerative disorder caused by degeneration of the dopamine-synthesizing cells of the mesostriatal-mesocortical neuronal pathway in substantia nigra. Parkinson's disease (PD) is characterized by well-known motor symptoms, however the presence of non-motor symptoms, such as cognitive impairment, emotional disturbances and psychiatric symptoms are still underestimated. The important issues in PD research is that there has been a great progress in the management of motor symptoms however, very little attention has been given to emotional, cognitive and psychological impact of disease problem.

The impairment in affective processing in PD results in problem in recognition, regulation of emotions

and emotion representations. In a previous study, PD patients demonstrated a recognition deficit for negative (sadness and anger) and positive faces². Besides affective deficit, PD patients also exhibited problems in cognitive performance. The cognitive deterioration in PD encompasses impairment in performance related with executive function, working memory, visuospatial ability³, whereas other cognitive processes like language are less affected⁴. Further, there is an intact attentional functioning in simple attention tasks like digit span and spatial span in patients with PD⁵. Furthermore, a study revealed that the attentional deficit at early stage of PD may be due to the reduced ability to resist interference revealed by flanker compatibility studies⁶. The interference in aged matched population of older adults was less impaired in congruent stimuli in comparison to incongruent stimuli on flanker compatibility task⁷.

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Furthermore, the effects of attention and emotion on face processing was examined by studies using fMRI to assess the effect of fearful and neutral faces in processing of spatial attention. The result revealed a differential impact of attention and emotion on face processing as

the interference produced by emotional distracters in the emotional processing in conflict resolution task is independent of attention i.e. it processed automatically⁸. However, a meta- analysis on emotional influences on attention and perception showed that emotional stimuli compete for neural representation, require attentional resources i.e. processing of emotional stimuli is dependent on attention⁹.

Thus, the studies suggested that the mechanism of attentional processing of emotional stimuli remains unclear. Studies showed discrepancies related to emotion processing in non- demented patients and hence further studies are needed to illuminate the emotional profile of patients with PD. Further, very few studies have done assessing the attentional processing with emotional stimuli in patients with PD. The studies in past had revealed the dysfunction in processing of negative stimuli, however, the attentional processing of positive stimuli is still unclear, which needs to be evaluated. Thus, the present study has attempted to clear the contradictory quest of deficit in emotional processing of stimuli and intact of attentional processing. The present research was an attempt to examine the processing of emotion stimuli on a stimulus- response compatibility flanker task. The study assess and compares the differences in the processing of different emotions under different target congruency conditions. The patients with PD-MCI (Mild Cognitive Impairment) and PD-D (Dementia) have been excluded from the study to remove any cognitive variability.

Methodology Participants: Participants were selected from the OPD of the Department of Neurology, I.M.S., B.H.U. and they were screened by using clock

drawing test to exclude any cognitive impairment in PD patient. Seven PD patients and 7 age-matched healthy controls were recruited. The other parkinsonian disorders were excluded from the study.

Tools: Emotional Flanker task: The emotional flanker task has been designed and programmed in Superlab 4.0 version programming software. Emotional flanker task was designed using pictures selected from the International Affective Picture System (IAPS)¹⁰.

Stimuli: The stimuli consisted of colored pictures that were selected from the International Affective Picture System (IAPS) based on their normative valence ('Valence' refers to the nature of emotion: positive, neutral or negative) ratings. The target congruency had two levels: congruent—when all the emotional stimuli are either positive, negative or neutral, and incongruent—when the center emotional stimuli are of different emotional valence than flanker emotional stimuli. The content of pleasant pictures included puppies, family, children etc. (IAPS no. 1710, 2340, 2347), whereas the unpleasant picture included hospital, stiches, explosion etc. (IAPS no. 2205, 3195, 9940). The neutral set included pictures of buttons, spoon, basket etc. (IAPS no. 7001, 7004, 7010).

Experimental paradigm: The paradigm consisted of three emotional conditions: 5 low valence negative, 5 high valence positive, and 5 neutral pictures. Selected negative pictures with a mean valence rating of 1.63 (SD 0.6) and a mean arousal rating of 6.07 (SD 0.5). Positive pictures with a mean valence rating of 8.34 (SD 0.5) and a mean arousal rating of 5.27 (SD 0.6). Neutral pictures with a mean valence rating of 5.01 (SD 0.3) and arousal rating of 6.96 (SD 0.4).

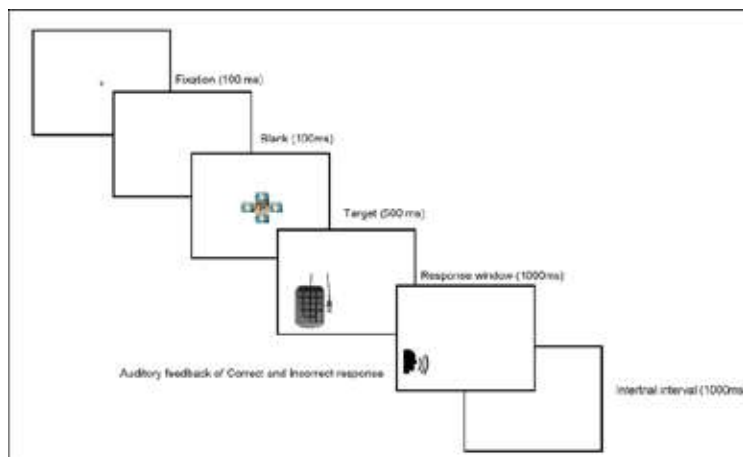


Figure 1: Schematic representation of trials in Emotional Attentional Task

Each trial consisted of six events. First, a fixation cross of 100ms duration was presented. A blank screen for 1000ms was presented before the appearance of target which lasts for 500ms. Patients were given 1000ms time for responding to the target. After the response, an auditory feedback was given about the correctness of response. The next trial of the experiment started after 1000ms of inter-trial interval(See Figure 1).

Experimental Design: A 2 (Group: PD patient & healthy control) x 3 (Valence: Positive, negative, neutral) x 2 (Stimulus congruency: Congruent & incongruent) x mixed factorial design with repeated measures on last two factors was used.

Procedure: Diagnosed patients were taken from outpatient department of hospitals. Screening of non- demented PD patient and healthy control was done using Hindi Mental State Examination. Rapport was established and then consent and biographical information was taken. The patients with at least 6 months of dopaminergic treatment were taken to control the motor problem. Further, a separate numeric key pad was used for their convenience in pressing the key. Three keys were assigned indicated by color red, green and yellow to respond to positive, negative and neutral stimuli respectively. The participants were asked to attend and respond to the center stimulus and ignore the other four emotional stimuli. Participants were asked to discriminate emotions as happy, sad and neutral and instructed to attend the central image. There are 18 number of trials in demo condition with an auditory feedback in hindi language of “Sahi” and “Galat”. In practice session of 32 trials, same auditory feedback

was given. After the practice session, two experimental sessions of 54 trials were administered without any feedback.

Dependent Measures: The reaction time and accuracy was computed. The measures of flanker compatibility effect constitutes the difference between different congruency conditions.

Results

Neuropsychological Assessment: Patients with cognitive impairment were excluded using clock drawing test. The UPDRS and Hoehn and Yahr staging were also used to measure motor impairment and the severity of the disease.

Cognito-affective Assessment: Repeated-measures analysis on 2(Group: PD patients, HC)×3 (Emotion: Positive, Negative and Neutral)×2 (Target conditions: Congruent, Incongruent) was performed with group (PD patients, healthy controls) as a between-group factor and target, valence emotion as within-group factor.

Response Latency: The analysis of reaction time result showed a significant effect of group ($F(1,12)=71.10, p = 0.012$) which revealed that patients with Parkinson disease performed poorer than healthy control. The main effect of target condition ($F(1,12)=214.47, p = 0.032$) was significant indicating that the incongruency trials showed high reaction time. The attentional modulation of different emotional valence condition was also found significant, $F(2,24)=23.93, p=0.001$, which suggest differential effect of emotional valence on attention performance (see Figure 2).

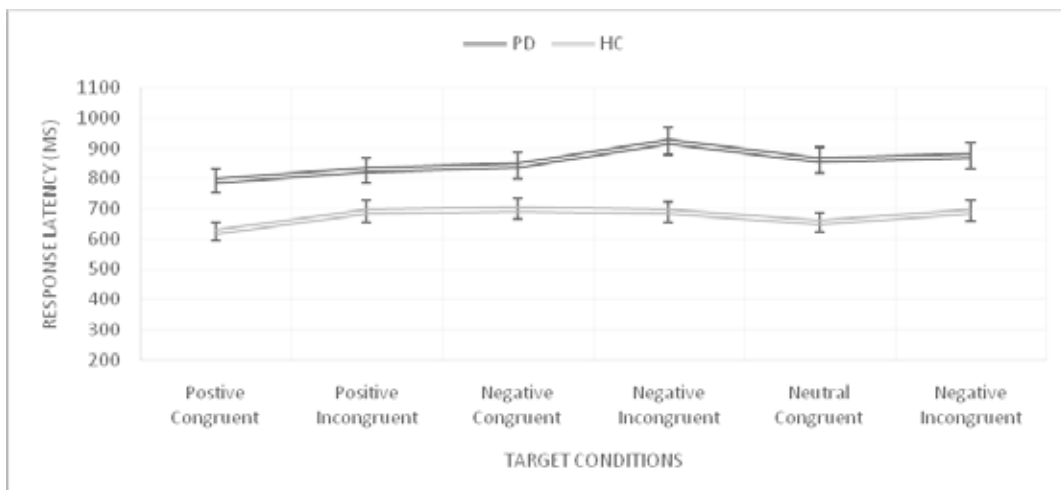


Figure 2: Graph showing mean reaction time of correct responses under different target conditions

The emotional stimuli of different valence state played an important role in attentional processing. The emotional stimuli with positive stimuli processed faster in comparison to negative and neutral valence stimuli as revealed by paired sample t test, $t(13)=4.207$, $p=0.001$. The paired sample t test between negative and neutral stimuli further revealed a significant difference, $t(13)=4.75$, $p=0.001$, it was found that response time taken in processing neutral stimuli was significantly less than negative valence stimuli.

Furthermore, a significant interaction was found between group and target condition ($F(1,12)=6.84$, $p=0.040$), showed that groups under congruent target condition was found better than incongruent target conditions. The interaction between group and valence conditions ($F(2,12)=8.21$, $p=0.002$) was also found significant indicating that group performed significantly better in positive than, negative and neutral valence conditions. The trials with positive emotional stimuli (PD: $M=746.14$ ms, HC: $M=663.28$ ms) were processed faster and accurately as compared to negative (PD: $M=829.00$ ms, HC: $M=674.28$ ms) and neutral stimuli

(PD: $M=837.57$ ms, HC: $M=696.57$ ms). However, the interaction between valence and target conditions ($F(2,12)=0.56$, $p=0.57$) was not found significant, which indicates that the effect of congruent and incongruent condition do not affect the performance in processing positive, negative and neutral condition.

Accuracy Performance: The accuracy data analysis showed a significant difference in group, $F(1,12)=3.53$, $p=0.085$ which revealed that patients with Parkinson committed more errors as compared to control. Further, the interaction between group and emotional valence were significantly different, $F(1,12)=0.369$, $p=0.695$ that revealed that trials with positive emotional stimuli (PD: $M=75.14$, HC: $M=85.64$) were processed more accurately as compared to negative (PD: $M=79.07$, HC: $M=86.85$) and neutral stimuli (PD: $M=79.05$, HC: $M=87.07$). However, a non-significant interaction was found between emotional stimuli and target, $F(1,12)=1.30$, $p=0.29$ which indicated that there was no difference in the effect of emotional stimuli on different congruency of target in patients with PD and healthy control (see Figure 3).

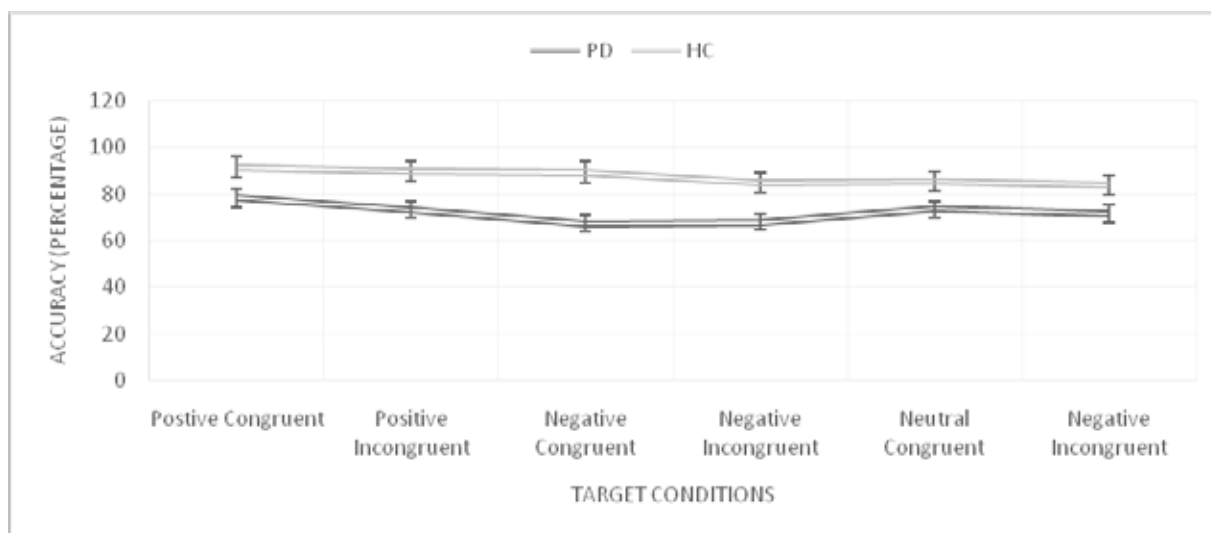


Figure 3: Graph showing mean reaction time of correct responses under different target conditions

Discussion

The study investigated the effect of emotional stimuli on a stimulus-response compatibility flanker task. In PD, an emotional symptom called facial amimia where patient's face becomes frozen and inexpressive due to the impairment in emotional processing which could relate with the problem in interpersonal relationship.

In light of this, the primary results of the present study reveals that the patient group reported more problems in processing emotional stimuli with negative valence than healthy control. These deficits were possibly due to the deficit in the regulation of negative emotion which is consistent with findings of a study¹¹. The findings of the present study further suggest that the response

processing to fear-eliciting stimuli is diminished, which is also consistent with a previous studies¹². Moreover, our study investigated cognitive aspect related to response inhibition processing related with emotions in non-demented PD patients. It was observed that response inhibition using flanker compatibility effect in PD and control did not differ in flanker effect which showed that there is no effect of congruency. One could argue that the deficits in emotional processing are an effect of general decline in cognitive functioning in PD. We excluded this possibility by not including PD-MCI (Mild Cognitive Impairment) and PD-D (Dementia) and only taken cognitively intact PD patients (PD-Non-cognitive Impairment (PD-NCI)). The finding of the present study agrees with the results of a study¹³ which revealed that emotion processing impairment among PD patients was not related to the patients' cognitive status.

The findings are discussed in terms of accuracy and response latency. The results of the present study suggest that emotional stimuli impair the performance on attentional task. First, performance in tasks of emotional attentional processing was impaired in PD patients compared to controls in line with previous data^{14,15} which means that performance on stimuli with different valence emotional stimuli under different target conditions was found different in healthy subjects and PD patients. The results are also consistent with¹¹ suggested that individuals with PD showed a lower attentional score for negative emotion than for relatively positive emotion. With regards to emotional deficit in processing emotional images in PD, our findings were relatively similar to a previous study¹⁶.

Although the present study address the deficit of emotional processing in PD patients, however the study also exhibit a limitation of small sample size of the patient. Thus future study can be done on larger sample of Parkinson patient. Future study can also be done using emotional faces in place of IAPS pictures. The present study also gives a direction to future study corroborating with fMRI investigation which can be used to identify the brain area activation.

Conclusion

In sum, the present study infer that the attentional processing of emotional images were slower in PD patients in comparison to matched healthy control. Further, result yielded a difference in performance on congruent and incongruent emotional trials in PD

patients, especially on negative incongruent conditions, however no such difference has been seen in matched healthy control. However, the analysis of accuracy results revealed no indication of diminished flanker compatibility effect on positive, negative and neutral stimuli which revealed that they recognized the emotional stimuli, however due to the differences in emotional valence and arousal the processing speed was affected as revealed by response latency measure.

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Declaration of Interest Statement: No

Ethical Clearance: The study protocol was approved by University Ethics committee and written informed consent was taken from all the participants and caregivers before the study.

References

1. Bora E, Walterfang M, Velakoulis D. Theory of mind in Parkinson's disease: a meta-analysis. *Behavioural Brain Research*. 2015 Oct 1;292:515-20.
2. Lin CY, Tien YM, Huang JT, Tsai CH, Hsu LC. Degraded impairment of emotion recognition in Parkinson's disease extends from negative to positive emotions. *Behavioural Neurology*. 2016;2016.
3. Caccappolo E, Marder K. Cognitive impairment in non-demented patients with Parkinson's disease'. *Cognitive Impairment and Dementia in Parkinson's disease*. 2010 Jan 7:179.
4. Barone P, Aarsland D, Burn D, Emre M, Kulisevsky J, Weintraub D. Cognitive impairment in nondemented Parkinson's disease. *Movement Disorders*. 2011 Dec 1; 26(14):2483-95.
5. Tröster AI. Neuropsychological characteristics of dementia with Lewy bodies and Parkinson's disease with dementia: differentiation, early detection, and implications for "mild cognitive impairment" and biomarkers. *Neuropsychology review*. 2008 Mar 1;18(1):103-19.
6. Wylie SA, van den Wildenberg WP, Ridderinkhof KR, Bashore TR, Powell VD, Manning CA, Wooten GF. The effect of Parkinson's disease on interference control during action selection.

- Neuropsychologia. 2009 Jan 1;47(1):145-57.
7. Rai P, Singh T, Singh IL, Tiwari T. Response inhibition processing between young and older adults. *Indian Journal of Health & Wellbeing*. 2017 Oct 1; 8(10): 1232-1236.
 8. Vuilleumier P, Armony JL, Driver J, Dolan RJ. Effects of attention and emotion on face processing in the human brain: an event-related fMRI study. *Neuron*. 2001 May 1;30(3):829-41.
 9. Pourtois G, Schettino A, Vuilleumier P. Brain mechanisms for emotional influences on perception and attention: what is magic and what is not. *Biological psychology*. 2013 Mar 1;92(3):492-512.
 10. Lang PJ, Bradley MM, Cuthbert BN. International affective picture system (IAPS): Technical manual and affective ratings. NIMH Center for the Study of Emotion and Attention. 1997;1:39-58.
 11. Gray HM, Tickle-Degnen L. A meta-analysis of performance on emotion recognition tasks in Parkinson's disease. *Neuropsychology*. 2010 Mar;24(2):176.
 12. Miller KM, Okun MS, Marsiske M, Fennell EB, Bowers D. Startle reflex hyporeactivity in Parkinson's disease: an emotion-specific or arousal-modulated deficit?. *Neuropsychologia*. 2009 Jul 1;47(8-9):1917-27.
 13. Herrera E, Cuetos F, Rodríguez-Ferreiro J. Emotion recognition impairment in Parkinson's disease patients without dementia. *Journal of the neurological sciences*. 2011 cNov 15;310(1-2):237-40.
 14. Bologna M, Fabbrini G, Marsili L, Defazio G, Thompson PD, Berardelli A. Facial bradykinesia. *J Neurol Neurosurg Psychiatry*. 2013 Jun 1;84(6):681-5.
 15. Marsili L, Agostino R, Bologna M, Belvisi D, Palma A, Fabbrini G, Berardelli A. Bradykinesia of posed smiling and voluntary movement of the lower face in Parkinson's disease. *Parkinsonism & related disorders*. 2014 Apr 1;20(4):370-5.
 16. Narme P, Bonnet AM, Dubois B, Chaby L. Understanding facial emotion perception in Parkinson's disease: the role of configural processing. *Neuropsychologia*. 2011 Oct 1;49(12): 3295-302.

Treatment Success Rate among Multidrug Resistant Tuberculosis Patients Registered Under Programmatic Management of Drug Resistant Tuberculosis Services in District Amritsar, Punjab, India

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Abstract

Background: MDR-TB has become an urgent public health problem worldwide, threatening the global TB control. The success rate of treating multi drug resistant remains very low.

Method: This cross-sectional study was conducted on all MDR-TB patients who were registered and being treated under PMDT services in Amritsar district from 1st January 2015 to 31st December 2016. The treatment outcome with their clinico-demographic determinants was ascertained. Data management and analysis was done by using Microsoft excel and SPSS.

Results: Out of 110 registered MDR-TB patients, 88 (80.0%) were males and 22 (20.0%) were females. The various treatment outcomes observed were- 36 (32.7%) cured, 20 (18.2%) treatment completed, 16 (14.5%) defaulted, 22 (20.0%) died, 11 (10.0%) regimen changed or shifted to XDR TB regime, 5(4.5%)transferred out. The success rate (cured+ treatment completed) was50.9%.

Conclusions: On statistical analysis, it was observed that age ($p=0.012$),weight band of patients under RNTCP ($p=0.040$) were significantly associated with the treatment outcome. Other factors like sex, residence, typeof tuberculosis and the HIV status of the patient did not affect the treatment outcome.

Keywords: Multi-drug resistant TB, Treatment outcomes, success rate.

Introduction

The emergence of Multidrug resistant TB (MDR TB) has created increasing constraints on effective tuberculosis control and has caused tremendous morbidity and mortality worldwide. Globally in 2017, there were an estimated 558 000 new cases of Rifampicin resistant TB (RR-TB), of which almost half

were in three countries: India, China and the Russian Federation. Among RR-TB cases, an estimated 82% had multidrug resistant TB (MDR-TB). Globally, 3.5% of new TB cases and 18% of previously treated cases had MDR/RR-TB, with the maximum proportions (>50% in previously treated cases) in countries of the former Soviet Union.¹ The treatment of MDR-TB, is long,expensive and requires the use of toxic drugs and has substantially lower success rates than for drug-sensitive TB.²

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Despite progress in tuberculosis (TB) control, the response to the multidrug resistant TB continues to be limited. Treatment success remains low, at 55% globally.¹ This is considered to be one of the major challenges to progress towards the country's targets to end TB by 2025. While prevention of development of

drug resistance is of paramount importance for ending TB, early detection and treatment completion are keys to interrupt on-going transmission.³ Therefore, it is imperative to analyze the treatment outcomes of MDR-TB patients treated by standardized 2nd line chemotherapy. Hence the present study was planned to investigate the treatment outcomes and to assess the impact of different demographic and clinical conditions on the outcome among MDR-TB patients.

Method

The study was a cross-sectional study conducted on all MDR-TB patients registered and being treated with second line anti-tuberculosis drugs under Programmatic management of drug resistant tuberculosis services in Amritsar City.

Study Sample: All MDR-TB patients registered from 1st January 2015 to 31st December 2016.

Inclusion Criteria: All drug sensitivity tested (DST) confirmed MDR-TB cases who signed written informed consent.

Exclusion Criteria: Critically ill patients and pregnant females were excluded from the study.

Data Collection and Analysis: A total of 110 patients registered with District Tuberculosis Centre(DTC), Amritsar and being treated with second line anti TB drugs were included in the study. A pre-designed and pre-tested proforma was administered to the subjects after taking his/her consent. The consent of the caretaker or guardian/parent was sought on behalf of all child participants. Questionnaire included questions regarding the socio-demographic and clinical profile, of the patients. The possible outcomes of the MDR TB patients under DOTS can be: cured, treatment completed, died, failure, defaulted, regimen changed/shifted to XDR and transferred out.³

Cured: Treatment completed as recommended by the national policy without evidence of failure and three or more consecutive cultures taken at least 30 days apart during CP are negative including culture at the end of treatment.

Treatment Completed: Treatment completed as recommended by the national policy without evidence of failure but no record that three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase.

Failure: Treatment terminated or need for permanent regimen change of at least two or more anti-TB drugs in CP because of lack of microbiological conversion by the end of the extended intensive phase or microbiological reversion in the continuation phase after conversion to negative or evidence of additional acquired resistance to FQ or SLI drugs or adverse drug reactions .

Died: A patient who dies for any reason during the course of treatment.

Transfer Out: A patient who has been transferred to another reporting unit (DR-TB Centre in this case) and for whom the treatment outcome is not known.

Regimen Changed/shifted to XDR: A TB patients need for permanent regimen change of at least one or more anti-TB drugs prior to being declared as failed/A MDR-TB patient who is found to have XDR-TB by an RNTCP certified CDST laboratory and who has subsequently switched to a regimen for XDR-TB treatment initiation.

Outcomes were classified as Favourable outcome which includes cured and treatment completed patients and Unfavourable outcome that includes cases with outcome as defaulted, died, transferred out and those who were shifted to XDR TB or changed regime. Cured and treatment completed, these together define treatment success.

All the information so collected was compiled, analyzed statistically with help of SPSS version 20. Chi-square test was used to evaluate differences in categorical variables and $p < 0.05$ was considered to be significant.

Ethics: The research proposal was approved by the college ethical committee at the time of commencement of the study.

Source of Funding: Nil

Conflict of Interest: Nil

Results

A total of 110 patients with a diagnosis of MDR-TB were registered under PMDT services in Amritsar city during 2015–2016. The total sample comprised of, 88 (80.0%) males and 22 (20.0%) females. The mean age of the patient is 33.13 years (SD \pm 12.4 years), ranging 11 to 68 years. 84 (76.4%) cases were in the age group of 11-40 years. Most of the patients 88(80.0%) were males

and 67(60.9%) patients resided in urban areas. Almost all patients,107(97.3%) had pulmonary tuberculosis and only 3(2.7%) had extra-pulmonary tuberculosis. Maximum patients 58(52.7%) belonged to weight band of 46-70 kg .Only 4 (3.6%) patients were HIV positive. 7(6.3%)patients were resistant to both drugs Rifampicin and Isoniazid.

Table 1: shows the distribution of cases according to their treatment outcomes. Out of the total 110 patients, 36 (32.7%) were cured, 20 (18.2%) were categorized as treatment completed, 16 (14.5%) patients defaulted, 22 (20.0%) died, in 11(10.0%) patients regimen was changed or shifted to XDR TB regime and 5(4.5%) patients were transferred out. Treatment success rate (cured and treatment completed) was 50.9% in the present study.

Table 2: depicts the clinical and demographic factors affecting treatment outcome in MDR TB cases. It is evident from the above table that favourable outcome was seen in younger age group i.e. 11-25 yrs. Out of 110 patients,30 (69.8%) patients had favourable outcome.

Unfavourable outcome was seen in 80.0% of patients of more than 55 yrs age. The results were found to be statistically significant (p=0.012). 43(48.9%) males and 13(59.1%) females had favourable outcome. The results were not found significant. Favourable outcome was significantly higher among patients with weight band 46-70 kg i.e 36(62.1%) as compared to patients belonging to other weight bands (p=0.040). Sex, residence, type of TB and HIV status of the patient were not significantly associated with treatment outcome.

Table 1: Treatment outcome of multidrug resistant TB patients

Outcome	Frequency	Percentage
Cured	36	32.7
Treatment completed	20	18.2
Defaulted	16	14.5
Died	22	20.0
Regimen changed/Shifted to XDR	11	10.0
Transferred out	5	4.5

Table 2: Distribution of cases showing the demographic and clinical factors affecting the treatment outcome.

Characteristics of Patient	Treatment Outcome		Significance
	Favourable* (n=56)	Unfavourable** (n=54)	
Age (Years)			
11-25 (n=43)	30(69.8)	13(30.2)	$\chi^2=10.892$ df=3 p=0.012
26-40 (n=41)	16(39.0)	25(61.0)	
41-55 (n=21)	9(42.9)	12(57.1)	
>55 (n=5)	1(20.0)	4(80.0)	
Sex			
Male (n=88)	43(48.9)	45(51.1)	$\chi^2= 0.737$ df=1 p=0.391
Female (n=22)	13(59.1)	9(40.9)	
Residence			
Urban (n=67)	34(50.7)	33(49.3)	$\chi^2=0.02$ df=1 p=0.966
Rural (n=43)	22(51.2)	21(48.8)	
Type of TB			
Pulmonary (n=107)	55 (51.4)	52 (48.6)	$\chi^2=0.381$ df=1 p=0.537
Extra-pulmonary (n=3)	1(33.3)	2 (66.7)	
Weight Bands			
26-45 (n=48)	19(39.6)	29(60.4)	$\chi^2=6.42$ df=2 p=0.040
46-70 (n=58)	36(62.1)	22 (37.9)	
>70 (n=4)	1(25.0)	3(75.0)	

Characteristics of Patient	Treatment Outcome		Significance
	Favourable* (n=56)	Unfavourable** (n=54)	
HIV Status			
Nonreactive (n=106)	55 (51.9)	51(48.1)	$\chi^2=1.115$ df=1 p=0.291
Reactive (n=4)	1(25.0)	3 (75.0)	

*Favourable outcome included Cured and Treatment completed; **Unfavourable outcome included Defaulted, Died, Regimen changed/shifted to XDR.

Discussion

In the present study it was observed that out of the total 110 patients, 76.4 % of patients were in age group of 11-40 yrs. Similar study by Nair et al in Chennai showed that 70% were in the age group of 15-44 yrs.⁴ The demographic profile of MDR-TB patients in our study was similar to other studies, with a majority of patients, 62(56.4 %), in the economically productive age group (26-55 years) with male patient predominance.^{5,6} Our study participants included 88 (80.0%) males and 22 (20.0%) females. The mean age of the patient was 33.13 years. A study conducted in Uttar Pradesh also revealed that more than 2/3rd of patients were male and the mean age was 32 years.⁷ Similar male preponderance was observed in the study by a study on MDR-TB patients in Cairo, Egypt and in Indonesia showing that out of the total, 72.9% and 68.6% were males respectively.^{8,9}

Table 1 revealed the outcome of the total 110 patients, 36 (32.7%) were cured, 20 (18.2%) completed treatment, 16 (14.5%) patients defaulted, 22 (20.0%) died, in 11 patients (10.0%) regimen was changed or shifted to XDR TB regime and 5 (4.5%) patients were transferred out. In the present study, treatment success rate, which consist of cured and treatment completed was 50.9%. The result is consistent with reported global (52%) and national (56%) MDR-TB treatment success rates.^{10,11}

MDR-TB treatment success rate recorded in a study conducted in patients from Chinese referral hospitals also showed similar success rate.¹² Another study done in china showed success rate of 57 %.¹³ A study undertaken to analyze the clinical profile and treatment outcome in pulmonary drug tuberculosis (TB) patients under programmatic management of multidrug resistant tuberculosis (PMDT) at a tertiary care center in Mumbai showed 48.4% of MDR-TB patients were successfully treated (cured + treatment completed), 43.47% were cured, 10.1% completed treatment, 13.04% died, 1.4% failed, 15.4% defaulted, 4.3% stopped treatment due to

adverse drug reactions and 11.5% transferred.¹⁴ Another study in Karnataka showed that at the end of treatment, 44.2% were cured, 12 defaulted, 9 died, 1 failure and 2 were under XDR TB evaluation.¹⁵ Studies in Portugal and China showed the treatment success of 62% and 68.3% respectively.^{16,17}

Table 2 shows the clinic-demographic determinants of treatment outcome. Our study observed that favourable outcome was significantly higher among the age group of 11-25 yrs. 30 (69.8%) patients had favourable outcome. Unfavourable outcome was seen in 80.0% of patients of more than 55 yrs age. Studies by Dengkui et al in Shanghai, Nair et al in Chennai and Gafar et al in South Africa on predictors of treatment outcome showed that unfavourable outcomes in MDR TB cases were significantly higher among cases >45 years.^{18,4,19}

Favourable outcome was significantly higher among patients with weight band 46-70 kg i.e 36(62.1%) as compared to patients belonging to other weight bands (p=0.040). A study by Agarwalla, *et al* on outcome of MDR patients that majority of the patients in this study are of low BMI (<18.5 kg/m²) and their success rate is significantly less compared to patients having BMI more than 18.5 kg/m².²⁰

Other factors like sex, residence, type of family and HIV status did not affect the treatment outcome.

Conclusion

Treatment of MDR-TB is major challenge due to the prolonged regimens, multiple drugs used and high incidence of drug toxicities. This is, in turn, contributes to poor treatment adherence and further exponential magnification of drug resistance which can have devastating consequences. The treatment success rate (cured and treatment completed) in the present study was 50.9% which is similar to global treatment success rates of a 55%. Favourable treatment outcome was

present in 50.9% cases. The predictors of unfavourable outcome were age ≥ 26 years and weight band of 26-45 under RNTCP

References

- World Health Organization. Global tuberculosis report 2018. Available from: <http://www.who.int/tb/publications/2019/en/>. Accessed on Sep29, 2019
- World Health Organization. Global tuberculosis report 2017. Available from <http://www.who.int/tb/publications/2018/en/>. Accessed on Sep18, 2019
- Guidelines on Programmatic Management of Drug Resistant TB in India. Central TB Division, Directorate General of Health Services, Ministry of Health & Family Welfare, Government of India, New Delhi, 2017
- Nair D, Velaytham B, Kannan T, Tripathy J P, Harries AD, Natrajan M, Swaminathan S. Predictors of unfavourable treatment outcome in patients with multi-drug resistant tuberculosis in India. *Int Union Against Tuberculosis and Lung Disease. PHA.* 2017;7(1):32-8.
- Kapadia VK, Tripathi SB. Analysis of 63 patients of MDR TB on DOTS plus regimen: An LG hospital, TB Unit, Ahmedabad experience. *GMJ.* 2013;68(2):52-7.
- Prasad R, Verma SK, Sahai S, Kumar S, Jain A. Efficacy and safety of kanamycin, ethionamide, PAS, and cycloserine in multidrug-resistant pulmonary tuberculosis patients. *Indian J Chest Dis Allied Sci.* 2006;48:183-6.
- Venkatesh U, Srivastava DK, Srivastava AK, Tiwari HC. Epidemiological profile of multidrug-resistant tuberculosis patients in Gorakhpur Division, Uttar Pradesh, India. *J Family Med PrimCare*2018;7:589-95.
- Mohammad A. Tag El Din, Ashraf A. El Maraghly, Abdel Hay R. Adverse reactions among patients being treated for multi-drug resistant tuberculosis at Abbassia Chest Hospital. *Egyptian J Chest Dis And Tuberculosis.* 2015;64(4):939-52.
- Manurung SMPF, Siagian P, Sinaga BYM, and Mutiara E. Factors related to successful treatment of drug-resistance tuberculosis in H. Adam Malik hospital, Medan, Indonesia. *IOP Conf. Series Earth Environ Sci.* 2018;125:012148
- World Health Organization. Global tuberculosis report 2016. Available from: <http://www.who.int/tb/publications/2019/en/>. Accessed on Sep29, 2019
- Zhao Y, Xu S, Wang L, Chin DP, Wang S, Jiang G, Xia H, Zhou Y, Li Q, Ou X. National survey of drug-resistant tuberculosis in China. *N Engl J Med.* 2012; 366(23):2161–70.
- Liu CH, Li L, Chen Z, Wang Q, Hu YL, Zhu B, Woo PC. Characteristics and treatment outcomes of patients with MDR and XDR tuberculosis in a TB referral hospital in Beijing: a 13-year experience. *PLoS One.* 2011;6(4):e19399.
- Alene, Kefyalew Addis, et al. “Treatment outcomes of patients with multidrug-resistant and extensively drug resistant tuberculosis in Hunan Province, China.” *BMC Infectious Diseases.*2017;17:573.
- Waghmare MA, Utpat K, Joshi JM. Treatment outcomes of drug-resistant pulmonary tuberculosis under programmatic management of multidrug-resistant tuberculosis, at tertiary care center in Mumbai. *Med J DY Patil Univ* 2017;10:41-5.
- Neeta PN, Prashanth N, Ramaprasad G, Gangadhar Goud T, Sameena A R B. A study on outcome of standardized treatment in multidrug resistance tuberculosis patients. *Int J Community Med Public Health.* 2016;3:257-63
- Chen Y, Yuan Z, Shen X, Wu J, Wu Z, Xu B. Time to multi-drug-resistant tuberculosis treatment initiation in association with treatment outcomes in Shanghai, China. *Antimicrob Agents Chemother.* 2018;62:e02259-17.
- Oliveira O, Gaio R, Villar M, Duarte R. Predictors of treatment outcome in multidrug-resistant tuberculosis in Portugal. *Eur Respir J.* 2013;42:1747–9.
- Lia D, Gea E, Shenb X, Weia X. Risk Factors of Treatment Outcomes for Multi-drug Resistant Tuberculosis in Shanghai, 2009-2012. *Procedia Environ Sci.* 2016;36:12 – 9.
- Gafar MM, Nyazema NZ, Dambisya YM. Factors influencing treatment outcomes in tuberculosis patients in Limpopo Province, South Africa, from 2006 to 2010: A retrospective study. *Curationis.* 2014;37(1).
- Agarwalla A, Bhattacharya S, Dey A, Kar S, Chaudhuri AD. Study of outcome of management of MDR-TB cases under programmatic condition in India. *J NTR Univ Health Sci* 2019;8:1-4.

Denture Identification Method: A Review

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Abstract

Context: Denture marking is accepted as a means of identifying dentures and persons in geriatric institutions, during war, crimes, and civil unrest, natural and mass disasters, post mortem and medico-legal investigations. This review highlighted the various method of denture marking and significance of placing identification marks on dentures.

Keywords: Denture marking, Geriatric, Identification

Introduction

Denture marking is accepted as a means of identifying dentures and persons in geriatric institutions, or post-mortem during war, crimes, civil unrest, natural and mass disasters. Due to the lack of a comprehensive fingerprint database, dental identification is growing as an essential part of forensic investigation. Prosthodontists are playing very important role in forensic dentistry as they are concerned with fabrication of various prostheses which can serve as an important tool for identification. The denture marking is important for the following reasons:¹

- a. It serves to identify an unknown denture wearer in cases involving amnesia or senility, loss of memory, psychiatric cases, homicide, suicide, victims of fire, explosion, floods, earthquake, plane crash, or war.
- b. In cases of lost and found, the denture can be returned to the owner.
- c. A rapid and accurate method other than finger printing is essential for identification of the individuals.

- d. In the laboratory, the dental technicians will find it easy to identify a denture, especially at the deflasking stage, if it is marked / labeled.
- e. To ensure the correct denture delivery to the respective patient.

Medicolegal Importance of Denture Marking Systems²:

1. Identification of the dead or deceased when all other means have failed.
2. Identification of individuals for forensic, social and legal reasons.
3. Victim identification in case of mass disasters like terrorism, bombings, earthquakes, hurricanes, typhoons, air crashes and other transportation mishaps.
4. Identification of mutilated and decomposed bodies when all other parameters like scars, tattoos, and facial features have failed.

Method of Denture Identification: Various method of denture marking have been reported in the literature. However, there are two main method in marking dentures, namely the surface method and the inclusion method. As compared to surface method, inclusions method are permanent but require more skills and are time consuming.³

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Surface Method:

Scribing or Engraving Method: In this method letters or numbers are engraved on the denture surface with the help of a small round dental bur.⁴

Disadvantage: Food entrapment occurs in the engraved grooves.

Embossing Method: In this technique name and other particulars of the patient are scratched on the master cast. After processing it produces stamped or embossed letters on the impression surface of dentures.⁵

Disadvantage: This technique has been associated with malignancy, possibly due to continued tissue irritation.

Invisible Ink Method: Harvey described a method wherein the patient's details are written with an invisible ink that is rendered visible by ultraviolet light. This is useful on acrylic resin dentures of those patients who object to normally visible identification marks.

Disadvantage: The mark is not readily visible and examination under special conditions is required to determine its presence.⁶

Fibre Tip Pen Method: Patient's details are written on the tissue-fitting surface or the polished surface of the denture with a fibre-tip pen. The patient's identification details are then covered by at least two thin coats of varnish in order to prolong the life of the marking.⁷

Disadvantage: This method resulted in an unesthetic denture.

Denture Bar Coding Method: A bar code consists of a machine-readable code of a series of bars and spaces printed in defined ratios. The technique described for denture bar coding involves printing a number code on paper, photographing the paper, making and transferring the negative to a piece of silk. An image of the bar code appeared on a prepared faience, by a machine that forced the paint through the silk, when heated to 860 degree C for 30 min in an industrial porcelain oven. The bar code is directly placed onto the denture surface and cyanoacrylate resin is painted to conceal the marking.⁸

Disadvantage: Incorporating the bar code into the curved denture flange is relatively cumbersome due to rigidity of the laminated strip.

Lenticular Card Method: In this technique a

lenticular lens is used to produce images with an illusion of depth, morph, or the ability to change or move as the image is viewed from different angles. Lenticular printing is a multi-step process consisting of creating a lenticular image from at least two or more existing images, and combining it with a lenticular lens. Each image is sliced into strips, which are then interlaced with one or more of the other images. These are printed on the back of a synthetic paper and laminated on the lens. The most common materials used for making lenticular images are polyvinyl chloride (PVC), amorphous polyethylene terephthalate (APET), acrylic, spectra, and polyethylene terephthalate glycol (PETG). The lens is incorporated in the channel cut on the denture and auto-polymerizing clear acrylic resin is added around and not on the identifier.⁹

Paper Strip Method: It utilizes onion skin paper. The acrylic resin fitting surface situated adjacent palatally between the ridge and the center of the palate is moistened with monomer on a small brush. The strip of typed paper is laid on this surface and the paper is moistened with the monomer. Clear resin is then placed over the paper before final closure of the denture flask.¹⁰

RFID Tags: RFID stands for radio-frequency identification, which is a wireless electronic communication technology. The radio-frequency identification (RFID) system consisted of a data carrier, or tag, and an electronic handheld reader that energizes the transponder by means of an electromagnetic field emitted via the reader's antenna. It then receives the coded signal returned by the transponder and converts it into readable data.¹¹

Advantages: This method is a cosmetic, effective labeling method permitting rapid and reliable identification of the wearer.

- b.) They are preferred because of their small size (8.5×2.2 mm).
- c.) A large amount data can be stored in them.
- d.) No special training is required to set the tag in the denture.
- e.) The chip is resistant to disinfectants and solutions of 1% hypochlorite, 4% chlorhexidine, and 4% sodium perborate.

Photographic Method: In this technique patient's photograph is embedded in the denture with the help of clear acrylic resin.

The name, age and geographic location of the patient are written on the obverse of the photograph using a micro-tip graphite pencil. The marker is particularly useful in the countries with low literacy rate where a photograph is the easiest method of identification.¹²

Advantage: The identity is easily ascertained by lay persons with the unassisted eye.

Incorporation of Min. I. Dent: Patient's details are typed on Min. I. Dent denture identification strip and the strip is heated in an oven at 325 degree C for 30 s to 1 min. This allows shrinkage of lettering or numbers and the strip becomes a chip. The chip is trimmed to required size using carbide bur. A groove is cut into the denture and the chip is incorporated into the groove and sealed with orthodontic resin.¹³

Lead Foil: A piece of lead foil from a used IOPA radiographic film is cut and patient's details are engraved with a sharp pointed pen or instrument and is embedded in the denture with the help of clear acrylic resin.¹⁴

Advantage: This technique is easy to operate. b.) It is economical. c.) It is radiographically visible.

Ceramic Crown Engraving Method: After baking the opaque layer of porcelain, dentin porcelain is applied and initials of name of the patient or letters are carved with the brush. Stains are applied on carved initials followed by enamel porcelain application shaped with soft brush so that the initials are maintained. Few initials can be carved in crown and bridges due to lack of available space.¹⁵

Conclusion

Denture marking should be compulsorily carried out for hospitalized patients, unconscious patients and patients in geriatric institutions. There is a strong need to adopt an international policy for denture marking and international collaboration should be encouraged, with different opinions from the world-wide community of forensic odontologists discussed and with the aim of reaching some kind of consensus for the future.

Conflicts of Interest: The authors declare that there is no conflict of interest regarding the publication of this paper.

Source of Funding: Self

Ethical Clearance: Ethical clearance has been taken from Institutional Ethical Committee

References

1. Woodward JD. Denture marking for identification. *J Am Dent Assoc* 1979;99:59–60.
2. Pyke TF. Personal identification from artificial dentures. *Aust Dent J* 1970;15:495–8.
3. Haines DH. Identification in mass disasters from dental prosthesis. *Int J Forensic Dent* 1973;1:11–5.
4. Luthra R, Arora S, Meshram S. Denture marking for forensic identification using memory card: an innovative technique. *J Indian Prosthodont Soc* 2012;12(4):231-5.
5. Millet C, Jeanin C. Incorporation of microchips to facilitate denture identification by radio frequency tagging. *J Prosthet Dent*. 2004;92:588-90.
6. Bali SK, Naqash TA, Abdullah S, Mir S, Nazir S, Yaqoob A. Denture Identification Method: A Review. *International Journal of Health Sciences & Research* 2013;3(4):100-4.
7. Kamath PG. Engraved fixed restorations and denture micro-labeling to facilitate identification through forensic dentistry. *J Indian Prosthodont Soc* 2005;5:79-81.
8. Murray CA, Boyd PT. A survey of denture identification in United Kingdom. *Br Dent J* 2007;203(11):E24.
9. Reeson MG. A simple and inexpensive inclusion technique for denture identification. *J Prosthet Dent* 2001;86:441-2.
10. Agüloğlu S, Zortuk M, Beydemir. Denture barcoding: a new horizon. *Br Dent J* 2009;206(11):589-90.
11. Rajendran V, Karthigeyan S, Manoharan S. Denture marker using a two-dimensional bar code. *J Prosthet Dent* 2012;107:207-8.
12. Datta P, Sood S. The various method and benefits of denture labeling. *J Forensic Dent Sci* 2010; 2(2):53-8.
13. Jain A, Mahoorkar S. Denture identification using unique identification authority of India barcode. *Journal of Forensic Dental Sciences* 2013;5(1):60-3.
14. Nalawade SN, Lagdive SB, Gangadhar SA, Bhandari AJ. A simple and inexpensive bar-coding technique for denture identification. *Journal of Forensic Dental Sciences* 2011;3(2):92-4.
15. Colvenkar SS. Lenticular card: A new method for denture identification. *Indian J Dent Res* 2010;21:112-4.

Repair of Cast Partial Denture Made Easy: An Alternative Approach

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Abstract

Context: Patients wearing cast partial denture might face breakage of denture due to any reasons. The ideal approach for repair of broken cast partial is electro soldering. This paper presents an alternative approach for repair of cast partial denture using heat cure acrylic resin.

Keywords: Repair of denture, Electro soldering, Cast Partial Denture.

Introduction

Despite careful planning and competent construction with materials of good quality occasional breakage and distortion of Cast Partial Denture is seen.

Breakage can be either of the acrylic, major or minor connectors, clasps or the tooth. Need for repair may arise due to careless handling by the patient, inadequate mouth preparation, poor construction, metal fatigue,

loss of fit, careless handling in the laboratory⁽¹⁾. Ideally electro-soldering is used to repair cast partial denture which is a process of building up of a localized area with a filler metal or joining two or more metal components by heating them below their solidus temperature and filling the gap between them using a molten metal. ^(2,3)

This clinical report describes an alternative approach for repair of cast partial denture using heat cure acrylic resin.

Clinical Report: A 51-year-old male reported to the department of Prosthodontics with the chief complaint of broken maxillary cast partial denture. On examination, a fracture was observed on both ends of the longitudinal component (strap) of the major connector that was joining the anterior and posterior palatal strap (Fig.1). To repair this cast partial denture the ideal procedure was electro soldering, but an alternate approach was planned. This clinical report describes an alternate approach to repair the broken cast partial denture using heat cured acrylic resin.



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Fig. 1: Broken cast partial denture Fig. 2: Broken Partial denture on cast

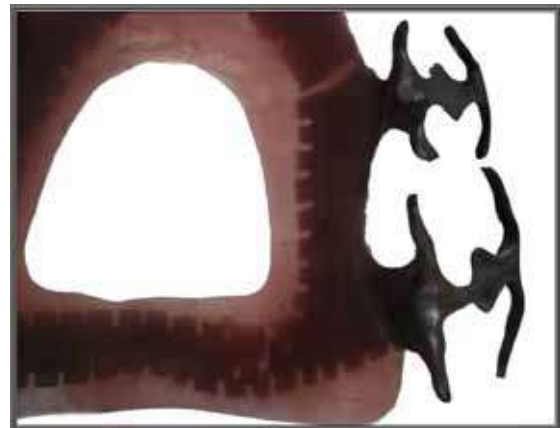


Fig. 5: After acrylization Fig.6: Through light



Fig. 3: Mechanical grooves for retention Fig. 4: Wax up



Fig. 7: Intraoral Placement of Cast Partial

Procedure: An impression of maxillary arch was made using alginate with the broken cast partial denture in place. After retrieving the impression, the cast partial denture was removed from the impression and impression poured in die stone. After the cast had set the fractured fragments of cast partial denture were approximated on the cast (Fig.2). Once approximated, mechanical grooves were made on both ends of the broken cast partial denture using a disc and a mandrel to enhance mechanical bonding between metal and acrylic resin (Fig.3). Wax up of the cast partial denture was completed and it was acrylized in usual manner (Fig.4). The final product was finished and polished to prevent affinity towards food debris (Fig.5). When seen through light the thickness of acrylic resin and the joint can be appreciated (Fig.6). The repaired cast partial denture was then placed intraorally and checked for the fit (Fig.7). Any difficulty in placement or any occlusal discrepancy was eliminated.

Advantages:

1. Comparatively easy to repair
2. Less technique sensitive
3. Economical
4. No complicated equipment required

Disadvantages:

1. Only major & minor connectors can be repaired
2. Can be bulky
3. Less thermal perception
4. Shrinkage can cause distortion
5. Less strength compared to metal
6. If not polished, then can cause irritation

Discussion

Breakage of cast partial denture is very uncommon which can be a result of careless handling by the patient, inadequate mouth preparation, poor construction, metal fatigue, loss of fit, careless handling in the laboratory. Electro soldering is the process by which broken cast partial dentures are repaired which involves the process of building up of a localized area with a filler metal joining two or more metal components by heating them below their solidus temperature and filling the gap between them using a molten metal. Advantages of this technique includes adequate strength in thin sections, less bulky, non-irritating and light weight, whereas disadvantages include technique sensitivity and is expensive.

The technique described in this paper uses heat cured acrylic resin for the repair of broken cast partial denture. The advantages include less technique sensitivity hence easy to repair, economical and less complicated equipments are required. The disadvantages include bulkiness to the cast partial denture, shrinkage of heat cure resin can cause distortion, less strength than metal and if not polished well can cause irritation.

Conflict of Interest: None

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References

- 1) Grasso J, Miller E. Removable partial prosthodontics. St. Louis: Mosby Year Book; 1991.
- 2) Kenneth J. Anusavice, Phillips Science of Dental Materials. 11th Edition, Elsevier:2003
- 3) McCracken's, Removable Partial Prosthodontics. 8th Edition: CBS Publishers.2005.

Indigenous Healing Practices and Beneficiaries' Perception

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Abstract

Context: For centuries, the concept of indigenous healing has been regarded as a non-invasive medical practice, and despite the development of clinical treatments, many people still depend on it for mental health. It is estimated that in developing countries, 80% of the population living in rural areas depend on indigenous healers for their healthcare needs (WHO, 2001). Despite the establishment of modern hospitals and educational institutions, people from the southern region of Karnataka believe that unnatural occurrences are due to Bhootas (Spirits) and a certain portion of the population attribute mental illness to witchcraft and supernatural causes. In order to overcome these obstacles, people approach healers for a miracle solution. Acknowledging the significant role of the belief system of people seeking the help of traditional healers for various problems, the present study was conducted to understand the perception of the beneficiaries regarding indigenous healing. Based on the findings, the study concluded that the belief system remains prominent in every aspect of the life of individuals who seek the help of healers, while indigenous healers need to be trained in order to provide better mental healthcare to the patients.

Keywords: *Mental illness, Traditional healers, Beliefs, Beneficiaries, and Patris*

Introduction

Beliefs and help-seeking behaviours are highly correlated and greatly influenced by culture¹ as it significantly contributes in determining the different causes of mental illness, and shapes the treatment process accordingly.² It provides an explanation of the causes for the sufferings of the people and ways through which it can heal their problems.³ It contributes to the manifestation of mental illness and attributes the cause of mental illness as a supernatural power, magical spirit, or possession by evil spirits.⁴ More than two-thirds of people with mental illness and their family members have strong belief in the supernatural causation of mental

illness, and this belief forces them to consult traditional healers before resorting to modern healthcare.

South India is a land of temples, where belief in the efficiency of 'pujas' and 'temple worship' is very strongly rooted.⁵ The practice of traditional healing follows the belief that "various supernatural influences operating in the environment affect an individual's physical and mental health", and pursues treatment for health problems through rituals and spiritual healings performed by healers.⁶ Traditional healing therefore, 'the sum total of all the knowledge and practices, used in diagnosis, prevention and elimination of physical, mental, and social imbalance and depending on practical experience and observation handed down from generation to generation'⁷.

History of Traditional Healing Practices in India: Initially, traditional healing practice was an integral part of the semi-nomadic and agricultural tribal societies. As per archaeological evidence, the existence of traditional healing can be dated back to 6000 BC,

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where reference to evil spirits, possession, black magic, and traditional method of treatment can be found in the Vedas⁸. According to the Atharvaveda, committing of sin in the present or even past life, transgression from the normal divine prescribed course of life, disrespect of gods, witchcraft by enemies, and evil spirits of different types are some of the major factors that lead to different diseases.⁹ Apart from the Atharvaveda, the Ashtanga Ayurveda, which builds on the idea that health and illnesses are determined by the balance of various elements, humours, and qualities in the body. Besides the gross physical body, a person is conceived as consisting of two other bodies, the subtle body and the causal body of which only the subtle body is relevant with respect to mental illness.¹⁰

Characteristics of Traditional Healing: Traditional healing has its own unique characteristics. As observed by Dala K., one of the distinguishing characteristic of the healing practices in rural India is the role of sacredness.¹¹ The whole weight of the community's religion, myths, and history enters the sacred therapy as the therapist proceeds to mobilize strong psychic energies inside and outside the patient. Traditional healing is considered to be holistic and aims at the overall well-being of the person and it takes the body, self, and society within a framework of dynamic equilibrium. The holistic approach takes into consideration the values, passions, beliefs, social interaction, and spiritual orientation of a person in its healing practices. Most of the healers act as mediators between the physical and the metaphysical. One can frequently find healers who are known for their ability to host a deity or spirit and under whose spell they acquire supernatural powers to control the minds of their visitors and heal them. The healer becomes the medium through which others can communicate with the deities and spirits. They get visions and can dispense favours at will. As diviners, they are presumed to be in direct communication with the supernatural and derive healing powers through divine grace. They are both feared and revered by the local community.¹¹

Types of Traditional Healers: Generally, traditional healing can be grouped into two types, viz., 'Swasthik' and 'Tamasik'. They differ in the method and materials used in the healing. The Swasthik form of healing is commonly practiced by people belonging to a higher caste. They are well versed in Sanskrit and have knowledge about the Vedas. The Tamasik form of healing is practiced by the lower castes. They indulge in violent practices and conduct occult practices after

midnight or on new moon days in a place of cremation.¹² The practice of traditional healing varies from region to region and is identified by various names. In Rajasthan, folk healers are called bhopas and mantarjanawals, wherein bhopas get possessed by a deity and speak directly to the supplicants. They are usually the attendants of a shrine. Mantarjanawals possess secret and powerful charms through which they treat their clients.¹³ In central India, healers are called as Jankars and Barwas. The jankars treat through divination and are believed to be able to find the causes of various problems through divination. The barwas work with the assistance of a superhuman force and get into a self-induced trance by consuming liquor and inhaling camphor.¹⁴ In Tamil Nadu, the devil dance is performed by the mistress of the community. This form of worship and healing is similar to the bhutharadana of Dakshina Kannada and Teyyam of Kerala, which propagates the belief that illnesses and misfortunes are caused 'Bhootas' or spirits.¹²

Rationale for the Study: The coastal region of Karnataka contains several cultural and religious sites, where apart from deities or God, Spirits or Bhootas are also propitiated, and it is believed that illnesses and misfortunes are caused by 'Bhootas'. Despite the establishment of modern hospitals and educational institutions, people of this region believe that unnatural occurrences are due to the Bhootas or devil spirits, and a certain portion of the population attribute mental illness to witchcraft, punishment for sins, and supernatural causes. So to overcome these obstacles, people approach traditional healers for solutions. The treatment is sometimes physically painful and expensive. Hence, this study has been undertaken to understand the factors responsible whereby people approach traditional healers and the type of treatment they receive thereof keeping in mind the significant role of the belief system.

Objectives of the Study: The study has been conducted with the following objectives:

1. To know the demographic details of the beneficiaries of traditional healing;
2. To determine the factors responsible whereby people approach traditional healers;
3. To know the opinion of the beneficiaries about the cause of their present problems; and
4. To find out the remedies as suggested by the healers.

Materials and Method

The present study has adopted the descriptive research design, which provides demographic details of the beneficiaries of traditional healing as well as their opinion about the causes for their problems and the solutions suggested by the healers. People from rural and urban areas of the two districts, i.e., Dakshina Kannada and Udupi, who have sought the help of traditional healers were considered as samples for the study and selected through purposive sampling technique. Altogether thirty beneficiaries, who had approached Mantravadis (Shamans), Naga Patri (Spirit Dancer for the Serpent), Kola and Dharshana cult artists (Spirit Dancer for the Demi-God), and an Astrologer for various problems, were interviewed via a semi-structured interview schedule at the shrine of the healers.

Findings:

Demographic Profile of the Beneficiaries: The demographic variables of the beneficiaries who sought the help of traditional healer reveals that most of the respondents were male (63.33 percent), and 46.66 percent of the adults who sought the help of healers were self-employed (60 percent), 40 percent had solicited the help of Dharshana Patris, 23.33 percent had met an Astrologer, and 13.33 percent had sought for a solution from Kola cult artists. In order to know whether people seeking the help of traditional healers for their health problems was due to the unavailability of healthcare facilities, the distance between the respective houses of the beneficiaries to the hospital was assessed, and it was found that for 30 percent of the respondents, the distance was 20 km, for 16.66 percent of the respondents, the distance was only 10 km from their home, whereas 20 percent were unaware of the availability of healthcare facilities.

The demographic data of the present study denotes that, in spite of the availability of healthcare facilities nearby people depend on traditional forms of treatment. Similar results were found in an earlier study,¹⁵ which denoted that a large number of people depended upon traditional and complementary healing for all sorts of problems and some portion of the population specifically depended on healers for psychological problems. This could be due to the broad use of traditional and complementary healing modalities and belief in spirituality and less faith in psychiatric treatments that people depend on traditional healing.

**Table 01: Demographic Profile of the Beneficiaries
N=30**

Variables		Frequency	Percentage
Age (in years)	20- 30	05	16.66
	31-40	14	46.66
	41- 50	08	26.66
	51 and above	03	10.00
Gender	Male	19	63.33
	Female	11	36.66
Education	No Formal Education	01	3.33
	Primary/ Secondary	09	30.00
	PUC	11	36.66
	Graduation	09	30.00
Marital Status	Single	07	23.33
	Married	22	73.33
	Widower/ Widow	01	3.33
Place of Residence	Rural	22	73.33
	Semi- urban	07	23.33
	Urban	01	3.33
Type of Family	Joint family	11	36.66
	Nuclear family	19	63.33
Occupation	Unemployed	03	10.00
	Student	01	3.33
	Housewife	04	13.33
	Agriculture	01	3.33
	Beedi rolling	03	10.00
	Self-employed	18	60.00
Type of healer	Kola cult artists	04	13.33
	Dharshana cult artists	12	40.00
	Mantravadi	03	10.00
	Naga cult artists	04	13.33
		07	23.33
	Astrologer		
Distance between house and hospital (in kms)	Don't know	08	26.66
	0-10	05	16.66
	11- 20	09	30.00
	21- 30	06	20.00
	31 and above	02	6.66

Table 02: Reasons for Approaching Traditional Healers

	Variables	Frequency	Percentage
Reasons	Job-related	15	50.00
	Curse of the Serpent	05	16.66
	Health Issues	16	53.33
	Future Prediction	02	6.66
	Addiction	13	43.33
	Possession	03	10.00
	No Hope in Life (Depression)	04	13.33
	Infertility	13	43.33
	Marriage Issues	10	33.33
	Problems with Relationship	02	6.66
	Foreign Visit	13	43.33

It was found in the study that people approached healers for various reasons, which were job-related (50 percent), the curse of the serpent (16.66 percent), marriage issues (33.33 percent), addiction (43.33 percent), health issues (53.33 percent), and depression (13.33 percent). Almost 10 percent of them opined that the major reason for their present problem was spirit possession, and this result was replicated in a similar other study,¹⁶ which found that the respondents attributed possession as the cause for their problem. The result significantly contributes to understanding the cultural beliefs of the people living in the rural area.

Table 03: Opinion of Beneficiaries about the Cause of Present Problem

Opinions	Number of Respondents	Percentage
Unaware	15	50.00
Black magic	03	10.00
Dhosha (Curse)	05	16.66
Curse of the Serpent	03	10.00
Disturbed by the Soul	03	10.00
Uncertainty about Future	1	3.33
Total	30	100

Table 03 denotes shows that 50 percent were unaware of the causes of their problem, 10 percent believed that it was due to the curse of the serpent, few (10 percent) opined black magic (10 percent) as the reason for their sickness, whereas 16 percent felt the reason for their present problem as Doshha (Curse). The findings revealed that the respondents attributed

to a supernatural cause (spirit possession and curse of the serpent) for their difficulties. Similar results were identified in other research works¹⁷, where it was noted that most of the rural people (83.55 percent) had opined that black magic was the major cause for their health problems.

Table 04: Remedies Suggested by Healers

	Variables	Frequency	Percentage
Remedies	Herbs / Coconut/ Lemon/ Kumkum	18	60.00
	Homa (A ritual wherein religious offerings are made to the fire)	03	10.00
	Prayer	06	20.00
	Visit to temples	12	40.00
	Talisman	03	10.00
	Serpent worship	15	50.00
	Consult doctor	03	10.00
	Exorcism	09	30.00
	Removal of black magic	06	20.00
	Solution for dosha (Curse)	09	30.00
	Animal sacrifice	06	20.00

The study attempted to understand the various mental health treatment method adopted by the healers and found that Herbs / Coconut/Lemon/ Kumkum was the common treatment method adopted by the healers (60 percent), exorcism was adopted for spirit possession (30 percent), 40 percent of the beneficiaries were asked to visit temples such as the Dharmastala and Subhramanya, and serpent worship was suggested for 50 percent of the respondents. The findings clearly show that the healers suggested treatments based on the cultural beliefs of the patient. In South India, serpent worship has its own significance in the treatment of mental illness. Even in the present study, most of the healers suggested this remedy to their clients, who presented complaints of possession.

A couple of studies^{18,19} showed similar results, where the healers had prescribed remedies for problems based on the cultural beliefs of the patients. It is believed that the various cultural beliefs and practices associated with mental illness persuade the patient and his/her family members to delay seeking professional help. Apart from cultural beliefs, there are various other factors associated with the method of treatment suggested by the healers

such as the level of education of the healers, nature of the problem, and the financial status of the client.

Recommendations: This study reflects the influence of culture on the health-seeking behaviour of the patient, who delays in seeking psychiatric care. So there is a need for sensitizing healers in early identification for optimum management of mental disorders and to ensure timely referral of the patients to psychiatrists. Mental health professionals need to come forward to enhance the knowledge of the general public on mental health issues, and proper mental health policies need to be developed with due consideration towards the cultural beliefs and practices of the people and the healers. The indigenous forms of psychotherapy may effectively treat certain psychological diseases, and therefore, indigenous healers need to be trained in order to provide better mental healthcare to the patients.

Conclusion

The association between culture and mental illness is deep rooted in our country and will continue in the future. The present study denotes that strong cultural beliefs of rural people force them to depend on religious and spiritual healing. The study has covered a minimum population, so it would be difficult to generalize the result, but in spite of the availability of healthcare services in districts like Udupi and Dakshina Kannada, people depend on folk healing. So it is necessary to create awareness among people and orient them to follow modern mental health services.

Conflict of Interest: I declare no conflict of interest.

Source of Funding: Self

Ethical Clearance: This study is a part of the PhD study on “Indigenous Healing in mental Health”. Ethical clearance has been taken from the Research Ethical Committee of the Central University of Kerala, Kasaragod.

References

1. Biswal R, Subudhi C, Acharya SK. Healers and healing practices of mental illness in India: The role of proposed eclectic healing model. *J Health Res Rev* 2017;4:89-95. Downloaded from <http://www.jhrr.org> on Sunday, July 1, 2018
2. Chittaranjan Subudhi. Culture and Mental Illness 2014. Retrieved from https://www.researchgate.net/publication/270762975_Culture_and_Mental_Illness on 14.02.2018.
3. Jyoti Anand. Concept, Characteristics and Process of Psychological Healing 2006. Retrieved from <http://ipi.org.in/texts/ajit/Concept%20of%20Psychological%20Healing.pdf> on 16.02.2018.
4. Wagner, W., Duveen, G., Themel, M. & Verma, J. The modernisation of tradition: Thinking about madness in Patna, India. 2006. *Culture and Psychology*, 5, 413-446.
5. Alen. Psychiatry in India. Shri. Rajesh C Bhalani, Bhalani. 1984. Book Depot, Medical Book Seller, Mumbai.
6. Kurihara T, Kato M, Reverger R, Tirta IGR. Pathway to psychiatric care in Bali. *Psychiatry Clin Neurosci*. 2006;60(2):204-10.
7. Iddrisu. Healing and medicine in traditional African societies, a reflection of the worldview. 2017. *UDS International Journal of Development*. Vol. 3(2). 2017.
8. Ramashankar. Traditional Healing Practices in North East India. *Indian Journal of History of Science*, 50.2 (2015) 324-332.
9. Ravi Abhyankar. Psychiatric Thoughts in Ancient India. *Mens Sana Monogr*. 2015. 13(1). 59-69. Retrieved from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4381323/> on 13.02.2018
10. Mita Majumdar. Seven Chakras and Our Health – (Muladhara to Sahasrara). The Medindia Medical Review Team on Jun 14, 2018 downloaded from <https://www.medindia.net/patients/lifestyleandwellness/seven-chakras-and-our-health.htm> on Sunday, July 1, 2018
11. Dalal AK. Concept, Characteristics and Process of Psychological Healing. *IpiOrg.in*. 1991;9:1-24. Downloaded from http://www.ipi.org.in/texts/ajit/Concept_of_Psychological_Healing.pdf on Sunday, July 1, 2018
12. Gurnasagari. Faith Healing. 1990. Unpublished thesis. Submitted to Mangalore University
13. Carstairs G. Protective elements in traditional Culture, a journal of psychiatry and social research. 1977. vol. 21. pp. 307-312.
14. Anne Kristine. Traditional Healing Meeting Modern Health Care Policy - Culturally Sensitive Health Care Practices for the Indigenous People. 2009. Unpublished Thesis. Submitted to Faculty of Social Sciences, Oslo University College

15. Sexton, Tore Sorlie. Use of traditional healing among Sámi psychiatric patients in the north of Norway. *International Journal of Circumpolar Health* 2008.67:1,p137-148
16. Madhura Lohokare. Recovering from Psychosocial Traumas: The Place of Dargahs in Maharashtra. *Journal of Economic and Political View*. 2009. Vol. 44,(16), 255-257 WHO Traditional Medicine Strategy 2002–2005. Retrieved from http://www.wpro.who.int/health_technology/book_who_traditional_medicine_strategy_2002_2005.pdf on 17.02.2018.
17. Pradhan SN, A study of help-seeking behaviour of Psychiatric patients *Journal of Kathmandu Medical College*. 2019. Vol. 2, No. 1, Issue 3, Jan.-Mar. p21-24.
18. Sorsdahl. Explanatory models of mental disorders and treatment practices among traditional healers in Mpumulanga, South Africa. *African Journal of Psychiatry* 2010;13:284-290
19. Somasundaram. Mental Health: Concepts and Treatment in The Siddha (Tamil) System of Medicine. *ASEAN Journal of Psychiatry*, 2015. Vol. 16 (2), XX-XX.

Effectiveness of Distraction Versus Cutaneous Stimulation on Venipuncture Pain Response among Children

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Abstract

Introduction: Intravenous procedure is invariably painful for children. Non-pharmacological techniques such as distraction and cutaneous stimulation provide coping strategies that help to manage and reduce perception of pain and decrease anxiety without medications.

Aim: To compare the effectiveness of passive distraction (group I) versus cutaneous stimulation (group II) on venipuncture pain response among children.

Materials and Method: A quantitative two group post-test only single centered study was conducted among 100 children, between the age group of 3 to 7 years attending a selected hospital and undergoing venipuncture at a given time. OUCHER Scale (Asian Version- Male and Female) was used to assess pain response to compare the effectiveness of passive distraction and cutaneous stimulation aimed at decreasing pain by applying ice pack over the site of procedure. The comparison of effectiveness of interventions was computed by using independent 't' test.

Results: The result showed that the mean pain score of group I (passive distraction) and group II (cutaneous stimulation) was 4.68 ± 2.66 and 3.48 ± 2.16 , which was statistically significant ($p = 0.01$).

There was a significant association between selected clinical aspects of children like being afraid of coming to hospital, being hospitalized and fear of needles with the pain score at $p < 0.05$ among children received distraction technique, whereas there was no association between the selected clinical aspects of children with the pain score in group received cutaneous stimulation.

Conclusion: In the present study cutaneous stimulation was found more effective pain relieve strategy than passive distraction during venipuncture. Hence, all the health care professionals should use optimal non-pharmacological pain management techniques in all aspects of paediatric practice and improve children outcomes to an extent as possible while maintaining high quality health care.

Keywords: *Passive distraction, Ice pack application, Non pharmacological techniques.*

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Introduction

The experience of illness and hospitalisation is an unpleasant and stressful condition which often requires various examinations, investigations, treatment or procedures that are associated with pain, anxiety and fear in children. The International Association for the Study of Pain (IASP) defines pain as an unpleasant

sensory and emotional experience associated with actual or potential tissue damage. Children are vulnerable and under-served population and every child has different perception of pain, and the meaning of pain also differs from child to child¹.

The most frequently performed minor invasive procedures by nurse is venipuncture but for children the procedure-related pain can be worse than that of the illness itself². Children requiring needle stick such as injections, IV cannulation and blood sampling view these procedures as frightening and painful. Since, children have little experience and understanding of the pain and disease process, unfamiliar and negative feelings can cause intimidation and considerable distress for them^{3,4}. Hence, managing procedural anxiety and fear can provide both short term and long term benefits by increasing adherence and reducing avoidance behaviour in medical care⁵.

Pediatric pain management entails the use of pharmacological and non-pharmacological interventions to control pain⁶. Non-pharmacological techniques such as distraction, relaxation, guided imagery, hypnosis, music therapy, acupuncture and cutaneous stimulation provide coping strategies that help to manage and reduce perception of pain and decrease anxiety without medications. Non-pharmacological procedures or techniques are generally less expensive and can be performed independently by a nurse. It also helps to avoid potential drug's side effects, decrease anxiety, provide a sense of control, enhance comfort and promote rest and sleep⁷.

Focussing one's attention on pain makes the pain worse and getting the attention away from the pain reduces its severity. Distraction is a cognitive-behavioural intervention which draws attention or engaging a child in a wide variety of pleasant activities which helps children to focus attention on something other than pain and the anxiety. A narrative review was conducted by Vetri Buratti C, et al,⁸ found that active and passive distraction techniques to be extremely effective in reducing distress and pain in children undergoing venipuncture.

In interactive distraction the child cognitively engages with the distracting stimulus whereas in passive distraction, child visually or auditory observes the distracting stimulus. The distraction activities such as listening to music, singing a song, blowing bubbles,

playing a game, watching television or a video, focusing on a picture while counting, guided imagery and breathing techniques, helps to increase the tolerance for pain, facilitates coping and decrease the sensitivity for pain⁹.

MacLaren J E, et al¹⁰ and Bellieni C V, et al¹¹ conducted a study on comparison of distraction strategies for children receiving venipuncture and found passive distraction was more effective than active distraction, as the children's distress interfere with their ability to interact with the distractor.

Cutaneous stimulation is defined as stimulation of the skin and underlying tissues for the purpose of reducing pain impulses, muscle spasm or inflammation. Cutaneous stimulation is a physical intervention performed by several method such as simple rhythmic rubbing, use of pressure or electric vibrators, massage with hand and application of heat or cold at the site before injection. Cold application relieves pain by slowing the ability of pain fibers to transmit pain impulse and decrease the sensitivity of tissues and create a sensation of numbness, thus it can be used as a local anesthesia for short periods¹². An experimental study was conducted by Ahmed Alalo F M, et al¹³ in 2016 to examine pain intensity after an ice pack application prior to venipuncture and the results revealed that the application of an ice pack was effective in reducing pain intensity among children.

Perception of pain in paediatrics is complex, and encompass physiological, psychological, behavioural, and developmental factors¹⁴. Even though non-pharmacological techniques are effective in reducing procedural pain in children but the professional practice of nursing within the Pediatric environment is challenging and it is often not being effectively applied¹⁵.

The above review of literature emphasizes that non pharmacological techniques are effective in reducing procedural pain. Hence, the present study was undertaken with the aim to compare the effectiveness of passive distraction versus cutaneous stimulation on venipuncture pain response among children.

Materials and Method

A quantitative two group post-test only single centered study was conducted among 100 children between the age group of 3-7 years. Permission to conduct the study, ethical clearance certificate and a

written informed consent was obtained before starting data collection.

The study subjects, who met the inclusion criteria were selected by simple random sampling (lottery method) and assigned in two equal groups (group I- distraction technique group and group II- cutaneous stimulation group).

Hypothesis: H₁: There is significant difference in pain response after intervention between group I and group II during venipuncture.

The Data Collection Instruments Included:

Tool I: Semi structured interview schedule for collecting demographic data of children and

Tool II: OUCHER Scale (Asian Version- Male and Female) ¹⁶ was used to assess pain response to compare the effectiveness of passive distraction, by drawing attention of the child away from pain showing film video songs and cutaneous stimulation, that refers to the stimulation of the skin and underlying tissues aimed at decreasing pain by applying ice pack over the site of procedure for 3 minutes.

The comparison of effectiveness of interventions with distraction versus cutaneous stimulation was computed by using independent ‘t’ test (Levene’s Test

for Equality of Variances) IBM SPSS Version- 20.0. The association between the pain score of subjects in group I and group II with the selected aspects of child was computed using chi-square test.

Result

In the present study the mean age of children of group I was 4.84 ± 1.34 and of group II was 4.94 ± 1.45. Majority (72%) of the children attended OPDs because of fever. Majority of the children (72%) accompanied their mothers, 21% with fathers and 7% with grandparents. Majority of the parents belonged to the age group of 20-30 years.

Table 1: Comparison of the effectiveness of distraction versus cutaneous stimulation on venipuncture pain response among children n=100

Groups	N	Mean	SD	T value	P value
Group I (Distraction technique)	50	4.68	2.66	2.47	0.01*
Group II (Cutaneous stimulation)	50	3.48	2.16		

* Significant at 0.05 level.

Table 1 shows that there was a significant difference in pain response (P=0.01) after intervention between group I and group II during venipuncture. n=100

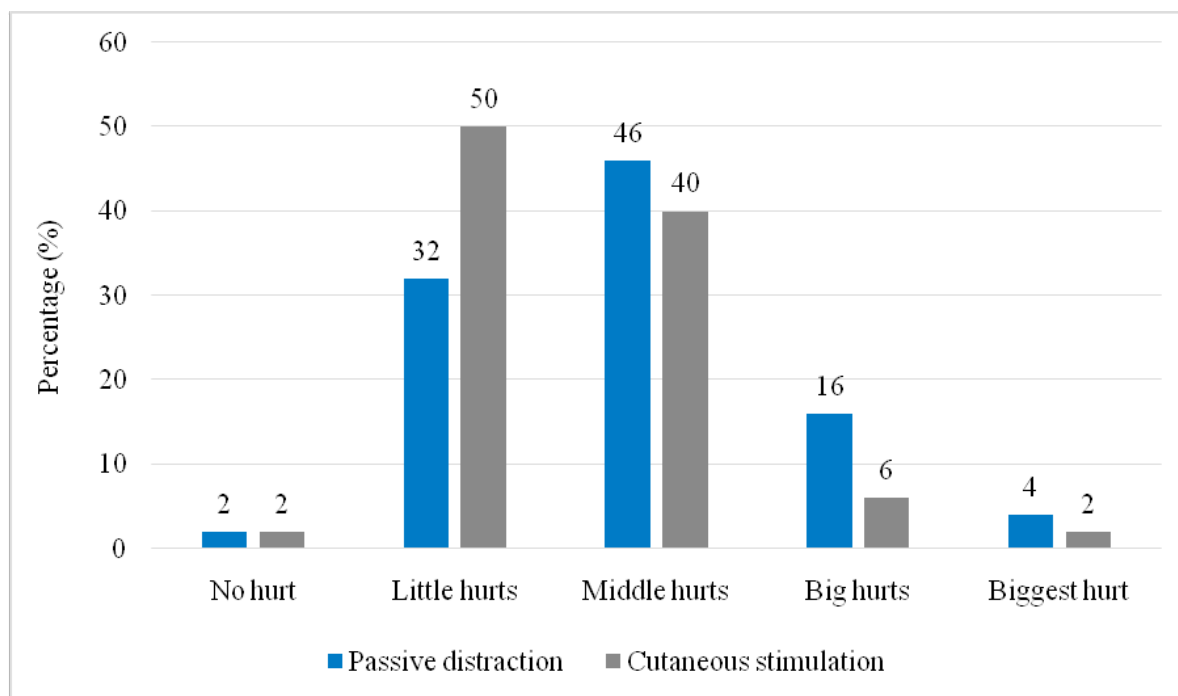


Figure 1: Percentage distribution of pain score of subjects of group I and group II during venipuncture

Discussion

The present study results shown that the mean pain score (4.68 ± 2.66) of group received distraction therapy during venipuncture were comparatively more than that of group received cutaneous stimulation (3.48 ± 2.16). The findings of the present study was supported by the study conducted by Kiran N et al¹⁷ which revealed that icepack application significantly decreases pain during venipuncture. A study was carried out by Hasanpour M, et al¹⁸ to evaluate the effect of local cold therapy and distraction in pain relief using penicillin intramuscular injection in children and found that the local cold therapy was effective in reducing IM injection related pain. This study findings were contradicted by Sahar Mahmoud El-Khedr Abd El-Gawad, et al¹⁹ in which interactive distraction technique had a positive pain relieve effect and was better than cutaneous stimulation in relieving children's pain during vein-puncture.

A quasi-experimental study was undertaken by James J, et al²⁰ revealed that use of animated cartoon as a distraction strategy has a significant effect on reducing the perception of pain among children at pre, during and post venipuncture. Whereas in a survey done by the researcher before the present study, revealed that more than watching cartoon videos, the children were more interested and get distracted by watching the film song videos. Hence, in the present study, children were distracted by showing the new film song videos.

Environmental and psychologic factors exert a powerful influence on children's pain perceptions. Children's reaction to pain are influenced by their developmental age, their previous experience with illness, separation, their innate and acquired skills and the support system available.

In the present study the association between the pain score of children with the selected demographic variables like age of the child, gender, area of residence, birth order of the child, parental age, number of children in the family, relationship of family member to the child, previous hospitalization, previous experience of venipuncture were not significant at $p < 0.05$ in both group I and group II. Whereas, few earlier studies noted and recognized that females suffer more pain than males. In a study conducted by Gaikwad N S, et al²¹ to assess the effectiveness of ice application on pain response prior to intravenous procedures among children, revealed that there was significant association between pain scores with age of children ($\chi^2 = 8.816$), gender of children (χ^2

= 5), and weight of children ($\chi^2 = 4.909$) in experimental group.

The findings of present study revealed that there was no influence of relationship of family member to the child on level of pain perception but the presence of parents during blood draw helped the children to remain more comfortable whereas, in a study conducted in Chandigarh by James J²⁰ reported that the perception of pain in children was significantly less when father was present with the child as compared to mother or grandparents. This may be due to the increased stress and anxiety among mother and grandparents compared to the father, which influenced the child.

In the present study there was a significant association between selected aspects of child like being afraid of coming to hospital, history of previous hospitalization, previous venipuncture and usual reaction of the child to the venipuncture with the pain score at $p < 0.05$ among children received distraction technique, whereas there was no association between the selected clinical aspects of children with the pain score in group received cutaneous stimulation.

Attending hospital itself is a stressful situation for children. In the present study, all children had previous experience of injections or blood draw, hence on entering the treatment room itself most of the children were distressed. Patient's expectations of how much pain they should have also influence how much pain they feel²².

In the present study the researcher found implementing cutaneous stimulation was comparatively easier than distraction technique for children between the age group of 3-7 years. Ice is been used from long ago as a topical pain reliever but ice pack should not be applied for longer time as it can cause local vasoconstriction, which can delay the absorption of drug, thus should be avoided in cases requiring quick drug absorption.

Implementing non-pharmacological method in the hospital is an independent nursing intervention and children between the age group of 3-6 years use transductive reasoning as they lack understanding of cause and effect relationships. Therefore, unnecessary pain can harm the nurse-patient relationship, whereas proper knowledge and use of alternative techniques can improve patient care and satisfaction that will bring the best possible outcome for their patients in each unique scenario.

Limitation: The limitation of the present study was the fear and distress of the children from previous pain experience prior to the procedure which facilitated less cooperation during the procedure. Hence, a few cases, the researcher found difficult to distract and refocus the attention of a child away from pain and anxiety during venipuncture and they were excluded.

Conclusion

Non pharmacological techniques are easy to apply, safe, non-invasive, inexpensive and have a positive pain relief effect during venipuncture, which give the child a sense of control over the situation and their behaviour. There was significant difference in pain response after intervention between passive distraction and cutaneous stimulation. In the present study cutaneous stimulation was found more effective pain relieve strategy than passive distraction during venipuncture. Hence, all the health care professionals should use optimal non-pharmacological pain management techniques in all aspects of paediatric practice and improve children outcomes to an extent as possible while maintaining high quality health care.

Conflict of Interest: Nothing specific- can use the study findings with proper citation of authors name.

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References

1. Mathews L. Pain in children: neglected, unaddressed and mismanaged. *Indian Journal of palliative care*. 2011 jan;17(suppl):S70-S73. doi:10.4103/0973-1075.76247
2. Berman A, Snyder S, Kozier B. *Fundamentals of Nursing: concepts, process, and practice*. Pearson Education; 8 edition, 2008; 1187-1230.
3. Baucher H, Woring C, Vinci R. Effect of skin refrigerant and age on pain responses of infants receiving immunization. *Research in nursing and health* 1991;87(4):544-548.
4. Kharach S. Pain treatment: Opportunities and challenges. *Achieves of paediatric and achieves of medicine* 2003; 157(11):1054-1056.
5. Orenius T, Saila H, Mikola K, and Ristolainen L. Fear of injections and needle phobia among children and adolescents: An overview of psychological, behavioral and contextual factors. Volume 4: 1-8, 2018. doi: 10.1177/2377960818759442 journals.sagepub.com/home/son.
6. Balan S. Approach to joint pain in children. *Indian journal of Pediatrics*. 2016;83(2):135-139. doi:10.1007/S12098-015-2016-8
7. Wong DL, Hockenberry MJ. *Text book of infants and children*. 7th ed. St. Louis: Elsevier;2003. P. 993-995.
8. Buratti CV, Angelino F, Sansoni J, Fabriani L, Mauro L, Latina R. Distraction as a technique to control pain in pediatric patients during venipuncture. A narrative review of literature. *Prof Inferm*. 2015 Jan-Mar; 68(1):52-62. doi: 10.7429/pi.2015.681052.
9. Demir Y. Non-pharmacological therapies in pain management, pain management –current issues and opinions, Dr. Gabor Racz (Ed.), ISBN: 978-953-307-813-7, InTech, 2012. Available from: <http://www.intechopen.com/books/pain-management-current-issues-and-opinions/non-pharmacological-therapies-in-pain-management>
10. MacLaren JE, Cohen LL. A Comparison of distraction strategies for venipuncture distress in children. *J Pediatr Psychol*. 2005 Feb; 30(5): 387–396, Available from: <https://www.ncbi.nlm.nih.gov/pubmed/15944166>
11. Bellieni CV, Cordelli DM, Raffaelli M, Ricci B, Morgese G, and Buonocore G. Analgesic effect of watching TV during venipuncture. *Arch Dis Child*. 2006 Dec; 91(12): 1015–1017. doi: 10.1136/adc.2006.097246.
12. Sr. Nancy. Stephanie's Principles and practice of Nursing. Volume one. 5th edition. N. R Publishing house. P. 323
13. Alalo FMA, Ahmad A E, El Sayed HMN. Pain intensity after an ice pack application prior to venipuncture among school-age children: An experimental study. *Journal of education and practice*. 2016; 7(36):16-25. Available from: <https://files.eric.ed.gov/fulltext/EJ1126518.pdf>
14. Gupta HV, Gupta VV, Kaur A, Singla R, Chitkara N, Bajaj KV, et al. Comparison between the analgesic effect of two techniques on the level of pain perception during venipuncture in children up to 7 years of age: a quasi-experimental study. *J Clin Diagn Res*. 2014 Aug; 8(8): PC01–PC04. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4190764/>

15. Srouji R, Ratnapalan S, Schneeweiss S. Pain in children: Assessment and Nonpharmacological Management. *Int J Pediatr.* 2010. Available from: <https://www.hindawi.com/journals/ijpedi/2010/474838/>
16. Beyer JE. How to use the Oucher; 1983 Available from: http://www.oucher.org/the_scales.html
17. Kiran N, Kaur S, Marwaha RK. Effect of icepack application at the site prior to venipuncture on intensity of pain among children. *Nursing and midwifery research journal.* 2013 October; 9(4). Available from: <http://medind.nic.in/nad/t13/i4/nadt13i4p160.pdf>
18. Hasanpour M, Tootoonchi M, Aein F, Yadegarfar G. The effects of two non-pharmacological pain management method for intramuscular injection pain in children. *Acute pain.* 2006 Jan; 8(1):7-12.
19. El-Gawad SMEA, Elsayed LA. Effect of interactive distraction versus cutaneous stimulation for venipuncture pain relief in school age children. *Journal of nursing education and practice.* 2015;5(4). doi.org/10.5430/jnep.v5n4p32. Available from: <http://www.sciedu.ca/journal/index.php/jnep/article/view/5816>
20. James J, Ghai S, Rao KLN, Sharma N. Effectiveness of “animated cartoons” as a distraction strategy on behavioural response to pain perception among children undergoing venipuncture. *Nursing and midwifery research journal.* 2012 July; 8(3). Available from: medind.nic.in/nad/t12/i3/nadt12i3p198.pdf.
21. Gaikwad NS, Naregal PM, Mohite VR and Karale RB. A Study to assess the effectiveness of ice application on pain response prior to intravenous procedures among children at tertiary care hospital. *Asian journal of pharmaceutical research and health care.* 2017; 9(4):167-173. Available from: <http://www.informaticsjournals.com/index.php/ajprhc/article/view/15793/15335>
22. Hansen GR, Streltzer J. The Psychology of Pain. *Emerg Med Clin N Am.* 2005; 339–348. Available from: <http://williams.medicine.wisc.edu/painpsychology.pdf>

A Study on Customer Attitude and Shopping Intention Towards Health Care Products

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Abstract

Context: The study aims to identify various factors that influence purchase intention towards health care products. The study purpose of the paper is to recognize various purchase intention factors. A survey of 100 respondents was carried out with the help of the questionnaire. The researcher used Anova and Regression analysis to check the hypothesis and to analyse the data. The result identified various attracting features that lead to purchase of health care product. Involvement and awareness towards healthy life style and time management played great impact over the customer shopping intention. This paper provide insights to the manufactures of health care products about the various determinants that the customer consider being most important and significant contributor in decision making process before making the purchase.

Keywords: Health care products, Customer attitude, Shopping intention

Introduction

Health care products are being purchased by lot of the customer. Health care products involves gym equipment's, fitness drinks, organic products, Blood pressure apparatus, Thermometer and weighing scale etc. People purchase these products irrespective of their profession. The customer in the urban areas increasingly showing interest to purchase more of the health care products. People in this era gain whole lot of information about health related issues from various sources. With the introduction social media application such as Facebook and other application are loaded with various influencers. Most of the influencers based on the experience without having professional degree influencing people to purchase health care products. The influencer are being followed by lot of the people. There are various factor that influence customer to purchase the health care products.

The study consist of four factors such as involvement and awareness towards healthy life style, increased beauty consciousness, Cost effective and time management. People are involved highly towards leading healthy life style because of the various information available over the various sources. The health care products customer showing constant interest towards beauty consciousness. Products like vitamin c capsule and biotin capsule are taken by the women for take care of their skin routine and also maintain healthy hair. The cost effective factors also influence customer purchase intention. Every time customer finds it difficult to get appointment to the doctors to their busy life. The customer try be to very rational on spending their each and every penny. They tend to monitor their health at the home with some basic knowledge. Most of the customer try to take treatment at their home trying to solve the health issue with natural remedy. The next factor is time management. The customer in the urban areas are busy on doing their chores. Instead of running to hospital people find it easy to monitor their health at the home. These factors are influenced by the customer attitude which in turn these attitude strongly make customer to affect shopping intention of the customer. The results designate that various factors have impact on the consumers while purchasing health care products. The

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outcomes have very strong inferences to manufacturers of health care products.

Review Of Literature: Moschis, (2008) The article points the inclinations and promotion inferences of the advanced customer division. The study focused only on health care products and services. The article concluded with a huge deviation found inside the customer mature market division with respect to numerous marketing health care offers. The study offered the suggestion to the marketers of health care products to produce products and the various services in accordance to the need of the established consumer division⁵.

Paulus, (2000) The article paper focus on the theory of Pareto. The study analysed if the alteration attempted towards the united health care affects income distribution pattern. The article result shows that commencement of combined health care adds value to those who need care services, provider's givers of informal care⁶.

Marshall (2009), The study article concentrates on the health care system that are prevailed around the USA, various plans that are listed on the insurance. The study also addresses the customer driven health care related plans and convention regarding various service providers. The study objective is to explore the social marketing needs of customer driven health care. The study concluded with a various suggestion on where and which part research must be conducted in the respective topic on the future study³.

Yeon Kim (2011) This article is about the customer shopping behaviour towards the organic personal care products. The study addressed the diminishing effect on customer attitude and the shopping intention relationship. The article concludes that atmospheric awareness and exterior awareness influence customer attitude positively toward chemical free personal care products. The study came with suggestion on effective strategies used in marketing to raise the shopping intention to buy chemical free products⁸.

Srinivasan, R. (2016) The researcher analysed Himalaya Company in this study. The study focused on the various strategy that Himalaya face to stay concentrate on difference plan. The study concluded with the reason of focused differentiation to pay higher for competitor than its other competitor. The study also demonstrate on how Himalaya overcome such limits⁷.

Guo, K. (2005), This study focus on the health care

sector. The approach is made on the service management line. The study concluded with the suggestion to the managers of health care to apprehend and drill the 4 key points to focus effectively on how to become effective health care leaders. The study also give use full information on the health care in the service line management approach²

Moschis, (2013), The article focus on the preference of the customers for the data sources. The study showed innumerable approaches of shopping recommendation for medications and makeup items. The study pointed the specific explanation on why customer choose particular medication stores and people preference to rely on very particular brand and health related issues. The study on the article employed large data from the national level and study demanded various analytical procedures. The result of the article concluded with various plans to effectively appear to aged consumers on the whole and as well to the other specific lines on the areas⁴.

Anthony. D. Ross (2009), The study focus on the problem related purchase on the area relating to health care. The studies focused on the new and second hand products on the emerging large health care providers. The study proposed a methodology for assessing research on large health care providers and in making decision. The study conclude with recommendation on various screening and choosing customers to be able to offer the new and second hand products¹.

Objectives of the Study:

1. To study the demographic profile of the customer who purchase health care products
2. To find the impact of health care products on customer attitude and shopping intention

Hypotheses of the Study:

1. There is no significant difference on demographic profile of the customers who purchase health care products
2. There is no significant impact of health care products on customer attitude and shopping attention

Result and Discussion

The researcher adopted opportunity sampling method to get the information from the respondents. The study was conducted around the Chennai city.

The Chennai city has variety of health care service providers and variety of income group of people which is one of the most vivacious metropolitan in South India. The Questionnaire circulated to 100 members. The questionnaire consist of three parts. The first part consist of demographic factors. The second part of the questionnaire consist shopping habits of the customer who purchase health care products. The third part of

questionnaire are framed according to the Likert scale. The statistical data was done using SPSS. The researcher employed Anova test to check significance for the demographic factors and Regression test was used to find the Impact for the study.

Influence Of Monthly Income Of The Customer Perception Towards Shopping Intention Of Health Care Products.

Table 1: ANOVA						
		Sum of Squares	df	Mean Square	F	Sig.
H1	Between Groups	401.361	1	401.361	81.035	.000
	Within Groups	485.389	98	4.953		
	Total	886.750	99			
H2	Between Groups	356.295	1	356.295	353.606	.000
	Within Groups	98.745	98	1.008		
	Total	455.040	99			
H3	Between Groups	409.417	1	409.417	138.673	.000
	Within Groups	289.333	98	2.952		
	Total	698.750	99			
H4	Between Groups	39.883	1	39.883	12.830	.001
	Within Groups	304.627	98	3.108		
	Total	344.510	99			

It was presented in the above table H1 Involvement towards healthy life style (F= 81.035, P=.000) H2 Increased beauty conscious (F=353606, P=.000) H3 Cost-effectiveness (F=138.673, P=.000) H4 Time management (F= 12.830, P=.001) are statistically significant at 5% level.

Influence Of Employment Status Of The Customer Perception Towards Shopping Intention Of Health Care Products

Table 2: ANOVA						
		Sum of Squares	df	Mean Square	F	Sig.
H1	Between Groups	710.529	3	236.843	129.026	.000
	Within Groups	176.221	96	1.836		
	Total	886.750	99			
H2	Between Groups	386.983	3	128.994	181.956	.000
	Within Groups	68.057	96	.709		
	Total	455.040	99			
H3	Between Groups	180.418	3	60.139	11.138	.000
	Within Groups	518.332	96	5.399		
	Total	698.750	99			
H4	Between Groups	113.296	3	37.765	15.680	.000
	Within Groups	231.214	96	2.408		
	Total	344.510	99			

It was presented in the above table H1 Involvement and awareness towards healthy life style (F= 129.026, P=.000) H2 Increased beauty conscious (F=181.956, P=.000) H3 Cost-effectiveness (F=11.138, P=.000) H4 Time management (F=15.680, P=.000) are statistically significant at 5% level.

Regression Analysis. 1: In this regression analysis table 1, table 2, table 3 Customer attitude acts as intermediate variable between the factors and shopping intention of the customer. So the customer attitude is treated as a dependent variable and the other factors are considered as independent variable for the analysis

Table 3: Model summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.749 ^a	.561	.543	.881
b. Dependent Variable: att_sum				

From above table it is found that $r = .749$ r square = .561 and adjusted r square .543. This implies the factors create variance over the customer attitude. The cumulative influence of four variables of customer

attitude is ascertained through the following one way analysis of variance.

Table 4: ANOVA^b

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	94.393	4	23.598	30.411	.000 ^a
	Residual	73.717	95	.776		
	Total	168.110	99			
a. Predictors: (Constant), ss_sum, he_sum, fiv_sum, lbi_sum						
b. Dependent Variable: att_sum						

Table 2 presents that $F = 30.411.107$ $p = .000$ are statistically significant at 5 % level. This indicated all the four variable cumulatively responsible for customer attitude. The individual influence of all this four variables is clearly presented in the following co-efficient table.

Table 5: Coefficients^a

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	8.698	.898		9.685	.000
	H1	-.297	.054	-.683	-5.511	.000
	H2	-.168	.090	-.276	-1.863	.066
	H3	-.073	.059	-.104	-1.227	.223
	H4	.427	.048	.871	8.978	.000
a. Dependent Variable: att_sum						

From the above table it shows that H1 Involvement and awareness towards healthy life style (Beta=-.683, $t = -5.511$, $p = .000$), H2 Increased beauty conscious (Beta= -.276, $t = -1.863$, $p = .066$), H3 cost –effectiveness (Beta=-.104, $t = -1.227$, $p = .223$), H4 Time management (Beta=.871, $t = 8.978$, $p = .000$). The Involvement and awareness towards healthy life style and the Time management factor are significant statistically at 0.05. This indicates that the involvement and awareness towards healthy life style and time management factors affects attitude of the customer to purchase health care products.

Regression Analysis. 2: In this regression analysis table 1, table 2, table 3 Customer attitude acts as intermediate variable between the factors and shopping intention of the customer. Here in this part table 3,4,5

the customer attitude is treated as independent variable and the shopping intention factor are considered as dependent variable for the analysis.

Table 6: Model Summary^b

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.923 ^a	.853	.846	.902
a. Predictors: (Constant), si_sum				
b. Dependent Variable: att_sum				

From the above table it is found that $r = .923$ r square = .853 and adjusted r square = .846. This implies the factors create variance over the shopping intention of the customer. The cumulative influence of purchase intention is ascertained through the following one way analysis of variance.

Testing of Hypotheses:

1. There is no significant difference among the demographic factors of the customers who purchase health care products - Rejected
2. There is no significant impact of health care products on customer shopping intention- Rejected

Findings and Conclusion

The present study had given information about various factors that influence customer attitude to purchase a health care products. This study gives insights to the manufacturers to look out the customer attitude that affect shopping intention towards health care products. The outcome of the paper suggests manufacturers to focus on all the other factors that affect the customer buying attitudes and shopping intention to purchase health care products. The study also has some limitation. The data collected are only in Chennai city. The sample was also restricted to 100 only. The questionnaire was issued to customer who purchase health care products. The opportunity method on sampling done for the study, thus inherently brings all limitation to it. Finally this finding may not be applicable to the other geographical areas.

- The factors determining customer shopping intention of health care products are Involvement and awareness towards healthy life style, Increased beauty consciousness, cost effectiveness and time management.
- The following factors such as involvement and awareness towards healthy life style, Time management, Since urban areas peoples today are showing interest towards healthy life style as peoples life span of the are getting lower when compared to our before generations. And for the second factor time management, people these days are running out of their time in the busy bee life. People find it difficult to spend time even for the families so people considering time management they tend to purchase the health care products to monitor health related issues.

Conflict of Interest: Nil

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Bibliography

1. Anthony.D.Ross “Strategic Purchases of Bundled Products in a Health Care Supply Chain Environment,” A journal on Decision Sciences institute, 2009, Volume 40, Issue2, Pages 269-293.
2. Guo, K. and Anderson, D. “The new health care paradigm”, *Leadership in Health Services*, 2005. Vol. 18 No. 4, pp. 12-20. <https://doi.org/10.1108/13660750510625733>
3. Marshall, K., Skiba, M. and Paul, D., “The need for a social marketing perspective of consumer driven health care”, *International Journal of Pharmaceutical and Healthcare Marketing*, 2009. Vol. 3 No. 3, pp. 236-257. <https://doi.org/10.1108/17506120910989660>
4. Moschis, G. and Bovell, L., “Marketing pharmaceutical and cosmetic products to the mature market”, *International Journal of Pharmaceutical and Healthcare Marketing*,. 2013. Vol. 7 No. 4, pp. 357-373. <https://doi.org/10.1108/IJPHM-04-2013-0020>
5. Moschis, G. and Friend, S. “Segmenting the preferences and usage patterns of the mature consumer health care market”, *International Journal of Pharmaceutical and Healthcare Marketing*, 2008. Vol. 2 No. 1, pp. 7-21. <https://doi.org/10.1108/17506120810865398>
6. Paulus, A., van Raak, A., van Merode, F. and Adang, E., “Integrated health care from an economic point of view”, *Journal of Economic Studies*, 2000. Vol. 27 No. 3, pp. 200-210. <https://doi.org/10.1108/01443580010326175>
7. Srinivasan, R., “Himalaya: head-to-heel herbal healthcare”, *Emerald Emerging Markets Case Studies*, 2016. Vol. 6 No. 3, pp. 1-29. <https://doi.org/10.1108/EEMCS-06-2015-0137>
8. Yeon Kim, H. and Chung, J. “Consumer purchase intention for organic personal care products”, *Journal of Consumer Marketing*, 2011. Vol. 28 No. 1, pp. 40-47.

Oral Health Literacy and its Relationship with Level of Education and Self-Efficacy among Patients Attending a Dental Rural Outreach Clinic in India

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Abstract

Objective: To evaluate the relationship between Oral health literacy (OHL) with the level of education and self-efficacy among adults (age 18-77 years) patients attending a dental outreach clinic in Udupi Taluk.

Basic Research Design: A cross-sectional study of adult patients attending a dental outreach clinic by convenience sampling.

Method: Information was obtained about patient's sociodemographic factors along with the self-efficacy by using Dental Copings Belief's scale (DCBS) questionnaire and OHL was assessed by using a word recognition instrument Rapid Estimate of Adult Literacy in Dentistry (REALD-30). One way ANOVA and Pearson's χ^2 test were used for analysis.

Participants: 200 adult patients age range of 18- 77 years who wanted to seek dental care in a dental outreach clinic.

Main Outcome Measures: Oral health literacy (OHL) and Self efficacy (DCBS).

Results: In this study the OHL was significantly associated with the level of education of patients. Among the 200 subjects who claimed to be able to read and write English language and had completed education till class 10th; more than 50% of the subjects had Low (≤ 21) OHL scores. Only 12.5% of the total study population had High OHL (≥ 26) and were clearly able to understand simple dental terminology. Moderate levels of literacy was recorded in 75.6% in graduate and postgraduates indicating that even these people partially understood dental terms. There was no significant association between oral health literacy and self-efficacy.

Conclusion: Our study suggests level of education to be a strong indicator of the OHL in the Indian Population. Further research to develop new instruments to measure the OHL, in a culturally diverse country like India, which has people of different mother tongues should be encouraged.

Keywords: Oral health; health literacy; self- efficacy; community outreach

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Introduction

The concept of Oral health literacy (OHL) has developed over several years and the existing literature is ever increasing in this field. Health literacy refers to the ability of individuals to obtain, understand and act upon health information and to make appropriate health decisions. ⁽¹⁻³⁾ Oral health literacy (OHL) refers to the

degree to which individuals have the capacity to obtain, process and understand basic oral health information and services needed to make appropriate health decisions.⁽⁴⁾ This concept has not yet gained sufficient weight age in regular dental practice.

Oral Health literacy is like a bridge between the dental care provider's instructions and the comprehension, thereby abiding of the patient to the same. This role of OHL makes it important for the dentist to ascertain the level of OHL of the patient before any procedure and then treat the patient according to the level of understanding of the patient. After identification of the level of OHL attention should be paid by the dentist to communicate with the public and remove literacy-related barriers to information, decision making, and healthful action.⁽⁵⁾ A significant number of patients may have a low level of oral health literacy, which possibly interferes with their ability to process and understand oral health information. Providers should identify patients who are having difficulty understanding and using dental health information and address their needs.⁽⁶⁾

According to Paasche-Orlow and Wolf conceptual model of causal pathways between health literacy and health outcomes the effect of literacy on health outcomes is mediated by patient-level and extrinsic factors grouped as ⁽¹⁾ access to and utilization of health care, ⁽²⁾ provider-patient interaction, and self-care.⁽⁷⁾ Many factors are related to OHL but amongst the recent ones focus has been given to those that affect behavior because behavior is amenable to change. A successful dental practice is not only related to dental treatment provided, but also to the patient's attitude and behavior towards the treatment.⁽⁸⁾ Individual health practices such as oral self-care are based on personal choices.⁽⁹⁾ According to the model proposed by Lee et al., Personal characteristics such as self-efficacy mediate and/or modify the impact of literacy on oral health behaviors.⁽¹⁰⁾

Self-efficacy-Perceived self-efficacy is concerned with people's beliefs in their capabilities to produce given attainments.⁽¹¹⁾ Perceived self-efficacy is a judgment of capability to execute given types of performances and outcome expectations are judgments about the outcomes that are likely to flow from such performances. Perceived efficacy has a pivotal role because it affects behavior and its impact on other determinants such as goals and aspirations; outcome and expectations. Self-efficacy appraisals reflect the level of difficulty individuals believe they can surmount.⁽¹¹⁾

The aim of the present study was to evaluate the relationship between Oral health literacy (OHL) by using Rapid Estimate of Adult Literacy in Dentistry (REALD-30) with the level of education and self-efficacy by using a questionnaire on Dental Coping Beliefs Scale (DCBS) among adult (age 18-77 years) patients attending a dental outreach clinic in Udupi Taluk.

Objectives:

- 1) To evaluate the Oral health literacy in adults visiting a dental outreach clinic in India by using word recognition instrument- Rapid Estimate of Adult Literacy in Dentistry (REALD-30).
- 2) To evaluate the Self-efficacy using Dental Coping Beliefs Scale (DCBS) questionnaire in the same subjects.
- 3) To evaluate the relationship between OHL with level of education.
- 4) To evaluate the relationship between OHL and self-efficacy.

Method

Sample and data collection- A convenience sample of participants (N=200) was recruited from patients presenting for an initial consultation to a dental rural clinic in Udupi. Written informed consent was obtained for all study participants. Study Design- A Cross-sectional questionnaire study. Inclusion Criteria were- subjects who claimed to be able to read English words, subjects more than 18 years of age but younger than 80 years, subjects who had completed education till a minimum of 10th class, subjects without cognitive impairment, subjects without vision or hearing problems and subjects without obvious signs of drug/alcohol intoxication. Exclusion Criteria: were subjects who are not able to read English words, subjects less than 18 years of age and more than 80 years, subjects who have completed education less than 10th class, subjects not willing to participate in the study, subjects with psychiatric disorders and subjects with other severe systemic illness. Ethical clearance was obtained from the Kasturba Hospital Ethics Committee, Manipal before commencement of the study (IEC 277/2014). Informed consent was obtained from all patients prior to the start of the study. The Oral Health Literacy Assessment was done using REALD-30 which is a word recognition instrument which has 30 dental related words arranged in order of increasing difficulty.⁽¹²⁾ The words were read

aloud by the subject to the interviewer. The participants were asked not to phonetically deduce the words, but rather to skip a word if they did not know it. One point is given to each word pronounced correctly (zero point if incorrectly). The REALD-30 score was categorized as Low (≤ 21), Moderate (22 to 25) or High (≥ 26).⁽¹³⁾

In addition to the above, each patient completed a questionnaire regarding Self-efficacy. This questionnaire was a part of Dental Coping Beliefs scale (DCBS).⁽¹⁴⁾ The participants were asked to mark only one response to each question. Total Self- efficacy was calculated by adding each of the responses. It had 9 questions and the responses were recorded on a Likert scale. The responses were-(1) Strongly agree, (2) Agree, (3) Neither, (4) Disagree and (5) Strongly disagree. Additionally, socio-demographic data was included in the questionnaire -Age, gender, education, occupation, monthly income.

Data Analysis: Statistical analysis was performed using SPSS (version 16.0).One way ANOVA was used to assess the relation between REALD-30(categorized-low, moderate, high)and self-efficacy (continuous variable). Pearson’s χ^2 test was used to assess association between education and REALD-30. The level of significance was set at 0.05.

Results

The study population consisted of 200 English speaking adults who visited the dental outpatient clinic. Questionnaire was administered to 200 adults and the response rate was 100.0%.The mean age of the respondents 38.33 years who were in the age range of 18 to 77 years. Among the respondents 41% were males and 59% were females. An individual’s completion of the entire questionnaire was ensured by checking for it during the oral health examination. The respondents were asked to complete the incomplete forms. The demographic characteristics of the participants are presented in Table 1. The distribution of REALD-30 is presented in Table 2 of which 12.5% people have high OHL, 30.5% have moderate OHL and 57.0% have low OHL. Self-efficacy in results have been presented in Table 3. The self-efficacy range is 9-29 with a median of 18.0. The co-relation between REALD and Self efficacy was analyzed by One way ANOVA and presented in Table 4. There was no significant association between

OHL and self-efficacy. Pearson’s χ^2 test was used to test for association between Education and REALD has been presented in Table 5. The OHL was significantly associated with the level of education of patients. 6.0% of the participants completed high school education, 33.0%Intermediate/PUC, 58.5% Graduate/Post graduate and 2.5% Profession/ Honors.

Table 1: Distribution of study participants according to socio-demographic characteristics

Variables		Participants (%) N=200
Gender	Male	82 (41%)
	Female	118(59%)
Age (years)	Mean	38.33
	Range	18-77
Socioeconomic status	Middle	159(79.5%)
	Low	41(20.5%)

Table 2: Distribution of REALD-30

	Frequency	Percentage
High	25	12.5%
Moderate	61	30.5%
Low	114	57.0%
Total	200	100.0%

Table 3: Distribution of Self efficacy

	Median	Range	Standard Deviation
Total Self efficacy	18.00	9-29	3.73

Table 4: One way ANOVA- Co-relation between REALD and Self efficacy

		N	Mean Self-efficacy	Standard deviation	Sig.
REALD	High	25	18.520	4.204	0.983
	Moderate	61	18.442	3.909	
	Low	114	18.377	3.548	
Total		200	18.415	3.727	

Table 5: Association between Education and REALD

			REALD			Total	Significance
			High	Moderate	Low		
Education	High school	Count	0	0	12	12	0.001*
		%	0%	0%	10.5%	6.0%	
	Intermediate/ PUC	Count	6	14	46	66	
		%	24.0%	23.0%	40.4%	33.0%	
	Graduate/ Post graduate	Count	17	46	54	117	
		%	68.0%	75.4%	47.4%	58.5%	
	Profession/ Honors	Count	2	1	2	5	
		%	8.0%	1.6%	1.8%	2.5%	
Total	Count	25	61	114	200		
	%	100%	100%	100%	100%		

Pearson's X^2 is taken as 0.001* as significant

Discussion

The aim of this study was to evaluate the oral health literacy (OHL) and its relationship with self-efficacy among adult patients attending a dental outreach clinic. To the best of our knowledge this is the second study done in India to assess the OHL using REALD-30 as the assessment tool and the first study done to look closely into the association between OHL and self-efficacy in an adult Indian population in an outreach dental clinic. In this study the OHL was significantly associated with the level of education of patients which is similar to the findings of another study on Health Literacy.⁽¹⁵⁾

The dental copings beliefs scale was used to assess self-efficacy. DCBS helps the oral health professional in understanding a patients' belief either in internal or external controls and also the ability to which patient perceives himself/herself to be able to perform given tasks.⁽¹⁴⁾ In the present study, there was no significant association between oral health literacy and self-efficacy. The self-efficacy has been assessed using a self-reported questionnaire, thus this finding could be attributed to the social desirability bias.

Among the 200 study English speaking subjects who had completed education at least till 10th class, who participated in the study OHL scores were very low in more than 50% of the subjects (57%-low OHL). These subjects scored less than 21 which mean these patients are likely to struggle to understand simple dental terminology which is used by the dentists while communicating to the patients. Only 12.5% of the total study population had High OHL (≥ 26). This means only a little more than 10%

of the whole of the study population is actually clearly able to understand the dental terms used by the dentists. Only moderate levels of literacy was recorded in 75.6% in graduate and postgraduates indicating that even these people understand only some of the dental terms and not all. The findings in the present study indicate that even in an Indian population with a basic level of education who are able to read and write in English have low levels of Oral health literacy. Similar findings are reported by M D'Cruz et al.,2014.⁽¹⁶⁾

Demands for reading, writing, and numeracy skills are intensified due to health-care systems' complexities, advancements in scientific discoveries, and new technologies. In this study there was no significant association between Oral health literacy and caries status and periodontal status. This could be attributed to the fact that the oral health literacy was taken by a word recognition instrument the REALD-30 which has several limitations.

This instrument is only a word recognition instrument and does not take into account whether the individual comprehends the dental words. Also, pronunciation of words vary in the Indian population due to a difference in dialect. It is possible that incorrect pronunciation may not necessarily mean that meaning of the word is also not known, more so among individuals with lower levels of education.⁽¹⁷⁾ Therefore, the evaluation of oral health literacy via a word recognition instrument like REALD may be misleading. Due to these reasons, an association of oral health literacy with DMFT or CPI is difficult to assess.

Newer tools for assessing oral health literacy should be developed which test comprehension along with simple word recognition. Then the level of health literacy can be measured accurately and associated with oral health outcomes like caries status and periodontal status.

Conclusion

Demands for reading, writing, and numeracy skills are intensified due to health-care systems' complexities, advancements in scientific discoveries, and new technologies.⁽¹⁸⁾ Poor health literacy has been described as a “silent epidemic” which needs to be taken care of by professionals and policy makers in order to improve quality of health care delivery, reduce costs and disparities. ⁽¹⁸⁾ The “roots of health literacy problems have grown as health practitioners and health care system providers expect patients to assume more responsibility for self-care at a time when the health system is increasingly fragmented, complex, specialized, and technologically sophisticated”. ⁽¹⁹⁾ Thus dentists should identify patients who are having difficulty understanding and using dental health information and address their needs.

Considering the importance of measuring oral health literacy and the numerous instruments available for the same, it becomes imperative to determine the applicability of the particular instrument to be used in the population under consideration.⁽¹⁵⁾ Thus, for further research in the field of oral health literacy in a culturally diverse country like India with people of different mother tongues, other instruments which measure oral health literacy rapidly and also test comprehension of the participants should be developed.

There is no known conflict of interest for this study. There was no funding obtained for this study.

References

1. HHS (U.S. Department of Health and Human Services). 2000. Healthy People 2010: Understanding and Improving Health. Washington, DC: U.S. Department of Health and Human Services
2. Ratzan SC, Parker RM. Introduction. Selden CR, Zorn M, Ratzan SC, Parker RM, Editors. In: National Library of Medicine Current Bibliographies in Medicine: Health Literacy. Vol. NLM Pub. No. CBM 2000-1. Bethesda, MD: National Institutes of Health, U.S. Department of Health and Human Services.
3. Ratzan SC. Health literacy communication for the public good: Health Promotion International, Oxford University Press 2001:16 (2), p207-213.
4. National Institute of Dental and Craniofacial Research. The invisible barrier: literacy and its relationship with oral health. A report of a workgroup sponsored by the NIDCR, USPHS, DHHS. J Public Health Dent. 2005; 65: 174-82.
5. Rima E. Rudd. Oral health literacy: correcting the mismatch. Journal of Public Health Dentistry 2012; 72: S31-S33.
6. M Jones, J Y. Lee, R. G Rozier. Oral health literacy among adult patients seeking dental care. JADA 2007; 138 (9): 1199-1208.
7. Paasche-Orlow MK, Wolf MS. The causal pathways linking health literacy to health outcomes. Am J Health Behav. 2007 Sep-Oct;31 Suppl 1:S19-26.
8. Schou L. The relevance of behavioural sciences in dental practice. Int Dent J. 2000; Suppl Creating A Successful:324-32.
9. Hollister MC, Anema MG. Health behavior models and oral health: a review. J Dent Hyg. 2004 Summer;78(3):6.
10. J Y. Lee, K Divaris, A. D Baker, et al. The Relationship of Oral Health Literacy and Self-Efficacy with Oral Health Status and Dental Neglect. Am J of Public Health. 2012 May 102(5): 923-929.
11. Bandura A. Guide for constructing Self-efficacy scales, Self-Efficacy Beliefs of Adolescents: Information Age Publishing 2006, p307-337.
12. JY Lee, R. G Rozier, SYD Lee, et al. Development of a Word Recognition Instrument to Test Health Literacy in Dentistry: The REALD-30 -A Brief Communication. J Public Health Dent 2007; 67 (2):94-98.
13. Meggan M.H., Caleb L. Corwin, et al. The impact of oral health literacy on periodontal health status. J Public Health Dent 2014; 74: 80-87.
14. Wolfe GR, Stewart JM et al. Use of Dental Coping Beliefs Scale to measure cognitive changes following oral hygiene interventions. Community Dentistry and Oral Epidemiology 1996; 24: 37-41
15. Rathnakar U.P, A Kamath, MURval, et al. Applicability of the rapid estimate of adult health

- literacy in medicine – short form among patients attending a university hospital in southern India. *International J. of Healthcare and Biomedical Research* 2014; 3(1): 196-205
16. A M D’Cruz and M R Aradhya. Health literacy among Indian adults seeking dental care experiences. *J Public Health Dent* 2014; 74: 195–201.
 17. J Y Lee, R G Rozier, S Y D Lee, et al. Development of a Word Recognition Instrument to Test Health Literacy in Dentistry: The REALD-30 -A Brief Communication. *JPublic Health Dent.* 2007 ;67 (2):94-98.
 18. Bohlman LN, Panzer A, Hamlin B, et al. Health literacy: a prescription to end confusion. Washington: National Academies Press 2004, p1-25.
 19. Parker RM. Health literacy: a challenge for American patients and their health care providers. *Health Promot International.*2000; 15(4): 277–83.

Perception and Prevalence of Substance Use among Undergraduate Medical Students in Mumbai

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Abstract

Introduction: Substance Use is a major public health concern due its potency to lead to long term addiction and its effects on an individual's health. Medical students follow general young adult patterns and are not exempt from the consequences of substance use, which may include injuries, work and social impairment, violence, risky sexual behaviour, cardiovascular disease, cancer, and death. In lieu of the same, it is crucial that the perception towards and prevalence of Substance Use in Undergraduate Medical Students be assessed.

Objectives: To study the Perception and Prevalence of Substance Use among Undergraduate Medical Students in Mumbai.

Method: This study was conducted among Undergraduate Medical Students in Mumbai with help of a pre-structured online questionnaire. A total of 250 participants were included in the study. The Data were entered and analysed using SPSS (Version 20). Descriptive statistics was done thereon.

Results: Majority (70.3%) agreed that substance abuse was a common problem in medical students and felt that Alcohol (71.8%) and Tobacco (20.9%) were the most commonly used substances. 91.3 % perceived that substance use was most common in the age group 18-30 years and 52.9% felt that male gender had a tendency to lean towards substance use. Prevalence of substance use was 68.8%.

Conclusion: There is a high prevalence of substance use amongst medical students. An integrated approach involving multiple stakeholders is integral to target the same.

Keywords: Substance Use, Undergraduate Medical Students, Perception, Prevalence.

Introduction

Substance Use is a major public health concern due its potency to lead to long term addiction and its effects

on an individual's health. Medical students follow general young adult patterns and are not exempt from the consequences of substance use, which may include injuries, work and social impairment, violence, risky sexual behaviour, cardiovascular disease, cancer and death.⁽¹⁻³⁾ Over the years, there has been an increase in the use of various substances such as alcohol, tobacco and cannabis by medical students. Studies from various countries reported the prevalence of excessive drinking among medical students ranging between 7% and 45%, and the prevalence of use of drugs such as cannabis and ecstasy ranging between 4% and 45%⁽⁴⁻⁸⁾. In India, alcohol use figures vary widely from 3.8% to 21.0%, with men 9.7 times more likely to regularly use alcohol

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as compared to women. (9-11) Prevalence of smoking has been estimated as 26.0% in males and 4.0% in females.¹² A variety of factors can be attributed to the increasing prevalence of substance use in undergraduate medical students. Constant Academic Stress, Burnout, Depression, Peer Pressure etc. are some of the factors which facilitate substance use in Undergraduate Medical Students. Family and Social stressors can also lead to students feeling emotionally disturbed and not knowing how to cope with these constant stressors can further lead to substance use in them. Additionally, student perceptions regarding substance use and their potential benefits may also contribute to substance use. Young students who consume various such substances may easily get addicted to them in the future, thereby making them a high risk group. In lieu of the same, it is crucial that perceptions and prevalence of substance use in undergraduate medical students be assessed and measures to combat the same be taken. This study will thereby explore the perception and prevalence of Undergraduate Medical Students towards substance use.

Materials and Method

This study was conducted among Undergraduate Medical Students in Mumbai. It was a layered study of 250 participants. The study was conducted in compliance with all the ethical principles to be followed for medical research which involves human subjects.¹³ Ethical approval for the study was obtained from DY Patil – School of Medicine, Navi Mumbai. An informed consent was obtained from all these participants and confidentiality of subjects was maintained. The first stage of the study was on their perception of substance use. In the second stage of the study, an online structured questionnaire was mailed to the students who participated in the first stage. This questionnaire was formulated by review of literature on the topic and discussion with experts. The questionnaire was validated by seven subject experts. The final content validity ratio – after the corrections suggested by the experts was more than 0.99 per item and hence all the changes done in questions were incorporated in the final questionnaire. The first part of the online questionnaire covered the demographic details of the participant while the second part covered questions to assess the perception related to substances

commonly used, factors responsible for the same along with questions on individual use etc. The study duration was one year April 2017-March 2018. The data was entered and analysed using Statistical Package for Social Sciences (Version 20). For the purpose of statistical significance, a p-value of less than 0.05 was taken as the essential criteria for showing a significant association. Descriptive statistics was used thereon.

Results

A Total of 250 participants were included in the study. There were 111 males (44.4%) and 139 females (55.6%), thereby having a higher female participation. Mean age of the participants and Standard Deviation was 21.54 ± 4.95 years. Various other characteristics of the study participants are described in Table 1.

Table 1: Characteristics of Study Participants

Variable		Male	Female	Total	%
Year of Study	1st Year	10	21	31	12.4
	2nd Year	9	14	23	9.2
	3rd Year	33	45	78	31.2
	4th Year	33	22	55	22
	Intern	26	37	63	25.2
Age (in years)	18-20	41	44	85	34
	21-23	57	73	130	52
	24-26	13	22	35	14
Residence	Hostelite	60	55	115	46
	Localite	51	84	135	54
	Total	111	139	250	100

In this study, gender ($X^2=1.44$, $p = 0.23$) and age ($X^2=0.2$, $p = 0.9$) did not have a statistically significant association with ever use of substance. However, a statistically significant association was found between the year of study ($X^2=9.87$, $p = 0.042$) and substance use. It was seen that there was a higher prevalence of substance use in hostilities as compared to localities and this difference was statistically significant ($X^2 = 5.92$, $p = 0.015$). The prevalence of substance use amongst the participants was 68.8%. Table 2 illustrates the prevalence of substance use amongst both male and female participants.

Table 2: Association between substance use and gender, age, residence

	Variable	Use of substance		X ²	p-value			
		Yes	No					
Gender	Male	72	39	1.4402	0.2301			
	Female	100	39					
Age	18-20	59	26	0.2018	0.904			
	21-23	88	42					
	24-26	25	10					
	Year of study	1st year	15			16		
Year of study	2nd year	19	4	9.8682	0.0427*			
	3rd year	51	27					
	4th year	40	15					
	Intern	47	16					
	Residence	Hostelite	88			27	5.9155	0.015*
		Localite	84			51		

As depicted in Figure 1, 72 out of 111 males and 100 out of 139 females agreed to have consumed substance/s at some point in their lives. They were categorised as ever-users.

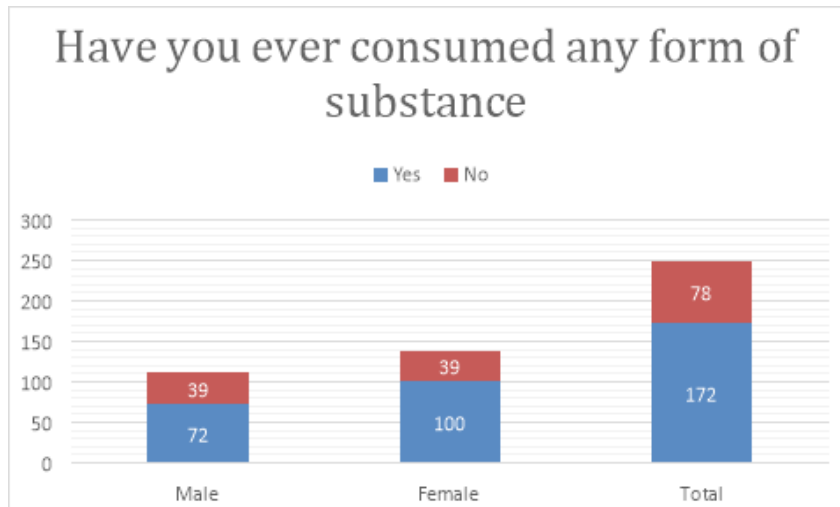


Figure 1: Prevalence of Substance Use

Majority of the participants (70.3%) agreed that substance use was a common problem in medical students while only 15.7% strongly agreed to the same. In contrast, 19.2% of the participants disagreed

to the same and a mere 1.3% strongly disagreed. The perception difference of students (substance use: non-users and ever-users) towards substance use being a common problem is illustrated in Table 3.

Table 3: Perception Difference on Substance Use being a common problem in medical students (Non users v/s-Ever Users)

Response	Non-user						Ever-user					
	Male	%	Female	%	Total	%	Male	%	Female	%	Total	%
Agree	48	39.70%	73	60.30%	121	70.30%	22	43.10%	29	56.90%	51	65.40%
Strongly Agree	13	48.10%	14	51.90%	27	15.70%	7	63.60%	4	36.40%	11	14.10%
Disagree	11	47.80%	12	52.20%	23	13.40%	9	60.00%	6	40.00%	15	19.20%
Strongly Disagree	Nil	Nil	1	100%	1	0.60%	1	100.00%	Nil	Nil	1	1.30%
Total	72		100		172		39		39		78	

Alcohol was the most common substance used (69.2%) followed by Tobacco (20.9%). In comparison, substances such as Cannabis (8.7%), Amphetamines (0.6%) and Heroin (0.6%) formed a minor proportion of the substances used by students. Table 4 illustrates the substances commonly consumed.

Table 4:Substances commonly consumed

Response	Male	%	Female	%	Total	%
Alcohol	46	38.7	73	61.3	119	69.2
Amphetamines	0	0.0	1	100.0	1	0.6
Cannabis	8	53.3	7	46.7	15	8.7
Heroin	1	100.0	0	0.0	1	0.6
Tobacco	17	47.2	19	52.8	36	20.9
Total	72		100		172	

Majority participants (91.3%) perceived that the age group of 18-30 years was most commonly affected by substance use. The perception difference of students (substance use: non-users and ever-users) towards age groups commonly affected is illustrated in Table 5.

Table 5: Perception Difference: Age group affected

Age	Non-user						Ever-user					
	Male	%	Female	%	Total	%	Male	%	Female	%	Total	%
18-30	34	49.3	35	50.7	69	88.5	66	42	91	58.0	157	91.3
30-45	1	50.0	1	50.0	2	2.6	4	80.0	1	20.0	5	2.9
45+	Nil	Nil	Nil	Nil	Nil	Nil	1	100.0	Nil	Nil	1	0.6
Not stated	4	57.1	3	42.9	7	9.0	1	11.1	8	88.9	9	5.2

91 participants (52.9%) felt that males had a higher tendency to lean towards substance use while 10 (5.8%) felt that females had a tendency to lean towards substance use. In contrast, 31 (39.7%) felt that gender didn't matter with regards to substance use; while a mere 3 (3.8%) didn't know if gender impacted substance use. Peer Pressure was the major factor participants believed to have been responsible for substance use followed by curiosity and depression. The factors presumed to be responsible for substance use as per consumers and non-consumers is shown in Figure 2.

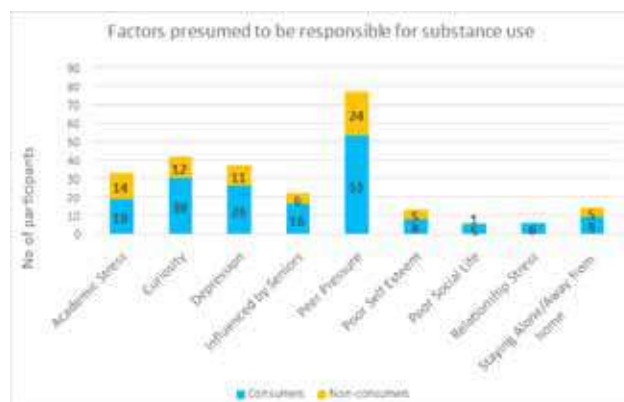


Figure 2: Factors presumed to be responsible for substance use as per non- users and ever-users

Majority (62.8%) claimed that they did not expose themselves to substance use due to fear of addiction, followed by a mere 12.8% claiming they were just not keen and 10.3% claiming that they opted not to due to fear of cancer. Additionally out of substance users, 33.1% claimed that the substances were available on campus while 66.9% denied the same. In comparison, 37.2% of non – users agreed that the substances were available on campus while 62.8% disagreed. With regards to potential benefits of substance use, majority substance users (71.5%) felt that it did not have any benefits. Table 6 illustrates the perception of substance users towards potential benefits of taking various substances.

Table 6: Perception of Substance Users towards potential benefits of various substances

Response	Male	%	Female	%	Total	%
Yes	7	77.8	2	22.2	9	5.2
No	53	43.1	70	56.9	123	71.5
May be	8	34.8	15	65.2	23	13.4
I don't know	4	23.5	13	76.5	17	9.9

Out of 172 participants who were substance users, 34.3% claimed that they did try quitting substance use, 41.9% said they didn't while 23.8% claimed they would not do that. Figure 3 illustrates the proportion of substance users who tried quitting v/s those who did not.

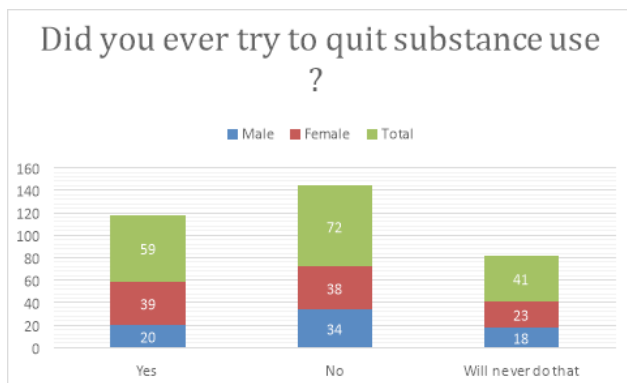


Figure 3: Proportion of Substance Users who tried to quit Substance Use

Discussion

Substance use is a growing concern in medical students. The prevalence of substance use amongst undergraduate medical students in our study was 68.8%. There is a wide variation in the reporting of substance use prevalence among Indian medical students. The

prevalence has been known to be reported from 32.5 % to as high as 81%.¹⁴ A higher prevalence was witnessed among female participants – 58.1% while male participants had a prevalence rate of 41.9%. Similarly, Boland M et al found an increase in alcohol use rates in females.¹⁵ However, the difference in our study was not statistically significant. Previous studies have shown substance use to be more common in males.^{16,17} Majority students who consumed substances were in the age group of 21-23 years. Similar results were obtained by Mir AR et al, who found that substance abuse was initiated majorly by students in the age group of 20-23 years.¹⁸ However, the association between age and substance use was not statistically significant in our study. A statistically significant association was found between the year of study ($X^2=9.87$, $p = 0.042$) and substance use. Pre-Final Year students (3rd Year) students had a higher prevalence of substance use followed by Interns. One of the reasons for the same could be attributed to the fact that the leisure time is more is more in third professional year as compared to first and final year while in internship the student is in a constant stress of post-graduate entrance exams. Likewise, in the study done by Mir AR et al, substance abuse was highest amongst 3rd year medical students.¹⁸ It was seen that there was a higher prevalence of substance use in hostelities as compared to localities and this difference was statistically significant ($X^2=5.92$, $p = 0.015$). Similarly, Kumar P et al found that more hostellers were found to be drug consumers than non-hostellers.¹⁹ Majority of the participants (70.3%) also agreed that substance use was a common problem in medical students, thereby highlighting the fact that it is an issue and needs to be addressed. Alcohol (69.2%) was the most commonly used substance followed by Tobacco (20.9%). In comparison, substances such as Cannabis (8.7%), Amphetamines (0.6%) and Heroin (0.6%) formed a minor proportion of the substances used by students. Similar results were obtained in a study done by Jaiswal HS et al wherein alcohol and tobacco were found to be the most commonly used substances.²⁰ Likewise, Tockus D et al showed that with respect to the drugs most commonly used by medical students, alcohol use was more prevalent (70.45%) followed by cigarette (27.3%) and marijuana (10.2%).²¹ The reason why alcohol and tobacco could be the most commonly used substance amongst a variety of studies is their easy availability and lack of stringent legal regulations regarding their consumption by adults and alike. Majority participants (91.3%) perceived that the age group of 18-30 years was most commonly affected by substance use. This highlights the fact that not only first year students

but also professionals form a vulnerable group for substance use. With regards to gender and substance use, 52.9% of the participants felt that males had a higher tendency to lean towards substance use. Similar results were obtained in a study done by Shafiq M et al, wherein male gender was found to be a predisposing factor for drug use as perceived by the students.²² Peer Pressure was the major factor participants believed to have been responsible for substance use followed by curiosity and depression. Likewise, Deressa W et al found that peer's influence was one of the important factors for students to practice substance use.²³ Additionally, Chatterjee et al and Boniatti et al. observed that curiosity was one of the factors for substance use.^(24, 25) Mesquita EM et al stated the stressful nature of the medical program as an initial cause and motivator for drug consumption.²⁶ Majority (62.8%) claimed that they did not expose themselves to substance use due to fear of addiction, followed by a mere 12.8% claiming they were just not keen and 10.3% claiming that they opted not to due to fear of cancer. These findings could have been synonymous with the fact that medical students are comparatively more aware about the health hazards of substance use and long term chemical dependency, which could have influenced their choice to not opt for the same. Additionally out of substance users, 33.1% claimed that the substances were available on campus while 66.9% denied the same. In comparison, 37.2% of non – users agreed that the substances were available on campus while 62.8% disagreed. Though the proportion of participants who claimed substances were available on/near the campus is comparatively lesser than those who denied it, the easy availability and proximity to college area could be a factor for a higher prevalence as well. With regards to potential benefits of substance use, majority substance users (71.5%) felt that it did not have any benefits. This is contrary to the high prevalence and leaves room for a further research into driving factors for substance use since despite being aware that there are no benefits of the same, the prevalence is still high. In contrast, the proportion of students (5.2%) who claimed substance use did have potential benefits was very minor and additionally 13.4% claimed that maybe the substances have benefits while 9.9% didn't know. Out of 172 participants who were substance users, 34.3% claimed that they did try quitting substance use, 41.9% said they didn't while 23.8% claimed they would not do that. This also highlights the high burden of substance use in correlation with the small proportion of students who tried to quit substance use.

Limitations: Owing to the fact that a convenient sample size was taken, the study results cannot be generalized. Additionally, the fact that a proportion of students belonged to affluent private medical colleges; this could have also impacted the prevalence figures and was also a contributing factor for selection bias. Lastly, since the study design was cross-sectional in nature – no causal inference could be determined.

Recommendations: Substance use is a major public health issue. There are comparatively few studies done in India on perception of medical students towards substance abuse. Counselling sessions should be conducted in various medical colleges to sensitize students to deal with stress and coping mechanisms so as to avoid long term chemical dependency. Media coverage regarding substance use and its hazards can impact students on a large scale. Media and its various resources as well campaigns can be an effective mode of behaviour change communication for students. Mere reporting of the increasing prevalence is not enough; there is a cumbersome need for targeted intervention programs to target the same through a variety of channels including involving medical school authorities, students and media portals. Additionally, there is scope for future research to get a more detailed understanding of the issue through qualitative studies.

Conclusion

There is a high prevalence of substance use amongst medical students. A variety of factors influence substance use in medical students and each of these needs to be addressed. Thereby to combat this issue on a large scale, a series of interventions with a variety of modules are required.

Conflict of Interest: None

Source of Funding: None

Ethical Approval: It was obtained from DY Patil School of Medicine, Navi Mumbai. Informed Consent was taken from all participants.

References

- 1) Center for Behavioral Health Statistics and Quality Behavioral health trends in the United States: results from the 2014 national survey on drug use and health: (HHS No. SMA 15-4927, NSDUH Series H-50). Available from: <http://samhsa.gov/data>. (Accessed on 2nd January, 2019).

- 2) Centers for Disease Control and Prevention Alcohol and your health. Available from:<http://www.cdc.gov/alcohol/pdfs/alcoholyourhealth.pdf>. (Accessed on 19th May, 2018)
- 3) Aristeiguieta CA. Substance abuse, mental illness, and medical students: the role of the Americans with disabilities act. *JAMA*. 1998; 279:80.
- 4) Akvardar Y, Demiral Y, Ergor G, Ergor A. Substance use in a sample of Turkish medical students. *Drug Alcohol Depend*. 2003; 72(2):117–21.
- 5) Jodati AR, Shakurie SK, Nazari M, Raufie MB. Students' attitudes and practices towards drug and alcohol use at Tabriz University of Medical Sciences. *East Mediterr Health J*. 2007;13(4):967–71.
- 6) Frank E, Elon L, Naimi T, Brewer R. Alcohol consumption and alcohol counselling behaviour among US medical students: cohort study. *BMJ*. 2008; 337:a2155.
- 7) Newbury-Birch D, White M, Kamali F. Factors influencing alcohol and illicit drug use amongst medical students. *Drug Alcohol Depend*. 2000; 59(2):125–30.
- 8) Horowitz A, Galanter M, Dermatis H, Franklin J. Use of and attitudes toward club drugs by medical students. *J Addict Dis*. 2008; 27(4):35–42.
- 9) Neufeld KJ, Peters DH, Rani M, Bonu S, Brooner RK. Regular use of alcohol and tobacco in India and its association with age, gender, and poverty. *Drug Alcohol Depend*. 2005; 77(3):283-291.
- 10) Murthy P, Manjunatha N, Subodh BN, Chand PK, Benegal V. Substance use and addiction research in India. *Indian J Psychiatry*. 2010; 52(5):189-199.
- 11) Deepa M, Pradeepa R, Anjana RM, Mohan V. Noncommunicable diseases risk factor surveillance: Experience and challenge from India. *Indian J Community Med*. 2011; 36(Suppl 1):S50-S56.
- 12) Goel N, Khandelwal V, Pandya K, Kotwal A. Alcohol and tobacco use among undergraduate and postgraduate medical students in India: A multicentric cross-sectional study. *Central Asian journal of global health*. 2015; 4(1).
- 13) ICMR. National Ethical Guidelines for Biomedical and Health Research involving Human Participants; 12 October, 2017. Available from: http://www.icmr.nic.in/guidelines/ICMR_Ethical_Guidelines_2017.pdf. (Accessed on 22nd December, 2018).
- 14) Rai D, Gaete J, Girotra S, Pal HR, Araya R. Substance use among medical students: time to reignite the debate. *Nat Med J India*. 2008 Jan 1;21(2):75-8.
- 15) Boland M, Fitzpatrick P, Scallan E, et al. Trends in medical student use of tobacco, alcohol and drugs in an Irish university, 1973–2002. *Drug Alcohol Depend*. 2006;85(2):123–128
- 16) Smith DR, Leggat PA. An international review of tobacco smoking among medical students. *J Postgrad Med*. 2007; 53(1):55–62.
- 17) Tobacco Control in Medical Schools of India. (The India, Global Health Professional Student's Survey, 2006) Ministry of Health and Family Welfare, Government of India, Nirman Bhavan, Maulana Azad Road, New Delhi-110 011, India. Available from: <http://www.mohfw.nic.in/India%20Global%20Health%20Professional%20Student%20Survey,%202006.pdf> (Accessed on 2nd January, 2019).
- 18) Mir AR, Mahesh SH, Rajanna MS, Ashok J, Singh D. Substance abuse pattern among medical college students in Tumkur, Karnataka, India: a cross sectional study. *International Journal of Community Medicine and Public Health*. 2016 Dec 21; 4(1):238-42.
- 19) Kumar P, Basu D. Substance abuse by medical students and doctors. *Journal of the Indian Medical Association*. 2000 Aug; 98(8):447-52.
- 20) Jaiswal HS, Jaiswal SS, Jain SL. Patterns of substance use in first year and final year medical students: a cross sectional study. *Int J Recent Surg Med Sci*. 2017; 3(2):98-101.
- 21) Tockus D, Gonçalves PS. Detection of drug abuse by medical students from a private university. *J Bras Psiquiatr*. 2008; 57 (3):185-7.
- 22) Shafiq M, Shah Z, Saleem A, Siddiqi MT, Shaikh KS, Salahuddin FF, Siwani R, Naqvi H. Perceptions of Pakistani medical students about drugs and alcohol: a questionnaire-based survey. Substance abuse treatment, prevention, and policy. 2006 Dec;1(1):31.
- 23) Deressa W, Azazh A. Substance use and its predictors among undergraduate medical students of Addis Ababa University in Ethiopia. *BMC public health*. 2011 Dec; 11(1):660.
- 24) Chatterjee T, Haldar D, Mallik S, Sarkar GN, Das S, Lahiri SK. A study on habits of tobacco use among

- medical and non-medical students of Kolkata. *Lung India: Official Organ of Indian Chest Society*. 2011 Jan; 28(1):5.
- 25) Boniatti MM, Zubaran C, Panarotto D, Delazeri GJ, Tirello JL, Feldens MO, et al. The use of psychoactive substances among medical students in Southern Brazil. *Drug Alcohol Rev*. 2007; 26(3):279-85.
- 26) Mesquita EM, Nunes AJ, Cohen C. Evaluation of medical students' attitudes towards drug abuse by colleagues in the academic environment. *Archives of Clinical Psychiatry*. 2008 Jan 1; 35 (suppl 1): 8-12.

An Assessment of Trust in Medical Profession amongst People Residing in a Semi: Urban Area, Tamil Nadu

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Abstract

Introduction: The fundamental basis in health care system and relationship is Trust. Trust is a set of expectations that the health care provider will do the best for the patient. The word “Trust” has been in a state of crisis over the last decade in India particularly in medical profession. Unlimited and implicit access to health care system and medical information from a varied range of source helps patients in one way and in contrary to that it may also misinform and adversely affect “Trust” in medical profession.

Objectives:

- To assess trust in medical profession among people (>18 years) residing in a semi urban area of Tamil Nadu.
- To assess the factors affecting Trust in medical profession.

Methodology: A community based cross-sectional study was conducted during February 2019 in Thirumazhisai, a semi-urban township in Chennai. 150 Men and Women above 18 years were included in the study. Data Collection was done using semi structured questionnaire. TMP (Trust in Medical Profession) scale was used to measure trust in medical profession.

Result: 56.4% have good trust on Doctors and 44.33% have trust lower than the expected score based on TMP scale. Trust was higher among unemployed, women, people below poverty line, those not suffering from chronic illness though statistical association could be established only with socio economic status(p 0.04) and system of medicine followed (p 0.01).

Conclusion: The trust in doctors have largely been reduced and hence understanding this would lead to better ways of responding to patients requests that preserve or enhance patients trust, leading to better outcomes.

Keywords: *trust in medical profession, TMP scale, semi urban area.*

Introduction

The fundamental basis in health care system and relationship is **Trust**. Trust is a set of expectations that the health care provider will do the best for the patient. Research shows that the number of hospital jobs increased by 306% in 2015 and hence it's the high time that we focus on the basis “TRUST”⁽¹⁾. The word “Trust”

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has been in a state of crisis over the last decade in India particularly in medical profession. Generally public in today's world have unlimited and implicit access to health care system and medical information from a varied range of source, this access helps patients in a way and in contrary to that it may also misinform and adversely affect "Trust" in medical profession. Views also varied by sex, age, health, education, income, number of visits/years with physician, past dispute with a physician, and satisfaction with care⁽²⁾. Trust also depends on patients willingness to seek care, reveal sensitive information, submit to treatment and follow physician. Measurement of trust also suggest an important tool for monitoring performance of individual providers and health

plans⁽³⁾. Trust in doctors is found to have five main domains: Fidelity, competence, honesty, confidentiality and global trust⁽⁴⁾. Importance of studying Trust is twofold – at macro-level, Trust is an indicator of support for the health system and changes in the health system and at micro-level, there is relationship between trust and peoples' behaviour in real choice situations.

Methodology: A community based cross-sectional study was conducted in Thirumazhisai, a semi-urban area of Chennai during February 2019. Thirumazhisai is the urban field practice area under department of Community Medicine, Saveetha Medical College and hospital. The study population included men and women who have completed 18 years of age residing in Thirumazhisai for more than 6 months. Sample size was calculated to be 150 using formula for cross sectional study with an anticipated population proportion of 40 %⁽⁵⁾, confidence level of 95% at 5% significance level and allowable relative error of 20%. A two stage sampling technique was used to enrol individuals to the study. There are 15 municipal wards in Thirumazhisai and each ward has 10 to 15 streets. At the first stage simple random sampling was done to select one street from each ward. A ward wise list of all the streets was prepared. One street was selected by lot method from each of the 15 wards. Systematic random sampling was done to select 10 households from each ward. The first family was selected randomly from street wise list of family folders maintained in Urban Health Centre of Saveetha Medical College at Thirumazhisai using random number tables. Every third house was visited starting from the randomly selected house till 10 houses were covered. Only one member (above 18 years) per household was chosen to avoid cluster bias.

Data was collected orally by interview method using structured questionnaire which included sociodemographic profile and TMP(TRUST IN MEDICAL PROFESSION) scale⁽²⁾ to measure trust in Medical Profession. TMP scale is a validated 11-item 4 point likert scale

(Table 1) with responses grading from Strongly agree, Agree, Disagree, Strongly disagree. Here maximum score is 1 for strongly agree and 2,3 and 4 for agree, disagree and strongly disagree respectively. In the questionnaire the negative format question is also changed and recoded according to the format above. Total TMP score was calculated for each individual by adding the scores of the 11 questions. The maximum possible score would be 44 (least trust) and minimum score will be 11 (maximum trust) Mean score was taken as the cut off for categorising into good trust (a score less than mean) and reduced trust (score more than mean).

The study was initiated after obtaining approval from institutional ethical committee of Saveetha Medical College. Informed consent was obtained from the study participants and confidentiality of data was assured and maintained throughout the study. Data was entered in Microsoft Excel and analysed using SPSS software. Qualitative data is expressed as frequencies and proportions, quantitative data were summarised as mean (standard deviation). Chi-square test was applied for bivariate analysis to find association between Trust and qualitative factors like age category, gender, occupation, education, socio economic status (APL/BPL), presence of chronic disease and system of medication followed. Logistic Regression was done for multivariate analysis.

Results

A total sample of 150 people of both men and women above 18 years of age were interviewed. Analysis of the demographic data revealed that there were more number of women about 60.66% and males about 39.33%. Mean (SD) age of the study population was 43.3 (15.6). Majority of people interviewed were in the age group of 18-40 years of age(51.33%). 38 % of the study population were unemployed followed by 23.3 % unskilled workers. 82% were educated till High school or above. 18 % were Below Poverty Line (BPL) with respect to the ration card that was possessed.

The mean(SD) TMP score of the study population was 21.3 (6.214). The maximum score obtained was 37 and minimum was 14. A score below mean (21.3) was

considered as “Good Trust” for comparison purpose in our study . Among the study population 85(56.7%) individuals were found to have “good” trust in medical profession while 65 (43.3%) had reduced trust. When 61% of the males in our study population was found to have good trust, only lesser number of females (53.84%) had good trust in Medical profession . While all the four participants above 80 years had good trust in Medical profession, 62.5% of those in the middle age group (40-60) had good trust. Trust did not vary significantly among the various occupational groups. Trust is higher amongst those belonging to below poverty line (74.1%) while only 52.8% of APL card holders were found to have good trust. Other factors influencing trust also were analysed and showed that trust has been slightly lower(51.1%) amongst people having at least one of the chronic diseases(hypertension, Diabetes Mellitus, cardiovascular disease, bronchial asthma) and it is 59.2% amongst people without any chronic disease .Trust also varied according to the system of medicine followed by the individuals as shown in Table 2.

Bivariate analysis was done using chi-square to test the statistical association between the various factors and trust in medical profession (table 2). Socioeconomic status (p value - 0.04) and system of medicine followed by the participants (p value- 0.010) had a significant association with Trust. Multivariate analysis by logistic regression with “good trust” as the dependant variable did not reveal significant association with any of the independent variables.

The most important quality of a doctor that can influence the trust in medical profession as perceived by the study participants were as follows: 44% of the participants perceived verbal communication as most important followed by behavioural competence(25%), comfort level(16%)and simple elegant appearance(15%). Question number 11 in TMP (table 1) which individually measures the over all trust showed that 74% of the study participants agreed that they “trusted their doctor completely”.

Table 1: 11-item Trust in Medical Profession(TMP scale)

1.	Doctors care their patients health more than or as similar to their parents
2.	Doctors care more about their convenience than their patients medical need
3.	Doctors are thorough and careful
4.	Completely trust Doctors about which medical treatments are best
5.	Doctors are honest in telling their patients about different treatment option available
6.	Doctors think about what is best for their patients
7.	Doctors do not pay full attention to what patient tells
8.	Doctors use their best skills and efforts
9.	You have no worries on putting your life in Doctors hand
10.	Doctors would never mislead you about anything
11.	You trust your doctor completely

Table 2: Factors associated with trust in medical profession

Factors	Good trust n(%)	Reduced trust n(%)	P value (chi-square)
Age			0.139
18-40	42(54.5%)	35(45.5%)	
40-60	30(62.5%)	18(37.5)	
60-80	9(42.9%)	12(57.1)	
>80	4(100%)	0(0%)	
Gender			0.387
Male	36(61%)	23(39%)	
Female	49(53.8%)	42(46.2%)	

Factors	Good trust n(%)	Reduced trust n(%)	P value (chi-square)
Occupation			
Professional	4(66.7%)	2(33.3%)	0.717
Semi-professional	9(47.4%)	10(52.6%)	
Skilled	21(63.6%)	12(36.4%)	
Semi-skilled	21(60%)	14(40%)	
Unemployed	30(52.6%)	27(47.4%)	
Socioeconomic Status			
APL	65(52.8%)	58(47.2%)	0.044*
BPL	20(74.1%)	7(25.9%)	
System of medication			
Allopathy	65(55.6%)	2(44.4%)	0.010*
Homeopathy	1(12.5%)	7(87.5%)	
Ayurveda	15(71.9%)	6(28.1%)	
Unani	4(100%)	0(0%)	
Chronic Disease			
Present	24(51.1%)	23(48.9%)	0.224
Absent	61(59.2%)	42(40.8%)	

*significant at p<0.05



Figure 1: Distribution of trust in medical profession

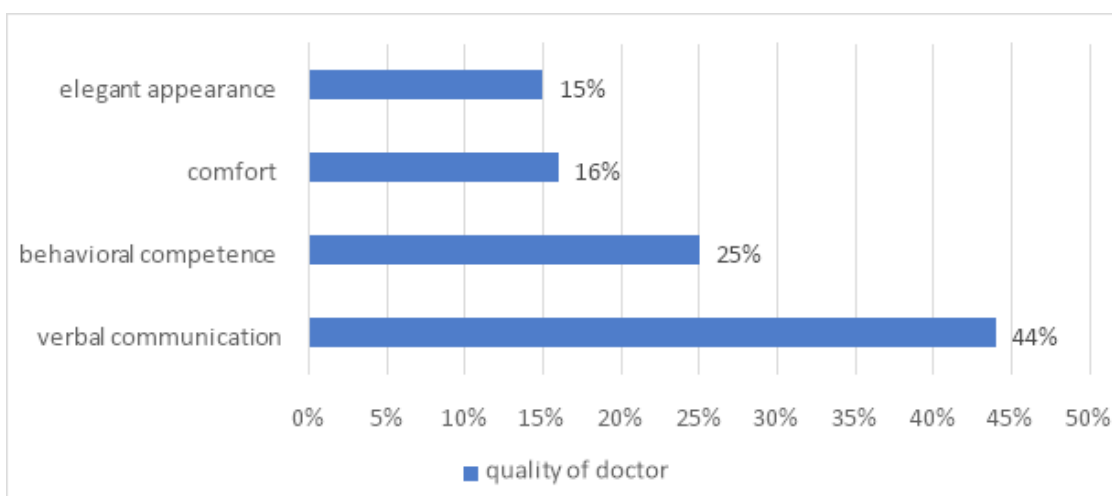


Figure 2: Perceived quality of a doctor that influence trust

Discussion

A cross sectional study was done to assess “trust in medical profession” among adults population in a semi-urban township of Chennai, TamilNadu. Proportion of females and unemployed persons were more in our study population when compared to census figures of Tamil Nadu.⁽⁶⁾ This may be due to the reason that the data collection was done during day time when males who were engaged at their occupation were not available at household . In this study based on the score calculated trust in medical profession is found to be 56.7% have good trust and about 43.3% have reduced trust and which is similar to study conducted in China by Da-Hai Zhao et al showed that the 67% has strongly trusted and about 33% had reduced trust.⁽⁷⁾ Since this is a cross sectional study, deducing a continuous trend in long term was not possible. Mean score in this study is 21.3 out of 44 and in the previous study by Da-Hai Zhao et al the mean score is 35.4 out of 50 (5 point likert 10 item scale)⁽⁸⁾ . Here it's important to note that level of trust is good in middle age group (40-60) in this study and is compared to study conducted in north-east Poland by Marcinowicz et al⁽⁹⁾ . Based on the Table- 1, question number 3 “ Doctors are thorough and careful “ scored the highest about 68% and shows that the public is confident with Doctors knowledge and which is one of the factor influences trust in medical profession. Question number 8 in Table 1 “Doctors use their best skills and efforts” scored the least about 42% and shows that public has less confidence in transparency and skills in medical profession. During interrogations some people have lower Trust but were reluctant to express to medical students. Here the reduced trust may be due to recent media coverage of unethical practices by the doctors.

Factors affecting trust was studied and there is statistical significance obtained between two independent variables, socio economic status and the system of medications followed and Trust. Economic factors were found to be determinant of trust in doctors by studies done by Birkha et al and Gopichandran ^(10,11) . Another study done in older population by Guerrero et al also showed similar result ⁽¹²⁾. Consistent results with association of trust in medical profession and system of medicine were not available. In this study participants perceived verbal communication and behavioural competence as more important and physical appearance as less important factor in influencing trust. Similar results were seen in another study done in rural and urban setting of Tamil Nadu⁽¹³⁾ .

One of the limitations of this study is that it was conducted in a single geographic area . The representativeness of study population was not adequate as the data collection was done during day time and hence the responses of males and working group could not be captured fully.

Conclusion

The final outcome from this study is that 56.7% has good trust and 43.3% have reduced trust in medical profession. Trust have been higher among unemployed, women, people below poverty line, those following alternate systems of medicine and those not suffering from chronic illness though statistical association could be established only with socio economic status(p 0.04) and system of medicine followed (p 0.01). Doctor's verbal communication skills was perceived by majority(44%) of the study participants as the most important quality that would determine trust in medical profession which should be focused on . The study would recommend the medical professionals to build up a close relationship with their patients and be still more transparent to avoid unethical issues. The trust in doctors have largely been reduced and hence understanding this would lead to better ways of responding to patients requests that preserve or enhance patients trust, leading to better outcomes.

Conflict of InterestL: Nil

Source of Funding: Nil

Ethical Clearance: Approval was obtained from Institutional Research Board of Saveetha Medical College and Hospital, Thandalam, Chennai.

Reference

1. John. Right Patient. An Essay on Right patient <http://www.rightpatient.com/blog/6-things-medical-institutions-gain-patient-trust/> [Accessed: 10 August 2019.
2. Hall MA, Camacho F, Dugan E, Balakrishnan R. Trust in the medical profession: conceptual and measurement issues. *Health ser Res* 2002;37:1419-39.
3. Thom DH, Hall MA, Pawlson LG. Measuring patients' trust in physicians when assessing quality of care. *Health Aff (Millwood)* 2004;23:124-32.
4. Steven D Pearson. Patients' Trust in Physicians: Many theories, Few Measures and Little Data.

- Boston : Journal of General Internal Medicine;2000 jul;15(7):509-513
5. Collier R. Professionalism: the importance of trust. *CMAJ*.2012;184(13):1455-1456.doi:10.1503/cmaj.109-4264.
 6. Census2011coin. Census2011coin. [Online]. Available from: <https://www.census2011.co.in/census/state/>.html [Accessed 10 September 2019]
 7. Yi Yong Lee, Choon Ta Ng, M Ghazalie siti Aishah. Public Trust in primary care doctors,the medical profession and the Health care system among Redhill residents . Singapore: *Annals of the Academy of Medicine*; 2007;36(8):655-61.
 8. Researchgatenet. Research Gate. [online]. Available from: https://www.researchgate.net/publication/298918284_Patient_Trust_in_Physicians_Empirical_Evidence_from_Shanghai_China [accessed on10 September 2019]
 9. Researchgatenet. ResearchGate. [Online]. Available from: <http://lup.lub.lu.se/search/ws/files/24176727/24176687.pdf> [Accessed 10 august 2016]
 10. Birkha uer J, Gaab J, Kossowsky J, Hasler S, Krummenacher P, Werner C, et al. (2017) Trust in the health care professional and health outcome: A meta-analysis. *PLoS ONE* 12(2): e0170988. doi:10.1371/journal.pone.0170988.
 11. Gopichandran V, Chetlapalli SK. Dimensions and determinants of trust in health care in resource poor settings--a qualitative exploration. *PLoS One*. 2013;8(7):e69170. Published 2013 Jul 16. doi:10.1371/journal.pone.0069170
 12. Guerrero N, Mendes de Leon CF, Evans DA, Jacobs EA. Determinants of trust in health care in an older population. *J Am Geriatr Soc*. 2015;63(3):553–557. doi:10.1111/jgs.13316
 13. Gopichandran V, Chetlapalli SK. Factors influencing trust in doctors: a community segmentation strategy for quality improvement in healthcare. *BMJ Open*. 2013;3(12):e004115. Published 2013 Dec 2. doi:10.1136/bmjopen-2013-004115

Li-Fi Based Automated Patient Healthcare Monitoring System

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Abstract

Context: Now a days, patient healthcare monitoring systems have realized lots of consideration. This monitoring system repeatedly peer the patient health for the earlier recognition of any physical fall in health. In previous days, Wi-Fi technology was used to transmit the data regarding patient health which cause some health disorders due to its harmful radio waves. To overcome this hazardous problem, Li-Fi (Light Fidelity) is proposed which has no harmful radiation effect with fast and secure communication than Wi-Fi. For more secure, bastion algorithm is used to make the data more immune to attacks by the encryption of data using block cipher encryption and proficient linear post processing to the ciphertext. In the proposed work, the data's are obtained using Arduino and then the statistical data's are manipulated using deep learning algorithms for sending the emergency alert to the doctor.

Keywords: Patient monitoring; Li-Fi; Bastion algorithm; Secure Li-Fi; Healthcare VLC.

Introduction

The goal of Patient Monitoring is to provide an early detection of any health deterioration with reliability and accuracy and to provide warning or alarm. At present, the healthcare monitoring system attains more importance because patients were continuously monitored and examined without any human interventions. This monitoring system is also helpful to the home dwelling chronic or elderly patients. The health status details of a patient such as temperature, ECG, and heart rate were observed using temperature sensor, ECG sensor and Heart rate sensor. The rapid growth of wireless communication led to the problem of efficient use of an electromagnetic spectrum. The most standard wireless technologies use the lowest part of the electromagnetic spectrum in the range of 3KHz-300GHz namely Radio waves. The details collected were transmitted to the receiver using Wi-Fi technology which uses Radio frequency band of an electromagnetic spectrum. This

radio signal transmitted form Wi-Fi antenna will be received by the Wi-Fi receiver like mobile phones and computers equipped with a Wi-Fi card. It causes some health problems like development of insomnia, affect cell growth, cardiac stress and reduce brain activity. Hence, it was not allowed in Operation theatre due to the radiation consequences because Wi-Fi blocks the signal from monitoring equipment and affect the medical equipment.

Li-Fi, a wireless technology that make use of visible light communication or infrared and near UV spectrum waves to resolve the problem of radio waves. The household LED bulbs also utilized for data transmission at a rate of 224 gigabits per second. In medical, Li-Fi was allowed in operation theatres rather than Wi-Fi to use internet and to regulate medical equipments. Hence, it is favourable for robotic surgeries in hospitals and for automated strategies.

Related Work: Nowadays, a patient health monitoring system attains more importance to observe patients remotely using Wireless Sensor Network (WSN)^[1-4]. It also helpful for an home dwelling patients who are aged persons^[5-6] or affected by chronic diseases includes hypertension^[7-9].

Along with ECG, monitoring heart rate was necessary to measure frequency at what rate the blood

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was pumping^[10-11] and respiration also essential to measure the breathing rate of a patient while sitting, sleeping, lying down or standing^[12]. Some techniques observe both breathing and heart rate using a Vital-Radio by inhalation and exhalation^[13] and a Dynamic Time Warping algorithm^[14]. Real time monitoring systems also were implemented for both hospitalized or leading regular life activities^[15] and also monitored using wearable sensors^[16]. Pervasive patients also observed with a sensor based healthcare system^[17]. Through this monitoring system, doctor stress and medical errors were reduced and overall flexibility also improved in observing the patients^[18].

Later, a mobile patient monitoring system uses Visible Light Communication system to pass on the ECG and PPG (blood pressure) details to doctors through high illumination LED. This LED transmits the details by switching between on and off condition as the light signal and received by photodetector^[19]. This technology was also used in automated billing system to reduce human effort and to avoid standing in queues for billing things through mobile application using Li-Fi module and payment was done by mobile banking^[20].

Due to radiation effect, Wi-Fi was restricted in hospitals. The problem in Li-Fi was, during transmission it is necessary to make sure that it ensures confidentiality. Hence, Elliptic Curve Diffie Hellman and Secure Hash Algorithms were used to provide security which use key and authentication to make it difficult to hack data in hospitals^[21]. If the key used for encrypting the data is exposed, the confidentiality must be maintained. To ensure confidentiality of an encrypted data, Bastion algorithm was used even when the key was opened. In bastion, the cipher text blocks were stored in multiple storage systems, so the adversary has to gain the encryption key, and to compromise all systems to win back the plaintext^[22].

Proposed System: The proposed system uses Li-Fi to transmit data using visible light communication and requires Line of sight condition. It is an optical communication technology that utilizes visible light rays between the frequency range of 400-800 THz, as an optical carrier for data transmission for a short range wireless communication system. Li-Fi transmits data in binary form as shown in fig 1.



Fig 1: Data transmission

The principle of Li-Fi technology is based on amplitude modulation, the light source in a standardized way. LEDs were switched on and off much faster with the operating speed of less than 1 microsecond and achieves

speeds of up to 1 Gbps, so which cannot be detected by human eyes. Fig 2 shows the patient monitoring system using Li-Fi.

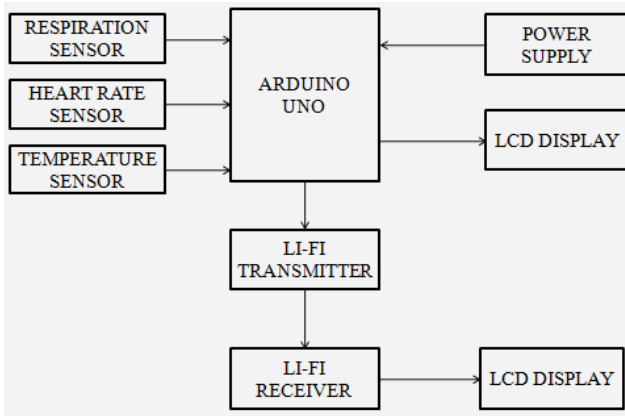


Fig 2: Block diagram

Transmitter Section: In Li-Fi, data was transmitted using LED bulb through a LED driver circuit which controls LED on and off. If the LED is on, binary value 1 will be transmitted and if is off, binary value 0 will be transmitted. LED can be flickers on and off in a rapid manner that provide good chance to transmit the data. It is feasible to encode the data by changing the rate of LEDs flicker to give different strings of 0's and 1's. The intensity of LED was regulated rapidly hence, on and off condition of LED cannot be noticeable by human eye, so the output appears constant. The data rate of Li-Fi can become greater by using an array of LED to transmit different data streams to achieve parallel communication. The data from respiration sensor, heart rate sensor and temperature sensor were fed to Arduino uno that convert an analog signal into digital output because Li-Fi transmits data as a binary stream by switching the LED on and off quickly. The Li-Fi transmitter encodes the signal using on off keying technique and encrypt the signal using secret key cryptography before transmission. Fig.3 shows the transmitter side of proposed system.



Fig 3: Li-Fi transmitter

Receiver Section: The photodetector at the receiver section receives the light signal and retrieves back into an electrical signal, then fed to a Li-Fi receiver where it decodes and decrypt the signal and removed the noise in the signal. This signal then fed to Arduino uno and viewed in the LCD display. Fig. 4 shows the receiver section on Li-Fi unit.

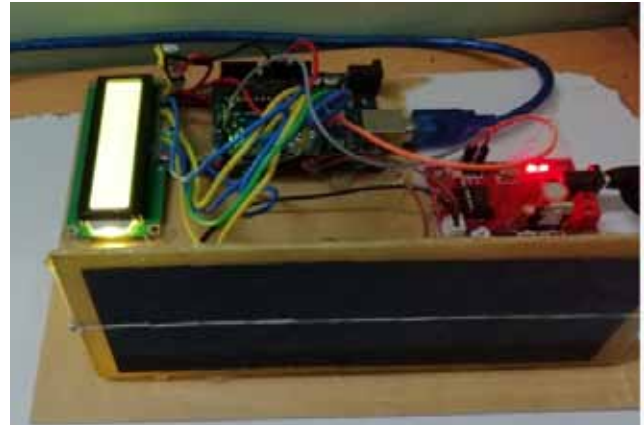


Fig 4: Li-Fi receiver

Security: Bastion Algorithm In patient monitoring, health details of the patient or any medical data or report were transmitted to the doctor or medical man. In that case, the data must be transmitted more securely. Hence the data were encrypted and decrypted. The process of converting a information or data by an algorithm into an unreadable or unusable form using key is called encryption. The encrypted data is called ciphertext and the original data is called plaintext. Decryption is the reverse process of encryption to recover the original data from ciphertext using the same key.

The data will be encrypted using some standard encryption techniques. If the encryption key is leaked, for assuring data confidentiality, the only way is to restrict the access of an adversary (opponent) to the ciphertext (example, distributing the ciphertext to multiple domains). Even though, the data is encrypted and distributed over multiple domains, adversary with an suitable key can compromise a server in a domain and decrypt ciphertext block stored therein. To counter such adversary, an efficient scheme Bastion, proposed to guarantee confidentiality even the key is revealed, ensures that an original data cannot be reclaimed until the adversary access at most all but two ciphertext blocks. Bastion pulled off this by combining the standard encryption function and efficient linear transform in similarities with AONT (all-or-nothing transform). AONT is not an encoding technique but utilized before

encryption as a pre-processing step in Li-Fi based systems. Bastion departs from existing AON encryption technique requires a pre-processing step of block cipher encryption for the AONT which is followed by another round of block cipher encryption. But Bastion first complete the encryption of data using one round of block cipher encryption followed by efficient linear post-processing to the ciphertext. Bastion relaxes the conception of all-or-nothing encryption with improved performance. In bastion, for an input with a security parameter k , the key generation algorithm of Bastion gives an output key $K \in \{0,1\}^k$ for the block-cipher which is used to encrypt the set of input blocks that results ciphertext $q' = q'[1], \dots, q'[p+1]$. Then, Bastion follows a linear transform to q' as follows. Let $n = p + 1$ and assume A to be an $n \times n$ matrix where element $a_{i,j} = 0^1$ if $i = j$ or $a_{i,j} = 1^1$. Bastion computes $q' = q \cdot A^{-1}$ and decrypt q' using K where matrix A is invertible and $A = A^{-1}$.

Results

To overwhelm the drawback of radiation concern in Wi-Fi technology data observed from patients will be transmitted using Li-Fi. It uses visible light part of the electromagnetic spectrum for data transmission. It supports data rate from 100 kbps -100 Mbps for various modulation scheme. The data observed from a patient was first fed to an Arduino that converts analog data to digital data. This data was encrypted into unreadable form using bastion algorithm and then transmitted as light using Li-Fi transmitter by flickering LED. The photodetector in receiver converts light to a digital signal and decrypt the signal which is again fed to another Arduino in receiver that recovered the transmitted data from the digital signal. This will be viewed using LCD. The bastion algorithm ensures that data confidentiality that only receiver can access the data sent, no other adversaries cannot access the data even the key was known.

The fig.4. Shows the respiration rate i.e. count of number of breaths per minute. The conventional respiration rate is 12 to 20 breaths per minute. The rate below 12 or above 25 breaths are considered abnormal. It is necessary to measure respiratory rate because patients affected by asthma, anxiety, pneumonia, congestive heart failure, lung disease or drug overdose may vary from normal rate.



Fig 4: Respiration value

Fig :5 shows the temperature value. The normal body temperature is 98.6°F. Above that is considered as fever and below that is hypothermia. Hence it is necessary to measure body temperature because it reveals our health information like hormonal health, metabolic rate etc.



Fig 5: Temperature value

Fig. 6 shows the heart rate of a patient which measures the cardiovascular fitness assessment. The normal heart rate is 60 to 100 bpm. When it is less than 60 bpm, considered as bradycardia and more than 100 bpm is considered as tachycardia.

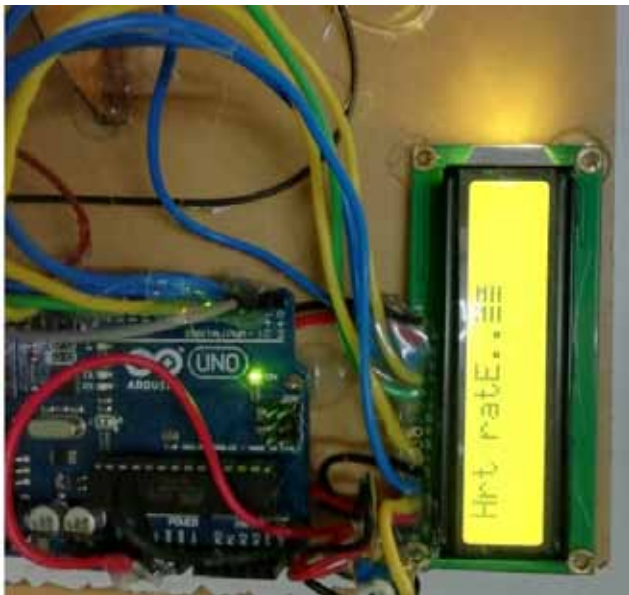


Fig 6: Heart rate

These measured data will be transmitted to receiver using Li-Fi which has some advantages and better throughput over other wireless communication that shows graphically in fig.7.

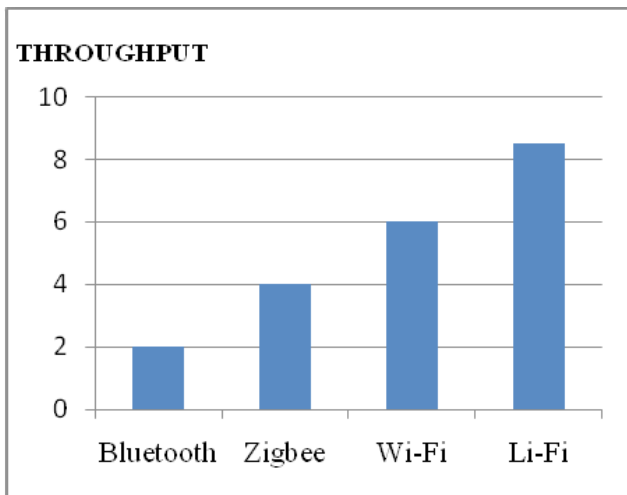


Fig 7: Li-Fi vs other technologies

Here, the data obtained from various sensors by placing the sensors on the patient’s body were converted to a digital form using analog to digital convertor present in the Arduino UNO. It regulates this digital signal to the 5V level. Then the signal was fed to the transmitter where it was transmitted as optic pulses using LED driver circuit which control the LED’s on and off condition to transmit data in a rapid manner. Then it was received by the solar panel to convert this light into electrical signal and then given to the Arduino. Based on the signal voltage level and health data, which is referred with predefined vales,

the abnormal or any deviation from normal value was detected. The alert through SMS or alarm will be sent automatically to the doctor using Li-Fi technology.

Conclusion

In this paper, healthcare monitoring system using Li-Fi technology was proposed which has certain advantages over Wi-Fi technology. Because of the radiation effect exist in Wi-Fi, it was restricted in some areas like aircraft, hospitals, nuclear power plant etc. In hospital, the radio waves may affect the patient health and also the medical equipments. Hence it was not allowed during operation. But Li-Fi provide safe, fast and secure data transmission on low power because it uses visible light spectrum instead of radio waves which never cause any harmful effect on humans. For security during transmission, data will be encrypted using standard encryption techniques. If the encryption key is exposed, data confidentiality will be guaranteed using an efficient algorithm called Bastion. It ensures confidentiality by distributing the encrypted data across multiple storage systems. It limits theopponent to access the encrypted data because the data was distributed to multiple systems, hence the adversary cannot compromise all system to access the data stored therein.

Conflict of Interest: Nil

Source of Funding: Self only

Ethical Clearance: The proposed work (topic) which is performed using noninvasive sensors on healthy human subjects. Here, only the Li-Fi Technology is introduced for high speed transmission with non-harmful radiation as it is using LED’s to transfer the data. Hence ethical committee clearance may not be required.

References

1. Jindal A, Liu M. Networked computing in wireless sensor networks for structural health monitoring. IEEE/ACM Transactions on Networking (TON). 2012 Aug 1;20(4):1203-16.
2. Aminian M, Naji HR. A hospital healthcare monitoring system using wireless sensor networks. J. Health Med. Inform. 2013 Feb;4(02):121.
3. Torabi N, Leung VC. Realization of public m-health service in license-free spectrum. IEEE journal of biomedical and health informatics. 2013 Jan;17(1):19-29.
4. Alumona TL, Idigo VE, Nnoli KP. Remote moni-

- toring of patients health using wireless sensor networks (WSNs). *IPASJ International Journal of Electronics & Communication (IJEC)*. 2014 Sep;2(9).
5. Yan H, Huo H, Xu Y, Gidlund M. Wireless sensor network based E-health system-implementation and experimental results. *IEEE Transactions on Consumer Electronics*. 2010 Nov;56(4):2288-95.
 6. Khan UM, Kabir Z, Hassan SA. Wireless health monitoring using passive WiFi sensing. In 2017 13th International Wireless Communications and Mobile Computing Conference (IWCMC) 2017 Jun 26 (pp. 1771-1776). IEEE.
 7. Yen YS, Chiang WC, Hsiao SF, Shu YP. Using WiMAX network in a telemonitoring system. In 2011 3rd International Conference on Computer Research and Development 2011 Mar 11 (Vol. 1, pp. 313-318). IEEE.
 8. Kim KA, Shin SY, Suh JW, Park C, Cha EJ, Bae HD. Home healthcare self-monitoring system for chronic diseases. In 2012 IEEE International Conference on Consumer Electronics (ICCE) 2012 Jan 13 (pp. 486-487). IEEE.
 9. Li WJ, Luo YL, Chang YS, Lin YH. A wireless blood pressure monitoring system for personal health management. In 2010 Annual International Conference of the IEEE Engineering in Medicine and Biology 2010 Aug 31 (pp. 2196-2199). IEEE.
 10. Park J, Cho J, Choi J, Nam T. A zigbee network-based multi-channel heart rate monitoring system for exercising rehabilitation patients. In TENCON 2007-2007 IEEE Region 10 Conference 2007 Oct 30 (pp. 1-4). IEEE.
 11. Pawar PA. Heart rate monitoring system using IR base sensor & Arduino Uno. In 2014 Conference on IT in Business, Industry and Government (CSIBIG) 2014 Mar 8 (pp. 1-3). IEEE.
 12. Patwari N, Brewer L, Tate Q, Kaltiokallio O, Bocca M. Breathfinding: A wireless network that monitors and locates breathing in a home. *IEEE Journal of Selected Topics in Signal Processing*. 2014 Feb;8(1):30-42.
 13. Adib F, Mao H, Kabelac Z, Katabi D, Miller RC. Smart homes that monitor breathing and heart rate. In Proceedings of the 33rd annual ACM conference on human factors in computing systems 2015 Apr 18 (pp. 837-846). ACM.
 14. Lee S, Park YD, Suh YJ, Jeon S. Design and implementation of monitoring system for breathing and heart rate pattern using WiFi signals. In 2018 15th IEEE Annual Consumer Communications & Networking Conference (CCNC) 2018 Jan 12 (pp. 1-7). IEEE.
 15. Abdullah A, Ismael A, Rashid A, Abou-ElNour A, Tarique M. Real time wireless health monitoring application using mobile devices. *International Journal of Computer Networks & Communications (IJCNC)*. 2015 May;7(3):13-30.
 16. Liang T, Yuan YJ. Wearable medical monitoring systems based on wireless networks: A review. *IEEE Sensors Journal*. 2016 Dec 1;16(23):8186-99.
 17. Triantafyllidis AK, Koutkias VG, Chouvarda I, Adami I, Kouroubali A, Maglaveras N. Framework of sensor-based monitoring for pervasive patient care. *Healthcare technology letters*. 2016 Aug 12;3(3):153-8.
 18. Puvaneshwari S, Vijayashaarathi S. Efficient Monitoring system for cardiac patients using Wireless Sensor Networks (WSN). In 2016 International Conference on Wireless Communications, Signal Processing and Networking (WiSPNET) 2016 Mar 23 (pp. 1558-1561). IEEE.
 19. Tan YY, Chung WY. Mobile health-monitoring system through visible light communication. *Bio-medical materials and engineering*. 2014 Jan 1;24(6):3529-38.
 20. Rani T.P, Anees B, Geetha Priya N, Mahalakshmi S. Automated Billing System Using Li-Fi (Light Fidelity). In 2016 International Journal of Industrial Electronics and Electrical Engineering. 2016 Jun; 4(6).
 21. Sindhu M, Priyanka M, Swedha AK, Ranjana RA, Sujatha R. Cryptography Based Secured Lifi for Patient Privacy And Emergency Health Care Service. *International Journal of MC Square Scientific Research*. 2017;9(1):86-97..
 22. Karame GO, Soriente C, Lichota K, Capkun S. Securing cloud data under key exposure. *IEEE Transactions on Cloud Computing*. 2017 Feb 16.

A Low Cost Hardware Based Fall Detection and Call for Help System for Elderly Person

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Abstract

Context: Aging is common for a Human being. Especially an old aged person needs attention due to weakening in their physical capability. Fall is one of the major problems faced by elderly persons during their daily day activities. Falls are caused due to accident, loss of consciousness. Fall poses a serious impact on health issues of an elderly person. Fall detection is one of the necessary actions to be taken. So the fall detection system is needed. Thereby here the development of the system includes methodology based on sensor-video integration technology. The event of fall occurrence can be detected using the sensor as well as the camera and the acquired information is sent as messages and live video feed to the user in case of emergency through making use of Wi-Fi technology.

Keywords: Accelerometer Sensor, camera, video, emergency, Wi-Fi, message, fall detection.

Introduction

With the increase in population, concerning the persons around the age groups of 60 years and above needs help in one way or another who are living independently in a home environment after the family members left for their work. The following figure shows the causes of fall.

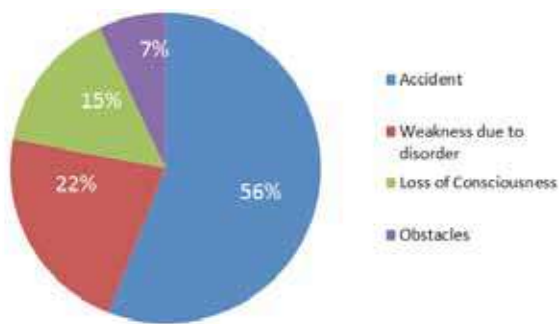


Fig 1: Causes offall

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According to World Health Organization^[1], the old aged group increases quickly in population, the percentage of fatal fall rates increase gradually in age groups from 65 to 85 and above shows the detail about the fall risk of old aged person. Many accidental falls occurs and causes injuries and health issues lead to long term among them. Considering as the main issue the system should be developed in order to help old aged people in best way, detecting the fall occurrence especially will assist them during that crisis. On the account of the importance of detecting the fall occurrence, the risk of falling can be avoided. The major challenge and problem among older person is falling. Fall may lead to extend of death among them if it is handled. Various fall detection systems were designed in order to bring at low cost and better efficient one. Many systems include methodology based automatically detect the fall event using acoustic sensors^[2] and also the system involves creating signatures for each activity and classifying the fall event using Doppler radar and analyzing the difference in time of signatures and representing in time frequency signals^[3,8] and taking the features of each posture of body and segmenting them to detect the fall event^[5]. The system used in identifying the fall event based on which uses, namely infrared^[14], Tri axial accelerometer sensors^[12], fibers optic^[15], ultrasonic sensor^[16], floor

pressure sensing sensors^[18], wearable cameras^[9-11,21] and using smartphone.

Proposed Model: Here the fall detection system is developed and implemented with the aim to achieve low cost, reliable and efficient one to serve as useful one. In addition to that a web camera separately connected to them to record the video automatically if the event is to befall occurrence. Firstly the prototype is developed by a Raspberry Pi board for sending message.

Now nextly this system is developed based on raspberry Pi 3 model B+ board, for storage as well as it has built in Wi-Fi chip for accessing internet connection and subsequently to reduce the cost.

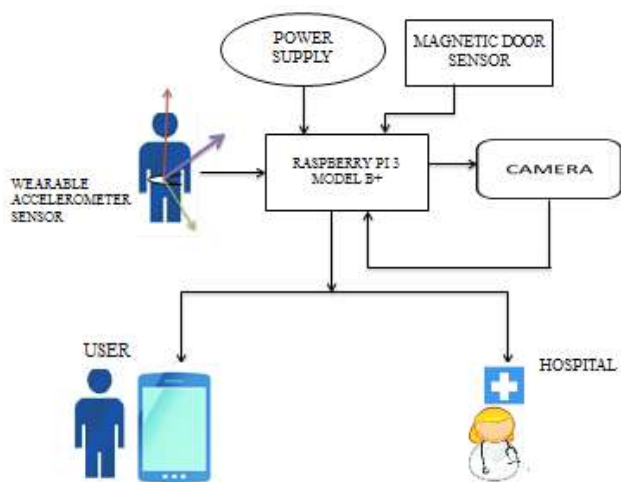


Fig 2: Proposed Model

And there are many visions based devices available for fall detection these days. The implemented fall detection system will notify the rescuers with the message as well as live video feed in order to provide assistance. The system can be easily be installed and established with wireless communication.

Proposed Fall Detection System: The fall detection system consists of tri axis accelerometer sensor and web camera for capturing the fall event. This sensor will sense the acceleration, velocity and position of the person. Thereby with the acceleration values obtained from the sensor will be compared with the fixed threshold value. Using this data the fall event occurrence can be detected and a message will be send as alert to the rescuers to assist them. By means of the Wi-Fi technology, communication can be made easier. A web camera is used for capturing image of the fall event. Here both the sensor and video technology has been used. Additionally, magnetic door sensor is used

as for detecting the door activities such as door open and the door close.

The main aim is to detect fall and handle the emergency situation in correct manner without any delay. The timing plays an important part in this system. Based on the occurrence, Fall can be fatal or not but causes some serious impact in the health of the aged person. Health of the person can be seriously damaged due to their natural weakness. This fall detection system will probably provide immediate action in the way of message form to respective hospital and member of the family utilizing the python programming language. Elderly person who lives independently in home environment after the family members left for daily activities outside. Here the following fig 3 and fig 4 shows the proposed fall detection system and python programming setup.



Fig 3: Proposed Fall Detection System

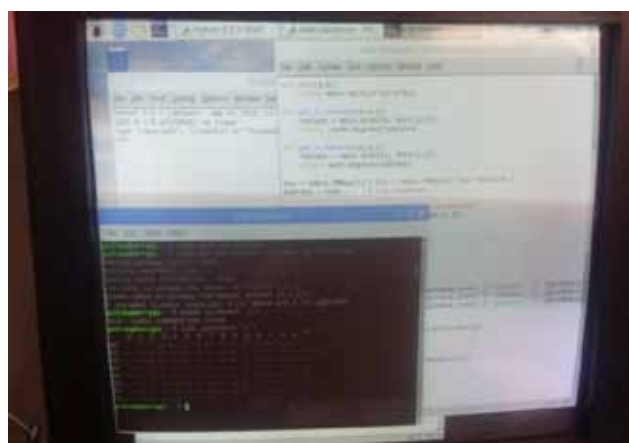


Fig 4: Python Programming Setup

In the python programming setup, utilizing the GPIO library the coding is done. Programming language plays an vital role in the software part. The types of fall are shown in the following table 1.

Table 1:

S.No.	Types of Fall
1	Normal fall
2	Falling forward
3	Falling right
4	Falling left
5	Falling backward
6	Falling due to loss of conscious state
7	Falling due to obstacles (furniture).
8	Accidental fall

Algorithm Description: The algorithm used for fall detection system is as follows. The First step of the algorithm involves the acquiring the raw data from the 3 axis of the accelerometer sensor namely X, Y, Z axis. This axis, which gives the details of roll and pitch. This accelerometer sensor value will be higher compared with the normal acceleration value.

Normally the movement of older person will have low acceleration values. But when fall occurrence takes place means the acceleration value of the person will be higher than the normal acceleration. These acceleration values can be compared with the threshold values. The values from the 3 axis of the accelerometer can be calculated as follows

$$\|F_A\| = \sqrt{F_{AX}^2 + F_{AY}^2 + F_{AZ}^2} \tag{1}$$

From the above equation (1), the data from each axis can be calculated and compared with threshold value. The algorithm is based on threshold based method. Now the steps involved for the fall event and door event are tracked one by one.

The steps how the proposed fall detection system will work are given as

The variables are used for assignment as the accelerometer sensor is a digital one. So the values will be 0 and 1.

Input: ox; fall detection x, y, z axis values are detected by the sensor.

Input: m; magnetic force value detected by the sensor.

Output P, K; P=1 if fall detection, K=1 if door opened, P=0, K=0 if it is off state.

- 1: Start.
- 2: Set the ox threshold value, x, y, z axis.
- 3: Set the m distance and time.
- 4: Connect fall detection sensor and magnetic door sensor to Raspberry Pi.
- 5: Repeat
- 6: Read ox from sensor.
- 7: Read m from sensor.
- 8: If $ox \leq x$ then $P=1$
 - {Send SMS for registered mobile number, Trigger camera to ON state, Ask request for video Send video same number}.
- 9: If $m \text{ distance} > \text{distance} \ \& \ m \text{ time} \leq \text{time}$ then
 - $K=1$
 - {Send SMS for registered mobile number}.
- 10: Else Set $P=0, K=0$ and go to step 4.
- 11: Until 1000ms.
- 12: End.

Now, the working of the proposed fall detection system is as follows will clearly give the idea of the system how it detects falls and proceed with the information to the next stage. The accelerometer sensor is fixed to the body as in the belt part so that the acceleration value varies for each activity. But the obtained value can be compared with the predefined value.

This whole system will provide only the detail of the fall event and the other activities of the person. Time delay is set in order to determine the duration. The advantage of this system is monitoring of 24 hours is not needed.

The condition of the person can be judged from this kind of system to provide assistance without any delay. Taking the health as the main concerns the fall detection system will be helpful.

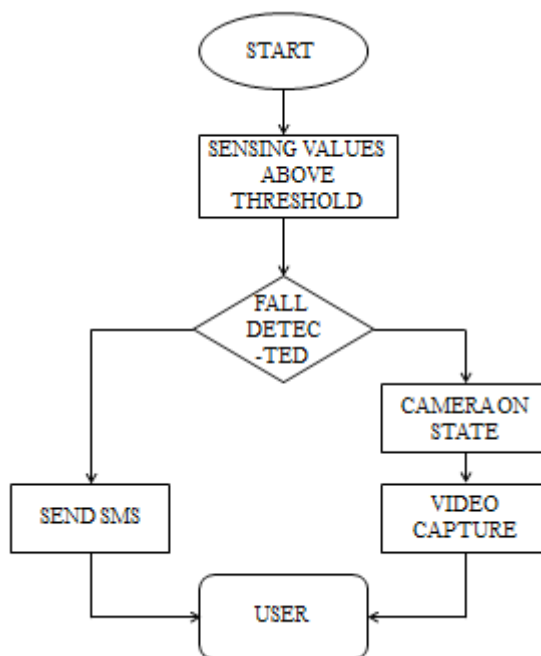


Fig4: Flowchart of the Proposed System

The fall detection system works based on the methodology of accelerometer sensor which plays a vital part of the system. The sensed value of the sensor from the axis based on the calculation exceeds the value of threshold value means the system works continues the process as given in the flowchart otherwise it stays away. This system mainly focuses on detecting the fall not just only intimating by message. Video feed brings the rescuers to handle the situation correctly. Health issue caused due to fall event can be serious or minor problem to the affected elderly person but needs some attention to them.

Alert System: The real time monitoring system includes the live video feed with the every movement of the person [19]. Here the alert system is developed using Raspberry Pi 3 model b+ has built-in Wi-Fi chip to access internet connection where wireless communication is established in which the message is sent to family members and hospital for providing assistance in emergency situations. The alert is made through SMS and MMS to user mobility.

This important feature can be added to the alert system in future based on pre-set time and the time taken by the system to send the message and video to the user

without the false alarm rate it. The time delay is set as 2 mins it is enough for the fallen person to recover from the fallen state to normal state. Directly the image of the fall event is provided visually to the user to take action for the event .communication are made easily to the nearest hospital and member of the family

Here magnetic door sensor is utilized to monitor the door is closed or in open state with the addition to detecting the fall event. When the person does not recover for a long period of time, the fall detection system will come to the state that the assistance is needed for the person immediately from the video.

Here the video captured by the camera will be sent to the user or care unit to know the status of the fall event as well as recovery. The condition of the person can be severe or less .This fall detection will continuously check for the fall event whereas the privacy of the person is protected. Privacy of the person is also considered as the vital aspect of the fall detection system. This alert system will provide information about the status of the person in home environment who lives independently thereby helpful for family member and hospital The following figure 5 shows the fall detected scenario.



Fig 5: Fall Detected Scenario

Based on the fall event occurrence the message is sent to the user as alert to make a call for help immediately in order to avoid the condition of the person severe. The false rate of the fall occurrence will be less compared to other fall detection system. The size of the video sent to user mobile has some limitations. The size of the file plays an important role so that the captured image can be sent as alert to the user. The video consists of continuous frames. Here web camera is used with high resolution so that the picture quality will be high. The following fig 6 shows the alert message and fig. 7 shows the video sent to user’s mobile for notification.

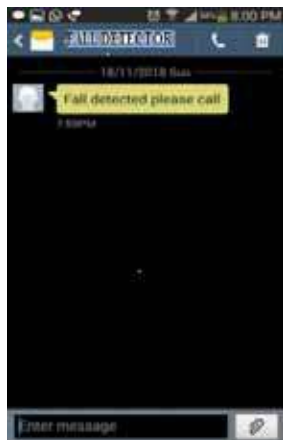


Fig 6: Alert message



Fig 7: image of the fall event

Here SMS message and video message to 2 different users is shown in the above figures.

Results and Discussions

A. Parameters: The parameters needed for calculations are in order to measure the performance of the system as follows .They are

- Sensitivity
- Specificity
- Accuracy

And it is defined as Sensitivity=TP/TOT P.

Specificity=TN/TOT N.

Accuracy= (TP+TN)/TOT Event.

Where TP= True Positive.

TN=True Negative.

TOT P = Total Positive.

TOT N= Total Negative.

Based on the proposed fall detection system, performance of the system is desirable. The fall rate occurs due to some above mentioned reasons. Hence the false rate of falls can occurs sometime due to the increase in the acceleration value so based on the calculation., it can be analyzed but using the web camera which gives an advantage of viewing the event whether the fall occurs or not and also the recovery status. Capturing the fall event is an additional feature added to the system. Therefore the fall detection system has provided satisfactory for the user with the capability of visually analyzing the situation. Compared to other fall detection system monitoring the other activities is evaded. And the only fall event is needed so this system is suitable for fall detection. The following table shows the result in terms of percentage

Table 2:

PARAMETERS	PERCENTAGE
Accuracy	96%
Sensitivity	96.6%
Specificity	97%

Conclusion

Here we designed a fall detection system using

Sensor-video integration technology. Our work offers a way in protecting the privacy of the person during the detection of fall occurrence. This system gives a novel approach to send the information in the form of video as MMS messages as well as SMS. An Experiment carried out shows the results obtained for detecting the fall occurrence in the independent home environment gives an accuracy of high level which is desirable for fall detection system.

In future work, the improvement of the system will be based on how to reduce the false alarm rate to some extent.

This fall detection system is very efficient, low cost and reliable one.

Ethical Clearance: Self (own inputs are taken and data are collected from no external source)

Source of Funding: Self

Conflict of Interest: Nil

Reference

- [1] World Health Organization, World Health Organization. Ageing, Life Course Unit. WHO global report on falls prevention in older age. World Health Organization; 2008.
- [2] Li Y, Ho KC, Popescu M. A microphone array system for automatic fall detection. *IEEE Transactions on Biomedical Engineering*. 2012 May;59(5):1291-301.
- [3] Liu L, Popescu M, Rantz M, Skubic M. Fall detection using Doppler radar and classifier fusion. In *Proceedings of 2012 IEEE-EMBS International Conference on Biomedical and Health Informatics* 2012 Jan 5 (pp. 180-183). IEEE.
- [4] Mellone S, Tacconi C, Schwickert L, Klenk J, Becker C, Chiari L. Smartphone-based solutions for fall detection and prevention: the FARSEEING approach. *Zeitschrift für Gerontologie und Geriatrie*. 2012 Dec 1;45(8):722-7.
- [5] Yu M, Rhuma A, Naqvi SM, Wang L, Chambers J. A posture recognition-based fall detection system for monitoring an elderly person in a smart home environment. *IEEE transactions on information technology in biomedicine*. 2012 Nov;16(6):1274-86.
- [6] Casares M, Ozcan K, Almagambetov A, Velipasarlar S. Automatic fall detection by a wearable embedded smart camera. In *2012 Sixth International Conference on Distributed Smart Cameras (ICD-SC) 2012 Oct 30* (pp. 1-6). IEEE.
- [7] Ozcan K, Mahabalagiri AK, Casares M, Velipasarlar S. Automatic fall detection and activity classification by a wearable embedded smart camera. *IEEE journal on emerging and selected topics in circuits and systems*. 2013 Jun;3(2):125-36.
- [8] Wu M, Dai X, Zhang YD, Davidson B, Amin MG, Zhang J. Fall detection based on sequential modeling of radar signal time-frequency features. In *2013 IEEE International Conference on Healthcare Informatics 2013 Sep 9* (pp. 169-174). IEEE.
- [9] Chua JL, Chang YC, Lim WK. A simple vision-based fall detection technique for indoor video surveillance. *Signal, Image and Video Processing*. 2015 Mar 1;9(3):623-33.
- [10] Bian ZP, Hou J, Chau LP, Magnenat-Thalmann N. Fall detection based on body part tracking using a depth camera. *IEEE journal of biomedical and health informatics*. 2015 Mar;19(2):430-9.
- [11] Hernandez SD, DeLaHoz Y, Labrador M. Dynamic background subtraction for fall detection system using a 2D camera. In *2014 IEEE Latin-America Conference on Communications (LATINCOM) 2014 Nov 5* (pp. 1-6). IEEE.
- [12] Yuan X, Yu S, Dan Q, Wang G, Liu S. Fall detection analysis with wearable MEMS-based sensors. In *2015 16th International Conference on Electronic Packaging Technology (ICEPT) 2015 Aug 11* (pp. 1184-1187). IEEE.
- [13] Kau LJ, Chen CS. A smart phone-based pocket fall accident detection, positioning, and rescue system. *IEEE journal of biomedical and health informatics*. 2015 Jan;19(1):44-56.
- [14] Chen WH, Ma HP. A fall detection system based on infrared array sensors with tracking capability for the elderly at home. In *2015 17th International Conference on E-health Networking, Application & Services (HealthCom) 2015 Oct 14* (pp. 428-434). IEEE.
- [15] Feng G, Mai J, Ban Z, Guo X, Wang G. Floor pressure imaging for fall detection with fiber-optic sensors. *IEEE Pervasive Computing*. 2016 Apr;15(2):40-7.
- [16] Chang YT, Shih TK. Human fall detection based on event pattern matching with ultrasonic array

- sensors. In 2017 10th International Conference on Ubi-media Computing and Workshops (Ubi-Media) 2017 Aug 1 (pp. 1-4).IEEE.
- [17] Shen RK, Yang CY, Shen VR, Chen WC. A novel fall prediction system on smartphones. *IEEE Sensors Journal*. 2017 Mar 15;17(6):1865-71.
- [18] Minvielle L, Atiq M, Serra R, Mougeot M, Vayatis N. Fall detection using smart floor sensor and supervised learning. In 2017 39th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) 2017 Jul 11 (pp. 3445-3448). IEEE.
- [19] Carecams Website. Available online: <https://www.carecams.co.uk/peace-of-mind-cameras> (accessed on 30 November 2017).
- [20] Li X, Nie L, Xu H, Wang X. Collaborative fall detection using smart phone and Kinect. *Mobile Networks and Applications*. 2018 Aug 1:1-4.
- [21] Xu T, Zhou Y. Elders' fall detection based on biomechanical features using depth camera. *International Journal of Wavelets, Multi resolution and Information Processing*. 2018 Mar 24;16(02):1840005.

Real Time Dengue Prediction Using Machine Learning

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Abstract

Context: Dengue is generally spreading the endemic zones for atmosphere zones. In a whole world, transmitted to an individual by an Aedes Aegyptus mosquito, dengue load in India is expanding at an upsetting rate. The commitments of expanded versatility, both vector and human populaces, urbanization and atmosphere changes are the most critical factors to clarify the expanding episode of dengue. Generally, the different calculations looked at, it was wasteful to evaluate the exactness for early dengue illness expectation. The recommended framework is to build up an application for Smart Prognosis Dengue (SPD) Model for AI development to foresee constant Dengue illness. It will continue with unmistakable AI approaches going from basic classifiers like Decision Tree, Logistic Regression. Thus, the Logistic Regression Algorithm gives the most extreme exactness precision will analyse for the dengue expectation. By utilizing both the equipment and programming setup, it joins the AI ideas with the expectation calculation and furthermore gives the framework can be altered to produce risk alert and area explicit forecasts.

Keywords: Machine Learning, Logistics Regression Algorithm, Raspberry Pi 3, GSM Module, GPS Module

Introduction

Dengue Disease & Dengue Hemorrhagic Disease is a critical significant ailment in both metropolitan and country regions of the nature. Aedes mosquito's family including Aedes Aegyptus mosquitoes, Aedes Albopictus mosquitoes, convey as the superior transmittal method for dengue irresistible infection. Essential dengue infection in people frequently realize a scope of expository manifestations, of fever to potentially pernicious dengue disorder, and powerful antiviral specialists equipped for treating dengue disease are not accessible at present.

The most demanding reason for this task is dengue infection forecast utilizing different spaces like AI calculations. At first, recognize the appearances of dengue experiences patients and forecast starts this

distinguishing proof. The informational collections are utilized for pre-preparing and to estimate exactness precision. The different AI calculations are examined in the approaching areas.

Accordance with the World Health's Organizations (WHO), dengue infection has bent over worldwide over hasty quintet decades. Around 200 to 750 million new infectious illnesses happen once per year alongside 70 nations. Numerous analysts are chasing away at part to anticipate and control the spread. In the advanced years, expanded research has concentrated on a scene the study of disease transmission utilizing machine learning approaches for better infection forecast.

In this desire significant to determine the appropriate of data acquired by various hospitals and health care units for the early detection along with controlling of dengue. Most patients recuperate inside around multi-week. Nonetheless, a few patients turn out to be more awful and create extreme stomach torment, tireless retching, discharge (gums, nose, under the skin, gastrointestinal), and inconveniences including the heart, liver, and lungs. Presently, treatment is strong and antibodies proceed a work in progress. In spite of the evidence that dengue is regional in no below than 100 nations in the tropical

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zone and subtropical zone, these territories occasionally experience expanded hazard when mosquito populaces increment in vicinity to powerless human residence. Natural variables are known to impact the commonness of mosquito vectors and the dangers of people getting to be tainted with dengue.

By cause of the likelihood of serious effects and demise, there is incredible enthusiasm for anticipating these ailment flare-ups. Because of general wellbeing worries about the spread and expanding degree of dengue, the US Center for Disease Prediction and Control, the US Departments of Defense, the US Departments of Health's and Human Service, the US Departments of Homeland's Security, and different US government organizations combined to support a Dengue Prediction Challenge venture in 2015. The central point of the venture was on foreseeing key measurements for verifiable dengue seasons utilizing just information from timeframes before those seasons.

Related Study: In order to state that, in this exploration displays the examination about the expectation of DHF in Bandung authorization utilizing K-Means Clustering as pre-handling strategy and Support Vectors Machines (SVM) calculations as order technique as indicated by authentic information of DHF and climate information. The most impact situation is marking class situation since K Means Clustering name technique demonstrates exactness [1].

In this paper clearly explained, in this exploration we consultation about Naive Bayer's algorithm for classification that describes utilization for dengue disease prediction. The preeminent aspiration of this related survey is, to resolve proper prediction system for dengue. The methodology used to diagnose a patient is modified NB predictor algorithm [2].

In this proposed paper, the dengue representation for the vulnerability map for nation Malaysia in the area of state Selangor and its areas, which is observed to be most astounding dengue episodes happened in 2014, as the ascent of rates were impelled from month of May till June the greatest number of occurrences can be restricted for the specific directions [3].

It offers a method to classify mosquitoes using SVM with the feature of MFCC. From the test results, they so that the conclusion obtained SVM using Kernel is better than previous research using back-propagation. This research may also be improved by classification using

the Neural Networks, as well as other data retrieval method to get higher accuracy [4].

In proposed paper, the fundamental inspiration of this procedure is to characterize information and give appropriate route to the applicants for removing valuable data from information. It effectively recognizes a reasonable calculation for the exact present calculation result from it. They distinguish calculation based on their outcome investigation and the preciseness of the forecast [5].

In the proposed methodology, household clustering of dengue is to be done by using dengue serotypes depending upon the age group through applying K-means Clustering Algorithm is increasing the proficiency of the output [6].

Proposed System: In a proposed system, the "Smart Prognosis Dengue Model" is to prediction of dengue that adopts the Logistics Regression Algorithm, as it supports heterogeneous data types and provides statistical measures with a better predictive power. Traditionally, various algorithms are used to predict the dengue cases. It is not sufficient method to give a correct accuracy, when compared to Gradient Boosting Algorithm. The Gradient Boosting Regression (GBR) calculations are fundamentally utilized for foreseeing the information, and in GBR are utilizing Ensemble Technique. When endeavour to foresee the objective variable utilizing any AI strategy, the primary driver of distinction in real and anticipated qualities are noise, difference, and bias. Group decreases these components (with the exception of commotion, which is an unchangeable mistake). A gathering is only an accumulation of indicators which meet up (for example mean everything being equal) to give the last expectation.

The final product of a fitted relapse examination is that known highlights and can foresee the obscure yield esteem. Here is the procedure that boosting relapse pursues,

1. Predict an underlying assessment of 0.0
2. Use the genuine qualities to ascertain the blunder in the underlying forecast.
3. Split the information into gatherings utilizing the highlights of the information, with the objective of putting information with comparative mistake into a similar gathering. For each gathering, locate the normal blunder

4. For each datum point in that gathering, add the normal blunder to the present forecast
5. Calculate the new mistake for each point for the new expectation
6. Then recurrent the cycle over again beginning at stage 3 the same number of times as wanted. For anticipating the information, the Gradient.

Boosting Regression (GBR) calculation is utilized, and in GBR are utilizing Ensemble Technique. When the attempt to anticipate the objective variable utilizing any AI strategy, the primary driver of contrast in genuine and anticipated qualities are commotion, fluctuation, and predisposition. Gathering lessens these variables (with the exception of commotion, which is a final mistake). A gathering is only an accumulation of indicators which meet up (for example mean all things considered) to give the last expectation. The takeaway is that powerless students are best joined in a way that enables everyone to solve a constrained segment of the issue.

Any machine learning routine can be utilized as a weak learner student. Neural nets, support vector machines or some other would work, yet the most generally utilized weak learner is the decision tree.

Generally, Its incorporated with Mean Square Error for improving the levels of performance as it's a part of measure, how close a fitted line is to the data points. It can use a new configuration computer called Raspberry PI with GSM and GPS module. This application can also contribute and generates the risk maps and its location-specific predictions.

Methodology

A.Data Pre-Processing: The dataset contains all the data which the learning model should learn for making the right forecasts. The crude information may have many varieties in the estimations of each element which may prompt off base outcomes. Thus the learning procedure will pre-process the dataset.

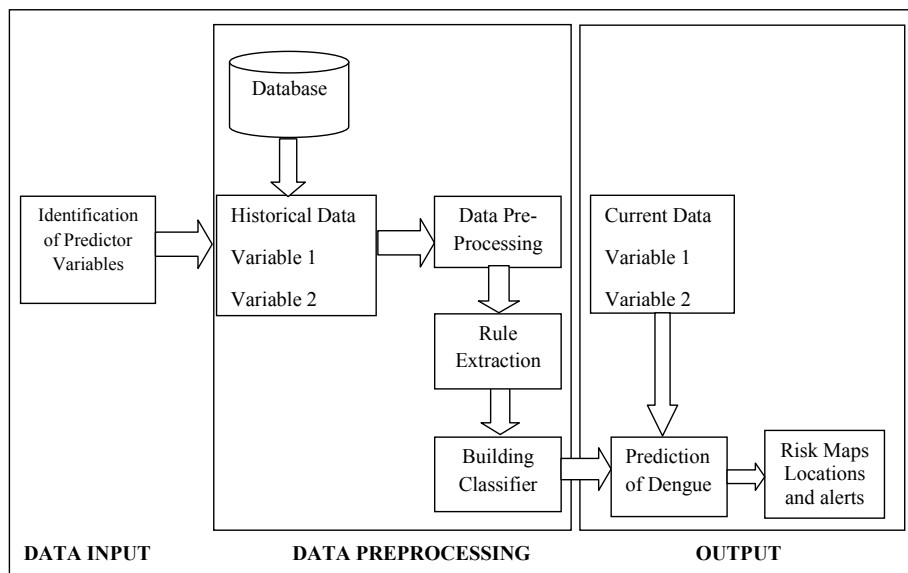


Fig 1: Smart Prognosis Dengue (Spd) Model

B. Prediction of Missing Values:

- **Removal of Data Occurrences:** The information occasion which has a missing an incentive for any element was evacuated. On these lines expelled the untrustworthy information point from the preparation set and yet, it has decreased the dataset estimate from 5000 to 1000
- **Filling the Missing Values:** The missing qualities in the datasets were doled out the most much of

the time happening an incentive for that include. By utilizing the bundle “Pre-processing” and the usefulness “Imputer()” from scikits.learn.

- By seeing that utilizing the second methodology (for example Imputer) the outcomes were progressively exact

C. Segregating the Dataset Into Standardization:

They can be an enormous variety in the measures of a component over the sufficient dataset. This

will make it troublesome for the model to gain proficiency with the information legitimately. It makes vital to institutionalize the info. It very well may be actualized by taking out the mean from the rate of each credit and scaling to unit changes. For this occurrence, utilizing the usefulness of “Standardscalar()” to decide from the preparing package.

D. Conversion of Array To Nominal Values: The component "states" in the dataset incorporates the names of three states. Its need to change over character esteems to numerical esteem. By applying the equivalent by utilizing LabelEncoder() usefulness of the pre-handling bundle.

E. Integration of Raspberry Pi With Generates the Alert Maps: At long last, to execute the content in Raspberry Pi 3, to foresee the dengue is there or not with given side effects. On the off chance that dengue ailment is found for the individual, raspberry pi coordinating with machine learning concepts to intimate the dengue sickness is found or not. It can likewise send and advise the cautions to influenced individual or specialist. Alongside that, it very well may likewise create risk map areas utilizing GPS and GSM modules.

Algorithm: In Dengue Prediction Model are mainly using two algorithms and they are;

1. Logistic Regression Algorithm(LRA)
2. Mean Square Error (MSE)

Logistic Regression Algorithm: Logistic Regression is an exceptional among the most utilized Machine Learning calculations for parallel grouping. Logistic Regression is go-to technique for double order. It gives you a discrete paired result among 0 and 1. Calculated Regression estimates the connection among the needy variable and the at least one determining factors, by assessing probabilities utilizing its natural strategic function. These desires should then be changed over into a paired number that one numerous really make a forecast. This work of Logistical Regression Algorithm likewise called a sigmoid capacity. The strategic capacity, additionally called the sigmoid capacity was created by analysts to portray properties of populace development in nature, rising rapidly and maximizing at the conveying limit of the earth. It’s an S-shaped bend that can take any genuine esteemed number and guide it into an incentive somewhere in the range of 0 and 1,

however never precisely at those points of confinement.

The key limit, also called the sigmoid capacity was made by examiners to depict properties of masses improvement in nature, rising quickly and boosting at the passing on farthest point of the earth. It’s a S-shaped twist that can take any certifiable regarded number and guide it into a motivating force some place in the scope of 0 and 1, yet never correctly at those purposes of restriction. $1 / (1 + a^{-\text{esteem}})$

Where a is the base of the typical logarithms (Euler’s number or the EXP () work in your spreadsheet) and regard is the genuine numerical regard. It is used to predict twofold outcomes for a given course of action of self-sufficient components. The yield of Logistical Regression is a sigmoid twist (or even more broadly known as S-twist). In vital regression, there are two achievable event 0 & 1. That object occurs, or it doesn’t. It uses a cut-off a motivating force to make our desire more straightforward. Self-sufficient segments or factors can be hard and fast or numerical elements. Logistical Regression is used to check discrete characteristics (regularly twofold characteristics like 0/1) from many free factors. It anticipate the probability of an appearance by capable data to a logit work. It is similarly called logit regression. These techniques recorded underneath are every now and again used to help improve determined to backslide models join coordinated effort terms, take out features, regularize frameworks, using a non-straight model.

Mean Square Error: The Mean Square Error (MSE) is an estimating capacity the regular even of the errors- that is, the normal squared contrast between the assessed qualities and what is assessed. MSE is a hazard work, relating to the normal estimation of the squared blunder misfortune. The way that MSE is quite often entirely positive (and not zero) is a direct result of arbitrariness or in light of the fact that the estimator does not represent data that could create progressively exact assessments. The MSE is a proportion of the nature of an estimating - it is dependably non-active, and qualities more like zero are better. MSE can speak to the contradiction between the real perceptions and the perception esteems anticipated by the model. In this unique circumstance, it is utilized to decide the degree to which the model fits the information just as in the case of expelling some illustrative factors are conceivable without altogether the model’s prescient capacity.

VI. Experimental Setup Testing Results:

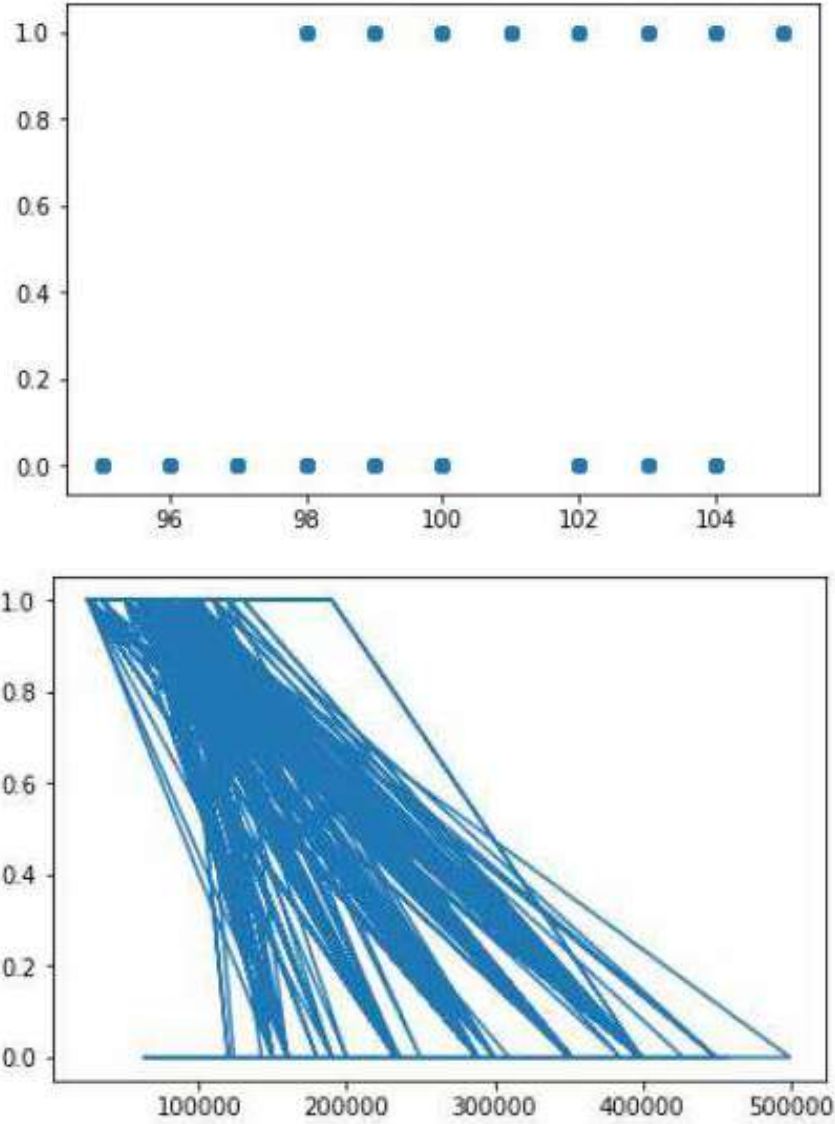


Fig 2: Matplots Representation

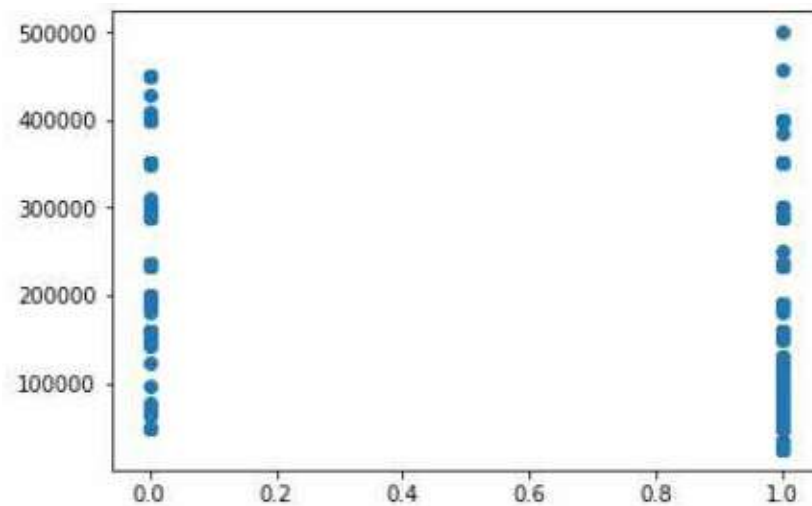


Fig 3: Software Configuration

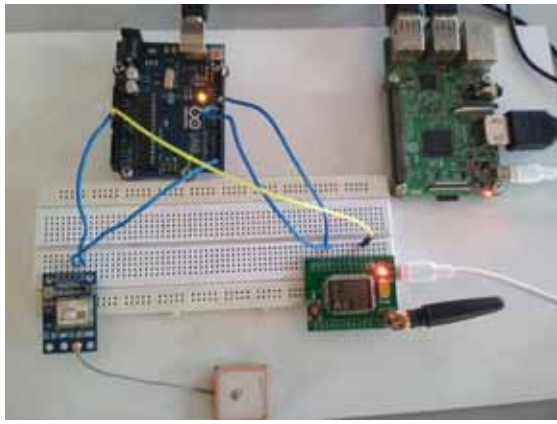


Fig 4: Hardware Configuration Notify When Dengue Is Found



Fig 5: Alert Message and Locations

Conclusion

The proposed conceptual smart prognosis dengue (SPD) recommend advanced method of predetermine and early detection of dengue cases. A standard for predicting the forthcoming dengue outbreaks incorporating Logistic Regression Algorithm. From the undertaken experiments, it shows that Logistical Regression Algorithm capable to obtain good generalization ability compared to Gradient Boost Algorithm, thus enhance the forecast accuracy and Mean Square Error. In the substantial foresight scenario, there are several numbers of factors having their influence on dengue outbreak such as Fever, Platelets, Temperature, Vomiting and Fatigue, etc. The suggested model will useful to governance, specifically Ministry of Health Sector in arranging plans and identifying initiatives needed for the purpose to strengthen dengue control.

Besides, it will also give precedence to the people in understanding and taking precaution steps in preventing dengue epidemic from becoming pervasive.

Source of Funding: Self

Ethical Clearance: The dataset inputs are taken from UCI or Kaggle website. It is an open source online website. Hence there is no ethical clearance will be needed

Conflict of Interest: Nil

References

- [1] M.Mufli Muzakki, Fhira Nhita. The Spreading Prediction of Dengue Haemorrhagic Fever (DHF) In Bandung Regency Using K-Means Clustering and Support Vector Machine Algorithm: IEEE. 2018: 453-458.
- [2] Ms.Harshada Somwanshi, Mr.Pramod Ganjewar. Real-Time Dengue Prediction using Naive Bayes Predicator in the IOT: IEEE.2018: 725-728.
- [3] Nirbhay Mathur, Vijanth S. Asirvadam, Sarat C. Dass. Spatial-temporal Visualization of Dengue Incidences Using Gaussian Kernel: IEEE. 2018.
- [4] Lukman, A. Harjoko, C.K. Yang. Classification MFCC features from Culex and Aedes aegypti Mosquitoes Noise using Support Vector Machine: IEEE. Sep.2017: 17-20.
- [5] Kashish ara Shakil, Sharma Anis, Mansaf Alam. Dengue Disease Prediction using Weka Data Mining Tool: IEEE.2017:
- [6] P.Manivannan, Dr. P. Isakki. Dengue Fever Prediction using K-Means Clustering Algorithm: IEEE.2017:5(1).
- [7] I. Rafique, M. Arif, N. Saqib, S. Siddiqui, M. A. Munir, I.A. Malik. Dengue knowledge and its management practices among physicians of major cities of Pakistan: IEEE.2016: 392–396.
- [8] Wajeehaa Farooqi, Sadaf Ali. A Critical study of selected classification algorithms for dengue fever and dengue haemorrhagic fever: IEEE. 2016:
- [9] Mohd Khalit Othman, Mohd Shahrul Nizam Mohd Danuri. Proposed Conceptual Framework of Dengue Active Surveillance System in Malaysia: IEEE. 90-95.
- [10] M. Hamid, H. Lugova, A. Mon, V. Knight. Awareness and practice related to dengue infection among military cadets in Malaysia: IEEE. 2015.

- [11] L. L. Hermann, S. B. Gupta, S. B. Manoff, S. Kalyanarooj, R.V.Gibbons, B. A. G. Coller. Advances in the understanding, management and prevention of dengue: 2015:153–159.
- [12] Shermon S. Mathulamuthu, Vijanth S. Asirvadaml, Sarat C.Dass², Balvinder S. Gile, Loshini T. Predicting Dengue Incidences Using Cluster Based Regression on Climate Data: IEEE. 2016.
- [13] M. U. Kraemer, M. E. Sinka, K. A. Duda, A. Q. Mylne, F. M. Shearer, C. M. Barker. The global distribution of the arbovirus vectors *Aedes aegypti* and *Ae. Albopictus*: IEEE. 2015.
- [14] P. Siriyasatien, A. Phumee, P. Ongruk, K. Jampachaisri, K. Kesorn. Analysis of significant factors for dengue fever incidence prediction: IEEE.2016: 1–9.
- [15] Ramandeep Kaur, Gaurav Gupta, Gurjit Singh Bhatthal. Demographic Analysis of Dengue Fever Using Data Mining: IEEE.2017:

An Survey on Breast Cancer in Machine Learning

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Abstract

Context: With the fast development of information in biomedical and social insurance networks, it has been a troublesome assignment to separate learning rapidly from accessible information. Breast cancer ahead of time can diminish the hazard rate of life; numerous investigations have demonstrated the relationship of AI calculations in various malady expectation. As health care needs timely and accurate performance for diagnosis, we are making use of data for better understanding about stage of cancer, prediction, effective decision making, maintenance of breast cancer record, organizing structured and unstructured data to give accurate results. This paper summarizes a traditional survey and the importance of dataset in health care machine learning can be implied.

Keywords: Health care, prediction, diagnosis.

Introduction

Breast cancer was the most hazardous disease after lung disease. Early discovery can endure the general population lives since it is simpler to treat and keep the tumor from extended. Tumor is the irregular development of cells. Enduring, the X-beam was the main technique that was utilized to distinguish the bosom malignant growth. In any case, numerous another strategies have been produced and proposed for distinguishing process that are more proficient than x-beam technique, for example, neural systems, artificial consciousness, and information mining.

Health care communities have advanced in achieving the accuracy using big data analytics. The main potential of Big-data lies in the delivery of the proper medicine, using an accurate decision support system for clinical results like extracting literature, changing

times, growing voluminous amount of data continuously with speed and yield better models with high precision results. The four main characteristics of big data are high Volume of data, Variety forms of data, Velocity of streaming data, Veracity of data. Now-a-day's, Big-data gaining importance in terms of precision medicine, which is mainly targeted activities like analyzing daily activities, the patient's genetics, and the environment etc., Analyzing human genome is one of the keys to human health. Large data storage and digitization of records also needs Big-data.

AI has made an extreme improvement throughout the years to help redemption of precise outcomes without human intercession and for better comprehension of crafted by human. It gives sorts of Artificial Intelligence (AI) that helps a framework with the capacity to learn independent from anyone else without being modified unequivocal. It involves six steps for complete process are collecting the data, cleaning the data, analyzing the data, training the data, testing the data and obtaining their result. An AI calculation is managed supervised and unsupervised algorithm. Supervised Learning is a technique, which uses labelled data for learning and then making predictions. The algorithm is trained with a specific task driven ability to map the output with the input given. The sort of supervised learning algorithms are called classification, and prediction. Examples

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of supervised learning types are SVM, K-NN, Naïve Bayes, Neural Networks, Ensembling method, and Decision trees. Labels are not required in unsupervised Learning. This technique involves in finding out the similarities among the input and based on similarities, it groups the data. Clustering is one of the best examples for unsupervised Learning. On clustering technique, the clusters are divided based on their similarities that lie among clusters. K- Means and Hierarchical are types of clustering techniques.

Literature Survey:

A. A Hybrid Model to Support the Early Diagnosis of Breast Cancer: Davi Carvalho, Plácido Rogério Pinheiro, Mirian Calópe Dantas Pinheiro¹ have proposed the Hybrid Model to help the early finding of Breast Cancer, which is utilized as a help in diagnosing. Hybrid model is more accuracy than Bayesian Network. The main objective of the Multi-Criteria Decision Analysis is accomplished an ideal to recognize the most persuasive characteristics of breast cancer. It can be used to obtain accuracy as 95.7% of success, 1.7% of doubt and 2.8% of failure. Given a sufficiently vast database this device will most likely gone through a great many cases in almost no time and alarm the cases with high shot of having breast cancer. Besides with a bigger database, the outcomes will be progressively steady and precise. We will keep on attempting to improve the outcomes and lessen the quantity of individuals who have a late analysis or a superfluous horrendous medical procedure.

B. An Application of Classification Techniques on Breast Cancer Prognosis: andeep Chaurasia, Prasu Chakrabarti, Neha Chourasia² have proposed the Supervised learning is a strategy in which a lot of delegate input-yield sets is displayed to the system. The test has been performed on the Breast cancer malignant growth dataset utilizing three grouping procedures: Naïve Bayes, Decision Tree, and Neural Network. The author can be compared their overall results for benign class is highest in Naïve Bayes classification with 98.65% with 437 true and 6 false predictions in contrast with Neural Network having 94.09% class prediction with 446 true and 28 false predictions and for Decision tree with 96.87% with 433 true and 14 false predictions. The prediction class for malignant class is highest in Neural Network classification with 94.67% with 12

true and 213 false prediction a compared to Naive Bayes algorithm with 91.8% class precision with 21 true and 235 false predictions and in Decision Tree with 90.08% precision with 25 true and 227 false predictions. So the efficiency of Neural Network is highest to predict the malignancy in breast cancer with +2.87% more than Bayesian classification and +4.59% more than Decision Tree.

C. Interpretability of Artificial Hydrocarbon Networks for Breast Cancer Classification:

Hiram Ponce et al.³ have proposed an Interpretability of Artificial Hydrocarbon Networks for Breast Cancer Classification, in which counterfeit hydrocarbon organizes, an AI calculation is changed over into the standard based and tree-based model with high exactness. The proposed methodologies comprised of two stages are data similitude and bunch ID, to assemble a tree-model of the hidden conduct of fake hydrocarbon systems. Diverse atomic parameters of the technique were recognized for interpretability. At that point, we investigated this strategy in the bosom disease characterization utilizing an outstanding open dataset. It can be used for tools are 10 cross fold validation. For the most part, AHN portrays about the component of synthetic inside a natural particle of tumor advancement in the Breast. Information likeness and group arrangement are the two fundamental techniques utilized in AHN classifier. The exactness acquired is 97.85%.

D. Using Machine Learning Algorithms for Breast Cancer Risk Prediction and Diagnosis:

Hiba Asri, Hajar Mousannif, Hassan Al Moatassime, Thomas Noel⁴ have proposed the performance comparison between different machine learning algorithms are support Vector Machine (SVM), Decision Tree, Naive Bayes and k-Nearest Neighbors on the Wisconsin Breast Cancer datasets. The tools used for 10 cross folds validation with Wisconsin dataset has 699 instances with two classes of Malignant (65.5%) and Benign (34.5%). The highest accuracy with the lowest error rate by SVM is 97.13%.

E. Prediction of Breast Cancer using Voting Classifier Technique:

U. Karthik Kumar, M.B. Sai Nikhil and K. Sumanga H⁵ have proposed the prediction of breast cancer by using the voting classifier technique in which they have included the algorithms are Decision tree, SVM, and Naive Bayes. Voting is one of the method of ensemble learning. The properties

which contribute less in exactness and in the forecast of disease are expelled utilizing the positioning calculation. The attributes which contribute less in accuracy and in the prediction of cancer is removed using the ranking algorithm and used 10 Cross-fold validations for avoiding missing values and over fitting in the subsets. Out of all algorithms, Naive Bayes has yielded high accuracy.

F. Automated annotation and classification of BI-RADS assessment from radiology reports:

Sergio M. Castro, Eugene Tseytlin, Olga Medvedeva, Kevin Mitchell, Shyam Visweswaran, Tanja Bekhuis, Rebecca S. Jacobson⁶ have developed a technique which improves the quality assurance of healthcare. It manually analyzes the radiology data reports of mammography. It used the methodology of NLP along with PART. The evaluation is performed on 2159 radiology reports. Selections of the type of radiology documents are made using an output of a rule-based approach called BROK algorithm. The accuracy obtained using PART is 93%, better when compared with Naïve, and SVM. Limitations in this approach are Brooks is ambiguous due to multiple BI-RADS.

G. Breast Cancer Detection using K-nearest Neighbor Machine Learning Algorithm:

Moh'd Rasoul Al-hadidi, Abdulsalam Alarabeyyat, Mohannad Alhanahna⁷ have discussed about two techniques in which, first using an imaging technique for pattern extraction and feature process (noise of the image is eliminated using a Wiener filter), second is to predict the breast cancer using ANN and logistic regression. It used 209 images that were extracted from 50 patient's cases. These images were used for training, testing, and validating processes. In ANN and logistic regression model yielded with 93% accuracy for 209 images.

H. Neural Network Techniques for Cancer Prediction: A Survey:

Shikha Agrawal, Jitendra Agrawal⁸ have discussed a survey on Cancer Prediction. By Using multilayer perceptrons accuracy gained was 97.1% and PNN yields accuracy of 96%. Future enhancement of the work can be improved using numerous neurons in the hidden layer.

I. Identification and analysis of novel microRNAs Proceeding from fragile sites of human cervical cancer: Computational and experimental

approach: G. Reshmi a, S.S. Vinod Chandra b, V. Janki Mohan Babu⁹ have described a novel approach 'Mphred' which first recognizes initial-microns and then post-microns. Zuker's Energy minimization method was used for validation; the validity of 95.60% is gained along with 98.5% specificity and 92.4% sensitivity.

J. Prediction of Cancer Class with Majority Voting Genetic Programming Classifier Using Gene

Expression Data: Topon Kumar Paul et al¹⁰ have proposed an approach, in which different type of cancer and machine learning applications over patient's gene expression data is addressed. As the samples for training the genetic data are limited, most of the method cannot overcome over fitting problem so majority voting genetic programming classifier is proposed for classifying microarray data. The experiment is performed mainly on four data sets, using the proposed model and yielded the best accuracy on prostate cancer with 90.59% and lung carcinoma with 95.50%.

K. Using automatically extracted information from mammography reports for decision-support:

Selen Bozkurt et al¹¹ have introduced a system for decision-support to identify the lesions, that are malignant in nature among mammography reports. It used algorithm are NLP, Bayesian Neural network. The reports of free depicted objects are taken as an input and then using these two approaches, the probabilities of malignancy to each injury in mammography is given as output. The accuracy obtained is 97.58% (precision -98.3%, and recall-98.8%).

L. Fully automatic classification of breast cancer microarray images:

Nastaran Dehghan Khalilabad et al¹² discussed about a strategy called Microarray picture that is utilized for conclusion of destructive cells in the completely programmed characterization of bosom disease microarray pictures. The small scale exhibit imaging strategy helpful for extricating genome datasets (which is taken for DNA); the way toward removing the genome includes three stages called granulating, quality choice from DNA and characterization. A choice tree calculation is utilized continuing and 95.23% exactness is gotten in the visualization of sorts of bosom malignant growths.

Proposed System: The proposed framework aims to utilizing the health care record results as section to

help even advances the analysis of Breast Cancer. It can be used to predict and analysis a breast cancer in a difficult situations. It used to obtain their better accuracy in a breast cancer. Obtained result which used to make decision in a early stage of the breast cancer by using machine learning algorithm.

Conclusion

This paper condenses the examination usefulness in setting up enormous systems in human services utilizing huge information and the utilization of various AI calculations for guess of the malady. The commitment made by numerous specialists for the use of various machine calculations alongside precision is similarly appeared.

Ethical Clearance: Nil

Source of Funding: Self

Conflict of Interest: Nil

References

- [1] DaviCarvalho, PlácidoRogerioPinheiro,MirianCa líopeDantasPinheiro.A Hybrid Model to Support the Early Diagnosis of Breast Cancer.Elsevier B.V .2016.
- [2] Chaurasia, S., Chakrabarti, P., Chourasia, N.An Application of Classification Techniques on Breast Cancer Prognosis. International Journal of Computer Applications.2012
- [3] H. Ponce and M. de Lourdes Martinez-Villaseñor. Interpretability of artificial hydrocarbon networks for breast cancer classification. International Joint Conference on Neural Networks (IJCNN). 2017.
- [4] HibaAsri, HajarMousannif. Using Machine Learning Algorithms for Breast Cancer Risk Prediction and Diagnosis. Elsevier B.V. 2016.
- [5] U. Karthik Kumar, M.B. Sai Nikhil. Prediction of Breast Cancer using Voting Classifier Technique. IEEE 2017.
- [6] sergio M. Castro, Eugene Tseytlin, Olga Medvedeva, Kevin Mitchell, ShyamVisweswaran. Automated annotation and classification of BI-RADS assessment from radiology reports.Elsevier. B.V. 2017.
- [7] Moh`dRasoulAl-headed, AbdulsalamAlarabeyyat. Breast Cancer Detection using K-nearest Neighbor Machine Learning Algorithm.IEEE 2017
- [8] ShikhaAgrawal, JitendraAgrawal. Neural Network Techniques for Cancer Prediction: A Survey. Elsevier B.V 2015.
- [9] G. Reshmi a, S.S. VinodChandra b, V. Janki Mohan Babu. Identification and analysis of novel microRNAs Proceeding from fragile sites of human cervical cancer: Computational and experimental approach. Elsevier B.V 2011
- [10] Topon Kumar Paul and Hitoshi Iba. Prediction of Cancer Class with Majority Voting Genetic Programming Classifier Using Gene Expression Data. IEEE.2009.
- [11] SelenBozkurt, Francisco Gimenez, Elizabeth S. Burnside, Kemal H. Gulkesen. Using automatically extracted information from mammography reports for decision-support. Elsevier B.V.2016.
- [12] NastaranDehghanKhalilabad a, Hamid Hassanpour. Fully automatic classification of breast cancer microarray images. Elsevier B.V.2017

Health of the Elderly in India: A Socio-Legal Study

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Abstract

Context: To study the health and social problems of the elderly and their attitude towards life. Materials and Method: Descriptive study carried out in the Field practice area of the Department of Community Medicine in South India. A total of 213 elderly patients (60 years old and above) who attended the outreach clinics were interviewed using a pre-tested schedule. Findings were described in terms of proportions and percentages to study the socio-economic status of the samples and its correlation to social problems. Results: Around 73% of the patients belonged to the age group of 60-69 years old. Nearly half of the respondents were illiterate. Around 48% felt they were not happy in life. A majority of them had health problems such as hypertension followed by Arthritis, Diabetes, Asthma, Cataract, and Anemia. About 68% of the patients said that the attitude of people towards the elderly was that of neglect.

Keywords: *Elderly, Morbidity, Social and Health Problems*

Introduction

“One who always serves and respects elderly is blessed with four things: Long Life, Wisdom, Fame and Power”- *Manusmriti Chapter 2:121*.

“Trees grow over the years, rivers wider, Likewise, with age, human beings gain immeasurable depth and breadth of experience “and wisdom. That is why older persons should be not only respected and revered; they should be utilized as the rich source to society that they are.”- *Kofi Annan*.

“A society for all ages is one that does not caricature older persons as patients and pensioners. Instead, it sees them as both agents and beneficiaries of development. It honors traditional elders in their leadership and consultative roles in communities throughout the world.” -*Kofi Annan* United Nations Secretary-General 1 October 1998.

“It is not sufficient to add years to life but the more important objective is to add life to years”-

WHO Slogan. S: The popular saying, “*old is Gold*” which implies the gravity of aged on the earth. All the things get aged. The things around us both animate and inanimate go through this aging process. The things which don’t have life earn currency and given a due place and reverence on account of aged.

The thing such as old swords, old Icon, old buildings, Cars and so forth. Are revered due to their aged. On contrary, the objects which have life such as animals, human beings are thrown useless things. The old people are not treated well and they need special care and policies for their autumn days. The increasing number of aged population, due to advancement in medical sciences, health care etc, amount a problem on both developed as well as developing countries¹. The policy makers and social scientists focus their attention to abate the seriousness of the problem, which pose before countries, particularly third world countries. For understanding the problem of these aged, we have to know the basic concepts like aging.

Aging is natural, inevitable and ubiquitous phenomenon. Everyone should confront this process,

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if he/she lives. It is irreversible one. Literally it refers to the effects of age. Commonly speaking, it means the various effects or manifestation of old age. In this sense, it refers to various deterioration in the organisms. Aging has been viewed differently by different persons. To politicians and Industrialists, it means power and wealth whereas to a middle class employee, it amounts to a forced retirement. To biologists and social scientists, it is a field of research on biological cells and problems on individual respectively. Handler defined "Aging is the deterioration of nature organism resulting from the dependent essentially irreversible changes intrinsic to all members of a species such that, with the passage of time. They become increasingly unable to cope with the stresses of the environment thereby increasing the probability of death"². Becker defines aging in the broader sense as "Changes coursing in an individual as the result of the passage of time". He adds "Aging consists of two simultaneous components of anabolic building up and catabolic breaking down". Comfort regards it as "the total effect of all changes which occur in a living being with increasing chronological age and which render it more vulnerable or less viable". Birren and Renner define "aging refers to the regular changes that occur in mature genetically representative organisms living under representative environmental conditions as they advance in chronological age". According to Hurlock, old age is the closing period in the life span. It is a period when people move away from previous, more desirable periods or times of usefulness. Stieglitz has rightly observed that "aging is a part of living.

Aging begins with conception and terminates with death. It cannot be arrested unless we arrest life. We may retire aging or accelerate it but we cannot arrest while life goes on, because it is essentially an element in living"³

Demographic Profile of Elderly in India: India, the world's second most crowded nation, has encountered a sensational statistic progress in the previous 50 years, involving very nearly a significantly increasing of the populace beyond 60 years old years. This example is ready to proceed. It is anticipated that the extent of Indians matured 60 and more seasoned will ascend from 7.5% in 2010 to 11.1% in 2025 UNDESA (United Nations Department of Economic And Social Affairs, 2008)⁴. This is a little rate point increment, yet a surprising figure in supreme terms. As per UNDESA information on anticipated age structure of the populace (2008), India had more than 91.6 million older in 2010

with a yearly expansion of 2.5 million old somewhere in the range of 2005 and 2010. The quantity of old in India is anticipated to arrive at 173 million out of 2026 and the share of older persons, above 60 years, in 2050, in India's population is projected to increase drastically by 20 percent.

Rundown figures veil the unevenness and complexities of the statistic progress inside India crosswise over Indian states with various degrees of financial improvement, social standards, and political settings. Anticipated appraisals of populace structure in 2025 for North India hold a "pyramidal" shape, while for south India, the portion of the older populace is required to grow significantly. Straight development in the number of inhabitants in the older is normal in the following 100 years, with more extreme slopes of increment in focal and east India and leveling off of supreme quantities of old in the north, south, west, and upper east .

A few important characteristics of the elderly population in India are noteworthy. of the 8.5% of the population who are elderly, two-thirds live in villages and nearly half are of poor socioeconomic status (2016 report by the ministry for statistics and programme implementation). Half of the Indian elderly are dependents, often due to widowhood, divorce, or separation, and a majority of the elderly are women (70%). of the minority (2.4%) of the elderly living alone, more are women (3.49%) than men (1.42%). Thus, the majority of elderly resides in rural areas, belongs to low SES, and is dependent upon their families.

While the southern states (Andhra Pradesh, Karnataka, Kerala, and Tamil Nadu) might be viewed as the greatest drivers of maturing in India, other Indian states (quite Haryana, Himachal Pradesh, Maharashtra, Orissa, and Punjab) are likewise encountering an old populace blast, to a great extent in provincial regions. Enormous scale investigations of the wellbeing practices of this developing old Indian populace are rare. In any case, data assembled from various overviews and provincial and neighborhood studies point to the high commonness of a few dangerous practices, for example, tobacco and liquor use, and physical dormancy. With these stressors, typically, total information contrasting the 52nd (1995–1996) and 60th Rounds (2004) of the National Sample Survey (NSS) propose a general increment in the reports of infirmities and usage of human services administrations among the old. Access

to administrations, be that as it may, is uneven the nation over.

An analysis of morbidity patterns by age clearly indicates that the elderly experience a greater burden of ailments (which the National Sample Survey Organisation defines as illness, sickness, injury, and poisoning) compared to other age groups (see National Sample Survey Organisation, 2006, Fig. 1), across genders and residential locations. The elderly most frequently suffer from cardiovascular illness, circulatory diseases, and cancers, while the non-elderly face a higher risk of mortality from infectious and parasitic diseases. In developed countries advancing through demographic transition, there have been emerging epidemics of chronic non-communicable diseases (NCDs), most of which are lifestyle-based diseases and disabilities. In contrast, India's accelerated demographic transition has not been accompanied by a corresponding epidemiological transition from communicable diseases to NCDs. As indicated in Figure 15-1, the Indian elderly are more likely to suffer from chronic than acute illness. There is

a rise in NCDs, particularly cardiovascular, metabolic, and degenerative disorders, as well as communicable diseases. While cardiovascular disease is the leading cause of death among the elderly, multiple chronic diseases afflict them: chronic bronchitis, anemia, high blood pressure, chest pain, kidney problems, digestive disorders, vision problems, diabetes, rheumatism, and depression. Concurrently, the prevalence of morbidity among the elderly due to re-emerging infectious diseases is quite high, with considerable variations across genders, areas of residence, and socioeconomic status. It is projected that NCD-related disability will increase and contribute to a higher proportion of overall national disability, in step with the graying of the population. However, a very significant shortcoming of most of the above studies is the use of self-reported data, which, in the absence of autopsies and physician examinations of patients, represents enormous lacunae in data on the conditions affecting the elderly. More detailed studies are needed, other than surveys, to extract information on the epidemiology of health conditions experienced by the elderly.

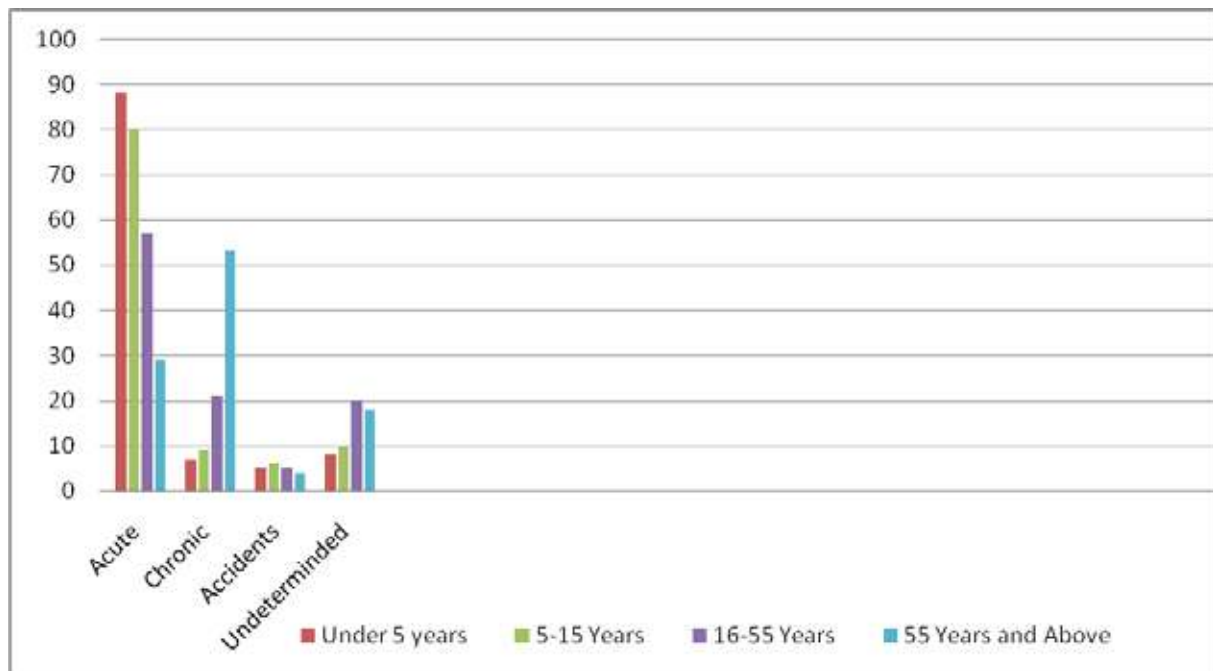


Figure 1: Burden of Illness Type Among Indians. Source: Dror, Putten-Rademaker, and Koren (2008).

Social Factors: A more intensive take a gander at the writing on access to human services uncovers variety over an age angle. More established Indians have revealed higher paces of out-patient and inpatient

visi. The age angle in older wellbeing access is overlaid by social determinants of wellbeing⁵. For one, there is a feminization of the old populace; as indicated by the 2001 registration, the sexual orientation proportion

among the Indian old matured 60 years and more seasoned is 1,028 females for 1,000 guys. It is normal that by 2016, 51% of India's old will be ladies (in provincial regions, this extent will be a lot higher). More ladies report weakness status when contrasted with guys, but a far more noteworthy extent of men is hospitalized when contrasted with females (87 versus 67 for each 1,000 matured people).

Neglected well being needs are progressively articulated among the 33.1% of the old in India who in 2001 were accounted for to have lost their mates, of whom a bigger relative extent is female (half of female old are widows versus just 15% of male older who are single men). Studies have demonstrated that widows are lopsidedly helpless against incapacity, ailment, and poor medicinal services use because of various portability, business, property, and monetary limitations.

Notwithstanding sexual orientation and conjugal status, religion, standing, instruction, financial autonomy, and sanitation have bearing on older wellbeing. Tally displaying of information from the 52nd Round of the NSS shows that the quantity of infections endured by an old individual, determined freely for rustic (Poisson Model) and urban populaces (Negative Binomial Model), incorporate age, sexual orientation, education, accessibility of drinking water and a latrine office, and family unit month to month utilization use. Another investigation of Uttar Pradesh (UP) and Maharashtra found that the older elderly (70 years and more seasoned) were altogether more averse to look for treatment contrasted with the 60–69 age classification, while Muslims were somewhere in the range of 62% and 49% bound to look for treatment in UP and Maharashtra, separately, contrasted with Hindus. This investigation found that old in booked clan/planned standing (SC/ST) classifications were 54% more uncertain and other in reverse classes (OBC) 35% more averse to look for treatment for existing diseases in Maharashtra contrasted with different ranks. At long last, secondary school graduates were twice as likely in UP and multiple times as likely in Maharashtra to look for treatment contrasted with the uneducated gathering. Be that as it may, in the previously mentioned examination, a greater part of the older experienced various bleakness conditions, which makes translating the exhibited outcomes troublesome. The nonattendance of thoroughly structured examinations that evaluate the sorts and seriousness of different sickness conditions in the old further features this reality utilizing information

from a similar review, inferred that 9.5% of provincial occupants and 4.2% of urban occupants report absence of access to everyday necessities of drug, near twofold that of apparel and sustenance.

Broad Health Coverage: Planning and Needs A pathway to national wellbeing change has been imagined by the Planning Commission in the number one spot up to the twelfth Five-Year Plan for India. In October 2010, a High-Level Expert Group (HLEG) was gathered by the Planning Commission to prescribe changes in wellbeing financing, medicate obtainment, network cooperation in wellbeing, wellbeing the executives, and physical and money related standards for wellbeing and HR. Arranging older wellbeing in a more extensive system of all inclusive access and moderateness of Universal Health Coverage (UHC) can possibly change the auxiliary conditions that hamper the prosperity of the matured. We abridge a portion of the manners by which UHC may serve these capacities, all through showing the proof holes that will be required for these capacities to be met.

Key UHC changes relevant to access incorporate the arrangement of extra HR at the Sub-Health Center level (per 5,000 populace), just as the presentation of an extra Community Health Worker (like an Accredited Social Health Activist) in rustic and low-salary urban regions⁶. These changes would guarantee that notwithstanding existing needs of maternal and youngster wellbeing, rising needs in NCD control, just as activity on social and physical hindrances to get to, can be tended to locally (i.e., pair with Village Health and Sanitation Committees and their urban identical). Future research may help decide the extent of consideration at the Sub-Health Center level and the scope of promotive administrations gave at the town/network so as to take into account the necessities of India's older.

It has been proposed by the HLEG, additionally, that a fundamental bundle of consideration (including essential, optional, and tertiary-level administrations) be cashless at purpose of administration using a National Health Entitlement Card⁷ (which would likewise fill in as an identifier for Electronic Medical Records, conveying quiet chronicles and care-chasing profiles). This arrangement will be especially valuable for the older poor, and will require advancement and a far reaching exercise in information accumulation and assemblage on both the client and supplier sides. To this end, methodological commitments from progressing

associate examinations, for example, the Longitudinal Study on Aging in India (LASI) and parallel endeavors universally will be very significant.

Various administrative instruments under the aegis of a recently proposed National Health Regulatory and Development Authority will guarantee wellbeing framework backing, accreditation, and nonstop wellbeing frameworks assessment. This procedure may profit, once more, from the developing base of research on old clients of the wellbeing framework, who may have a more drawn out length of collaborations with the framework just as incredible variety regarding need and weight, affected by changing social determinants. Wellbeing frameworks assessment will also need to reflect age-explicit horribleness and mortality designs, just as that of intersectional older gatherings (the bereaved old, matured of religious minority status, and others).

Conclusion:

The development of the older populace in the coming decades will carry with it exceptional weights of horribleness and mortality the nation over. As we have laid out, key difficulties to access to wellbeing for the Indian old incorporate social hindrances molded by sexual orientation and different tomahawks of social disparity (religion, position, financial status, shame). Physical obstructions incorporate diminished versatility, declining social commitment, and the constrained reach of the wellbeing framework. Wellbeing moderateness requirements incorporate restrictions in pay, business, and resources, just as the confinements of money related insurance offered for wellbeing consumptions in the Indian wellbeing framework.

Among the most critical discoveries that rose in building up this audit was the inadequacy of information on the weights of access and moderateness among older populaces in India. A noteworthy purpose behind this is standard wellbeing information gathering in India isn't intended to reflect or describe neurotic movement: a procedure wherein, by goodness of being alive longer than others, the older are bound to encounter a pathology,

prompting impedance, practical impediments, and at last incapacity. Numerous standard information accumulation strategies (National Sample Surveys, Census information, or passing endorsements) in India don't catch neurotic movement nor do they disaggregate dreariness and inability results among the older.

Ethical Clearance: is taken from Departmental Research Committee to Amity Law School, Amity University, NOIDA, U.P

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References

- 1 Acharya A, Ranson K. Health care financing for the poor: Community-based health insurance schemes in Gujarat. *Eco and Poli Wee.* 2005;141–4.
- 2 Alam M. Ageing in India: Socio-economic and Health Dimensions. New Delhi: Academic Foundation; 2006.
- 3 Goswami A, Reddaiah VP, Kapoor SK, Singh B, Dwivedi SN, Kumar G. Tobacco and alcohol use in rural elderly Indian population. *Ind Joul of Psy.* 2005;192–197.
- 4 National Sample Survey Organization. National Sample Survey 52nd Round Report. New Delhi: Ministry of Statistics and Programme Implementation, Government of India; 1996. The Aged in India: A Socio-economic Profile, 1995–96.
- 5 Duggal R. Poverty and health: Criticality of public financing. *Ind Jou of Med Res.* 2007; 309–317.
- 6 World Health Organization. Reducing Stigma and Discrimination against Older People with Mental Disorders. Geneva: World Health Organization and World Psychiatric Association; 2002
- 7 Eldercare: Demographic downside [Internet]. Kerala: India Today, April 2018[updated 2018]. Available from: [www.https://www.indiatoday.in/magazine/nation/story/20180507-branded-corporate-elderly-care-old-age-homes-1221657-2018-04-26](https://www.indiatoday.in/magazine/nation/story/20180507-branded-corporate-elderly-care-old-age-homes-1221657-2018-04-26)

Effectiveness of Rhythmic Chopping & Lifting Pattern on Shoulder Range of Motion and Upper Extremity Functional Index in Post: Mastectomy Patients

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Abstract

Objective: To determine the effect of Rhythmic chopping & lifting pattern on shoulder range of motion in Post-mastectomy patients.

Method: A total 40 subjects were taken according to inclusion and exclusion criteria. Each subject was assessed by using Shoulder goniometry and UEFI questionnaire.

Result: A statistical analysis showed that Rhythmic chopping and lifting PNF exercises showed significant improvement in the outcome variables concluding that it improves shoulder ROM and functional activities.

Conclusion: Analysis of all the data obtained through the outcome measures (UEFI Questionnaire and shoulder ROM) shows that Rhythmic chopping and lifting PNF exercises showed significant improvement in the outcome variables concluding that it improves shoulder ROM and functional activities.

Keywords: PNF, Rhythmic chopping and Lifting Pattern, UEFI, ROM, LDH.

Introduction

Breast cancer is an abnormal growth of cells that normally line the ducts and lobules.¹ Breast cancer is the most common female cancer worldwide representing nearly a quarter (25%) of all cancers.² In present scenario, breast cancer is reflected as an important public health problem for adult women residing in developing countries and showing prevalence is estimated around 2.5 million, with over 0.8 million new cases & 0.5 million deaths occurring each year.³

Changes in reproductive risk factors, dietary habits & increasing life expectancy it is causative factor of rising incidence of breast cancer in India. Study suggests that approximately 75,000 new cases occur in Indian women every year. Breast cancer can be invasive carcinoma or non-invasive carcinoma.

Treatment of breast cancer is classified into two types- Local therapy (surgery and radiotherapy) or Systemic treatment (chemo, hormone and targeted therapy).

Mastectomy: Mastectomy is removal of the entire breast, including the nipple, but no lymph nodes from under the arm or muscle tissue from beneath the breast is removed.

In a Modified radical mastectomy consists of removal of entire breast with lymph nodes in the axilla. The extent of lymph node dissection may vary from complete

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clearance to less extensive procedure. Mastectomy and adjuvant radiotherapy given to the mastectomy site and axilla increases the risk of impairment of shoulder function.⁴

Radiotherapy leads to release of reactive oxygen species causes vascular damage leads to hypoxia, while the alteration in LDH (lactate dehydrogenase) levels secondary to hypoxia enhances fibrosis and worsen it.⁵

Lennart Blomqvist et, al established that radiotherapy will cause fibrosis that results into reduction of ROM of shoulder joint in mastectomy patients .⁶

Pectoralis major, serratus anterior, upper trapezius, rhomboid are affected which causes reduction in flexion, external rotation, scapular elevation and retraction. Biceps, triceps, deltoid, latissimus dorsi are also affected.⁷

Complications: Estrogen withdrawal symptoms, arthralgias, fatigue, mood swings, anxiety, weight gain, peripheral neuropathy, reduced mechanical strength of bone, discomfort pain, decreased range of motion and weakness in the muscles of the shoulders and arms lymphedema may affect the daily operational activity and the overall functional ability associated with health and quality of life.⁸

Rhythmic Chopping & Lifting Method: Proprioceptive neuromuscular facilitation technique (PNF) is stretching technique. It has positive effect on active and passive ROM. It helps to improve functional movement through facilitation, inhibition, strengthening & relaxation of muscle group.⁹

Chopping & Lifting is one of the pattern of PNF in which combination patterns of bilateral asymmetrical thorax, upper extremity combined with neck along with contract relax technique.

In this technique the muscle is stretched isometrically, contracted for 7-15 seconds, briefly relaxed for 2-3 seconds, and then immediately subjected to a passive stretch that stretches the muscle even further than initial passive stretch. This final passive stretch is held for 10-15 seconds. The muscle is then relaxed for 20 seconds before the PNF technique is performed.¹⁰

Study conducted by Cochrane states that scapulohumeral rhythm can be initiated with active assisted ROM, PROM, Soft tissue scar mobilization and proprioception neuromuscular facilitation (PNF) exercises.¹³

Studies conducted previously by Neuromuscular Facilitation (PNF) techniques help in improving range of motion as it elongates the Golgi tendon organ that facilitates relaxation of the antagonist muscle. .

As PNF Technique is known to show significant effect in terms of pain reduction, correcting scapular dyskinesis and improving shoulder ROM, no study till date has checked the efficiency of Rhythmic Chopping & Lifting pattern in mastectomy patients. So the need of the present study is to check the effectiveness of single PNF technique i.e. Rhythmic Chopping & Lifting technique on shoulder range of motion and upper extremity functional index in Post-Mastectomy patients.¹⁴

Materials and Methodology

Subjects were selected from Krishna Hospital karad:

Inclusion Criteria:

- Unilateral carcinoma of breast.
- Subjects who underwent mastectomy procedure alone or along with radiation for breast carcinoma.
- Not involved in any other type of exercise protocol.
- Subjects who are interested to participate in the study

Exclusion Criteria:

- Infection in axillary area.
- Open wounds
- Plan or infection to undergo a reconstructive surgery with in intervention period.
- Previous history of trauma to shoulder, surgery, untreated pathology or dysfunction.
- Current or previous cervical Neuropathy.

Methodology: Study was conducted among post mastectomy patients in Krishna hospital karad. A total 40 subjects were taken according to inclusion and exclusion criteria. After taking ethical clearance from institutional ethics committee consents forms were given and taken consents from participants. The subjects were assessed by using shoulder goniometry and UEFI Questionnaire. The scores were according to the answers given by the subjects with the help of same Questionnaire and . Statistical analysis of collected data was done accordingly and hence result was obtained.

Result

I Within the group comparison:

Group A:

1. UEFI:

Parameter (Group A)	Pre	Post	Mean diff	t value	p value	Remark
UEFI	4.0±1.182	4.3±1.081	-0.3000	2.854	0.0102	Significant

The above table and graph shows pre and post comparison within the group. Post treatment there was significant improvement noted in shoulder and arm mobility.

2. Shoulder ROM:

Parameter (Group A)	Pre	Post	Mean diff	t value	p value	Remark
FLEXION	70.9±7.210	80±6.287	-9.550	12.698	<0.0001	Sig
EXTENSION	46.65±4.308	46.85±4.258	--.02000	1.710	0.1036	N.S.
ABDUCTION	80.5±6.469	81.1±7.029	-0.5500	1.599	0.1263	N.S
INTERNAL ROTATION	68.6±6.731	77.65±6.667	-9.050	14.860	<0.0001	Sig
EXTERNAL ROTATION	46.65±4.308	46.85±4.258	-0.2000	1.710	0.1036	N.S

The above table and graph shows pre and post comparison within the group. Post treatment there was significant improvement noted in flexion and internal rotation

Group B:

3. UEFI

Parameter (Group B)	Pre	Post	Mean diff	t value	p value	Remark
UEFI	6.2±1.182	6.4±1.903	-0.2000	2.179	0.0421	Significant

The above table and graph shows pre and post comparison within the group. Post treatment there was significant improvement noted in shoulder and arm mobility.

4. Shoulder ROM

Parameter (Group B)	Pre	Post	Mean diff	t value	p value	Remark
FLEXION	73.2±8.320	80±8.177	-7.450	11.447	<0.0001	Sig
EXTENSION	49.9±5.911	50.3±5.667	-0.4000	0.9016	0.3786	N.S.
ABDUCTION	72.25±10.192	75.1±5.418	-2.850	1.485	0.1541	N.S
INTERNAL ROTATION	71.55±7.141	78±6.483	-6.800	6.936	<0.0001	Sig
EXTERNAL ROTATION	56.9±8.620	57.35±8.604	-0.4500	0.3975	0.6954	N.S

The above table and graph shows pre and post comparison within the group. Post treatment there was significant improvement noted in flexion and internal rotation.

II. Between the group comparison:

5.UEFI

Parameter	Pre	Post	Mean diff	t value	p value	Remark
UEFI	7.0±1.182	8.0±1.903	-0.2000	2.179	0.0421	Significant

The above table and graph shows pre and post comparison within the group. Post treatment there was significant improvement noted in shoulder and arm mobility in group B according to the p values

6. Shoulder ROM

Parameter	Pre	Post	Mean diff	t value	p value	Remark
FLEXION	71±7.279	78.9±6.000	7.3000	3.459	0.0014	Sig
EXTENSION	48±4.662	50±5.771	2.350	1.417	0.1647	N.S.
ABDUCTION	74.4±9.484	75.1±5.418	0.7000	0.2866	0.7760	N.S
INTERNAL ROTATION	69.25±6.897	76±7.269	6.750	3.013	0.0046	Sig
EXTERNAL ROTATION	57.4±8.858	55.7±1.841	1.300	0.4914	0.6259	N.S

The above table and graph shows post comparison between the groups. Post treatment there was significant improvement noted in group B as compared to group A according to the p values.

Discussion

This study “Effectiveness of Rhythmic chopping & Lifting Pattern on Shoulder Range of Motion and upper extremity functional index in Post- Mastectomy Patients” was conducted to compare the effectiveness of conventional shoulder and thoracic mobility exercises and Rhythmic chopping and lifting PNF Pattern, and find out the effective technique that improves shoulder ROM and upper extremity functional index in post-mastectomy patients.

There is rapid increase in incidence of breast cancer, hence surgery along with chemotherapy is mandatory for treatment of cancer. Surgery leads to dissection of muscles and soft tissue structures and chemotherapy causes decreased joint mobility and muscle strength, pain, impairment in functions and disability in gross fine motor skills leading to limitations in activities of daily living.

The study was conducted with 40 subjects. The subjects were divided into two groups. Prior consent was taken from them. The subjects in first group received conventional shoulder and thoracic mobility exercises and in the second group received rhythmic chopping & lifting PNF Pattern. The interventions were carried out for alternate days per week for 4 weeks. The outcome measures for this study were ROM assessment and UEFI Questionnaire.

Previous studies state that therapeutic exercises that is AROM, PROM, AAROM, Stretching, strengthening are been used till date as a part of conventional treatment

Previous studies conducted by Kayla B. Hindle, Whitcomb, Wyatt O. Briggs, Junggi Hong concluded

that PNF technique increases ROM by increasing the length of the muscle and neuromuscular efficiency.

Studies conducted previously by Dr .Kayinat Hassan, Dr. Danish Nouman, Dr. Surandar Kumar concluded that Proprioceptive Neuromuscular Facilitation (PNF) techniques help in improving range of motion as it elongates the Golgi tendon organ that facilitates relaxation of the antagonist muscle.

Study conducted by Cochrane states that scapulohumeral rhythm can be initiated with active assisted ROM, PROM, Soft tissue scar mobilization, and proprioception neuromuscular facilitation (PNF) exercises .

Study conducted by Nicolaou Valentina, Stasinopoulos Dimitrios, Lamnisos Dimitrios states that PNF helps to improve quality of motion in various musculoskeletal diseases and in women with breast cancer.

Within the group comparison:

- Conventional Exercises:** Post training there was significant improvement noted with conventional exercises in UEFI (p=0.0102). Post training there was significant improvement in ROM for Shoulder flexion (p=<0.0001) and internal rotation (p=<0.0001), In abduction (p=0.1263), external rotation (p=0.1036), and Extension (0.10360 following p values showed that there was no significant difference in the outcome variables.
- Rhythmic chopping and lifting Method:** Post training there was significant improvement noted with PNF rhythmic chopping and lifting exercises in UEFI (p=0.0421). There was significant improvement in Shoulder flexion (p=<0.0001), and internal rotation (p=<0.0001). And no significant difference was noted within the outcome variables in abduction (p=0.1542) and external rotation (p=0.6954) and extension (0.3786).

Between the Group Comparison: Post test there was significant difference between outcome variables in UEFI ($p=0.0421$). Following are the p values which led to analysis of improvement in flexion($p=0.0014$), internal rotation($p=0.0046$).And no significant difference was noted between the outcome variables in abduction($p=0.7760$),external rotation($p=0.6259$) and extension (0.1647).

This study shows that Rhythmic chopping and lifting method showed significant improvement in the outcome variables concluding that it improves shoulder ROM and arm mobility.

Conclusion

Analysis of all the data obtained through the outcome measures (UEFI Questionnaire and shoulder ROM) shows that Rhythmic chopping and lifting PNF exercises showed significant improvement in the outcome variables concluding that it improves shoulder ROM and functional activities

Conflict of Interest: Do not have any conflicts of interest to declare.

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Ethical Clearance: The institutional Ethics Committee has given permission to initiate the research project entitled EFFECTIVENESS OF RHYTHMIC CHOPPING & LIFTING PATTERN ON SHOULDER RANGE OF MOTION AND UPPER EXTREMITY FUNCTIONAL INDEX IN POST- MASTECTOMY PATIENTS

References

1. Breast cancer-treatment guidelines for patients,version VIII, (SEPT 2006).
2. hreshtha MALVIA, Sarangdhara Appalaraju BAGADI, Uma S. DUBEY, Sunita SAXENA, Epidemiology of breast cancer in Indian women, (2017).
3. Mohite RV, Mohite VR, Socio Demographic and Clinical Profile of women with breast cancer: A cross sectional study from Western Maharashtra, India,(2015).
4. Vinay h Deshmukh, API:Vol 4.
5. Sharma M,et al,Limited mouth opening in oral submucous fibrosis : reasons,ramifications, and remedies, (2017).
6. Lennart Blomqvist, Birgit Stark, Natacha Engler & Maj Malm,Evaluation of arm and shoulder mobility and strength after modified radical mastectomy and radiotherapy,(2004)
7. Dlvashamley, Reza oskarochi, Elaine Sagden, Changes in shoulder muscle size and activity following treatment for breast cancerer, (2007)
8. Nicolaou Valentina, Stasinopoulos Dimitrios, Lamnisos Dimitrios. The effectiveness of the exercise program by the method Graham, in functional capacity and quality of life of women with mastectomy breast cancer. 2016 Vol 12.2.
9. Salameh Bweir Al Dajah, Soft tissue mobilization and PNF improve range of motion and minimize pain level in shoulder Impingement,(2014).
10. Susan S. Adler, DAOMINIEK Beckersn, Math Buck, PNF IN PRACTICE, second edition.
11. Prabhjot Gambhir, Functional Impairments Post Breast Cancer Surgery : A Correlational Study. (2014).
12. Kayla B. Hindle, Tyler J Whitcomb, Wyatt O. Briggs, Junggi Hong, Proprioceptive Neuromuscular Facilitation (PNF): Its mechanism and Effects on Range of motion and Muscular function. The Journal of Human Kinetics volume. 2012 March: 105-113.
13. Mary Lou Galantino, Nicole L. Stout. Exercise Interventions for Upper Limb Dysfunction Due To Breast Cancer Treatment. 2013 October
14. Dr. Kaniyat Hassan, Dr. Danish Nouman, Dr. Surandar Kumar. To Compare the Effectiveness of scapular PNF with Conventional Physiotherapy versus conventional physiotherapy in subjects with Shoulder Dysfunction After Mastectomy. Indian Journal of Research. 2019 February :2250-1991.
15. Suelen Helena da silva, Lydia Christmann espindola koetz, Eduardo schnem, et al,Quality of life after mastectomy & its relation with mucous strength of upper limb.(2014).

Current Research in Neuropathology and Pharmacotherapy of Alzheimer's Disease: A Review

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Abstract

Background: Alzheimer's disease (AD), a category of neurological degeneration generally seen in elderly people which is reflected by memory loss and affecting daily living activities.

Method: The data has been accessed from scopus, pubmed, science-direct and google-scholar which is included in this article.

The literature provide the information about pathological alterations of Alzheimer disease emphasizing on formation of neuritic plaques, beta amyloid protein, neurofibrillary tangle and also updates therapeutics used in Alzheimer's disease including cholinesterase inhibitors, ACE inhibitors, NMDA receptor antagonists, secretase inhibitors and anti-inflammatory drugs, herbal drugs and other naturals.

Results: The research on neuropathology and diagnosis of Alzheimer's disease are determinants of this study. The pathophysiology, diagnosis using biomarkers and therapeutics of disease has been summarized.

Conclusion: The aim of this review paper is to focus on how diagnosis and pharmacotherapy of Alzheimer's disease useful for researchers engaged in the experimental research.

Keywords: Alzheimer's disease, β -amyloid precursor protein, neurofibrillary tangles, Acetylcholinesterase inhibitors, Secretase inhibitors, biomarkers.

Introduction

Alzheimer's disease (AD) is approved as a chronic, irreversible neurodegenerative disorder in many countries which produces various cognitive impairments in old people. Alzheimer's disease (AD) is indicated

by memory loss and cognitive impairment which affect daily living activities. With an increase in the geriatric population in India, quantities of AD patients are increasing step by step⁽¹⁾. The neuropathologists had distinguished 64 instances of amyloid plaques and NFTs, a cause of disease, at the time of Dr. Alois Alzheimer, in autopsied brains of AD individuals⁽²⁾. The extracellular deposition of Ab called Amyloid plaques; saw in parenchymatous cells of brain and furthermore in cerebral blood vessels called cerebral amyloid angiopathy (CAA)⁽³⁾.

Currently such medications are approved by USFDA (US Food and Drug Administration), including five medications those are utilized for the treatment

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of cognitive manifestations of AD. NMDA receptor antagonist–memantine (Namenda) donepezil (Aricept), AChEIs –rivastigmine (Exelon), tacrine (Cognex) and galantamine (Razadyne, Reminyl) are drug of choice as per indications ⁽⁴⁾.

Pathophysiology of Alzheimer’s Disease: In 1907, AD is known to treat subsequent to recognizing the pathophysiology of AD when neuropathological features of this disease observed and described by amyloid plaques and hyperphosphorylated NFTs and different hypotheses have been proposed ⁽⁵⁾ (Fig-1). In last decade, it has been suggested that commonly used Ab hypotheses is responsible for complex pathophysiology of growing disease ⁽⁶⁾.

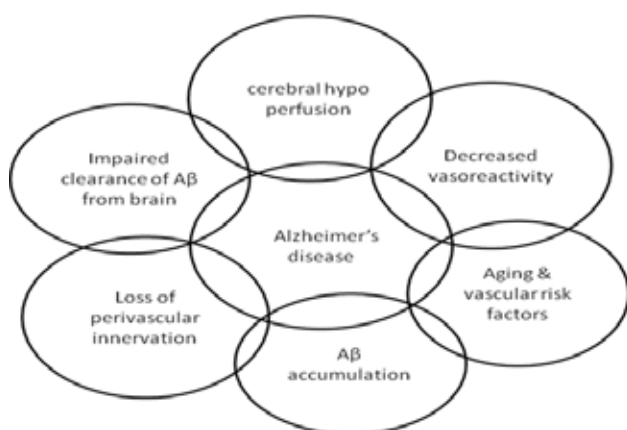


Fig 1: Various pathophysiological processes causing Alzheimer’s disease (AD)

In late stage, development of amyloid plaques is appeared in the older age of patients ⁽⁷⁾. The breakdown of APP is occurred by α -secretase which is further by action of β -and γ -secretases in amyloid cascade hypothesis ⁽⁸⁾. The activities of neurons and their related astrocytes are responsible for production of Ab42 oligomers. The cytokines like IL-1b, TNF-a, and IFN-g stimulate neighbour astrocyte-neuron which produces Ab42 oligomer ⁽⁹⁾. Working of neuron–astrocyte complex is affected by oligodendroglia (OLGs) which are destroyed by Ab oligomers ⁽¹⁰⁾. The aggregation of Ab oligomers also induces degeneration in neurons of AD patients ⁽¹¹⁾. It was proposed that receptor pharmacology of Ab activates neuroprotection mediating Ab42 monomers through signaling pathways of mediating receptors ⁽¹²⁾.

Use of Biomarkers In Alzheimer’s Disease: The cholinergic hypothesis of AD mechanism stipulates that most of cognitive manifestations are a result of cholinergic dysfunction ⁽¹³⁾.

Early Detection Strategies via Biomarkers: The magnetic resonance imaging and fluorodeoxy-glucose positron emission tomography determine hippocampus atrophy and cortical hypo-metabolism in AD progression. Advancements in science, radiology and system biology promotes use of biomarkers in AD research ⁽¹⁴⁾.

Biomarkers Using Cerebrospinal Fluid: Scientists have determined levels of Ab-42 peptide by knowing and total phosphorylated Tau protein (t-tau and p-Tau) and by estimating cerebrospinal liquid (CSF) which is responsible for neurodegeneration in AD. All three parameters have been proposed as one of the prevailing biomarkers for this disease which is independent of the apo-lipoprotein E (APOE) genotype ⁽¹⁵⁾. The accuracy in AD symptoms and combining CSF Ab with either t-tau or p-tau level ⁽¹⁶⁾.

Biomarkers Using Imaging Techniques: Beta-amyloid load in the brain can be estimated through positron emission tomography (PET) using amyloid ligands such as Pittsburgh compound B (PiB), florbetapir (AV-45). Amyloid PET is considered a strong biomarker which was incorporated in 2011 and re-evaluated by National Institute on Aging-Alzheimer’s Association diagnostic criteria for AD. In spite of being an amazing screening instrument in clinical trials, there is as yet limited evidence as a diagnostic tool for AD in clinical practice ⁽¹⁷⁾.

Biomarkers Using Genetic Screening: Early AD was related with special autosomal dominant mutations in amyloid precursor protein (APP), and/or presenilin 1 (PSEN1), or presenilin 2 (PSEN2). At present, genetic testing for both PSEN1 and PSEN2 lay down in one family member with early-beginning of AD¹⁸. Lanoisele’e et al. observed the occurrence of AD, proposing potential advantage of screening non-familial cases of AD for these mutations¹⁹. Late-onset AD is most normally connected with APOE4 allele which is situated on chromosome 19q13.2 including regulation of Ab aggregation and clearance ⁽²⁰⁾. Besides, carriers of this allele have a lower onset of disease and more hippocampal atrophy in dose-dependent manner ⁽²¹⁾.

Strategies Used For Treatment of Ad: Currently available medications N-methyl d-aspartate receptor antagonist (Memantine), acetylcholinesterase inhibitors (Rivastigmine, Galantamine, Donepezil) in the various stages of disease ⁽²²⁾. In AD, deletion of amyloid beta protein deposition is one of the most favorable targets for treatment.

Anticholinesterases:

The drugs can change cholinergic neurotransmission, have been approved from regulatory authorities for Alzheimer's therapy⁽²³⁾. Three ChEIs like Donepezil, Rivastigmine and Galantamine. Donepezil and Galantamine are usually used to get patients with mild to moderate AD. Rivastigmine inhibits both Acetyl cholinesterase and Butyryl cholinesterase associating the degradation of Acetyl choline⁽²⁴⁾

NMDA Receptor Antagonist (Memantine):

Memantine is a newer medication used in treatment of moderate to severe dementia. Its mechanism of action is a voltage-dependent, low-moderate affinity, uncompetitive NMDA receptor antagonism⁽²⁵⁾. Memantine blocks abnormal glutamate activity which causes neuronal cell death and cognitive dysfunction⁽²⁶⁾.

Angiotensin-converting enzyme (ACE) inhibitors: It has been seen that ACE inhibitors decrease aggravation in brains of AD patients⁽²⁷⁾. The mechanism includes transformation angiotensin I to angiotensin II. Another possibility is that angiotensin II is converted to angiotensin III after that to angiotensin IV. Angiotensin IV binds at AT₄ receptor sites, which are most predominant in the neocortex, hippocampus, and other areas and improves learning and memory⁽²⁸⁾.

Nonsteroidal Anti-inflammatory Drugs: Most researches on nonsteroidal anti-inflammatory drugs have concentrated on prevention instead of treatment of AD⁽²⁹⁾. Animal models have exhibited that anti-inflammatory cyclooxygenase-2 (COX-2) inhibitors (Rofecoxib) reduced oxidative stress yet nonspecific COX inhibitors (Flurbiprofen and Ibuprofen)⁽³⁰⁾.

Secretase Inhibitors: Secretases are enzymes forms plaques by breaking APP of cell membranes into β A fragment. Memoquin, an example of β -secretase inhibitors reduce β A production by inhibiting AChE and limits tau hyperphosphorylation in early developmental stage⁽³¹⁾.

Herbal Drug Treatment:

Polyphenols: e.g. Resveratrol found in red wine, peanuts and other plants, has been used to reduce oxidative stress, inflammation, β A and protect DNA thus, decrease in cell death. A moderate utilization of red wine decreases the danger of growing AD⁽³²⁾.

Curcumin: obtained from turmeric is used in

AD treatment. Curcumin has neuroprotective, anti-inflammatory, antioxidant activities and cause inhibition of β A formation and clearance of existing β A⁽³³⁾.

Ashwagandha: (also known as *Withania somnifera*) proposed to have neuroprotective, anti-inflammatory, antioxidant, AChE inhibitory, β A inhibitory activities which decrease in cell death³⁴. It has been found that its oral use reversed damage to hippocampus and brain cortex by diminishing neurite atrophy, restoring synapses and improving memory in mice⁽³⁵⁾.

Nutrients and Hormones: Alpha-lipoic acid acts as a prevailing micronutrient with various pharmacological and antioxidant properties⁽³⁶⁾. LA has been proposed to have anti-dementia in AD by altering antioxidant protective enzymes³⁷.

Polyunsaturated fatty acids: like omega 3-fatty acids (FAs), docosahexaenoic acid (DHA) found in high levels in the mammalian brain, neuronal membranes and myelin sheath. Their actions were observed by enhanced receptor binding and function of ion channels⁽³⁸⁾. The cognitive impairment occurs due to diminished serum DHA levels which obstruct learning and memory⁽³⁹⁾. As a result, the scientists have explored possibility of DHA supplement utilization may decrease risk of progression of AD⁽⁴⁰⁾.

Vitamin B₁₂ and folate: in low levels are shown to result into cognitive decline. AD patients have high levels of homocysteine which need to become low. Homocysteine levels seem to relate with aging but not with cognition. A combination of vitamins B₁₂ and B₆ and folate brought down homocysteine in people with mild to moderate AD⁽⁴¹⁾.

Retinol: commonly known as Vitamin A is essential for learning, memory and cognition. Vitamin A levels in the brain decline in AD people, therefore its need to improve. A metabolite of vitamin A, retinoic acid is known to slow cell death and protect from β A⁽⁴²⁾.

Lithium Compounds:

Are prescribed for some neurodegenerative disorders. Enhancement of bcl-2 levels (neuroprotective protein) in hippocampus and frontal cortex of the rat has been observed. It also inhibits GSK-3, which is involved in increasing levels of phosphorylated tau and believed to be a factor prompting β A plaques and cell death⁽⁴³⁾.

Melatonin: has antioxidant, anticancer properties

and also protects mitochondria against tau tangles and also reduces β A toxic effects⁽⁴⁴⁾.

Conclusion

The evidences have been proposed to suggest that A β has pivotal role in the pathogenesis of AD, which involves many complex secondary events in the disease. Novel developments like radiology, chemistry and system biology involved use of biomarkers to identify mechanism. Enormous development has proposed to make various strategies for AD treatment including anti-inflammatory, anti-amyloid, secretase inhibitor, antihypertensive, cholinesterase inhibitor, and some natural nutrients and hormones.

In this paper, authors have discussed the current research on diagnosis and pharmacotherapy of Alzheimer's disease which may be fruitful for researchers engaged in the experimental research.

Abbreviations: AD, Alzheimer's disease; ACh, acetylcholine; AChRs, acetylcholine receptors; AChEs, acetylcholinesterase; AChEIs, acetylcholinesterase inhibitor; ApoE, apolipoprotein-E; β A, beta amyloid; β -APP, β -amyloid precursor protein; NMDA, N-methyl d-aspartate.

Ethical Clearance: There is no need of Ethical Clearance for publishing this review article.

Conflict of Interest: The authors have no conflicting interests in writing this paper.

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References

1. Apostolova, L. G., Alzheimer Disease. Continuum (Minneapolis, Minn). 2016, 22, 419-434.
2. Pietrzik, C., Behl, C., Concepts for the treatment of Alzheimer's disease: molecular mechanisms and clinical application. *Int J Exp Pathol.* 2005, 86, 173-185.
3. Anand R., Gill, K. D., Mahdi, A. A., Therapeutics of Alzheimer's disease: past, present and future. *Neuropharmacology.* 2014, 76, 27-50.
4. Aisen, P. S., Cummings, J., Schneider, L. S., Symptomatic and Nonamyloid/Tau Based Pharmacologic Treatment for Alzheimer Disease. *Cold Spring Harb Perspect Med.* 2012, 2, a006395.
5. Kurz, A., Perneczky, R., Novel insights for the treatment of Alzheimer's disease. *Prog Neuropsychopharmacol Biol Psychiatry.* 2011, 35, 373-379.
6. Castello, M. A., Soriano, S., On the origin of Alzheimer's disease. Trials and tribulations of the amyloid hypothesis. *Ageing Res Rev.* 2014, 13, 10-12.
7. Cheignon, C., Tomas, M., Bonnefont-Rousselot, D., Faller, P., Hureau, C., Collin, F., Oxidative stress and the amyloid beta peptide in Alzheimer's disease. *Redox Biol.* 2018, 1, 450-464.
8. Chow, V. W., Mattson, M. P., Wong, P. C., Gleichmann, M., An Overview of APP Processing Enzymes and Products. *Neuromolecular Med.* 2010, 12, 1-12.
9. Dal Pra, I., Chiarini, A., Gui, L., Chakravarthy, B., Pacchiana, R., Gardenal, E., et al., Do astrocytes collaborate with neurons in spreading the "infectious" Ab and tau 644 drivers of Alzheimer's disease? *Neuroscientist.* 2015, 21, 9-29.
10. Rosenmann, H., Immunotherapy for targeting tau pathology in Alzheimers disease and tauopathies. *Curr Alzheimer Res.* 2013, 10, 217-228.
11. Vromman, A., Trabelsi, N., Rouxel, C., Béréziat, G., Limon, I., Blaise, R., β -Amyloid context intensifies vascular smooth muscle cells induced inflammatory response and de-differentiation. *Aging Cell.* 2013, 12, 358-369.
12. Armato, U., Chakravarthy, B., Pacchiana, R., Whitfield, J. F., Alzheimer's disease: an update of the roles of receptors, astrocytes and primary cilia (review). *Int J Mol Med.* 2013, 31, 3-10.
13. Ferreira-Vieira, T. H., Guimaraes, I. M., Silva, F. R., Ribeiro, F. M., Alzheimer's Disease: Targeting the Cholinergic System. *Curr Neuropharmacol.* 2016, 14, 101-115.
14. Frisoni, G. B., Visser, P. J., Biomarkers for Alzheimer's disease: a controversial topic. *Lancet Neurol.* 2015, 14, 781-783.
15. Lautner, R., Palmqvist, S., Mattsson, N., Andreasson, U., Wallin, A., Palsson, E., et al., Apolipoprotein E genotype and the diagnostic accuracy of cerebrospinal fluid biomarkers for Alzheimer disease. *JAMA Psychiatry.* 2014, 71, 1183-1191.
16. Dubois, B., Feldman, H. H., Jacova, C., Hampel, H., Molinuevo, J. L., Blennow, K., et al., Advancing research diagnostic criteria for Alzheimer's disease:

- the IWG-2 criteria. *Lancet Neurol.* 2014, 13, 614-629.
17. Johnson, K. A., Minoshima, S., Bohnen, N. I., Donohoe, K. J., Foster, N. L., Herscovitch, P., et al., Appropriate use criteria for amyloid PET: a report of the Amyloid Imaging Task Force (AIT), the Society of Nuclear Medicine and Molecular Imaging (SNMMI) and the Alzheimer Association (AA). *Alzheimers Dement.* 2013, 9, 1-16.
 18. Sassi, C., Guerreiro, R., Gibbs, R., Ding, J., Lupton, M. K., Troakes, C., Investigating the role of rare coding variability in Mendelian dementia genes (APP, PSEN1, PSEN2, GRN, MAPT, and PRNP) in late-onset Alzheimer's disease. *Neurobiol Aging.* 2014, 35, 2881.e1-2881.e6.
 19. Lanoisele'e, H. M., Nicolas, G., Wallon, D., Rovelet-Lecrux, A., Lacour, M., Rousseau, S., et al., APP, PSEN1, and PSEN2 mutations in early-onset Alzheimer disease: a genetic screening study of familial and sporadic cases. *PLoS Med.* 2017, 14, e1002270.
 20. Liu, C. C., Liu, C. C., Kanekiyo, T., Xu, H., Bu, G., Apolipoprotein E and Alzheimer disease: risk, mechanisms, and therapy. *Nat Rev Neurol.* 2013, 9, 106-118.
 21. Hostage, C. A., Roy, C. K., Doraiswamy, P. M., Petrella, J. R., Dissecting the gene dose-effects of the APOE epsilon4 and epsilon2 alleles on hippocampal volumes in aging and Alzheimer's disease. *PLoS One.* 2013, 8, e54483.
 22. Lleó, A., Current Therapeutic Options for Alzheimer's Disease. *Curr Genomics.* 2007, 8, 550-558.
 23. Arendt, T., Bigl V., Arendt, A., Tennstedt, A., Loss of neurons in the nucleus basalis of Meynert in Alzheimer's disease, paralysis agitans and Korsakoff's Disease. *Acta Neuropathol.* 1983, 61, 101-108.
 24. Colović, M. B., Krstić, D. Z., Lazarević-Pašti, T. D., Bondžić, A. M., Vasić, V. M., Acetylcholinesterase inhibitors: pharmacology and toxicology. *Curr Neuropharmacol.* 2013, 11, 315-35.
 25. Carvajal, F. J., Mattison, H. A., Cerpa, W., Role of NMDA Receptor-Mediated Glutamatergic Signaling in Chronic and Acute Neuropathologies. *Neural Plast.* 2016; 2016: 2701526.
 26. Rogawski, M. A., Wenk, G. L. The neuropharmacological basis for the use of memantine in the treatment of Alzheimer's disease. *CNS Drug Rev.* 2003, 9, 275-308.
 27. Wolfel, E. E., Effects of ACE inhibitor therapy on quality of life in patients with heart failure. *Pharmacotherapy.* 1998, 18, 1323-1334.
 28. Sink, K. M., Leng, X., Williamson, J., Kritchevsky, S. B., Yaffe, K., Kuller, L., Yasar, S., Atkinson, H., Robbins, M., Psaty, B., Goff, D. C., Angiotensin Converting Enzyme Inhibitors and Cognitive Decline in Older Adults with Hypertension: Results from the Cardiovascular Health Study. *Arch Intern Med.* 2009, 169, 1195-1202.
 29. Ong, C. K., Lirk, P., Tan, C. H., Seymour, R. A., An evidence-based update on nonsteroidal anti-inflammatory drugs. *Clin Med Res.* 2007, 5, 19-34.
 30. Umar, A., Boisseau, M., Yusup, A., Upur, H., Bégaud, B., Moore, N., Interactions between aspirin and COX-2 inhibitors or NSAIDs in a rat thrombosis model. *Fundam Clin Pharmacol.* 2004, 18, 559-563.
 31. Ghosh, A. K., Tang, J., Prospects of β -Secretase Inhibitors for the Treatment of Alzheimer's Disease. *Chem Med Chem.* 2015, 10, 1463-1466.
 32. Upadhyay, S., Dixit, M., Role of Polyphenols and Other Phytochemicals on Molecular Signaling. *Oxid Med Cell Longev.* 2015, 2015, 504253.
 33. Amalraj, A., Pius, A., Gopi, S., Gopi, S., Biological activities of curcuminoids, other biomolecules from turmeric and their derivatives - A review. *J Tradit Complement Med.* 2016, 7, 205-233.
 34. Kurapati, K. R., Atluri, V. S., Samikkannu, T., Nair, M. P. Ashwagandha (*Withania somnifera*) reverses β -amyloid1-42 induced toxicity in human neuronal cells: implications in HIV-associated neurocognitive disorders (HAND). *PLoS One.* 2013, 8, e77624.
 35. Kuboyama, T., Tohda, C., Komatsu, K., Neuritic regeneration and synaptic reconstruction induced by withanolide A. *Br J Pharmacol.* 2005, 144, 961-971.
 36. Packer, L., Witt, E. H., Tritschler, H. J., Alpha-lipoic acid as a biological antioxidant. *Free Radic Biol Med.* 1995, 19, 227-250.
 37. Maczurek, A., Hager, K., Kenklies, M., Sharman, M., Martins, R., Engel, J., Carlson, D. A., Münch, G., Lipoic acid as an anti-inflammatory and neuroprotective treatment for Alzheimer's disease. *Adv Drug Deliv Rev.* 2008, 60, 1463-1470.

38. Farkas, E., de Wilde, M. C., Kiliaan, A. J., Meijer, J., Keijser, J. N., Luiten, P. G., Dietary long chain PUFAs differentially affect hippocampal muscarinic 1 and serotonergic 1A receptors in experimental cerebral hypoperfusion. *Brain Res.* 2002, 954, 32-41.
39. Tully, A. M., Roche, H. M., Doyle, R., Fallon, C., Bruce, I., Lawlor, B., Coakley, D., Gibney, M. J., Low serum cholesteryl esterdocosahexaenoic acid levels in Alzheimer's disease: A casecontrol study. *Br J Nutr.* 2003, 89, 483-489.
40. Cunnane, S. C, Plourde, M., Pifferi, F., Begin, M., Feart, C., Barberger-Gateau, P., (2009) Fish, docosahexaenoic acid and Alzheimer's disease. *Prog Lipid Res.* 2009, 48, 239-256.
41. Reay, J. L., Smith, M. A., Riby, L. M., B vitamins and cognitive performance in older adults: review. *ISRN Nutr.* 2013, 2013: 650983.
42. Watson, J., Lee, M., Garcia-Casal, M. N., Consequences of Inadequate Intakes of Vitamin A, Vitamin B₁₂, Vitamin D, Calcium, Iron, and Folate in Older Persons. *Curr Geriatr Rep.* 2018, 7, 103-113.
43. Forlenza, O. V, De-Paula, V. J., Diniz, B. S., Neuroprotective effects of lithium: implications for the treatment of Alzheimer's disease and related neurodegenerative disorders. *ACS Chem Neurosci.* 2014, 5, 443-450.
44. Cardinali, D. P, Vigo, D. E., Olivar, N., Vidal, M. F., Brusco, L. I., Melatonin Therapy in Patients with Alzheimer's Disease. *Antioxidants (Basel).* 2014, 3, 245-77.

Prevalence of Thalassemia among Reproductive Age Group Women of Central Gujarat

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Abstract

Background: thalassemia is one of serious genetic blood disorder. To know about its suffering during or before child bearing to female will be great help to manage married life and can avoid children morbidity or disability.

Objective: study aimed to know prevalence of thalassemia among reproductive age group of females.

Method: Cross-sectional research design used to follow this prevalence from September 2018 to December 2018 among reproductive age group females of central part of Gujarat. House to house survey conducted by using predesigned, validated questionnaire to collect base-line information and blood sample collected and analyzed to know presence of thalassemia. Data was analyzed by using SPSS version 20 (Trial). Proportion, chi-square statistical tests used to know finding and interpret it.

Result: the overall prevalence of thalassemia among reproductive age group female is 3.679% which is almost nearer to India's prevalence of thalassemia.

Conclusion: Prevalence of thalassemia is higher in India especially in rural area where people having lack of knowledge about diseases

Keywords: HPCL, thalassemia, reproductive age, prevalence

Introduction

Thalassemia is a term derived from Greek word. Thalassemia is an autosomal recessive blood disease which lead to decreasing hemoglobin level through genetic defects in globin chain synthesis.

Thalassemia is one of serious genetic inherited disorder. It alters physiology of individual by loosing oxygen carrying capacity of Hb because of producing abnormal forms of Hemoglobin. Inability to carry oxygen leads to anemia which will be more serious in form of

thalassemia because of excessive destruction of RBC's. It is a genetic autosomal recessive disorder which cause genetic defect and leads to decreased synthesis of globin chains of Hb. Further based on abnormal chain sequence alpha and beta thalassemia exist. As it is inherited disease so parent carries this recessive gene.

Autosomalrecessive disease happen inheritantly, where both parent bring equal amount of receive gene and in thalassemia this defect lead reduced level of hemoglobin. Persons carrying only one of these genes are called 'carriers' as they do not suffer from any disease but carry the abnormal gene and transmit it to the next generation. Carriers cannot be recognized clinically but only by performing special blood tests. Where both mother and father are 'carriers', there is a chance that their children may inherit the abnormal gene from both parents and thus suffer from a severe thalassemia

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syndrome or a Sickle Cell syndrome or may be normal without any abnormal gene or carriers like their parents¹.

The present prevalence of thalassemia stated by WHO is 4.5% at world level while in India it varies from 0-17% but average can be counted as 3.5, where in Gujarat the prevalence rate is high². As per available statistic the highest prevalence of thalassemia remain at Gujarat (10 to 15%), which will further followed by other states in row as West Bangal (10.20%), Punjab (6.50%), Delhi (5.50%), Tamil Nadu (4%), Maharastra (1 to 2%) and Kerala (less than 1%)³. As prevalence is higher in Gujarat, so researcher took interest to find prevalence of thalassemia among reproductive age group females at Anand district of central Gujarat.

Estimation of prevalence will be informed to state government to take necessary action to handle the prevalence rate of thalassemia.

To support the significance of the research, researcher reviewed few studies result, few are like one study recommended that a routine premarital screening should be began so that high-risk marriage can be identified and prevent. Such step will further prevent happing of child suffering due to transfusion-dependency. These recommendations given by study after estimated higher prevalence of hemoglobinopathy⁴.

A cross section study conducted in Bhopal of India also shown all most similar recommendation with some of additional points to suggest public awareness about thalassemia kind of disease and complete facts should be known to all healthcare professionals working in community services and it's their duty to aware public about these diseases through periodic meeting⁵.

Material and Method:

Researchers used cross-sectional research design to achieve objective of study, and it covered in rural area of Anand Gujarat-North India. The data were collected from September 2018 to March 2019. A total of 958 female of reproductive age group were screened for thalassemia. The blood was collected by trained nursing staff. This study participants were combination or mixture of rural population involving them without discrimination with caste, religion. The sampling method used to recruit the sample were selected village randomly by lottery method.

Educational talks and audiovisual presentations were delivered to create awareness prior to get blood

sample for investigation. Informed consent was filled by participants prior to study.

Structured Performa used to gather base-line information which included age, income, marital status, kind of family, food habits, occupation, caste, religion, family history of blood disorders.

Blood samples of 5 ml were collected in ethylene diamine tetrachloride acetate (EDTA) vacuette. Laboratory findings were measured after as all investigations held in NABL accredited laboratory. To know the high-risk sample and selecting sample for hemoglobin electrophoresis the HbA₂ level identified and all participants having less than 4.0 % Hb asked to go for Hb electrophoresis for disease confirmation. The entire participants who fulfil inclusion criteria are included in study. The females those were suffer with communicable and life threaten conditions are excluded from the study.

Participants those were between 18-35 year, willing to go for phase II (if screen in phase I) and residing in rural area of Anand district were recruited. The subject those were belongs to 18-35 year of age. Women those were diagnosed with any blood related disorder like anaemia and sickle cell anaemia, pregnant or breast feeded and suffering with any communicable disease were excluded from study.

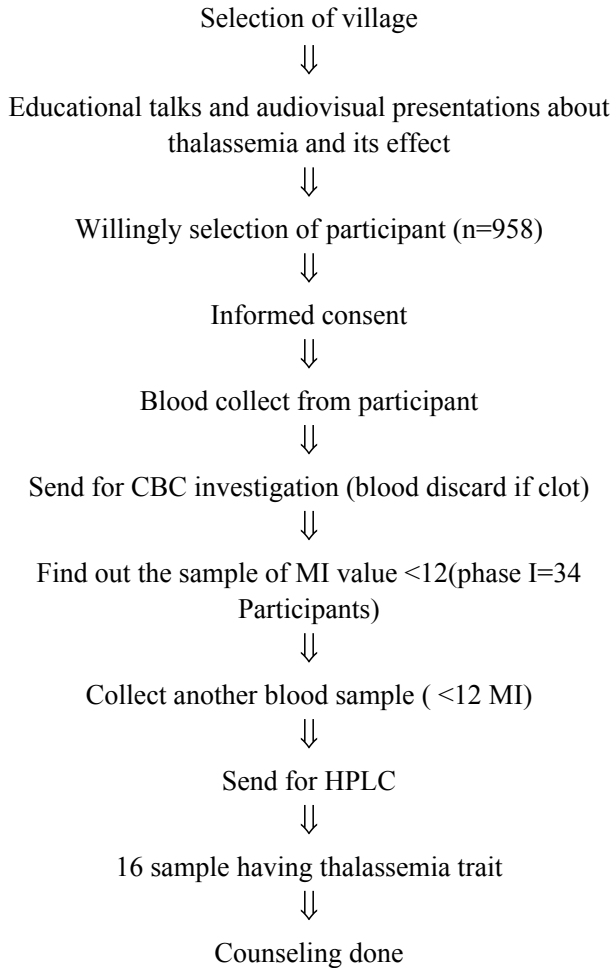
About Anand District: Anand District Panchayat have 8 taluka's (Tehsil) which having 351 gram Panchayat. The total population of Anand district is 18,56,872.

The sample size calculated with the prevalence of 5% and precision of 5% by using formula

$N = Z^2 PQ/L^2$ and calculated sample size is 850 by calculating 10% of drop out rate we finalised the sample size of 958.

Anand district have total 8 talukas and samples are recruited from each talukas in equally weight age manner. The researcher collected base line information before collection of blood sample. It was completely assumed that collected blood sample should reach to laboratory for testing within 2 hours of collection. All universal precaution taken for collecting, storing, and transporting the simple. Data were collected by house to house survey. All samples are tested at lab of NABH accredited hospital.

Flow of Data Collection:



Finding: Study estimated prevalence of thalassemia as per identified objective and it calculated 3.697. It means out of 1000 women, 3 to 4 females are vulnerable to become thalasaemic.

Table 1: shows prevalence of thalassemia

Count		Prevalence of Thalassemia = 3.679%
Normal	924	
Thalassemia	34	

The data related to marital status, educational qualification, having blood disorder, type of family, diet pattern and feeling of tiredness were collected.

Total 958 females were recruited for blood collection. Out of which 924(96.45) had not shown trait for thalassemia while 34 females (3.55) were considered as thalassemia trait. The mean MI value of thalassemia women were 10.92, mean HGB 9.66, mean MCV 62.08 and mean RBC value is 5.53 which is lesser than non thalassemia women.

Table 2: Frequency distribution of samples

N=958		
Marital status	Frequency	Percentage
No	140	14.6
Yes	818	85.4
Education		
Illiterate	124	14.45
Primary	544	56.78
Secondary	205	21.39
Higher secondary	85	8.90
Blood disorder		
Yes	61	6.36
No	897	93.63
Type of family		
Joint	830	86.63
Nuclear	128	13.36
Diet		
Vegetarian	683	71.29
Mixed	275	28.70
Feeling of tiredness		
Daily	321	33.50
Every week	333	34.76
Every 3 month	111	11.59
Never	193	20.15

Table 3; shows complete sample descriptive statistic

Descriptive Statistics N-958		
	Mean	Std. Deviation
MI Value	18.0614	4.34781
HGB	11.1910	5.09125
MCV	78.3230	11.56269
RBC	5.2413	18.01294

Table 4: shows descriptive statistic of Normal female and thalassemia female

		N	MEAN	SD
Normal Women	MI VALUE	924	18.32	4.20
	HGB		11.25	5.15
	MCV		78.92	11.25
	RBC		5.23	18.34
Thalassemia Women		N	MEAN	SD
	MI VALUE	34	10.92	0.77
	HGB		9.66	2.68
	MCV		62.08	7.51
RBC	5.53		0.65	

Blood investigation also revealed about level of hemoglobin among reproductive age group, it's surprised to know that 26.51% (254 sample) of whole samples having less than 10 gm hemoglobin.

Ethical Consideration: Researchers obtained ethical committee approval and written informed consent also taken on voluntary basis from each participants before enrolling them in study. Informed consent covers all possible risk and benefits of present study and further each participant informed that any point of time they can withdraw from study.

Conclusion

This study concluded with a clearly estimated prevalence of thalassemia among reproductive age group of females in rural part of Anand district is 3.69 which almost nearer to national prevalence. As a secondary data researcher also find out that 26.59% prevalence of mild anemic cases with less than 10 gm of Hb.

Researcher took this opportunity to suggest premarital counselling or genetic counselling to avoid future complications of thalassemia.

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Conflict of Interest: there is no conflict of interest

References

- 1. NHM Guidelines for Prevention and Control of Hemoglobinopathies in India-2016**
2. Lokeshwar MR. Late Hony. Surg. Cmde. Dr. Shantilal C. Sheth oration presentation during PEDI-CON 2006, Delhi, January 6th, 2006. Progress in the management of thalassemia. *Indian Pediatr* 2006;43:503-6.
3. Verma IC. Burden of genetic disorders in India. *Indian J Paediatr* 2000;67:893-8.
4. Mondal SK, Mandal S. Prevalence of thalassemia and hemoglobinopathy in eastern India: A 10-year high-performance liquid chromatography study of 119,336 cases. *Asian J Transfus Sci* 2016;10:105-10.
5. Bhatia P, Nagar V, Meena JS, Singh D, Pal DK. A study on the demographic and morbidity patterns of thalassemia patients registered at a tertiary-care center of central India. *Int J Med Sci Public Health* 2015;4:85-88
6. Mohanty D, Colah RB, Gorakshakar AC, Patel RZ, Master DC, Mahanta J, et al. Prevalence of β -thalassemia and other haemoglobinopathies in six cities in India: A multicentre study. *J Community Genet* 2013;4:33-42.

Prevalence and Risk Factors of Obesity among Women

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Abstract

Background: Obesity is a state throughout that there's a generalized buildup of humoring fat among the body, leading to a weight of quite two hundredth of the essential weight. Fatness invites disability, disease and premature death.^[1] Women are vulnerable to becoming overweight because of inadequate resources for physical activity, healthy food choices and family demands.

Objective:

1. To review the prevalence of obesity among women.
2. To determine risk factors of obesity among women.

Material and Method: A Quantitative approach with descriptive survey design was adopted for this present study. It was conducted among 300 adult women aged 20-60 years of selected wards of Athirampuzha Panchayat using simple random sampling method. BMI was calculated by WHO Asian classification and risk assessment check list was used to identify risk factors. Odd's ratio was used to examine association between obesity and risk factors.

Results: Prevalence of obesity was 24.3%. It was found that 66.2% of women were housewives. Common risk factors of obesity identified among women were consumption of bakery items (40%), family history and history of hypothyroidism (23.3%), excessive intake of fried item (35%), lack of exercise (34%), retained weight gain in relation to pregnancy (26.6%). Odds ratio shows significant positive association between obesity and risk factors [OR> 1].

Conclusion: Enhancing knowledge regarding regular physical activity and healthy dietary practices would obviously decrease the risk factors of obesity which would turn improve the health status of the women.

Keywords: Obesity, Prevalence, Risk factor, BMI, Women

Introduction

Obesity is promising sober health problem increasing hastily worldwide. Obesity is a state throughout that there's generalized buildup of humoring fat among the

body leading to a weight of quite two hundredth of the essential weight.^[1] Fatness invites disability, disease and premature death.^[2]

Obesity is considered as a 'hired gun lifestyle' disease. It is one of the leading preventable cause of death worldwide with increasing prevalence in both adults and children.^[3] Childhood obesity is a known precursor to adult obesity and other lifestyle diseases in adulthood.^[4] Adult hood obesity is the one of the most serious public health challenge of 21st century. According to World Health Organization, 1.2 billion people worldwide are formally classified as overweight. In the Indian setting, even with the increasing consciousness about health and

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fitness, more than 3% of the populations are obese. This is probably due to sedentary lifestyle of people. So there is an insistent need to create public awareness about the mechanisms of detection, prevention and treatment of obesity than ever before.^[5]

NFHS-3 has reported that more than 20% of urban Indians are overweight or obese. And in the northwestern Punjab, nearly 40% of all women are overweight or obese. Kerala is a second most state in obesity next to Punjab. That is 28% women and 18% of men aged 15 years to 49 years in Kerala were overweight or obese. The review also reported that 52.2% abdominal obesity was additional prevalent among women.^[6]

Obesity is a multi factorial phenomena and associates with age, sex, economical status, marital status, smoking, physical activity, education, traditions, levels of leisure time, parity, family history of obesity, alcohol consumption and dietary habits. In comparing to men, such determinant factors of obesity were normally accumulated in women. Women are vulnerable to becoming overweight because of inadequate resources for physical activity, healthy food choices and family demands.

The findings of many studies have shown that the incidence and the prevalence of obesity in women is higher in many countries compared to men and surprisingly the ratio is higher by 10–15% in women than in men and it is associated with socio economic status and lifestyle.^[7]

Women have more frequently opportunities to consume food and more likely to have greater volume of food available because they traditionally prepare meals for their families however more women are eating outside their home now a days on well as buying home food from restaurant food stall, fast food centers for their families^[8]. Among women of childbearing age, one potential pathway for the development of obesity has been through the retention of gestational weight gain.^[9]

In Kerala, life style diseases are common among women associated with multiple risk factors. Researcher experiences the fact that women are more conscious about their weight, but are unaware of healthy practices, it was necessary to have an accurate data to assess prevalence and risk factors of obesity among women in order to reduce future obesity burden.

Material and Method:

The present study was conducted in selected ward of Athirampuzha Panchayat, Kottayam among the women between the age group of 20-60 years during 2016. Sample consists of 300 was calculated on the basis of NFHS-3 data reported that prevalence of obesity among adult women in Kerala was 28% using $4PQ/D^2$ formula. [P=prevalence, Q=100-P, D=Allowable error]

Institutional ethics committee permission was obtained. And written informed consent of the study subjects was taken. Data for the present study was collected from women residing in 8, 9 and 10 wards of Athirampuzha Panchayat, Kottayam between the age group of 20-60 years. Wards were selected by lot method. A list of women in the age group of 20-60 years was obtained from the family survey register of JPHN. Samples were selected using tables of random numbers. Baseline information was collected using socio personal data sheet. Their height and weight were measured by measuring tape and standardized weighing scale. BMI was calculated with this measurement. BMI > 30 will be considered as obese based on WHO classification. The risk assessment checklist was used to identify the risk factors of obesity. Analysis was done using SPSS 16.0. Information Booklet regarding obesity, its prevention and management was prepared and given to the women after the data collection procedure. The content of the booklet was explained to each women and doubts were clarified.

Results

Table 1: Frequency distribution and percentage of women based on BMI (n=300)

Prevalence of obesity	f	%
BMI		
Under weight (<18.5)	18	6
Normal weight (18.5-24.9)	151	50.3
Over weight (25-29.9)	58	19.4
Obese (30 and above)	73	24.3

Table 1 depicts that 50.3% of the women were with normal (18.5-24.9) BMI. 24.3% were obesity, 19.4% were with overweight and only 6% were with underweight. Based on BMI table shows that prevalence of obesity (BMI > 30 and above) among women were 24.3%.

Table 2: Frequency distribution and percentage of women based on risk factors (n= 300)

Risk factors	Yes		No	
	f	%	f	%
Family history	70	23.3	230	76.6
History of PCOD	68	22.6	232	77.3
History of hypothyroidism	70	23.3	230	76.6
Excess intake of food	29	9.6	271	90.3
Consumption of ghee > three times/week	43	14.3	257	85.6
Consumption of fried items> three times /week	105	35	195	65
Consumption of egg with yolk > three times /week	58	19.3	242	80.6
Consumption of meat > three times/week	85	28.3	215	71.6
Consumption of bakery items/ ice cream / chocolate > three times/week	120	40	180	60
Lack of exercise	102	34	198	66
Stress in daily life	59	19.6	241	80.3
Excessive sleep	55	18.3	245	81.6
Retained weight during Pregnancy and postpartum care	80	26.6	220	73.3
Intake of steroids > three months	34	11.3	266	88.6
Intake of antipsychotics > three months	4	1.3	296	98.6
Intake of antiepileptics > three months	3	1	297	99

Table 5 shows the risk factors of obesity and findings reveals that 40% of the women were consuming bakery items, ice cream, and chocolate more than 3 times/week. 35% of the women were consuming fried items more than 3 times/week. 34% of the women had lack of exercise in their routine 28.3% of the women were consuming meat more than 3 times/week. 26.6% of women had weight gain during pregnancy and post partum care. 22.6% of the women had a history of PCOD, 23.3% of

the women had a family history of obesity and history of hypothyroidism. Table also shows that. 19.3% of the women were consuming egg with yolk more than 3 times /week. 14.3% of the women consuming ghee more than 3 times /week. 19.6% of the women were experiencing excessive stress in their life and also 18.3% of women had excessive sleep more than 8 hours per day and 11.3 % of the women were using steroid medication more than three months.

Table 3: Frequency distribution, and Odd’s ratio of women based on dietary habits (n=300)

Risk factor	Obese	Non obese	Odds ratio	CI Lower limit	CI Upper limit
	f	f			
Excess intake of food	19	10	7.46*	3.28	16.95
Consumption of ghee > three times/ week	24	19	5.22*	2.65	10.52
Consumption of fried items> three times /week	54	51	9.26*	5.08	16.88
Consumption of egg with yolk> three times /week	36	22	8.78*	4.66	16.55
Consumption of meat >three times/week	43	42	6.07*	3.43	10.75
Consumption of bakery items/ ice cream / chocolate > three times/week	56	64	8.38*	4.53	15.51

Table 3 depicts that Odd ratio is significant at 95% confidence interval[OR>1] and it shows that there is a positive association between obesity and dietary habits.

Table 4: Frequency distribution and Odd's ratio of women based on lack of exercise, stress in daily life, excessive sleep, retained weight during pregnancy and post partum care (n=300)

Risk factor	Obese	Non obese	Odds ratio	CI Lower limit	CI Upper limit
	f	f			
Lack of exercise	54	48	10.01*	5.47	18.31
Stress in daily life	24	35	2.61*	1.43	4.80
Excessive sleep	33	22	7.46*	3.95	14.08
Retained weight during Pregnancy and postpartum care	55	25	23.27*	11.94	45.34

Table 4 depicts that Odds ratio is significant at 95% confidence interval [OR>1] and it shows that there is a positive association between obesity and lack of exercise, stress in daily life, excessive sleep, retained weight during pregnancy and postpartum care

Table 5: Frequency distribution and Odd's ratio of women based on family history of obesity, history of PCOD, history of hypothyroidism (n=300)

Risk factor	Obese	Non obese	Odds ratio	CI Lower limit	CI Upper limit
	f	f			
Family history	40	30	7.68*	4.23	13.96
History of PCOD	27	41	2.57*	1.44	4.61
History of hypothyroidism	34	36	4.48*	2.51	8.00

Table 5 depicts that Odds ratio is significant at 95% confidence interval [OR>1] and it shows that there is a positive association between obesity and family history of obesity, history of PCOD, history of hypothyroidism

Discussion

The present study was carried out in the selected ward of Athirampuzha Panchayat among 300 adult women aged 20-60 years.

The first objective of the study: was to assess prevalence of obesity among women. The findings of the present study shows that prevalence of obesity was 24.3% and it is congruent with the findings of a cross-sectional study carried out on prevalence of overweight and obesity among adult population at Malaysia population aged 18-59 years old and it reveals that the prevalence of obesity among women was 22.9%.^[10] A study was undertaken in an urban slum in Chennai city to find out the prevalence of overweight and obesity among women aged 20 years and above revealed that prevalence of obesity was 19.8%.^[11] Another cross sectional study was conducted among 300 adults in Nellanadu Panchayath, a rural area in Trivandrum, Kerala shows that prevalence of obesity was 40.7% in women.^[12]

The second objective: was to identify the risk factors of obesity among women and findings revealed

that majority of women (40%) were consuming of bakery items/ ice cream / chocolate more than 3 times/ week. 35% of the women were consuming fried items more than 3 times/week. 34% of the women had lack of exercise in their routine 28.3% of the women were consuming meat more than 3 times/week. 26.6% of women had weight gain during pregnancy and post partum care. 22.6% of the women had a history of PCOD, 23.3% of the women had a family history of obesity and history of hypothyroidism.

The study findings are congruent with the findings of another study to review causes of obesity among adult at UK London, findings shows that risk factors for obesity were sedentary lifestyles, a high intake of energy-dense, micronutrient-poor foods, heavy marketing of energy-dense foods and fast food outlets, sugar-sweetened soft drinks and fruit juices, adverse social and economic conditions developed countries, especially in women.^[13]

The third objective of the study: was to find out association of obesity and risk factors. And findings reveals that [OR>1] there is a positive association was

found between obesity and all mentioned risk factors. The study findings are congruent with the descriptive epidemiological study was carried out among seven thirty adults of 15-64 yr age group in a village of West Bengal revealed that there is a significant association was found with age group, per capita income, tobacco use, alcohol consumption, physical activity, salt intake with food and intake of oils.⁴⁹

Conclusion

The major conclusion drawn from this study is that low levels of physical activity, intake of bakery items, stress in daily life, excessive sleep, retain weight after pregnancy were associated with a higher prevalence of obesity. Thus, participation in household activities and regular physical exercise could help in lowering the prevalence of overweight. And also educate adult women on the aspects of healthy dietary habits and desired lifestyles to prevent overweight/obesity and its associated ill effects.

Ethical Clearance: Taken from Institutional ethical committee. IEC no:86/2016

Conflict of Interest: None

Source of Funding: Self

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Reference

1. Patidar OP. Higher prevalence rate of CHD in 'apple type of obesity' cases as compared to 'pear type obesity' cases. Indian Journal of Clinical Practice. 2013 May;23(12):791-4.
2. Park K, Park K. Text Book of Preventive and Social Medicine, M/s. Epidemiology of chronic non-communicable diseases and conditions. 23rd ed. Jabalpur. M/s Banarsidas Bhanot publishers. 2015:298-392.
3. Sethi P, Thillai M, Nain PS, Ahuja A, Vayoth SO, Khurana P. Effects of Laparoscopic Sleeve Gastrectomy on Central Obesity and Metabolic Syndrome in Indian Adults-A Prospective Study. Journal of clinical and diagnostic research: JCDR. 2017 Jan;11(1):PC01.
4. S Shalimol U, Sudhi Sudhakaran & K Kumar, Dheeraj. (2018). Level of activity and obesity among high school children. Indian Journal of Public Health Research & Development. 9. 205. 10.5958/0976-5506.2018.00721.0
5. World Health Organization. Obesity Data and Statistics. WHO regional office for Europe. [internet] 2014 [cited by October 2014]; Available from <http://www.euro.who.int/en/health-topics/noncommunicable-diseases/obesity/data-and-statistics>
6. Girdhar S, Sharma S, Chaudhary A, Bansal P, Satija M. An epidemiological study of overweight and obesity among women in an urban area of north India. Indian journal of community medicine: official publication of Indian Association of Preventive & Social Medicine. 2016 Apr;41(2):154.
7. Saboo B, Talaviya P, Chandarana H, Shah S, Vyas C, Nayak H. Prevalence of Obesity and Overweight in Housewives and Its Relation with Household Activities and Socioeconomical Status. Journal of Obesity and Metabolic Research [Internet] January 2014 [cited 2016 March 13]; 1(1): 20-24 Available from <http://www.jomrjournal.org> IP: 180.215.120.152
8. Wang MC, Naidoo N, Ferzacca S, Reddy G, Van Dam RM. The role of women in food provision and food choice decision-making in Singapore: a case study. Ecology of food and nutrition. 2014 Nov 2;53(6):658-77.
9. Siega-Riz AM, Evenson KR, Dole N. Pregnancy-related weight gain—a link to obesity?. Nutrition reviews. 2004 Jul 1;62(suppl_2):S105-11.
10. Baharudin A. Escalating prevalence of overweight and obesity among Malaysian adults. Medical Journal of Malaysia. [Internet] 2013 [cited September 2015] Vol 70 (1): Available from <http://www.e-mjm.org/2015/v70s1/mjm-sept-suppl-2089.html>
11. Anuradha R, Ravivarman G, Jain T. The prevalence of overweight and obesity among women in an urban slum of Chennai. J Clin Diagn Res. 2011 Oct;5(5):957-60.
12. Bindhu AK, Jose RP, Beevi N. Prevalence of obesity and overweight among adults in a rural area

- in Trivandrum: a cross sectional study. *Int J Prev Ther Med.* 2014 Apr;2.
13. Swinburn BA, Caterson I, Seidell JC, James WP. Diet, nutrition and the prevention of excess weight gain and obesity. *Public health nutrition.* 2004 Feb;7(1a):123-46.
14. Sen J, Mondal N, Dutta S. Factors affecting overweight and obesity among urban adults: a cross-sectional study. *Epidemiology, Biostatistics and Public Health.* 2013 Jan 17;10(1).

Assess the Knowledge and Risk Factors among Pregnancy Induced Hypertension among Antenatal Mothers

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Abstract

Background of the Study: Hypertension, complicating 5-10% of all pregnancies worldwide, is a leading cause of maternal and fetal morbidity. The control of pregnancy-induced hypertension (PIH) appears difficult to achieve. Part of the reason for poor control of hypertension in these women might be limited PIH self-care knowledge.

Objective: to assess the knowledge and risk factors of PIH among antenatal mothers and to find out the association between knowledge and risk factors with selected demographic variables.

Materials and Method: Study was conducted on 110 antenatal mothers attending in Gynecologic OPD, AIMS, Kochi, Kerala. The research design used was non experimental descriptive design.

Result: The present study reveals that more than half of the mothers (63.6%) had average knowledge regarding PIH. Half of the mothers had the risk factors of family history of hypertension (50%) and followed by 32.7% had the habit of high non vegetarian food intake. A statistically significant association was observed for education and knowledge and comorbidities and knowledge of antenatal mothers. Significant association was found in risk factors and comorbidities of antenatal mothers.

Conclusion: The finding of the study shows that antenatal mothers had average knowledge related to PIH. Health care providers should implement the focused health education programme during antenatal visit

Keywords: Knowledge, Pregnancy Induced Hypertension, antenatal mothers, risk factors, Pregnancy.

Introduction

Pregnancy is a kind of miracle by the god and a mother's joy begins when new life is stirring inside and a tiny heartbeat is heard for the very first time. Pregnancy is the unique and exciting time in woman's life, as it highlights the woman's amazing creative and nurturing powers while providing a bridge to the future¹. Hypertensive conditions during pregnancy

contribute greatly to maternal mortality and morbidity around the world. It is the most common medical problem encountered during pregnancy, complicating 2-3% pregnancies. Approximately 1, 00,000 women die worldwide per annum because of Pregnancy Induced Hypertension (PIH). Although prompt recognition and treatment can greatly reduce the morbidity and mortality associated with pregnancy-induced hypertension and preeclampsia, the only known resolution is delivery of the fetus and placenta¹.

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Pregnancy induced hypertension is a common medical disorder seen associated with pregnancy, and it leads more complication when it unregistered. Maternal and fetal morbidity and mortality can be reduced by early recognition and institutional management.² Darling B Jiji conducted a study regarding a study to assess the

knowledge of risk factors about pregnancy induced hypertension and availability of supplies among health care workers in the selected health care facilities in Sebha, Libya. Finding of the study showed that majority of 76(55.1%) had adequate knowledge about pregnancy induced hypertension and 62(44.9) had inadequate knowledge about pregnancy induced hypertension .³

Maternal mortality in PIH is primarily due to low standard of care and delay in referral services. One of the most important functions of antenatal care is to detect high risk pregnancies and give them the necessary care .Early detection of pre-eclampsia and eclampsia is important in reducing the maternal and neonatal mortality and morbidity.⁴

Pregnancy-induced hypertension occurs in about 5-8% of all pregnancies. Although the cause of PIH is unknown, certain factors are known to increase the risk of PIH, such risk factors include that PIH mostly affects young women with a first pregnancy, pregnant women younger than 20 years and those older than 40 years, women with multiple fetuses, pregnant diabetics, pregnant women with preexisting hypertension or previous episodes of preeclampsia or PIH and pregnant women with preexisting renal disease.⁵

The present study is an attempt to assess the level of knowledge and risk factors regarding pregnancy induced hypertension. It also aims to find out the association between the level of knowledge and selected demographic variables.

Materials and Method

The Study was conducted on 110 antenatal mothers⁶ and the research design used was non experimental descriptive design. The subjects were selected by Convenience sampling technique based on inclusion criteria and a rapport was established with them. The researcher explained the purpose of the study and obtained an informed consent from them and the tools were administered. The demographic data and clinical data were obtained from the subject themselves. The data regarding knowledge and risk factors of pregnancy induced hypertension was obtained using self-prepared questionnaire and checklist. Each sample took 15 minutes to fill the questionnaire. The data obtained was analyzed using descriptive and inferential statistics and association using Chi Square.

Results

Out of 110 antenatal mothers majority of the subjects were belongs in the age group of below 25 years (44.5%), most of them were graduate (42.7%) and 76.4% women were unemployed. About (60.0%) were resided in city with in that (68.2%) are primi mothers and (69.1%) not had any history of co morbidities like GDM, thyroid dysfunction, heart diseases etc.

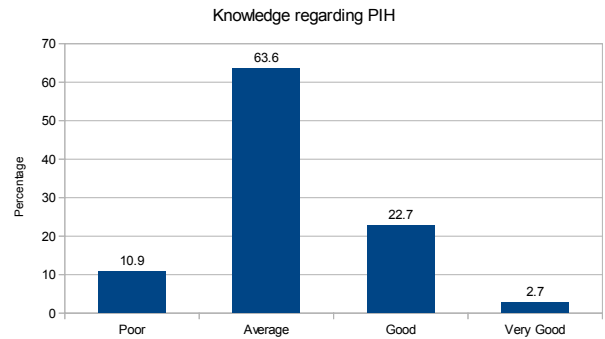


Figure 1: Distribution of subjects based on knowledge regarding pregnancy induced hypertension.

About 63.6% had average knowledge regarding pregnancy induced hypertension and 22.7% had good knowledge.

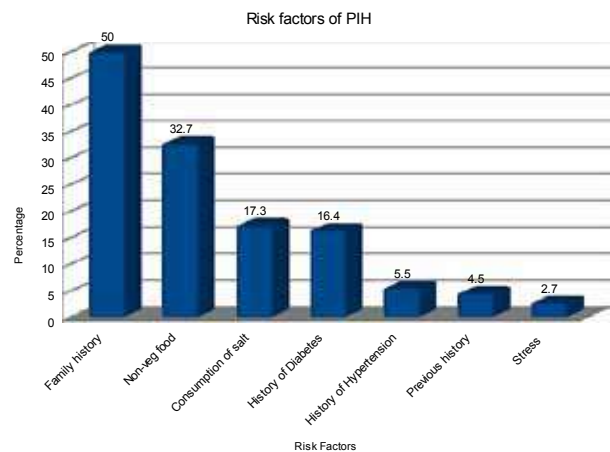


Figure 2: Assess the risk factors of PIH among antenatal mothers.

Risk factors of pregnancy induced hypertension are only 4.5% in women with previous history. 50% had family history of hypertension and no relevant history of twin pregnancy. 16.4% of mothers had history of diabetes, 5.5% had history of hypertension and there was no relevant history of renal disease. 17.3% mothers had habit of high salt intake, 2.7% had stress and about 32.7% had habit of high non veg food intake

Table 1: Association of level of knowledge among antenatal mothers and selected demographic variables
n=11

Variable	Category	Knowledge				Chi square	df	P value
		Average		Good				
		F	%	F	%			
Age	<= 25	39	79.6	10	20.4	1.186	2	.553
	25-30	31	70.5	13	29.5			
	>30	12	70.6	5	29.4			
Education	Below degree	50	84.7	9	15.3	6.978	1	.008
	Above degree	32	62.7	19	37.3			
Occupation	Unemployed	66	78.6	18	21.4	3.036	1	.081
	Employed	16	61.5	10	38.5			
Residence	Village	34	77.3	10	22.7	.287	1	.592
	City	48	72.7	18	27.3			
Parity	Primi	59	78.7	16	21.3	2.110	1	.146
	Multi	23	65.7	12	34.3			
Comorbidities	Yes	20	58.8	14	41.2	6.410	1	.011
	No	62	81.6	14	18.4			

Data in table 2 shows that there was significant association found in knowledge of antenatal mothers and education (p= .008) and level of knowledge with comorbidities (p=.011) among antenatal mothers. However no association was found between antenatal knowledge and selected variables like age, occupation, parity and residence.

Table 2: Association between risk factors of PIH and selected demographic variables

Variable	Category	Knowledge				Chi square	df	P value
		Average		Good				
		F	%	f	%			
Age	<= 25	11	22.4	38	77.6	1.479	2	.477
	25-30	7	15.9	37	84.1			
	>30	5	29.4	12	70.6			
Education	Below degree	12	20.3	47	79.7	0.25	1	.874
	Above degree	11	21.6	40	78.4			
Occupation	Unemployed	19	22.6	65	77.4	.628	1	.428
	Employed	4	15.4	22	84.6			
Residence	Village	11	25.0	33	75.0	.742	1	.389
	City	12	18.2	54	81.8			
Parity	Primi	19	25.3	56	74.7	2.790	1	.095
	Multi	4	11.4	31	88.6			
Comorbidities	Yes	2	5.9	32	94.1	6.719	1	.010
	No	21	27.6	55	75.4			

Data in table 3 shows that there was a significant association found in risk factors of antenatal mothers comorbidities. However no association found between age, education, occupation, residence and parity.

Discussion

Hypertension during pregnancy may lead to several problems to the mother and child. It was a major pregnancy complication, causing premature delivery, fetal growth retardation, abruption placenta, and fetal death, as well as maternal morbidity and mortality. The present study revealed that 63.6% had average and 22.7% had good knowledge regarding PIH. Another study conducted by Darling B Jiji to assess the knowledge of risk factors about pregnancy induced hypertension among 138 antenatal mothers revealed that majority 76(55.1%) had adequate knowledge about pregnancy induced hypertension and 62(44.9%) had inadequate knowledge about pregnancy induced hypertension.

In the present study explored risk factors of pregnancy induced hypertension were 4.5% of women with previous history of PIH. 50% of mothers had family history of hypertension. About 16.4% of mothers having history of diabetes, 6% having history of hypertension .17.3% mothers are having habit of high salt intake, 2.7% are in stress and about 32.7% having habit of non-veg food intake. Another study conducted by Leanne Bellamy to investigate pre-eclampsia and risk of cardiovascular disease and cancer in later life among 3488160 women revealed that after pre-eclampsia women have an increased risk of vascular disease. The relative risks for hypertension were 3.70 after 14.1 years weighted mean follow-up, for ischemic heart disease 2.16 after 11.7 years, for stroke 1.81 after 10.4 years, and for venous thromboembolism 1.79 after 4.7years⁷.

It was also identified in the present study, that there is a significant association between pregnancies induced hypertension and mother's educational status and comorbidities (previous history, family history, history of diabetes, history of hypertension, stress etc.). The finding was consistent with the study conducted by LA Rahman, NN Hari, N Salleh to investigate the association between PIH and low birth weight. This study revealed that there was a significant association of pregnancy induced hypertension with low birth weight⁸.

Conclusion

Pregnancy-induced hypertension is a common medical disorder seen associated with pregnancy, and it leads more complication when it unregistered. Maternal and fetal morbidity and mortality can be reduced by early recognition and institutional management. Early diagnosis and treatment through regular antenatal check-

up is a key factor to prevent hypertensive disorders of pregnancy and its complications.

Conflict of Interest: Nill

Source of Funding: Self

Ethical Aspects: Ethical clearance was obtained from Institutional Thesis Review Committee after presenting the proposal. Informed consent was obtained from the participants.

Reference

1. Joseph Sr J, Nayak S, Fernandes P, Suvarna V. Effectiveness of Antenatal Care Package on Knowledge of Pregnancy Induced Hypertension for Antenatal Mothers in Selected Hospitals of Mangalore. Nitte University Journal of Health Science. 2013 Mar 1;3(1):8.
2. Singh V, Srivastava M. Associated risk factors with pregnancy-induced hypertension: A hospital-based KAP study. *International Journal of Medicine and Public Health*. 2015;5(1).
3. Cabading ML, Benjamin BA. A study to assess the kn factors about pregna hypertension and the avai among health care worke health care facilities.
4. Podymow T, August P. Postpartum Course of Gestational Hypertension And Preeclampsia: 235. *American Journal of Obstetrics and Gynecology*. 2006 Feb 1;193:S76.
5. Pswarayi I. The relationship between pregnancy induced hypertension (PIH) self care knowledge and hypertension control among pregnant mothers aged 18 to 49 years in Bindura District.
6. Sajitha AT, Anju Philip T, Sarika TK. Effectiveness of Prenatal Education Regarding Practice on Antenatal Exercises and Minor Ailments among Pregnant Mothers. *Journal of Clinical & Diagnostic Research*. 2018 Sep 1;12(9).
7. Leanne Bellamy. Pre-eclampsia and risk of cardiovascular disease and cancer in later life: systematic review and meta-analysis. *BMJ*. 2007;pp.974-977.
8. Rahman LA, Hair NN, Salleh N. Association between pregnancy induced hypertension and low birth weight; a population based case-control study. *Asia Pacific Journal of Public Health*. 2008 Apr;20(2):152-8.

Improvement of Diabetic Patients' Knowledge Regarding Foot Problems: An Intervention Study

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Abstract

Background: Many diabetic patients are affected by diabetic foot, a devastating and potentially fatal condition mostly due to lack of knowledge of foot care. Aim of the study: to evaluate the effectiveness of nursing intervention program on patient's knowledge about diabetes and foot care.

Subjects and Method: This quasi-experimental study was carried out at the Diabetes and outpatient clinics of Beni-Suef University hospitals on a convenience sample of 158 adult diabetic patients. An interview questionnaire was used to collect data on patient's socio-demographic and diabetes characteristics and patient's health habits, in addition to, knowledge questionnaire and diabetic foot screening format which used to assess foot condition.

Results: The sample had an equal gender distribution, and mostly had intermediate education (41.1%), with 52.5% having their diabetes for less than five years, 77.2% had one or more abnormal physical finding in foot assessment. Overall, 32.9% had satisfactory knowledge before the intervention, and this significantly increased to 90.5% after the intervention ($p < 0.001$). In multivariate analysis, the study intervention was the main positive predictor of the knowledge score change.

Conclusion and Recommendations: A patient's education program is effective in improving patients' knowledge about diabetes and diabetic foot. It should be widely used in educating diabetic patients. A longer term study is proposed to investigate the impact of knowledge improvement on prevention of diabetic foot.

Keywords: Diabetic foot, Knowledge, Health education

Introduction

Diabetes mellitus (DM) is one of the chronic diseases which need active participation from patients to achieve good control and avoid complications [1]. According to the World Health Organization (WHO), the worldwide prevalence of diabetes in adults in the year 2014 amounted to 8.5%, with higher rates in developing

countries, including Egypt. The related mortality is expected to have a twofold increase from 2005 and 2030, with diabetic foot having a major contribution as a death cause [2].

As many as 8-17% of diabetic patients are affected by diabetic foot, and one in five of diabetic patients attending hospitals present with foot problems [3]. Although diabetic foot is an ominous complication of diabetes, it is one of the most amenable to prevention [4]. The condition presents with infection, ulcer formation, with possible deep tissue destruction leading to vascular and neurological disorders in the foot and lower extremity which leading to amputation of the lower limb

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with a rate reaching the double in comparison with non-diabetic people [5,6,7].

According to [8] the lack of knowledge of foot care and related deficient practices are significant risk factors for diabetic foot in diabetic patients. Thus, good patient education for those with high risk may prevent this deleterious complication. Moreover, a correct management of diabetic foot can prevent complications as gangrene and amputation. Nevertheless, diabetic patients often neglect proper foot care practice so long they do not have complications; additionally, patient education often starts after foot complications have already started. So, patient education is urgent, prominent and activities should give more focus to patient responsibility for own health [9,10].

Diabetes mellitus (DM) is a public health problem in Egypt, with high prevalence especially in rural communities. The risk factors for diabetic foot and related complications are also higher and are related to patients' socioeconomic status, especially education. These patients need to be educated regarding proper foot care, which would have a positive influence on their practices.

Aim of the Study: The aim of this study was to evaluate the effectiveness of nursing intervention program on patient's knowledge about diabetes and foot care.

Research Hypothesis: The percentage of patients with satisfactory knowledge will significantly increase after implementation of the educational program.

Subjects and Method

Design and setting: quasi-experimental design with pre-post assessment was used in carrying out this study at Diabetes and outpatient clinics at Beni-Suef University hospitals.

Subjects: A convenience sampling technique was used and all patients attending aforementioned settings during the time of study was eligible for the study upon fulfilling the inclusion criteria of being adult, diagnosed as having diabetes at least three months before, and have early signs of diabetic foot were participated in the intervention. Patients with any physical or mental disablement were excluded. The sample size was calculated to demonstrate an improvement of the percentage of participants with satisfactory knowledge

from a pre-intervention level of 50% by an Odds Ratio of 2.0 at 95% level of confidence and 80% power. Accordingly, using the Open-Epi software package, the required sample size was 137. This was increased to 158 to compensate for an expected dropout rate around 10%.

Data Collection Tool: The researchers used an interview questionnaire form and a diabetic foot screening format to collect required data

The interview questionnaire comprised four sections the first is patient's socio-demographic characteristics including age, gender, level of education, residence, marital status and job. A second section covered the characteristics of diabetes as the duration and mode of discovery, as well as the history of other chronic diseases, and perception of health. These two sections were developed by the researchers based on review literature. A third section, based on [11] addressed patient's health habits such as dietary regimen, physical activity, smoking, eye, dental, and foot care. It also comprised the habits of testing urine and blood, follow-up, as well as having DM card. The sum of healthy practices reported to be done was calculated and divided by the total number of practices and presented as a percent score; a higher percent score indicated healthier practices.

The last section was developed by researchers based on review literature the questionnaire consisted of knowledge test for pre-post assessment. It consisted to a series of True/False questions covering the definition, symptoms, complications, prevention, and treatment of diabetes, as well as questions on suitable diet, insulin injection, travel arrangement, foot care, and selection of suitable footwear. For scoring, the correct response for each item was scored 1 and the incorrect zero. Knowledge was considered satisfactory if the percent score was 50% or more and unsatisfactory if less than 50%.

The diabetic foot screening format: This was developed by the National Foot Treatment Center (1990), and was modified by the researchers to suit the aim of the study. It covered foot anomalies as Charcot, callous, dryness/cracks, etc.; foot infections as interdigital fungus and interdigital wounds; foot sensation as hypoesthesia, anesthesia, no sweating, etc. and atherosclerosis as inability to walk due to pain, cold extremities, absence of pulse, etc. The sum of the number of anomalies found by foot examination was calculated and divided by the

total number of possible anomalies and presented as a percent score; a higher percent score indicated more physical examination anomalies. The patient height and weight was also recorded to calculate Body Mass Index (BMI).

Pilot Study: The tools were rigorously revised by a panel of experts in nursing and medicine for validity, reliability, and modified according to their recommendations. Then, they were pilot-tested on a sample representing about 10% of the sample size. The tools were finalized in view of the pilot results. The pilot sample was not included in the main study sample.

Fieldwork: The study was carried out from October 2017 to April 2018. It was conducted through assessment, planning, intervention, and evaluation phases. The assessment phase was started after securing all needed permissions. The researcher met individually with the diabetic patients in the settings, explained the aim of the study and its process. After they were giving their consent they interviewed to fill the first tool. Then, foot examination was done using the second tool. In the planning phase, the researchers used the assessment data to develop an educational program that meets the identified diabetic patients' needs and to fill their knowledge gaps. The program covered various areas of diabetes disease. The researchers developed an illustrated booklet in simple Arabic language to help participants to retain knowledge.

The implementation phase involved application of the program to participants. This was done in small group sessions of 9-10 patients in the study settings while patients were waiting for service or after obtaining it. Each session lasted 45-60 minutes. The sessions were interactive with ample time given for questioning and discussions. Audiovisual aids were used in short presentations with demonstrations and brain storming. The program involved a theoretical part for diabetes knowledge, and a practical part including foot care practices such as skin care, proper nail cutting, selection of footwear, etc. By end of the program, its effectiveness in improving participants' knowledge was measured through a posttest using the knowledge section of 1st tool.

Administrative and ethical considerations: The data collection took place in collaboration with two Non-Governmental Organizations (NGOs), namely Women's Health and Resala company. Before starting

any data collection, official permissions to conduct the study were obtained from the medical and nursing directors of the study setting. The researcher explained the aim of the study and its procedures to eligible patients in simple terms to get their oral informed consent. They were informed about the rights to refuse participation or withdraw at any time and about the confidentiality of the study.

Statistical Analysis: Data entry and statistical analysis were done using SPSS version 20.0. Data were presented using descriptive statistics in the form of frequencies and percentages for qualitative variables, and means, standard deviations and medians for quantitative variables. Spearman rank correlation was used for assessment of the inter-relationships among quantitative variables and ranked ones. In order to identify the independent predictors of the knowledge score, multiple linear regression analysis was used.

Results

As presented in **Table 1**, more than half of the study sample had diabetes for less than five years (52.5%), and it was mostly discovered by chance (57.4%). One half of them experienced hypoglycemia (50.0%). The majority were overweight to obese (38.9%, 34.8%).

Regarding practices, **Table 2** demonstrates a wide variation as, some healthy practices were reported to be done by majority of patients including proper wound care (89.2%), & eye care (85.4%). Minority of them reported visiting dentist (3.2%), testing urine daily (7.0%), having DM card (22.2%), brushing teeth (24.7%) and foot care was reported by 72.2% of them. The median percent of total healthy practices was 47.1%.

Table 3 demonstrates that the most common abnormal findings of feet examination were dryness and cracks (49.4%), hypoesthesia (48.1%), leg/thigh pain (29.9%), and delayed wound healing (29.1%). In total, the majority (77.2%) had one or more abnormal physical finding.

As shown in **Table 4**, patients' knowledge about DM was variable before the study intervention. The majority had correct knowledge of the DM definition, symptoms, and prevention, as well as insulin injection and none of them had correct knowledge of foot care or suitable footwear. The implementation of the intervention led to significant improvements in all knowledge areas. Only 32.9% of the patients had satisfactory knowledge before

the intervention, which significantly increased to 90.5% after the intervention ($p < 0.001$).

Table 5, points to significant positive correlation between patients’ knowledge scores and healthy habits practice ($r=0.252$). It also shows positive correlations between knowledge and practice scores which negatively correlated with age. The duration of diabetes also correlated negatively with knowledge score in pre-test ($r=-0.241$).

The multivariate analysis (Table, 6) identified the study intervention as the main positive predictor of the knowledge score change, in addition to having DM card. On the other hand, having a lower health perception was a negative predictor of this score. The model explains 52% of the variation in the knowledge score.

Table 1: Describe disease and medical characteristics of patients in the study sample (n=158)

Items	Frequency	Percent
Duration of diabetes (years):		
<5	83	52.5
5+	75	47.5
Mode of discovery of DM:		
By chance	59	57.4
Symptoms/signs	85	53.8
Coma	14	8.9
Had hypoglycemia	79	50.0
Had diabetic coma	43	27.2
Other chronic diseases	74	46.8
Body Mass Index (BMI):		
Normal (<25)	42	26.6
Overweight (25-<30)	61	38.6
Obese (30+)	55	34.8
Mean±SD	29.3±7.2	
Perception of health:		
Good	19	12.0
Average	139	88.0

Table 2: Illustrate health habits practices for DM management among study sample (n=158)

Items	Frequency	Percent
Dietary habits:		
Follow dietary regimen	87	55.1
Take balanced diet	70	44.3
Take small frequent meals	94	59.5
Practice sports	93	58.9

Items	Frequency	Percent
No smoking	130	82.3
Use non-prescribed medications	92	58.2
Regular:		
Bathing	128	81.0
Brushing teeth	39	24.7
Visit dentist	5	3.2
Foot care	114	72.2
Eye care	135	85.4
Eye examination	51	32.3
Can test urine	17	10.8
Test urine daily	11	7.0
Lab test blood/urine	120	75.9
Proper wound care	141	89.2
Follow-up	115	72.8
Have DM card	35	22.2
Got instructions for DM care	50	31.6
Total practice score:		
Mean±SD	45.6±12.9	

Table 3: Clarify Foot examination findings among study sample (n=158)

	Frequency	Percent
Foot anomalies:		
Charcot / Callous	18	11.4
Dryness/cracks	78	49.4
Foot infections:		
Interdigital fungus	29	18.4
Interdigital wounds	39	24.7
Sensation:		
Hypoesthesia	76	48.1
Anesthesia	3	1.9
No sweating	13	8.2
Dryness	35	22.2
Bluish discoloration	9	5.7
Atherosclerosis:		
Leg/thigh pain	46	29.1
Inability to walk due to pain	40	25.3
Foot pain	20	12.7
Cold extremities	30	19.0
Absence of pulse	9	5.7
Delayed wound healing	46	29.1
BP >140/90	36	22.8
Presence of any anomalies:		
No	36	22.8
Yes	122	77.2
No. of anomalies:		
Mean±SD	3.3±2.5	

Table 4: Describe knowledge score among study participants pre and post intervention(n=158)

Knowledge	Pre		Post		X ²	p-value
	No.	%	No.	%		
Definition	134	84.8	149	94.3	7.61	0.006*
Symptoms	140	88.6	150	94.9	4.19	0.04*
Complications	122	77.2	146	92.4	14.15	<0.001*
Prevention	140	88.6	147	93.0	1.86	0.17
Treatment	114	72.2	147	93.0	23.97	<0.001*
Pancreas	94	59.5	151	95.6	59.02	<0.001*
Pancreas function	97	61.4	153	96.8	60.06	<0.001*
Suitable diet	89	56.3	109	69.0	5.41	0.02*
Insulin injection	144	91.1	155	98.1	7.52	0.006*
Travel arrangement	94	59.5	158	100.0	80.25	<0.001*
Foot care	0	0.0	153	96.8	296.61	<0.001*
Suitable footwear	0	0.0	141	89.2	254.61	<0.001*
Total knowledge:						
Satisfactory (50%+)	52	32.9	143	90.5		
Unsatisfactory (<50%)	106	67.1	15	9.5	110.90	<0.001*

(*) Statistically significant at p<0.05

Table 5: Correlation between patients’ knowledge, Health habits practice scores, clinical findings, and their certain socio demographic characteristics (n=158)

Items	Spearman’s rank correlation coefficient		
	Knowledge Score	Health habits practice score	No. of abnormal findings
Health habits practice score	.252**		
No. of abnormal findings	0.08	-0.15	
Age	-.306**	-.246**	0.00
Education	.248**	.232**	-0.02
Income	0.12	.170*	0.03
Duration of DM	-.241**	-0.11	-0.05
BMI	-0.10	-0.06	0.15

(**) Statistically significant at p<0.01

Table 6: Best fitting multiple linear regression model for patients’ knowledge score(n=158)

	Unstandardized Coefficients		Standardized Coefficients	t-test	p-value	95% Confidence Interval for B	
	B	Std. Error				Lower	Upper
Constant	25.57	6.57		3.891	<0.001	12.64	38.50
Intervention	35.97	1.99	0.71	18.073	<0.001	32.05	39.88
DM card	5.77	2.40	0.09	2.406	0.017	1.05	10.48
Lower health perception	-7.64	3.06	-0.10	-2.498	0.013	-13.66	-1.62

r-square=0.52 ANOVA: F=112.85, p<0.001

Discussion

The study findings indicate that only one-third of the diabetic patients in the study sample had satisfactory knowledge before the intervention. This increased significantly after implementation of the educational program, which leads to acceptance of the set research hypothesis.

The present study was carried out on a sample representing the population of diabetic patients in the fourth to fifth decades of their age. The diabetic state was mostly discovered by chance among these participants which is a commonly reported finding in previous research. It indicates low health awareness and health behavior among them. This result is in agreement with a study in Italy which revealed that about two-thirds of the diabetic patients discovered their disease just by mere chance [12].

Moreover, one half of participants in the current study reported having had hypoglycemia; additionally, more than one-fourth of them had previously experienced an attack of diabetic coma. This further indicates poor diabetic control among them, which is explained by the low practice scores as the study findings revealed, particularly regarding regular testing of urine for glucose. The reported rate of hypoglycemia is very high compared with the rates reported by [13]. In a study at the United States. Thus, the risk of hypoglycemic attacks is one of the most important indicators of good diabetic control as recommended by [14].

Majority of patients in the present study were overweight or obese. This result corroborates the poor control of diabetes among them as it reveals lack of strict following a DM dietary regimen. The importance of weight reduction and compliance with a dietary regimen was outlined in a systematic review [15]. However, to be effective in achieving good glycemic control, this regimen should lead to >5% weight loss. Thus, bariatric surgery could have an important preventive role in the management of recent onset diabetes [16].

Concerning foot care, the current study results showed that more than one-fourth of participants do not practice good foot care. It might indicate lack of proper patient education since only less than one-third of the patients reported having had instructions for DM care. Similarly, a low level of practice of diabetic foot care was demonstrated among Iraqi diabetic patients [17]. Hence, a study in Brazil underscored the importance

of patient education to improve their practice of good diabetic foot care [18].

The lack of good health habits practices among study sample was reflected on the prevalence of abnormal physical findings identified among them. The most common of these problems include dryness and cracks, hypoesthesia, pain, and delayed wound healing. The median number of abnormal findings was 4, indicating that at least one-half of the sample had four or more of these abnormal findings. In congruence with this, a study in Japan among diabetic patients found that calluses and cracks were the most prevalent signs of non-ulcerative diabetic foot [19].

Although patients' knowledge about DM was generally acceptable before the study intervention, but none of them had correct knowledge of proper foot care or suitable footwear. This might explain the high prevalence of abnormal physical findings among them in feet examination. In fact, the multivariate analysis revealed a negative relation between the knowledge score and the number of abnormal physical findings. Thus, a better knowledge score is associated with a lower number of abnormal findings. In agreement with this, a study in Malaysia by [20] found poor knowledge of diabetic foot care among participants. Also in congruence with the present study results, [21] in a study in Saudi Arabia reported that the majority of diabetic patients lacked correct knowledge of how to choose appropriate footwear.

Regarding the factors influencing patients' knowledge scores, the bivariate analyses revealed positive associations with the educational level, and negative associations with patients' age and duration of diabetes. The positive correlation with education is quite conceivable given the relation between the level of educational attainment and the general health behavior. The findings are in agreement with those of [22] whose study in China demonstrated that diabetic patients' knowledge increased with their level of education and decreased by age.

Nevertheless, the negative correlations with age and duration of diabetes revealed in the present study might be confounded by education given that the educational level of older age patients with longer duration of the illness might be lower compared with those from younger generations. None of these factors was found to have an independent influence on the knowledge score.

Meanwhile, having a DM card was identified as a positive predictor of the knowledge score, which indicates the importance of this as it reflects a positive health behavior. In line with this, the importance of carrying a wallet diabetes care card to protect the diabetic patient in case of any emergency was highlighted by United States department of Health and Human Affairs [23].

The implementation of the current intervention study was effective in improving patients' knowledge of DM in all of its areas. Moreover, the intervention was identified as the main positive predictor of the knowledge score in multivariate analysis, thus confirming its independent and significant positive effect. This success could be attributed to the fact that the program was tailored to their findings, and its content had direct applications to their care practices. A similar successful educational program was reported by [24] in an intervention study in Slovakia. On the same line, a pre-post intervention study in Brazil demonstrated significant improvements in diabetic patients' knowledge [25].

Conclusion and Recommendations

In conclusion, education program for diabetic patients proved to be effective in improving their knowledge of diabetes and diabetic foot. The program should be widely used in educating diabetic patients, particularly those at risk for diabetic foot. The developed booklet should be made available in diabetes care settings. The study could not assess the effect of the knowledge improvement on patients' practices, which is a limitation of the present study since these practices needed more time to be changed. Hence, a longer term study is proposed to investigate the impact of knowledge improvement on diabetic foot care.

Ethical Clearance: Taken before starting the research process from the research ethics committee at Faculty of nursing Beni-Suef University.

Source of Funding: This study is part of a project of Beni-Suef University Scientific Research Development Unit and the Support and Project Finance Office, funded by the United Nation Programs to fight poverty in developing countries.

Conflict of Interest: All authors shared substantially in fulfilling study & approved the final version to be published.

References

1. Sendur U.G., and Adas M.: Determinants of Awareness on Diabetes and its Complications. *Exp & Clin Endocrinol & Diabetes*; 2019, doi:10.1055/a-0840-3438.
2. WHO: Fact sheet: Diabetes Geneva: World Health Organization; 2017, [16.03.2017].[http:// www.who.int/ media Centre/factsheets](http://www.who.int/media/Centre/factsheets).
3. American Diabetes Association: Economic costs of diabetes in the U.S. in 2012. *Diabetes Care*; 2013, 36:1033-46.
4. Magbanua E. and Lim-Alba R. Knowledge and Practice of Diabetic Foot Care in Patients with Diabetes at Chinese General Hospital and Medical Center. *Journal of the ASEAN Federation of Endocrine Societies*; 2017, ISSN 2308-118X. Available at <http://asean-endocrinejournal.org/index>.
5. Jack L.L., Nathaniel G, Clark and Wiliam T. C.: Medical management of diabetic mellitus; 768; University of Vermont College of medicine. Burlington, Vermont, Dekker,inc .New York; 2000, ISBN:0-8247-8857-5.
6. Carlesso G.P., Gonçalves M.H.B., and Moreschi JD. Evaluation of diabetic patients' knowledge about preventive care of the diabetic foot, in Maringá, PR, Brazil. *Journal Vascular Brasileiro*; 2017, 16(2):113-118.
7. Taksande B.A., Thote M., and Jajoo U.N.: Knowledge, attitude, and practice of foot care in patients with diabetes at central rural India. *J Family Med Prim Care.*; 2017, 6(2):284-287.
8. George H., Rakesh P., and Krishna M. Foot care knowledge and practices and the prevalence of peripheral neuropathy among people with diabetes attending a secondary care rural hospital in southern India. *J Family Med Prim Care*; 2013, 2(1):27-32.
9. Yazdanpanah L., Nasiri M., and Adarvishi S. Literature review on the management of diabetic foot ulcer. *World J Diabetes*; 2015, 6(1):37-53.
10. Matricciani L., and Jones S. Who cares about foot care? Barriers and enablers of foot self-care practices among non-institutionalized older adults diagnosed with diabetes: An integrative review. *Diabetes Educ.*; 2015, 41(1):106-17.
11. Pender, N.J. Health promotion in nursing practice 3rd edition, Stamford, CT: 1996, Appleton & Lange.

12. Picchi S., Bonapitacola C., Borghi E., Cassanelli S., Ferrari P., Iemmi B., et al. The narrative interview in therapeutic education. The diabetic patients' point of view. *Acta Biomed*; 2018, 89(6-S):43-50.
13. Hollander P., Hill J., Johnson J., Jiang Z.W., Golm G., Huyck Setal. Results of VERTIS SU extension study: safety and efficacy of ertugliflozin treatment over 104 weeks compared to gliclazide in patients with type 2 diabetes mellitus inadequately controlled on metformin. *Current medical research and opinion*; 2019, 1-9]
14. Hussain S, & Chowdhury, T.A. The impact of comorbidities on the pharmacological management of type 2 diabetes mellitus. *Drugs*; 2019, 79(3), 231-242]
15. Franz M.J., Boucher J.L., Rutten-Ramos S., and VanWormer J.J. Lifestyle weight-loss intervention outcomes in overweight and obese adults with type 2 diabetes. *J Acad Nut. Diet*; 2015, 115(9):1447-63.
16. Bailly L., Schiavo L., Sebastianelli L., Fabre R., Morisot A., Pradier C., et al. Preventive effect of bariatric surgery on type 2 diabetes onset in morbidly obese inpatients: a national French survey between 2008 and 2016 *Surgery for Obesity and Related Diseases*; 2019, 15(3), 478-487]
17. Saber H.J., and Daoud A.S.: Knowledge and practice about the foot care and the prevalence of the neuropathy among a sample of type 2 diabetic patients in Erbil, Iraq. *J Family Med Prim Care*; 2018, 7(5), P. 967-974.
18. Borba A.K.O.T., Arruda I.K.G., Marques A.P.O., Leal M.C.C., and Diniz AD.S.: Knowledge and attitude about diabetes self-care of older adults in primary health care, *Ciencia & saude coletiva*; 2019, 24(1), 125-136]
19. Takehara, K., Oe, M., Ohashi, Y., Tsunemi, Y., Kadowaki, T., & Sanada, H. Differences Between Patient-Reported Versus Clinician-Observed Non-ulcerative Signs and Symptoms of the Foot in Patients With Diabetes Mellitus. *Journal of Wound Ostomy & Continence Nursing*; 2019, 46(2), 113-116]
20. Muhammad-Lutfi A.R., Zaraiyah M.R., and Anuar-Ramadhan I.M. Knowledge and Practice of Diabetic Foot Care in an In- Patient Setting at a Tertiary Medical Center. *Malays Ortho J.*; 2014, 8(3):22-26.
21. Al-Hariri M.T., Al-Enazi A.S., Alshammari D.M., Bahamdan A.S., AL-Khtani S.M., and Al-Abdul Wahab A.A. Descriptive study on the knowledge, attitudes and practices regarding the diabetic foot J of Taibah University Medical Sciences; 2017, 12(6) 492-96.
22. Chin Y.F., Yeh J.T., Yu H.Y., and Weng L.C. Knowledge of the Warning Signs of Foot Ulcer Deterioration among Patients with Diabetes. *J Nurs Res*; 2018, 26(6):420-426.
23. Agency for Healthcare Research and Quality [AHRQ], Diabetes Care Card. Accessed on February 15 2019 at: <https://innovations.ahrq.gov/quality-tools/diabetes-care-card>.
24. Nemcová, J., and Hlinková, E. The efficacy of diabetic foot care education. *Journal of clinical nursing*; 2014, 23(5-6), 877-82]
25. Figueira A.L.G., Boas L.C.G.V., Coelho A.C.M., Freitas M.C.F., and Pace A.E. Educational interventions for knowledge on the disease, treatment adherence and control of diabetes mellitus; 2017, *Revista latino-americana de enfermagem*, 25]

The Empowerment among Type 2 Diabetes Mellitus Patients

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Abstract

Context: TYPE 2 DIABETES MELLITUS is one of the most serious health concerns and policy agendas around the world. Diabetes is strongly associated with the patients' unhealthy lifestyle and behavioural patterns and socio-economic changes. New model of thinking is required to recognize whether the patients are in control of and responsible for the daily self-management of Type 2 Diabetes Mellitus. A descriptive study was conducted for a period of 4 weeks in 2018 in AIMS hospital. Objective is to assess the level empowerment among Type 2 Diabetes Mellitus, to find the association between Diabetes Empowerment Scale and selected variable. Method Data were collected by using Diabetes Empowerment Scale(DES). Collected data was analysed by using IBS SPSS software version 20.

Methodology: A quantitative research approach with convenience sampling technique was used for study the setting of the study was the sample size of Type 2 Diabetes Mellitus patient selected. A semistructured questionnaire used to assess demographic data and diabetes empowerment scale used to assess empowerment among type 2 Diabetic Patient.

Result: A sample size of 150 was available for analysis, ranging from 20 years to above with 43% of the subjects belongs to the age group above 65 years and majority are females. Using, diabetes empowerment scale, each domains of 'managing the psychosocial aspects of diabetes, assessing dissatisfaction and readiness to change and setting and achieving diabetes goal were measured and scored for each patient. The Data analysis revealed a statistical significance in age.

Conclusion: Using the empowerment approach, healthcare professional would help patients make informed decision in accordance with their particular circumstance.

Keywords: *Diabetes Empowerment Scale (DES), Type 2 Diabetes Mellitus(DM)*

Introduction

TYPE 2 DM is one of the most serious health concerns and policy agendas around the world. Diabetes is strongly associated with the patients' unhealthy lifestyle and behavioural patterns and socio-economic changes. Diabetes is the fifth leading cause of death in

most countries. According to National Diabetes Statistic Report, 2017 found that, India is the diabetes capital of the world with a projected 109 million individuals with diabetes by 2035. The disease currently affects more than 62 million Indians, which is more than 7.1% of India's adult Population. An estimate shows that nearly 1 million Indians die due to Diabetes every year and the average age of onset is 42.5 years. ¹

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New model of thinking is required to recognize whether the patients are in control of and responsible for the daily self-management of Type 2 DM. Such a new approach should be based on 'empowerment and involvement' to be more applicable to daily activities in diabetic patients. Rapid changes toward patient empowerment and increasing involvement of patients

in their care plan indicate more emphasis on disease prevention and health promotion and education than on mere disease and its treatment. Such changes make a step toward pervasive sense of responsibility among patients about their illness for their daily activities. Using the empowerment approach, healthcare professionals would help patients make informed decisions in accordance with their particular circumstances.²

Patient empowerment implies a patient-centred, collaborative approach that helps patients determine and develop the inherent capacity to be responsible for their own life. Empowerment is something more than certain health behaviours. Empowerment is more than an intervention, technique or strategy. It is rather a vision that helps people change their behaviour and make decisions about their health care. It has the potential to improve the overall health and well-being of individuals and communities, and to change the socio-environmental factors that cause poor health conditions. The main concept of this change is the tendency to change.³

Materials and Method

A descriptive study is conducted Amrita Institute of Medical Science, 2018 among 150 Type 2 DM patient. Patients selected according to the inclusion criteria for study were patient diagnosed Type 2 DM, who were able to read and write English/Malayalam. People with mentally challenge were excluded from the study. All patient informed about the aim of the study.

Data was collected by using DES, standard questionnaire developed by Michigan Diabetes Research Centre. Patient empowerment was measured by DES self reported scale with subscale reflecting three areas including managing psychosocial aspect of diabetes (9 items), Assessing dissatisfaction and setting and readiness to change (9 items), and setting and achieving diabetes goal (10 items). Each item have 5 response categories ranging 1 to 5 (1=strongly disagree, 2=somewhat disagree, 3=neutral, 4=somewhat agree and 5=strongly agree). Accordingly, the minimum and maximum scale values were 28 and 140, respectively.

Result

Tool 1: Section A: Demographic variable

Table 1: Distribution of subjects based on Socio-Demographic variable

Sl. no	Variables		Frequency	Percentage
1	Age (Years)	20-49	23	15
		50-64	62	42
		>65	65	44
2	Gender	Male	66	44
		Female	84	56
3	Education Status	Primary	23	15
		Secondary	73	49
		Higher secondary	23	15
		Graduation	31	21
4	Marital Status	Married	125	83
		Unmarried	25	17
5	Occupation	Home Maker	67	45
		Govt. Employee	27	18
		Private Sector	32	21
		Others	24	16
6	Income	Below 10,000	83	55
		Above 10,000	67	45
7	Place of residence	Rural	102	68
		Urban	48	32

Figure 1: Pie diagram showing distribution of subjects based on age

Table 1 show that, among the 150 subjects, majority 65 (44%) of the subjects were above 65 years and 84(56%) were female .Among the samples73(49%) of them have secondary education. In case of Marital status 125(83%) were married and 67(45%) are home makers. Most of them 83(55%) have income below 10,000 and 102(68%) were living in Rural areas.

Section B: Clinical Variable

Table 2: Distribution of subjects based on clinical variable

Sl. no	Variables	Frequency	Percentage
1	Family history of DM	51	34
	a)yes b)no	99	66
2	Duration	45	30
	a)<6 years b)>6 ears	105	70
3	Treatment	4	3
	a)diet	20	13
	b)drugs	26	17
	c) insulin	46	31
	d)both a & b	19	13
	e)both b & c	17	11
	f)a, b & c	18	12
4	Medical history	35	23
	a)no b)yes	115	77
5	Habit	5	3
	a)smoking	17	11
	b)alcoholism	7	5
	c)both a & c d) none of these	121	81
6	Complication	30	20
	a)diabetic neuropathy	19	13
	b)others c)nil	101	67

Table 2 represents the data regarding clinical variable shows that 60% have no family history of DM, 70% have duration DM is greater than 6 years, 37% have treatment is diet and drugs, 77% have other medical problem, 81% have no habit, 67% have no complication.

Tool 2: Diabetes Empowerment Scale

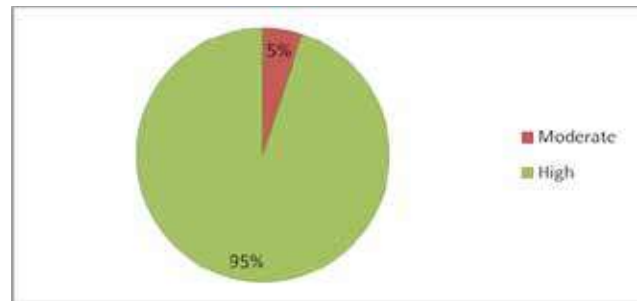


Figure 1: Pie diagram explain distribution of subjects based on total diabetes empowerment scale

Figure 1 represent that most of the subject 142(95%) have high DES score.

Table 3: Frequency distribution of subscales

Sub scale	Level	Frequency	Percentage
Subscale a	Moderate	9	6
	High	141	94
Subscale b	Moderate	4	3
	High	146	97
Subscale c	Moderate	9	6
	High	141	94

Table 3 illustrate 3 subscale distributions, Subscale A(managing psychosocial aspect of diabetes) most of subjects 141(94%) have high score. Subscale B (assessing dissatisfaction and readiness to changemost of the subjects 146(97%) have high score. Subscale C (setting and achieving diabetes goal) most of subjects 141(94%) have high score.

Discussion

The present study was undertaken to assess the empowerment among patient with Type 2 Diabetes Mellitus. The study was formulated with the following objectives.

The first objective of the study was determine the level of empowerment among Type 2 Diabetes Mellitus patients.

In the present study out of 150 subjects 142(95%) had high empowerment score and only 8(5%) had moderate empowerment score, that is majority had high empowerment among Type 2 Diabetes Mellitus.

Similar empowerment assessment study conducted by Anna Ninan in 2014shows that the better /high empowerment level. Effective patient empowerment is not achieved unless patient can receive the necessary

information and are educated about their health condition.⁴This, proves that patient with diabetes can be empowered to manage their chronic disease if they are adequately informed and educated..⁵

To summaries the discussion based on first objective it is markedly clear of empowerment of the participants was moderate to high.

The second objective of the study to find the association between diabetes empowerment score and selected demographic variables among patients with Type 2 Diabetes Mellitus.

Association between the total DES score and selected demographic variable like age, sex, education, marital status, occupation, income, place of residence and clinical variable like family history of DM, duration of DM, treatment, medical problems, habit, complications was done using chi- square.

In the present study, statistically association exist between total DES score and demographic variable age.

AzarTolconducted a study to determination of empowerment score in Type 2 diabetes patient and its related factors and there is an association between total empowerment score and age. Diabetes empowerment scale showed significant relationship between variables such as educational level($p < 0.001$), gender (0.007), age ($p < 0.001$) and duration of diabetes ($p < 0.001$). Persons correlation coefficient also revealed that empowerment of Type 2 diabetes patient has a reverse relationship with HbA1c($r = -0.75, p < 0.001$). Furthermore ordinal regression test that having diploma and higher education($p = 0.005$), and optimal and borderline HbA1c($p < 0.001$)were effective factors in empowering patient.⁶

Conclusion

Patients with Type 2 Diabetes Mellitus can be

empowered so that they can reduce the complications and able to improve their self esteem and self actualization.

Ethical Consieration: Study was presented in the research committee of Amrita College of Nursing for approval. The permission was obtained from head of the Department of Podiatry at AIMS, Kochi. Ethical clearance was obtained from thesis Review committee of AIMS.

Conflict of Interest: None

Surce of Funding: None

Reference

1. National Diabetes Statistic Report, 2017, Centers for Diseases Control and Prevention, 600 Clifton Road Atlanta, GA 30329-4027US <https://www.cdc.gov/features/diabetes-statistic-report/index.html>
2. AzarTol, FatemehAlhani, DavoudShojaeezadeh, Gholamreza Sharifirad, and Nahid Moazam, An empowering approach to promote the quality of life and self-management among type 2 diabetic patients, *JEduc Health Promot.* 2015; 4: 13.
3. Funell MM. Anderson R. From DSME to DSMS: Developing empowerment based Diabetes Self Management Support. *Diabetes Spectrum* 2007;20,
4. Sigurdardottir AK, Jonsdottir H. Empowerment in diabetes care: towards measuring empowerment. *Scand J Caring Sci* 2008; 22: 284-91.
5. Alhani F. Planning and evaluation of empowerment based family model in Iron deficiency Anemia, Doctorial dissertation TarbiatModares University, 2002.
6. AzarTol, Davood Shojaeezadeh, Golamreza Shari-firad, Fatemeh Alhani, Mohamadreza Mohajeri Tehrani, Determination of empowerment score in type 2 diabetes patients and its related factors, 2012.

Assessments of Pre: Competitive Psychological Variables Between South Zone Volleyball Players and Basketball Male Players

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Abstract

Context: The purpose of the study was to find out assessments of pre-competitive anxiety between volleyball players and basketball south zone male players. To achieve the purpose forty subjects were selected SRM IST Chennai. The age ranged between 18 to 25 years male players. The competitive state anxiety inventory II Burton (1990) questionnaire was used. The questionnaire consisted of III dimension, Cognitive anxiety, stress and self-confidence. This study showed that anxiety is required to measure the performance during competition. To compare pre-competitive anxiety between volleyball players and basketball south zone male players. Unpairedt-test was employed with the help of statistical packages of SPSS. To test the significant level was set as 0.05 level. The results showed that there was insignificance difference on Cognitive anxiety, stress and self-confidence between volleyball players and basketball players.

Keywords: Cognitive anxiety, stress, self-confidence, volleyball, basketball

Introduction

Pre competitive anxiety is considered as one of the most vital problems in the area of modern sports psychology. It has been noted for many years as one of the psychological factors. Specifically anxiety plays a central role in the sports competitions where every athlete undergo fear before, during and also after events.¹ Anxiety makes even the world most victorious athlete to experience nervousness. Factors such as fear of losing the game and be short of confidence provoke anxiety in the athletes. Anxiety is similar to worry and it is an unpleasant feeling that most face often when they are put to challenges.

Anxiety is considered to be normal and it is usually related to healthy emotions. But, if a person regularly suffers inconsistent degree of *anxiety*, it might result in medical related disorders.² Disorders pertaining to anxiety form a group of mental health identify that result in extreme nervousness, high fear, apprehension, and lot of worry. Anxiety is often distinguished from fear, which is suitable to cognitive and emotional linked responses to a supposed threat. Anxiety is related to the exact behaviors of fight-or-flight responses, protective behavior or break out.³ It happens in circumstances only perceived as unmanageable or inevitable, but not realistically so defines anxiety as “a future-oriented mood state in which one is not ready or prepared to challenge to cope with future negative actions and that it is a division between the dangers of future and present which helps in the division of anxiety and fear.⁴ Additional description of anxiety is pain, terror, fright and also uneasiness. In constructive psychology, anxiety is expressed as the intellectual state that leads from a difficult challenge for which the subject has deficient surviving skills.⁵

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Fear and anxiety can be made with a distinction in four areas in the period of emotional experience, sequential center, specificity of the threat, and forced direction.⁶Fear is little lived, near focused, thrust towards a particular threat, and made easy free from threat; anxiety, additionally it is long-acting, potential focused, generally focused towards a disperse threat, and supporting excessiveness.

Statement of the Problem: The purpose of the study was to evaluate the assessments of pre-competitive anxiety between volleyball players and basketball south zone male players.

Methodology: The present research was “assessments of pre-competitive anxiety between volleyball players and basketball south zone male players”. To achieve the purpose 40 south zone men players (20volleyball players and 20basketball players) were recruited as subject. The age ranged was 18 to

25years. To check pre-competitive anxiety of recruited subjects (CSAI -2) questionnaire was used.

The competitive state anxiety inventory 2 (CSAI -2) is a 27 item questionnaire consisted of 3 dimensions. Cognitive anxiety, stress and self-confidence. To score the CSAI-2 take all the scores for each item at face value with the exception of item 14, where you reverses the score.

Test Administration: After collection data it was proceed and analyzed with statistics to compare the subjects mean, standard deviation and unpaired t-test was employed with the help of statistical package of SPSS. The significance level was set at 0.05 level. Cognitive anxiety had the sum items as 1,4,7,10,13,16,19,22 & 25. Stress had the sum items as 2,5,8,11,14,17,20,23 & 26 and Self Confidence had the sum items as 3,6,9,12,15,18,21,24 & 27.

Table 1: Mean and Standard Deviation of Cognitive anxiety between volleyball players and basketball player’s south zone male players

Group	N	Mean	Standard Deviation	Standard Error of mean	t
volleyball players	20	22.60	4.29	0.89	1.2423
basketball players	20	21.40	6.96	1.50	

Significant at 0.05 level of confidence

Table 1 presents the mean and standard deviation with regards to south zone volleyball men players 22.60 and 4.29 whereas case of south zone basketball players 21.40 and 6.96 respectively. The value of t – value 1.2423 which is less than table value 2.048 at 0.05 levels. There is insignificant difference between cognitive state anxiety variables volleyball players and basketball players south zone male players.

Table 2: Mean and Standard Deviation of stress between volleyball players and basketball player’s south zone male players

Group	N	Mean	Standard Deviation	Standard Error of mean	t
volleyball players	20	22.25	3.25	0.69	1.0266
basketball players	20	21.24	3.47	0.81	

Significant at 0.05 level of confidence

Table 2 shows the mean and standard deviation with regards to south zone volleyball men players 22.25 and 3.25 whereas case of south zone basketball players 21.24 and 3.47 respectively. The value of t – value 1.0266 which is less than table value 2.048 at 0.05 levels. There is insignificant difference between cognitive state anxiety variables volleyball players and basketball players south zone male players.

Table 3: Mean and Standard Deviation of self-confidence between volleyball players and basketball player’s south zone male players

Group	N	Mean	Standard Deviation	Standard Error of mean	t
volleyball players	20	21.90	3.98	1.03	0.9963
basketball players	20	23.14	3.63	0.92	

Significant at 0.05 level of confidence

Table 3 presents the mean and standard deviation with regards to southzone volleyball men players 21.90 and 3.98 whereas case of southzone basketball players 23.14 and 3.63 respectively. The value of t – value 0.9963 which is less than table value 2.048 at 0.05 levels. There is insignificant difference between cognitive state anxiety variables volleyball players and basketball players southzone male players.

Discussing on Findings: The insignificant differences of cognitive anxiety, stress and self confidence between volleyball players and basketball players south zone male players. Analysis of student t-test showed the insignificant difference. Both a team players have high experience participation and won so many trophies and number of time they mentally well prepared for tournament.

Discussion on Hypotheses: It was hypothesized at the beginning of the study that there would be insignificance difference Cognitive anxiety, stress and self-confidence between of volleyball players and basketball players. The present study produced similar results. Hence, the first research hypothesis of the investigator was held true.

Conclusions

The results showed that there was insignificance difference Cognitive anxiety, stress and self-confidence between of volleyball players and basketball players.

Ethical Clearance: Nil

Source of Funding: Self

Conflict of Interest: Nil

References

1. Lizuka, P Anxiety and performance in young players, Sports Sci. 2005. 26(3) 73-75
2. Moran, A. Sports and Exercise Psychology. Routledge, London;2004
3. Athan, A.N. Copying with pre-competitive anxiety in sports sciences, Int J Phy Edu Sports and Health . 2013. 1(1),1-9
4. Louis,A. Psychology :Seven Editions. New York, 2003.
5. Krane V. Stress,situation criticality and softball performance. J Stren & CondRes. 1994. 8.58-71
6. Erceg, M. Milic, M. Pre-competitive self confidence in soccer players. Hb Sport Psyc .2003. 02(01),3-6

A Study to Find the Prevalence of Breast Engorgement among Lactating Mothers

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Abstract

Introduction: Breast engorgement problem was common in early days and also after weeks of breast feeding. This frequent problem can happen to lactating mother who don't or can't breast feed as well as those who do. It is usually caused by an imbalance between milk supply and infant demand, if engorgement left untreated it can lead to potentially serious issues including painful blebs, plugged milk ducts or mastitis.

Aim: The study aimed to find out the prevalence of breast engorgement among lactating mothers with vaginal delivery, Lower segmental caesarean section.

Materials and Method: A total of 90 women were selected from Saveetha Hospital and Saveetha Rural Health Centre, based on the inclusion criteria Saveetha Hospital and Saveetha Rural Health Centre, based on the inclusion criteria of Lactating mothers with Breast Engorgement and pain for atleast 2-3days who underwent vaginal delivery or lower segmental caesarean section. Exclusion criteria were lactating mothers with soft breast and non lactating mothers and other breast problems. After getting the consent from mothers and after explaining the Six Point Self-rated Engorgement Scale (SPES) and Visual Analogue Scale (VAS). They were asked to rate their level of engorgement and pain. The materials used were VAS and SPES.

Results: The study showed that the prevalence of breast engorgement among lactating mothers was 65%-75%.

Conclusion: The study concluded that the prevalence of breast engorgement among lactating mothers was 65%-75%. Breast engorgement is a major issue in the lactating mothers can leads to many problems like blocked milk ducts, feeding difficulties, a depressed milk ejection reflex, infection, inflammation of the breast and sore/cracked nipples.

Keywords: Breast engorgement, Vaginal delivery, Cesarean delivery, Breastfeeding, Visual Analogue Scale, Six Point Self-rated Engorgement Scale,

Introduction

Breastfeeding is a mother's gift to herself, her baby and the earth, there is no substitute for mother's milk. Colostrum is a yellowish liquid that contains important nutrients and antibodies that a baby needs right after birth [1]. During initial stages of Breastfeeding, mother breasts produce colostrum in small amounts. But after making a couple of days, they're going to increase in milk production. So breast becomes fuller and firmer.

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This swelling is not only caused by the greater amount of milk, but also by increased blood flow and extra lymph fluids^[2] in breast tissue. For most new mothers, these feelings of heaviness pass without problems when their baby feeding well and frequently. But some produce more milk than their breast can hold which makes them feel rock hard and uncomfortably full - a condition called engorgement. Breast engorgement is a problem^[3] that is commonly encountered in breast feeding mothers and it can lead to potentially serious issues^[4] including painful blebs, plugged milk ducts or mastitis. There are many lactating mothers suffering with breast engorgement^[5]. Severe engorgement can make it difficult to baby to latch on to the breast properly and feed well. Engorgement may even cause body temperature to rise around 99-100 degree F, it is also known as milk fever. . According to Academy of Breastfeeding Medicine Protocol Committee, breast engorgement is defined as “the swelling and distension of the breasts^[6]. Usually in the early days of initiation of lactation caused by vascular dilation as well as the arrival of the early milk. Breast engorgement during the first week of breast feeding and can also occurs as a result of delayed, infrequent or interrupted removal of milk from the breast^[7,8]. The factors which may place a mother at a higher risk of engorgement are failure to prevent or resolve milk stasis resulting from infrequent or inadequate drainage of the breasts^[9,10]. The main aim of the study is to find the prevalence of breast engorgement among lactating mothers with vaginal delivery, Lower segmental caesarean section in rural population.

Materials and Method

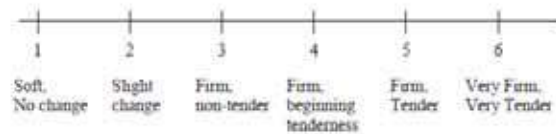
This was an observational study conducted in Saveetha Hospital and Saveetha Rural Health Centre and took nearly 3months to complete the study. A total of 90 lactating mothers belongs to rural areas who complains of engorgement and pain for atleast 2-3days were selected. Samples collected by convenient sampling with the inclusion criteria of lactating mothers with breast engorgement and pain for atleast 2-3days who underwent vaginal delivery or lower segmental caesarean section. Exclusion criteria were lactating mothers with soft breast, non lactating mothers, nipple problems such as nipple sore, nipple cracks, inverted nipple or postnatal complications in previous her vaginal delivery or lower segmental caesarean section. The patients were fully explained about the study and after getting consent from the mothers. They were also given a detailed explanation about the Six Point Self-rated

Engorgement Scale(SPES)^[11] and Visual Analogue Scale(VAS)^[12]. They were asked to rate their level of engorgement and pain. The outcome measures used were SPES and VAS.

Engorgement was assessed using Six Point Self Rated Engorgement Scale from 1 to 6

- 1- being soft, no change
- 2- being slight change
- 3- being firm, non-tender
- 4- being firm, beginning tenderness
- 5- being firm, tender
- 6- being very firm, very tender, [Any measure of 3- firm, no tender or more after baseline was the threshold for this subjective rating.]

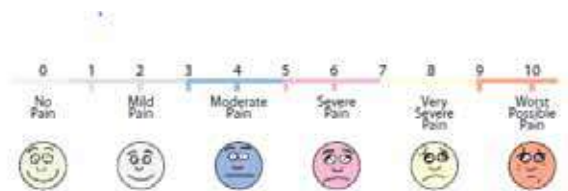
Figure 1. Six Point Self Rated Engorgement Scale



Pain was assessed subjectively by using the visual analogue scale, a subjective measure of self-rated pain on a numerical scale of 1-10

- 0-Being no pain
- 1-3 being mild pain
- 3-5 being moderate pain
- 5-7 being sever pain
- 7-9 being very severe pain
- 9-10 being worst possible pain [10 being the worst possible pain,5 moderate pain, 0 no pain] . The threshold for pain was having atleast one subsequent pain measure 3points or more above baseline.

Figure 2. Visual Analogue Scale

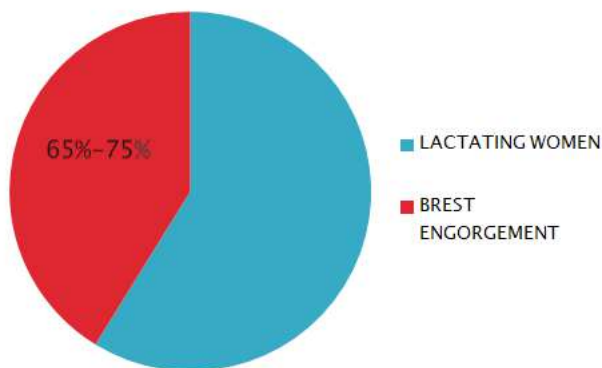


The participants in this study belongs to lower socio economic status and had no idea about breast feeding positions, breast care, breast engorgement and problems related to breast.

Results

Total samples of 90 belongs torural population were randomly selected as a part of the study. Lactating mothers were asked to rate their level of breast engorgement in their breast, according to SPES and also asked to rate their level of pain according to VAS. This study shows that 59-68 lactating mothers complained engorgement and pain in their breast. The result of the study was 65%-75%

Figure 3. Percentage of Breast Engorgement among Lactating Mothers.



Discussion

In this study breast engorgement was self-reported and diagnosed on the answers given by the lactating mothers. This study provides an opportunity to analyse the prevalence of breast engorgement among lactating mothers with vaginal delivery, lower segmental caesarean section. The samples were selected to find the prevalence with the help of Six Point Self-rated Engorgement Scale and Visual Analogue Scale. It is proven that SPES and VAS have their own validity and reliability. The SPES and VAS are valid diagnostic tools used for measuring breast engorgement and pain. SPES and VAS appears to be valid and reliable measures to assess breast engorgement and pain. Among 90 lactating mothers, this study showed that 59-68 lactating mothers complained engorgement and pain. Results showed that 65%-75% lactating mothers suffering with breast engorgement. Clearly health professionals should educate the mother who intends to breast feed that she is most likely to experience some degree of engorgement during the first two weeks post partum and perhaps for a longer duration. The health professional should not assume that the degree of engorgement or pattern is the same for every breast feeding mother. According

to Lawrence^[13], it is important that back pressure in the milk should be prevented from developing and eventually inhibiting milk production uncomfortable engorgement is best prevented by frequent breast feeding around the clock, since the infant is the most effective mechanism for removal of milk. Applebaum^[14] suggest that if the infant is sleepy or sucking is impaired temporarily, the mother's residual milk and high milk tension may be relieved by breast massage and manual expression.

Conclusion

The study concluded that the prevalence of breast engorgement among lactating mothers were 65%-75% in rural population. At present there is no approved medicine to 'dry up' milk supply and prevent engorgement. We need to identify effective preventive and treatment measures for engorgement with no side effects to mothers and the baby, which not only helps to relieve the discomforts of lactating mother but also helps to promote proper milk to the baby.

Ethical Clearance: Taken From saveetha College of Physiotherapy, Institutional Scientific Review Board.

Source of Funding: Self

Conflict of Interest: Nil

References

1. Meenal L. Godia and Neesah Patel. Colostrums – its composition., Benefits as a Nutraceutical-A Review 2013.
2. Newton post partum engorgement of the breast. American Journal of Obstetrics Gynecology 1951.
3. Pamela D. Hill, RN PhD and Sharron S. Humenick, RN, PhD Det al., "The occurrence of breast engorgement" 1994, 79-86. cited on 10th Oct 2012.
4. Roberta J. Hewat, Donelda J. Ellis A comparison of the effectiveness of two methods of nipple care 1987.
5. Humenick SS, J Hum Lact. Breast engorgement: patterns and selected outcomes. J Hum Lact 1994, 10: 87-93.
6. Academy of Breastfeeding Medicine Protocol Committee, Eglash A ABM clinical protocol #8: human milk storage information for home use for full-term infants 2010. (original protocol March 2004).
7. Lee WT A population-based survey on infant feeding practice 0(0-2 years) in Hong Kong: Breast-

- feeding rate and patterns among 3,161 infants below 6 months old. *Asia Pac J Clin Nutr* 2006, 15: 377-387.
8. Powarpriyanka, Basavaraj C, Ramannavar A, GeetaKurahade, AravindKurahade et al., comparative effect of ultrasound therapy with conventional therapy on breast engorgement in immediate postpartum mothers: A randomized controlled trial. *Integr Mol Med*, 2016 doi:10.15761/IMM
 9. Smriti Arora, Manju Vatsa, Vatsla Dadhwal A Comparison of Cabbage Leaves vs. Hot and Cold Compresses in the Treatment of Breast Engorgement. *Indian Journal of Community medicine* 2008, vol 33, Issue 3.
 10. Ligia de Sousa, Mariana Lourenco Haddad, Ana Marcia Spano Nakano, Flavia Azevedo Gomes [A non-pharmacological treatment to relieve breast engorgement during lactation: an integrative literature review] 2012.
 11. Donna Brown, Claire Langdon . Does Kinesio Elastic Therapeutic Taping Decrease Breast Engorgement in Postpartum Women? 2014, *Clinical Lactation*, 5(2).
 12. McLachlan et al. Ultrasound treatment for breast engorgement: A randomized double blind trial 1991.
 13. Lawrence et al Breastfeeding ; A Guide for the Medical profession st. Louis: cvmosby company 1989.
 14. Applebaum R et al The modern management of successful breast feeding. *Pediatr Clin North Am* 1970, 17:203-25.

Depression & Diabetes Has No Relation: A Cross Sectional Study in Tertiary Care Hospital of Eastern India

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Abstract

Background: Diabetes and depression is a growing concern now a day. Both have bidirectional relation. But few studies showed no association between two. Here we tried to find out whether there is any association between two.

Method : 96 patients were recruited in the study. They were assessed by structured interview by trained psychiatrist and diagnosed by ICD 10 diagnostic criteria. Severity of disease was assessed by Beck depression inventory (BDI).

Blood sugar was assessed by Fasting and Postprandial blood sugar and glycosylated haemoglobin (HbA1c).

Result: The p value of FBS, PPBS and HbA1c was 0.91, 0.957, 0.957 respectively. It signifies that in our study the two diseases have no association. Most of the patients were female and male to female ratio was 1 : 2. Mean age of the patients were 40.9±12.2 .30 patients were single which suggest that in our study depressive disorder were more common in married population. And most of the patients were unemployed about 54.167 percent people had no job.

Conclusion: In our cross sectional study we did not find any significant association between depression and diabetes.

Keywords: Diabetes, Depression, Glycosylated haemoglobin (HbA1c).

Introduction

Diabetes as well as depression is becoming an epidemic in India.⁽¹⁾As per projection of World Health Organisation the number of diabetes will increase by 122 percent in 20 yrs from 1995 to 2025.⁽¹⁾There will be 42 percent increase in developed countries and 170 percent increase in developing countries.The maximum increase will occur in India about 195 percent.⁽¹⁾

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And depression which is characterized by depressed mood,decreased energy,anhedonia,early morning awakening,lack of concentration, decreased appetite and suicidal ideation (ICD 10 diagnostic criteria), is on rise. According to world Health Organization Depression is responsible for great burden and 12 percent total year lived with disability.⁽²⁾

Depressive disorder is becoming a social burden and cause for increased mortality as a result of poor self care, higher incidence of noncompliance or treatment non adherence,decreased quality of life.⁽³⁾

Depression or Major depressive episode as per WHO is a major public health problem,that costs substantial sufferings,loss of productivity,higher rates

of morbidity and mortality and at last but not the least impaired quality of life. (4,5)Among the various causative factors depression is very much common in any chronic illness such as diabetes,cancer etc.(6)Low grade symptoms of depression in diabetes frequently missed.(7)Approximately half of diabetes patients use to experience low grade to sub threshold depression in their lifetime.(7)

The relationship of depression and diabetes is bidirectional.(8)Depression increases the risk of diabetes both by biological and behavioural factors.(9)The relationship of depression and diabetes described by a British Physician Thomas Willis.(10)As per his view diabetes is consequences of depression.And now this is widely discussed topic as chicken egg dilemma.

Co morbid diabetes and depression impairs the course and prognosis of both the disorders and utilises great public health and social resources.(11)

Depression is associated with both the types of diabetes,but there are some researchers who are strongly in favour of type 2 variant.(12)

Apart from the biological factors including activation of HPA axis,Sympathoadrenal system,diabetes is associated with poor health related behaviours of depression.(13)Obesity,physical inactivity is the risk factor of diabetes.(14)Another study found that glycemic control measured by glycosylated haemoglobin is directly proportional to the number of depressive episodes.(15)And severity of diabetic complication is also predicted by depression.(16)

Mezuk et al., 2008 stated that depression is correlated with 60% increase in type2 DM and type 2 DM has only 15% correlation with depression.(17)

Current study aims at prevalence of diabetes in patients of depression who never had been treated with antidepressants for their depressive episodes.

Methodology: The study was conducted by Department of Psychiatry and Department of Biochemistry of College of Medicine & Sagore Dutta Hospital, Kamarhati, Kolkata, WestBengal, after obtaining ethical clearance from institutional ethical committee.Informed consent was taken from patients before entering into the study.Biochemical tests were done at the Department of Biochemistry of the same institution.

Study Population: The study group comprised of patients having the diagnosis of depressive disorder .First episode depression was included in the study.

Study Design: This cross sectional was designed assess prevalence of DM in patients of depression in a tertiary care hospital of eastern zone of India .During the period of four months we recruited the patients having MDE as per our inclusion criteria. 1) age more than 18 yrs 2) Drug naïve (those did not receive any antidepressants in past) 3)Free from any psychiatric and medical co morbidities which can influence the metabolic profile and thus glycemic control.

Socio-demographic and clinical information was collected on a semi structured proforma designed for the study.Physical evaluation included measurements of body weight in kilogram (KG), height in centimeters (cm) and waist circumference (in cm) by a calibrated scale and recording of blood pressure (BP). Waist circumference was measured in cm using a measuring tape in the horizontal plane midway between the inferior margin of the ribs and the superior border of the iliac crest; measurement being recorded at the end of normal expiration in the standing position.Fasting blood sugar and PPBS were measured at Biochemistry laboratory of the institution.The venous blood samples were collected after 8 hrs of fasting incase of Fasting blood sugar (FBS) and 2hrs after having 75 gms of glucose in case of Postprandial blood sugar(PPBS) and glycosylated haemoglobin (HbA1c)..

Severity of depression was assessed among patients using Beck depression inventory (BDI).

Result

Table 1:Depression level * FBS level Cross tabulation

		FBS level		Total
		X	Y	
Depression level	Mild	28	6	34
	Moderate	47	7	54
	Severe	6	1	7
	Very severe	1	0	1
Total		82	14	96

X ≤ 126, Y >126 Chi square value= 0.541, df= 3, p value= 0.91

In our data patients were grouped into two,those having fasting sugar more than 126 mg/dl and those having less than and equals to 126 mg/dl.

Here among the patients with mild depression 6 were having fasting blood sugar more than 126 mg/dl. And 7 among Moderate, 1 among severe and nil having very severe having FBS level more than 126 mg/dl. And it shows that there were no association between the variables.

Table 2: Depression level * PPBS level Cross tabulation

		PPBS level		Total
		M	N	
Depression level	Mild	31	3	34
	Moderate	49	5	54
	Severe	6	1	7
	Very severe	1	0	1
Total		87	9	96

M ≤ 200, N > 200 Chi square value = 0.315, df = 3, p value = 0.957

Table 3: Depression level * HbA1c level Cross tabulation

		HbA1c level		Total
		A	B	
Depression level	Mild	31	3	34
	Moderate	49	5	54
	Severe	6	1	7
	Very severe	1	0	1
Total		87	9	96

A ≤ 7.0, B > 7.0 Chi-squares value = 0.315, df = 3, p value = 0.957

200 mg/dl was taken as PPBS standard. And similarly fewer patients were having blood sugar more than reference value. And p value is 0.957 which is not significant.

Regarding HbA1c, 7 was taken as standard. And only 9 patients have HbA1c level more than 7 and p value is 0.957 which is not significant.

Most of the patients were female and male to female ratio was 1 : 2. Mean age of the patients were 40.9 ± 12.2 .

Table 4: Sex distribution

		Frequency	Percent
Valid	F	64	66.7
	M	32	33.3
	Total	96	100.0

30 patients were single which suggest that in our study depressive disorder were more common in married population.

Table 5: Marital status

		Frequency	Percent
Valid	Single	30	31.25
	Married	66	68.75
	Total	96	100.0

And most of the patients were unemployed about 54.167 percent people had no job.

Table 6: Employment status

		Frequency	Percent
Valid	Employed	44	45.833
	Unemployed	52	54.167
	Total	96	100.0

Discussion

Here we tried to find out the relationship between depression and diabetes in a cross sectional study but we did not find any significant association between two. The previous studies stated that depression and diabetes were related bidirectional.⁽¹⁸⁾ Among 96 depressed patients of various grade we did not find any relation between two. This study is contradiction of previous studies. But one study was in our favour which stated that diabetes and depression has no association in clinical and genetic level.⁽¹⁹⁾

In current study we used structured interview and diagnostic criteria of ICD 10 to diagnose depression of varying severity. And blood sugar was assessed by fasting blood sugar, PP sugar after 2 hrs of meal, and HbA1c. But none of them shows any significant association with depressive disorder.

Previous studies had got several limitations. In these studies varying method were used to diagnose depression like diagnosis by physician, self reported questionnaire etc.^(20,21) But in our study we used structured diagnostic criteria of ICD 10.

In our study depression is more common in woman and unemployed persons which supports the previous studies.^(18,22)

And also married persons were affected by the disease process twice as common as single person which also contradiction of previous studies.⁽²³⁾

Married and unemployed persons were affected much more common which probably suggest the chronic

stress of a family man ends with the disorder which also costs the productivity and thus the vicious cycle runs.

But our study has got several limitations. It was a cross sectional study in a hospital based population which does not reflect the entire community as only a few patients with symptoms come to the hospital. And the study lacks the comparison group which could be used to assess comparison between the prevalence of depression among diabetes and non diabetic individuals.

Conclusion : We have studied in a tertiary care hospital of North Kolkata, which was not representative of whole community. Multicentric study using larger population sample and probably the genetic analysis will give better insight into the problem.

Conflict of Interest: Nil.

Source of Funding: Self

References

- King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: Prevalence, numerical estimates, and projections. *Diabetes Care*. 1998;21(9):1414-31.
- Egede LE, Ellis C. Diabetes and depression: global perspectives. *Diabetes Res Clin Pract*. 2010;87(3):302-12.
- Dhvale HS, Panikkar V, Jadhav BS, Ghulghule M, Dagaria A. Depression and diabetes: Impact of anti-depressant medications on Glycaemic control. *J Assoc Physicians India*. 2013;61(DEC):896-9.
- Katon WJ. The Comorbidity of Diabetes Mellitus and Depression. *Am J Med*. 2008;121(11 SUPPL. 2):8-15.
- Ferrari AJ, Charlson FJ, Norman RE, Patten SB, Freedman G, Murray CJL, et al. Burden of depressive disorders by country, sex, age, and year: findings from the global burden of disease study 2010. *PLoS Med*. 2013;10(11):e1001547.
- Katon WJ. Epidemiology and treatment of depression in patients with chronic medical illness. *Dialogues Clin Neurosci*. 2011;13(1):7-23.
- K W, J R, J C, L R, L C, J P. The Importance of Screening for Mild Depression in Adults with Diabetes. *Transl Biomed*. 2017;08(01):1-8.
- Alzoubi A, Abunaser R, Khassawneh A, Alfaqih M, Khasawneh A, Abdo N. 39.3.137 • Korean. *J Fam Med*. 2018;39(0):137-46.
- Fiske A, Wetherell JL, Gatz M. Depression in Older Adults. *Annu Rev Clin Psychol*. 2009 Apr;5(1):363-89.
- Katon W. Depression and diabetes: unhealthy bed-fellows. *Depress Anxiety*. 2010 Apr;27(4):323-6.
- Dejenie Habtewold T, Radie YT, Sharew NT. Prevalence of Depression among Type 2 Diabetic Outpatients in Black Lion General Specialized Hospital, Addis Ababa, Ethiopia. *Depress Res Treat*. 2015 Feb 19;2015:1-8.
- Chireh B, Li M, D'Arcy C. Diabetes increases the risk of depression: A systematic review, meta-analysis and estimates of population attributable fractions based on prospective studies. *Prev Med Reports*. 2019;14(October 2018):100822.
- Ducat L, Philipson LH, Anderson BJ. The mental health comorbidities of diabetes. *JAMA*. 2014 Aug 20;312(7):691-2.
- Qin L, Knol MJ, Corpeleijn E, Stolk RP. Does physical activity modify the risk of obesity for type 2 diabetes: A review of epidemiological data. *Eur J Epidemiol*. 2010;25(1):5-12.
- Holt RIG, de Groot M, Golden SH. Diabetes and Depression. *Curr Diab Rep*. 2014 Jun 18;14(6):491.
- E. A, T. H, D. K, A. I. Depression in diabetes mellitus: A comprehensive review. *Hippokratia*. 2012;16(3):205-14.
- Mezuk B, Eaton WW, Albrecht S, Golden SH. Depression and type 2 diabetes over the lifespan: A meta-analysis. *Diabetes Care*. 2008;31(12):2383-90.
- Campayo A, Gómez-Biel CH, Lobo A. Diabetes and Depression. *Curr Psychiatry Rep*. 2011 Feb;13(1):26-30.
- Samaan Z, Garasia S, Gerstein HC, Engert JC, Mohan V, Diaz R, et al. Lack of association between type 2 diabetes and major depression: Epidemiologic and genetic evidence in a multiethnic population. *Transl Psychiatry*. 2015;5(8):e618-6.
- Nouwen A, Winkley K, Twisk J, Lloyd CE, Peyrot M, Ismail K, et al. Type 2 diabetes mellitus as a risk factor for the onset of depression: A systematic review and meta-analysis. *Diabetologia*. 2010;53(12):2480-6.
- Wang J, Wu X, Lai W, Long E, Zhang X, Li W, et al. Prevalence of depression and depressive symptoms among outpatients: A systematic review and

- meta-analysis. *BMJ Open*. 2017;7(8):1–14.
22. McGee RE, Thompson NJ. Unemployment and Depression Among Emerging Adults in 12 States, Behavioral Risk Factor Surveillance System, 2010. *Prev Chronic Dis*. 2015;12:1–11.
23. Mushtaq R, Shoib S, Shah T, Mushtaq S. Relationship between loneliness, Psychiatric disorders and physical health ? A review on the psychological aspects of loneliness. *J Clin Diagnostic Res*. 2014;8(9):WE01–4.

Prevalence of Psychiatric Morbidities in Migraine: An Observational Study

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Abstract

Background: Migraine is a chronic episodic moderate to severe throbbing headache having many psychiatric co morbidities. Current study aims to detect epidemiology of psychiatric co morbidities in migraine.

Method: Patient aged 11-65 years selected by International classification of headache 3rd edition to have migraine. SRQ-24 and ICD-10 criteria was applied to detect psychiatric co morbidities.

Result: Anxiety was found to be prime co morbidity followed by depression.

Conclusion: Treating co morbidities may improve disease condition.

Keywords: Migraine, Co morbidity, Anxiety.

Introduction

As per International classification of headache disorder 3rd edition, migraine is characterized by chronic or episodic headache, pulsatile in nature associated with photophobia or phonophobia, aggravated by routine physical activity which causes avoidance of that situation.

Among the various types of headache the prevalence of tension type of headache is 38 percent and of migraine is 10 percent⁽¹⁾. And it is one of the debilitating disorder which causes functional⁽²⁾, cognitive⁽³⁾ and social impairment. It has become a social burden in terms of increased utilisation of health care cost by visiting the physician regularly or by consuming the drugs.⁽⁴⁾

Though migraine is second most common in primary headache disorder after tension type headache, but the

disability comes first⁽⁵⁾. Social burden of disease ranges from mild impairment to severe disability that limits the work like study, regular official job and routine household work. Migraine is associated with various comorbid conditions like impaired interpersonal relationship, psychosocial problem, cognitive impairment, neurological, gastrointestinal, autoimmune diseases, cardiovascular diseases.⁽⁶⁾

In most of the cases the headache is underestimated⁽⁷⁾ and also its comorbid conditions leading to loss of productivity for the society as it is mostly affecting the economically productive age groups. And the quality of life is also impaired in migraineurs⁽⁸⁾ and it use to severely impaired in associated psychiatric, neurological or medical disorders among the various psychiatric comorbidities Depressive disorder is one of most common in migraine patients⁽⁹⁾. In previous studies it estimated that anxiety and depressive disorders are ten times more common than general population. Substance abuse disorder, Panic disorder, phobia, Personality disorders are significantly associated with migraineurs. Significant percentage of people attempt suicide in very severe debilitating condition⁽⁹⁾. Among neurological symptoms epilepsy, allodynia, visual symptoms, vertigo and gait instability and impaired higher cognitive functions is

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important⁽¹⁰⁾. Apathy, impaired attention, executive functions use to get impaired⁽³⁾. It also decrease the school performances in school going children. Cognitive function is affected by age, frequency of attack, duration of headache.⁽³⁾ In studies it shows that cognitive decline is mostly associated with migraine with aura⁽³⁾.

Helicobacter pylori infection, irritable bowel syndrome, unexplained right upper abdominal pain, celiac disease cyclic vomiting syndrome are associated with migraine significantly.⁽¹¹⁾

In the current study we tried to find out psychiatric disease burden in migraine patients so that in future modifying the associated risk and comorbid condition disease course will be modified.

Methodology: The study conducted in department of psychiatry in College of medicine and sagore Dutta Hospital. It took about 6 months to collect the data. Ethical permission was obtained from institutional ethical committee. Informed consent was taken from all the patient before entering the study. In case of minors consents were taken from parents.

Inclusion Criteria:

1. Age 11 yrs to 65 yrs
2. With sound mental activity
3. Can give informed consent
4. Willing to participate in study

Exclusion Criteria:

1. Patients with mixed headache
2. Unsound mind
3. Not willing to take part in study
4. Those having organic brain lesion
5. Those having anatomical lesion in either CT scan or MRI

Patients were selected as per inclusion and exclusion criteria. They were diagnosed as per diagnostic guidelines in International classification of headache disorder 3 rd editions. Semi structured proforma was used to record the socio demographic data and to record the associated symptoms. Then SRQ 24 was administered to assess whether they have any psychiatric disturbances. SRQ is self reported questionnaire with N and P score. N score more than 6 and P score more than 2 was considered positive. After that they were diagnosed by ICD 10 diagnostic criteria. Anatomical lesions in CT scan or MRI were excluded from study.

Result

Table 1: Sociodemographic profile in migraine (n = 173)

Mean Age	32.9±10.4yrs (11 to 65 yrs, n=173)
Sex	Female-138(79.8%), Male-35 (20.2%) F:M = 3.94 : 1
Religion	Hindu – 48 (27.7%); Muslim – 121 (69.9%); Christian -4 (2.3%)
Marital Status	Married – 124 (71.7%), Unmarried-34 (19.7%), Divorced – 15 (8.7%)
Family history	Present – 37 (21.4 %), Absent- 136 (78.6%)
Occupation	Employed-63 (36.4%), Unemployed -110 (63.6%)
Education	Graduate 2(1.2%), Higher secondary 16 (9.2%), Secondary -39 (22.5%), Middle School – 75 (43.4%), Primary 41 (23.7%)
Aura	Present – 16 (9.2%), Absent – 157(90.8%)

Our population was mainly middle aged females with mean age 32.9±10.4yrs and female to male ratio was 3.94 : 1. As the local community around the hospital is predominantly Muslim, our study reflects disease affection mostly in Muslim, married (124) patients. Most of them did not have family history of migraine headache. Most of people were educated upto middle school (upto class VIII) and were unemployed. Aura was present in small number of patients.

Table 2: Psychiatry Diagnosis (n =173)

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No illness	88	50.9	50.9	50.9
	Alcohol Dependence	3	1.7	1.7	52.6
	Bipolar Disorder	9	5.2	5.2	57.8
	GAD	41	23.7	23.7	81.5
	MDE	19	11.0	11.0	92.5
	OCD	2	1.2	1.2	93.6
	Panic Dis	11	6.4	6.4	100.0
	Total	173	100.0	100.0	

50.9% patients did not have any psychiatric illness. So almost half of patients had various comorbid psychiatric illnesses. Most of the patients had generalized anxiety disorder (23.7%). And moderate depressive episode, panic disorder, bipolar disorder, alcohol dependence and obsessive compulsive disorder were psychiatric comorbid illness they have.

Table 3: Smoking

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	145	83.8	83.8	83.8
	Yes	28	16.2	16.2	100.0
	Total	173	100.0	100.0	

Table 4: Suicide attempt

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	154	89.0	89.0	89.0
	Yes	19	11.0	11.0	100.0
	Total	173	100.0	100.0	

Most of the patients were non smoker (83.8 %) and few patient (11%) attempted suicide in past.

Discussion

We studied in tertiary care hospital which crater predominantly Muslim population in urban area. Middle aged female population were affected mostly. Most of Indian population were villagers. Our study conducted to assess prevalence of migraine in urban area. The prevalence varies in different countries. One year prevalence rate 25.2% in one study from Karnataka⁽¹²⁾ The mean prevalence in European country 14.7%⁽¹³⁾. In one previous study occurrence of migraine higher in females than in males⁽¹⁴⁾.

Most of the patients did not have family history of migraine in our study which is consistent with the previous studies⁽¹⁵⁾. Large number of patients were married as it is explained by that the disease mostly affects the reproductive age group⁽¹⁵⁾.

Aura was present in small number of patients (9.2%) which is also consistent with previous studies.⁽¹⁵⁾

About 50% patients had various psychiatric illnesses. Among them most prevalent was generalized anxiety disorder (23.7%). Next in the list were moderate depressive episode, panic disorder, bipolar disorder, alcohol dependence and obsessive compulsive disorder.⁽¹⁶⁾ The causes of psychiatric comorbidity is recurrent attack of pain which causes agony and anxiety, and depressive disorder⁽¹⁷⁾. Epidemiological studies found that there are same pathophysiology underlying migraine and anxiety and depressive disorders⁽¹⁷⁾. But this is not the sole cause of the comorbidities as many patients with migraine did not have any psychopathology.

In the previous study percentage of suicide attempt in migraine headache is close to our finding⁽¹⁸⁾. But it

did not tell us whether there is actual increase of suicide rate than the general population as we did not have comparison group.

And another limitation of our study was we studied in a centre which was not representative of entire community.

Conclusion

The comorbid conditions adversely affect the prognosis and treatment responses in migraine headache. It is necessary for the therapist to assess the comorbid conditions and treat them accordingly so that disease course can be modified. To get the exact picture of disease comorbidity multicentric trial with large sample may be required.

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References

- Ahmed M, Bota R, Ariff M, Ajmal H Bin, Qaiser M. Prevalence of Different Types of Headache and Migraine Disability Assessment: A Cross Sectional Study among University Students. *Int J Med Sci Innov Res* www.ijmsir.com [Internet]. 2017;(2):371–7. Available from: www.ijmsir.com
- Test I, Scale IB, Survey SH, Affairs OJS, Neurologics M, Pharmaceuticals E, et al. *Mayoclinproc_84_5_007*. 2009;10461(May):422–35.
- Araújo CM de, Barbosa IG, Lemos SMA, Domingues RB, Teixeira AL. Cognitive impairment in migraine: A systematic review. *Dement Neuropsychol*. 2016;6(2):74–9.
- Joshi P. Economic and Social Impact of Micro. *IPE J Manag*. 2015;6(1):131–51.
- Steiner TJ, Stovner LJ, Vos T. GBD 2015: migraine is the third cause of disability in under 50s. *J Headache Pain* [Internet]. 2016;17(1):0–3. Available from: <http://dx.doi.org/10.1186/s10194-016-0699-5>
- Wang SJ, Chen PK, Fuh JL. Comorbidities of migraine. *Front Neurol*. 2010;AUG(August):1–9.
- Burton WN, Landy SH, Downs KE, Runken MC. The impact of migraine and the effect of migraine treatment on workplace productivity in the United States and suggestions for future research. *Mayo Clin Proc*. 2009;84(5):436–45.
- Anand KS, Sharma S. Quality of life in migraine. *Drug Dev Res*. 2007;68(7):403–11.
- Minen MT, De Dhaem OB, Van Diest AK, Powers S, Schwedt TJ, Lipton R, et al. Migraine and its psychiatric comorbidities. *J Neurol Neurosurg Psychiatry*. 2016;87(7):741–9.
- Lal V, Singla M. Migraine comorbidities - A discussion. *J Assoc Physicians India*. 2010;58(SUPPL APRIL2010):18–20.
- Cámara-Lemarroy CR, Rodriguez-Gutierrez R, Monreal-Robles R, Marfil-Rivera A. Gastrointestinal disorders associated with migraine: A comprehensive review. *World J Gastroenterol*. 2016;22(36):8149–60.
- Kulkarni G, Rao G, Gururaj G, Subbakrishna D, Steiner T, Stovner L. EHMTI-0333. The prevalence and burden of migraine in india: results of a population-based study in Karnataka state. *J Headache Pain* [Internet]. 2014;15(S1):B18. Available from: <http://www.thejournalofheadacheandpain.com/content/15/S1/B18>
- Stovner LJ, Andree C. Prevalence of headache in Europe: A review for the Eurolight project. *J Headache Pain*. 2010;11(4):289–99.
- Ray B, Paul N, Hazra A, Das S, Ghosal M, Misra A, et al. Prevalence, burden, and risk factors of migraine: A community-based study from Eastern India. *Neurol India*. 2017;65(6):1280.
- Bhatia M, Gupta R. Migraine: Clinical pattern and psychiatric comorbidity. *Ind Psychiatry J*. 2013;21(1):18.
- Teixeira AL, Costa EAC, Da Silva AA, Dos Santos IAM, Gómez RS, Kummer A, et al. Psychiatric comorbidities of chronic migraine in community and tertiary care clinic samples. *J Headache Pain*. 2012;13(7):551–5.
- Lake AE, Rains JC, Penzien DB, Lipchik GL. Headache and psychiatric comorbidity: Historical context, clinical implications, and research relevance. *Headache*. 2005;45(5):493–506.
- Breslau N, Schultz L, Lipton R, Peterson E, Welch KMA. Migraine Headaches and Suicide Attempt. *Headache J Head Face Pain*. 2012 May;52(5):723–31.

Economic Slow Down and it's Impact on Disease Burden in India

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Abstract

Context: Fall in employment, growth, incomes and investments are the more visible and obvious ill effects of an economic slowdown but there are far reaching impacts of an economic slowdown that aren't so immediate and visible. The aim of this study is to assess how these economic downturns have dented the health outcomes in India since 1990. We assess the non-fatal outcomes of public health using the morbidity measure DALY(Disability adjusted life years) caused by economic slowdown. We find that rise in income led to reduction in communicable, maternal, neo natal and nutrition diseases (CMNNDs) while it led to an increase in injuries and non-communicable diseases. An increase in unemployment was associated with an increase in disease burden for CMNNDs, non-communicable disease and injuries. Economic slowdown puts the people in a vulnerable position as loss of income and employment lead to increase in disease burden. The public health policy especially in developing nations must focus on social security protection to prevent such negative health outcomes during an economic slowdown.

Keywords: Disease burden, DALY, Morbidity Measures, Economic Slowdown

Introduction

A healthy population is a productive one. Achieving better public health not only has positive outcomes on the society but also makes economic sense as expenditure and economic loss from ill health can be prevented. While a growing economy creates opportunities for better health outcomes, the contrary can also be true. Public health deteriorates during an economic slowdown or during an economic crisis.

In today's globalized world, contagion of financial distress in one part of the world to the entire global economy is an expected effect. The 2008 global economic crisis led to the increase of mortality rates in every affected country.¹ Irrespective of the wealth of a nation, the poor and those who fell in to poverty because of loss

of Income or housing were hit the hardest. Developing countries with huge percentage of population living in poverty are particularly vulnerable. During an economic crisis there is huge financial stress on the poor as they suffer from lower incomes, they reduce the spending on both quantity and quality of nutrition which can have irreparable impact of their physical and psychological being and productivity.²

India's economy since 1990 has transformed dramatically due its trade openness. The Gross domestic product has been out on a growth trajectory since the New Economic policy in 1991.⁷ Increasing per capita incomes supported by steady economic growth leads to improvement in the nation's capacity to consume goods and services that promote public health.⁸ Post reforms, unemployment grew gradually due to increasing rural unemployment and predominance of casual workers. Spike in number of student population due to expansion in higher education, is another reasons attributes slow growth in the workforce.^{9,10} Temporary unemployment and unemployment in long term affects physical and mental health of the population.^{10,11}

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Earlier studies have studied public health by analyzing mortality rates and Public health expenditure.^{1,13-14} Mortality measures don't provide adequate information with respect ill health of a population. DALY(Disability adjusted life years) is becoming the commonly accepted measure to assess status of public health as it a comprehensive indicator comprising of both morbidity and mortality giving a picture about the healthy life expectancy lost due to ill health.¹¹ Therefore, present study gives a macro perspective and tries a new approach to assess the impact of an economic slowdown on public health by studying the Disease Burden.

Literature Review: Globalization has increased the potency of economic crisis by having a cascading effect on global economy. However, according to the decoupling theories, the emerging economies do not reflect the patterns exhibited by the developed nations during the rise and fall in the business cycle, as it is believed that the emerging economies are largely independent of each other.^{3, 4} However, the aftermath of an economic crisis characterized by capital flow reversal, pressure on the fiscal deficit due to stimulus packages provided by the government, corporate debt and currency depreciations was witnessed in India post 2008.¹⁴

Economic slowdown harmfully heightens the impact on mental health of the public. The stresses of unemployment and mortgages adds pressure to the primary attendees increasing depression, anxiety and alcoholism.⁵ Financial crisis can have a rapid impact on mortality related to suicide amidst the tumult in banking sector. Anticipation of job loss and social security aggravates the suicide prevalence.¹ Studies in developed countries which have well-functioning social security systems, have confirmed the immediate rise in suicides following a financial crisis.¹⁴

Demand for the public health care increases during economic slowdown as the incomes contract and public expenditure on private health care decreases.^{26,27} This can create increased pressure on the public health systems in the light of austerity measures and cuts in government spending thus leading to damaging effects on public health such as sharp increase in people report worsening health, suicides, drug abuse, violence and infectious disease burden.⁵ An immense pressure will be put on public health sectors as more people shift from private health services to public health service providers due to affordability issues. Poor health equity in regions

can decrease access to the needy in such situations as the non-poor grab the services.⁴ There is immense need to recognize the fragile nature of Public health in relation to turmoil in the business cycle. Due to the efforts of the Global Disease burden Initiative 2017, it has become feasible to study morbidity in India on multiple dimensions.

Data: The data on Public health for the period 1990 to 2016 is obtained from the broad study conducted as part of the Global Disease burden Initiative, 2017 by Indian Council of Medical Research, Public Health Foundation of India, and Institute for Health Metrics and Evaluation. The findings of this study are first of its kind on the basis of scale completed with the collaboration of 103 institutions and over 200 health scientists. The study provides estimates of all India and state level metrics for DALYs (Disability adjusted life years) for 333 disease conditions and injuries and 84 risk factors for each state of India from 1990 to 2016. The study uses the aggregates of DALY's for three broad categories namely, communicable, maternal, neonatal, and nutritional diseases (CMNNDs); non-communicable diseases (NCDs); and injuries. Disease burden is given by DALY gives relatively a deeper understanding on status of health when compared to mortality measures as it takes in to account the years of health life expectancy lost due to injury, disease and premature death.¹¹

Studies previously conducted on this topic have used unemployment rate as the primary measure of macro economy.^{1,13-14} The present study uses unemployment rate and Per capita income at constant prices as they comprise of two key determinants linking macro economy and health.² The unemployment rate has been sourced from International Labour Organisation and the per capita national income at constant prices has been sourced from World Bank Open data source.

Method

Linear regression technique is employed in the study to establish the impact of change in per capita income and unemployment on disease burden in India. We have used Gross National per capita income at constant prices which is adjusted for inflation. Unemployment rate captures the number of people actively seeking employed upon total number of people in the labour force. Per capita income and unemployment are the explanatory variables. Our predictor is DALY (Disability adjusted life years) which captures the disease burden that is the

healthy life expectancy years lost due injuries, disease and premature death with is the summation of YLL (Years of life lost) and YLD (years lived with disability) for a total of 333 disease conditions. Log transformation technique has been used to standardise the data as the values are non-negative. Linear regression is performed initially to analyse the impact of per capita income and unemployment of DALY for aggregate of all causes. Later the regression estimation will be performed to assess the impact of the independent variables on three categories namely communicable, maternal, neonatal, and nutritional diseases (CMNNDs); non-communicable diseases (NCDs); and injuries.

Results and Interpretations

Results of 42 linear regression models were computed to establish relationship between disease burden, Per-capita income and Unemployment for the time period 1990 to 2016 in India. It was noted that a percentage increase in per-capita income was associated with a 0.843 percent fall in disease burden for all causes across all ages. Similar effect was noted for the aggregate disease burden for communicable, maternal, neonatal and nutritional diseases (CMNNDs). A percentage rise in per capita income was associated with a 0.914 percent fall in disease burden for CMNNDs. By contrast, it was noted that the association was inverse for Non-communicable diseases and injuries. A percentage increase in per-capita income was associated with a 1.019 percent rise in non-communicable diseases and with a 1.049 rise in injuries.

A rise in per-capita income had varying effects on disease burden for different age groups. While increase in per-capita income led the decrease in disease burden for the age group under 5 and for 5 years to 14 years, an opposite relationship was observed for age groups 15 years and above. Relatively higher increase in disease burden was observed in Age group 15 to 49 years (with co-efficient 1.055) when per-capita income increased.

The effect of rise in per-capita income on disease burden was more distinct in female population with beta co-efficient of -0.905 when compared to the male population -0.68. For both female and male population increase in per-capita income was associated with a reduction in disease burden for age groups below 14 years and for age groups above 15 years the effect was reversed, where an increase in per-capita income was associated with an increase in disease burden.

The study attempts to associate another independent

variable with disease burden i.e. Unemployment. The results indicated a significant association between unemployment and disease burden. However, the beta coefficients of the linear regression models were lesser across disease categories, gender and age groups in comparison with per-capita income. An increase in unemployment was associated with an increase in disease burden for CMNNDs, non-communicable disease and injuries. The effect of unemployment was negligible with a beta coefficient of 0.06 on disease burden due to Non-communicable diseases. A positive relation between unemployment and disease burden was detected across age groups except for population in age group 50 to 69 years for both female and male populations, where an increase unemployment was negatively related to disease burden.

Discussion and Conclusion

Our results have shown that Economic slowdown leads to negative health outcomes on a nation. These results are consistent with the previous studies which have confirmed the negative health effects loss of income and employment can have on the population health.^{1,4} Increase in income is observed to be positively related to decrease in disease burden from communicable, maternal, neonatal and nutritional diseases. Increase in income can lead to better access to clean water, sanitation, quality health care, vaccinations, nutrition and insurance. India is also undergoing an epidemiological transition where there is shift in disease burden from CMMNDS as major contributor to NCDs and injuries. The epidemiological transition can be attributed to demographic transition (decreasing mortality and fertility) and social transition (increasing awareness and expectations about the health system) happening in a developing nation like India.³ These transitions seem to be affected by an economic slowdown as the disease burden among all these classifications showed a significant relation with change in income and employment.

Some of the previous studies have argued that road accidents increase with decrease in Unemployment. However, India witnessed a 65.1 percent rise road accidents 29.8 percent rise in cases of self-harm and 41.3 percent rise in falls from 1990 to 2016.³ According the results obtained by us an increase in unemployment and per capita income led increase in injuries. In India about 82.2 percent are employed in informal sector with little or no social security protection, which means that when joblessness goes up people take up hazardous jobs

which can increase the incidence of injuries due to poor working conditions.

Positive health effects of increase in per-capita income were observed only in very young population aged below 14 years. For the age groups above 14 years disease burden increased as income and employment increased. The working populations belonging to these age groups are exposed to many external environmental hazards which are the leading cause for increase in disease burden. Some of top risk contributors to disease burden with highest change since 1990 were High body-mass index (+281%), unsafe sex (+214%), High fasting plasma glucose (+127%), High total cholesterol (+106.2%), High systolic blood pressure (+89.3%) and low physical activity (+109%). These are the risk factors associated with rise non-communicable diseases which steadily become the top contributor for India's disease burden since last decade. Rise in non-communicable diseases is an issue that is plaguing middle and lower income nations like India. Increasing urbanization, over nutrition, sedentary lifestyles, pollution, shift in dietary habits and addictions are some of the causes of increase in non-communicable diseases in developing countries in spite of a steady increase in incomes and our results were in conformity with this view.^{6, 8}

The study relies entirely upon the morbidity estimates and its relation to the changes in income and employment. This can be a limitation as earlier studies on morbidity in India have indicated that there exists a problem of under self-reporting and underestimation of morbidity due its subjective nature. Accurate reporting morbidity depends upon awareness about general health conditions among populations. Many social, community and individual factors influence the reporting of morbidity, therefore collective morbidity reports may not entirely be representative of the actual morbidity figures among various sections of the nations. It is observed that this may be more valid for poorer populations and women.⁴ There exists immense scope for future research in the light of the findings of our study. India is a nation with huge population with immense diversity among its states. The associations established in the study can be extended to various states in India and the further addition of other socio economic determinants of health can provide deep insights on factors affecting morbidity in India.

The effects of economic fluctuations on public health is more potent in less developed countries with a weak

social security net especially in terms of unemployment insurance.⁴² The findings of the present study are also in line with the National health policy 2017, which aims to work towards strengthening the social security protection. The results obtained by this study attempts to throw some light on this issue and indicate a direction for National health policy decisions. India's state of public health is often linked to the quantum of public expenditure on health which is way below the world average. The findings of the study indicate along with increasing public expenditure on health, the government should focus on improving working conditions of unorganized workforce, social security protection in the event of unemployment and widen the scope of public health insurance to cover variety of diseases.

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Ethical Consideration: The study was approved by the Institutional Ethical Review Board (IERB).

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References

1. Stuckler D, Basu S, Suhrcke M, Coutts A, McKee M. The public health effect of economic crises and alternative policy responses in Europe: an empirical analysis. *The Lancet*. 2009 Jul 25;374 (9686):315-23.
2. Brinkman HJ, De Pee S, Sanogo I, Subran L, Bloem MW. High food prices and the global financial crisis have reduced access to nutritious food and worsened nutritional status and health. *The Journal of nutrition*. 2009 Nov 25;140 (1):53S-61S.
3. data.worldbank.org
4. Labonté R. The global financial crisis and health: scaling up our effort. *Canadian Journal of Public Health*. 2009 May 1;100 (3):173-5.
5. Gili M, Roca M, Basu S, McKee M, Stuckler D. The mental health risks of economic crisis in Spain:

- evidence from primary care centres, 2006 and 2010. *The European Journal of Public Health*. 2012 Apr 19;23 (1):103-8.
6. Walia S. Impact of global economic crisis on Indian economy: An analysis. *International Journal of Latest Trends in Engineering and Technology*. 2012 Jul;1 (2):31-6.
 7. Chatterji M, Mohan S, Dastidiar SG. Relationship between trade openness and economic growth of India: A time series analysis. *Journal of Academic Research in Economics*. 2014 Mar 1;6 (1):45-69.
 8. Subramanian SV, Belli P, Kawachi I. The macro-economic determinants of health. *Annual review of public health*. 2002 May;23 (1):287-302.
 9. Thomas JJ. India's labour market during the 2000s: Surveying the changes. *Economic and Political Weekly*. 2012 Dec 22:39-51.
 10. Cerra V, Saxena SC. What caused the 1991 currency crisis in India?. *IMF staff papers*. 2002 Jul 1;49 (3):395-425.
 11. Murray CJ, Lopez AD, World Health Organization. The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020: summary.
 12. India Labour Market Update ILO Country Office for India | July 2017
 13. Noelke C, Beckfield J. Recessions, job loss, and mortality among older US adults. *American journal of public health*. 2014 Nov;104 (11):e126-34.
 14. Cutler DM, Knaul F, Lozano R, Méndez O, Zurita B. Financial crisis, health outcomes and ageing: Mexico in the 1980s and 1990s. *Journal of Public Economics*. 2002 May 1;84 (2):279-303.

Effect of Self Myofascial Release Using Foam Roller Versus Tennis Ball in Subjects with Plantar Fasciitis: A Comparative Study

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Abstract

Background: Plantar fasciitis is a repetitive micro trauma overloaded injury of the attachment of plantar fascia at the inferior aspect of the calcaneum. It results into inflammation and thickening of the fascia causing heel pain. Myofascial release (MFR) is a manual therapy technique which can be used to release the tension developed in the thickened fascia. Self-Myofascial Release (SMFR) can be given with a variety of tools such as foam rollers and tennis ball. They are easy, harmless and cost effective method of giving SMFR. However, the efficacy of the technique in plantar fasciitis is not yet clear.

Objective: To compare the effect of SMFR technique using foam roller and tennis ball in subjects with plantar fasciitis.

Method: Thirty-two eligible patients were recruited for the study. They were allocated into either group A (n = 16) and group B (n=16). Group A was given SMFR with Foam roller and group B was given SMFR with tennis ball. The intervention was given for 2 weeks (5 days/week). Visual analogue scale (VAS) and Foot and Ankle Disability Index (FADI) outcome measures were taken both at baseline and after 2 weeks of intervention.

Results: Both group A and group B showed significant improvement in VAS and FADI after two weeks of interventions (p value <0.05). However between groups comparison were statistically insignificant (p value >0.05) for both the outcome measures.

Conclusion: This study concludes that SMFR with both foam roller and tennis ball showed improvement in pain and muscle function i.e. both interventions were equally effective. Neither of the method was found superior than the other.

Keywords: Heel pain, Plantar Fasciitis, Foam Roller, Tennis Ball, Self-Myofascial Release, Manual Therapy.

Introduction

Plantar fasciitis is a degeneration of the plantar fascia as a result of repetitive micro tears of the fascia

that lead to an inflammatory reaction.¹ Inflammation of the plantar fascia and other fascial structures is characteristic feature of plantar fasciitis.²

Plantar fasciitis or plantar heel pain is most commonly reported cause of inferior heel pain. In a course of a lifetime, it has been estimated that approximately 10% of general population are afflicted with plantar heel pain.³

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Plantar fasciitis prevails in both athletic and non

athletic populations and about 15% of adult foot complaints need clinical help.⁴ It is found to be more common in females when compared to males.⁵

Risk factors for plantar fasciitis are work related weight bearing, sudden gain in body weight, shoes with poor cushioning, athletic population, increased age, decreased ankle dorsiflexion, occupation involving prolonged standing and tightness of Achilles tendon.⁶

Heel pain is mostly noticed in morning, during initial steps of walking or after a short interval of inactivity. Pain gradually decreases with activity but tends to worsen by end of the day. Antalgic gait may be observed if the pain is severe.⁷

Therapists use various manual Myofascial therapies over the soft tissue to produce therapeutic changes in these tissues. A variety of interventions including structural integration, osteopathic soft-tissue techniques massage including connective tissue massage (CTM), myofascial trigger joint therapy and instrument assisted fascial release have been utilized.⁸ Also, treatment method like Orthosis (heel pads and arch supports), Non-steroidal anti-inflammatory drugs, local steroid injection, exercise for stretching the Achilles tendon, night splints, below knee cast are used commonly.⁹

SMFR is a technique used to treat myofascial restrictions and restore the normal soft-tissue extensibility. To increase myofascial mobility, foam roll and roller massager are commonly used tools. The clients use their body weight to apply pressure to the soft-tissues during the rolling motion with foam roller.¹⁰

Tennis ball is amongst the most resourceful aid used for self-massage. The ball can be placed on the floor or a wall or any other body part to apply definite pressure on the tight or aching site of the muscle. The main aim is to reach the area of the body which cannot be reached with the individual's own hands. The pressure applies by tennis ball should be large enough to release the tightness without irritating the nervous system. The resultant pain sensation should be considered as "good pain".¹¹

Heel pain associated with plantar fasciitis is common in both sedentary as well as in active individuals. Investigation regarding method used to treat plantar fasciitis is scarce, however, different interventions have shown to be beneficial but there is paucity in the literature regarding the effect of SMFR using a foam roller or tennis ball. Thus, the need of this study is to find out the

effect of plantar SMFR using foam roller and tennis ball in subjects with plantar fasciitis.

Methodology: The study was conducted between May 2018 to April 2019 in the department of physiotherapy, in a tertiary hospital of Mangalore, India. Obtaining ethical clearance from the institutional ethical committee from the university, participants diagnosed with plantar fasciitis by specialized physician were recruited. The participants of both the genders were included if they presented with clinical diagnosis of acute plantar fasciitis and were of age above 18 years, and they were excluded if they reported with calcaneal spur, fracture of foot and loss of plantar foot sensation. The participants were randomized by using chit method into two groups. Outcome measures were recorded by the therapist who was not a part of the study and was blinded to the interventions. Written informed consent was obtained from all the eligible participants.

Along with SMFR both groups also received ultrasound therapy over the entire length of the plantar fascia. Outcome measures VAS (Visual Analogue Scale) and FADI (Foot and Ankle Disability Index) were taken before and after the treatment sessions. Treatment was given for 10 sessions over a period of 2 weeks.

Group A: Smfr With Foam Roller: Participants were instructed to be in standing position and foam roller was given to roll under the affected sole starting from behind the head of metatarsals towards the heel focusing on medial arch for 2 minutes. They were asked to exert maximum pressure, till a point of discomfort but not pain (Figure 1) and Ultra sound therapy was given over the affected plantar surface of the foot with Intensity 1.0 W/cm² continuous mode and 3MHz depth for 7 minutes.

Group B: Smfr With Tennis Ball: Participants were instructed to be in standing position and tennis ball was given to roll under the affected sole starting from behind the head of metatarsals towards the heel focusing on medial arch for 2 minutes. They were asked to exert maximum pressure, till a point of discomfort but not pain (Figure 2) and Ultra sound therapy was given over the affected plantar surface of the foot with Intensity 1.0 W/cm² continuous mode and 3MHz depth for 7 minutes.

Statistical Analysis: SPSS software 16.0 was used to assess the data obtained. Independent sample t test was used for Group A and Group B to compare the pre and post measurements for VAS and FADI, within the group comparison was analysed by using paired t test.

The p-value less than 0.05, was considered significant for the study.

Results

The study consisted of 7 males and 9 females in group A and 4 males and 12 females in group B. The meanage in group A and B was 25.5 ± 7.37 and 26 ± 8.9 respectively. There was no significant difference seen

between both the groups with respect to age and gender ($p > 0.05$). Within the group analysis for the outcome measures VAS and FADI was done using paired t test (Table 1). A statistical significant difference was obtained within the group analysis ($p < 0.001$) for both the outcome measures in both the groups. However, no significant difference was seen between the groups analysis ($p > 0.05$), (Table 2 and 3).



Figure 1: Illustration of SMFR Technique with Foam Roller



Figure 2: Illustration of SMFR Technique with Tennis Ball

Table 2: between the group comparison of VAS

	GROUPS	N	MEAN	SD	t	P value
VAS – PRE	Group A	16	6.89	0.598	0.99	0.33
	Group B	16	6.65	0.782		
	Total	32				
VAS- POST	Group A	16	4.2	1.294	0.856	0.399
	Group B	16	3.81	1.222		
	Total	32				

Table 3: between the group comparison of FADI

	GROUPS	N	MEAN	SD	T	P value
FADI-PRE	Group A	16	63.75	6.159	-1.607	0.118
	Group B	16	67.625	7.4		
	Total	32				
FADI-POST	Group A	16	86.875	5.5	-1.677	0.104
	Group B	16	89.93	4.8		
	Total	32				

Discussion

The purpose of this study was to compare the effect of SMFR using foam roller versus tennis ball in subjects with plantar fasciitis. The results of the present study indicated that SMFR with both foam roller and tennis ball showed improvement in pain and muscle function i.e. both intervention were equally effective. Neither of the method was found superior than the other.

The exact mechanism behind the role of SMFR in improving plantar fasciitis is still not clear. Meltzer et al demonstrated that MFR causes apoptotic rate normalization, changes in cell morphology and reorientation of fibroblasts. This facilitates the healing processes by halting degeneration of plantar fascia which may possibly decrease the pain.¹² Also a study suggests that MFR helps to return the shortened fascial tissues to its normal length by collagen reorganization.¹³ MFR stimulates the afferent A delta fibers which causes segmental pain modulation, supporting the analgesic effect of MFR.³

A study suggested that SFMR using a foam roller can be used as an alternative to reduce pressure pain of latent muscle trigger points on gastrocnemius muscle.¹⁴ It has been proved by Le GAL J et al, SMFR using tennis ball on infraspinatus and pectoralis muscle of tennis players reduced pain and improved ROM (Range of Motion) of glenohumeral joint. The findings of the current study favored the above studies.¹⁵

Branca Romero et al conducted a study to compare the effects of vibration and non-vibration foam roller and proved that both protocols were effective in improving pain and joint ROM, but VFR (Vibrating Foam Roller) achieved greater short-term effects on pain perception and ROM.¹⁶ so, further studies are required to evaluate the effectiveness of foam roller to reduce pain.

A systematic review in 2015 showed that ROM of joints; muscle performance and pain can be effectively improved by foam rolling or roller massage. But as the method used in the studies were highly heterogeneous, no appropriate consensus has been developed on an optimal SMR program.¹⁷

However, a narrative review of 2016 by Kalichman L et al concluded that joint ROM increased significantly after using SMFR. The muscle force and performance didn't change. But there is scarcity of studies investigating the role of SMFR in lowering the myofascial pain.¹⁸

Conclusion

The present study shows that SMFR given with both tennis ball and foam roller reduced pain and improved function in patients with plantar fasciitis. However, on comparing the mean difference of both the groups foam roller SMFR was superior to tennis ball SMFR, although this difference was not statistically significant. Hence it can be inferred that foam roller SMFR and tennis ball SMFR both were equally effective in improving pain and function in patients with plantar fasciitis. The limitations of the study are the small sample size, short-duration of intervention, no control group and no long term follow up was taken.

Conflict of Interest: The authors had declared that there is no conflict of interest

Source of Funding; Self

Ethical Clearance: The study has been approved by the institutional ethics committee

References

1. Luffy L, Grosel J, Thomas R, So E. Plantar fasciitis. Journal of the American Academy of Physician Assistants. 2018;31(1):20-24.

2. Physiotherapy in Kleinburg: Advantage Physiotherapy: [Internet]. Advantagephysiotherapy.com. 2018 [cited 13 January 2018]. Available from <http://www.advantagephysiotherapy.com>
3. Ajimsha M, Binsu D, Chithra S. Effectiveness of myofascial release in the management of plantar heel pain: A randomized controlled trial. *The Foot*. 2014; 24(2):66-71.
4. Rome K, Howe T, Haslock I. Risk factors associated with the development of plantar heel pain in athletes. *The Foot*. 2001;11(3):119-125.
5. Reb C, Schick F, Karanjia H, Daniel J. High Prevalence of Obesity and Female Gender Among Patients With Concomitant Tibialis Posterior Tendinitis and Plantar Fasciitis. *Foot & Ankle Specialist*. 2015;8(5):364-368.
6. Barrett SJ, O'Malley R. Plantar fasciitis and other causes of heel pain. *Am Fam Physician*. 1999;59(8):2200-2206.
7. Cole C, Seto C, Gazewood J. Plantar fasciitis: evidence-based review of diagnosis and therapy. *Am Fam Physician*. 2005;72(11):2237-2242.
8. Simmonds N, Miller P, Gemmell H. A theoretical framework for the role of fascia in manual therapy. *J Bodyw Mov Ther*. 2012;16(1):83-93.
9. Singh D, Angel J, Bentley G, Trevino S. Fortnightly review: Plantar fasciitis. *BMJ*. 1997;315(7101):172-175..
10. Curran P, Fiore R, Crisco J. A Comparison of the Pressure Exerted on Soft Tissue by 2 Myofascial Rollers. *J Sport Rehabil*. 2008;17(4):432-42.
11. Tennis Ball Massage for Myofascial Trigger Points [Internet]. www.PainScience.com. 2018 [cited 12 January 2018]. Available from: <http://www.pain-science.com/articles/tennis-ball.php>.
12. Meltzer KR, Cao TV, Schad JF, King H, Standley PR. In vitro modeling of repetitive motion injury and myofascial release. *J Bodyw Mov Ther* 2010;149(2):162-171.
13. Schleip R. Fascial plasticity-a new neurobiological explanation: part 1. *J Bodyw Mov Ther* 2003;7(1):11-19.
14. Wilke J, Vogt L, Banzer W. Immediate effects of self-myofascial release on latent trigger point sensitivity: a randomized, placebo-controlled trial. *Biology of Sport*. 2018;35(4):349-354
15. Le GAL J, Begon M, Gillet B, Rogowski I. Effects of Self-Myofascial Release on Shoulder Function and Proprioception in Adolescent Tennis Player. *Journal of Sports Rehabilitation*. 2018;27(6):530-535.
16. Romero-Moraleda B, González-García J, Cuéllar-Rayó Á, Balsalobre- Fernández C, García D, Morencos E. Effects of Vibration and Non-Vibration Foam Rolling on Recovery after Exercise with Induced Muscle Damage. *Journal of Sports Science and Medicine*. 2019;18:172-180.
17. Cheatham S, Kolber M, Cain M, Lee M. The Effects of Self-Myofascial Release using a Foam Roll or Roller Massager on Joint Range of Motion, Muscle Recovery, and Performance: A Systematic Review. *Int J Sports Phys Ther*. 2015 Nov; 10(6):827-38
18. Kalichman L, Ben David C. Effect of self-myofascial release on myofascial pain, muscle flexibility, and strength: A narrative review. *Journal of Bodywork and Movement Therapies*. 2017;21(2):446-451.

A Study on the Impact of Demonetization on Utilisation of Private Health Care Services in a South Indian City

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Abstract

Background: Private sector plays a key role in India's healthcare system. The demonetization of Rs.500 and Rs.2000 currency notes on 8th November 2016 had a great effect on the Indian economy as well as day-to day lives. Hence this study was aimed at assessing the impact of demonetization on utilization of private healthcare services in Eluru, Andhra Pradesh.

Material and Method: This was a health-facility based cross-sectional study. Ten health facilities were involved and 200 study subjects from these facilities were interviewed using a pre-designed and validated questionnaire. The respondents' characteristics, their utilization of health services and overall experience with regard to healthcare was included in the questionnaire.

Results: When asked about the overall experience, 27pc of respondents said they were not affected, 49.5pc said they were affected but felt it tolerable, and 23pc said they were severely affected and suffered. 33.5pc of the respondents have postponed their visits to the health facility due to cash shortage. This was mostly seen in low income groups. Only 35pc of the respondents were willing to use credit/debit cards for cashless transactions.

Conclusion: Majority of respondents felt their healthcare was affected by demonetization but it was tolerable. The low income groups had highest impact. The penetration of cashless payments in private healthcare was very poor.

Keywords: Andhra Pradesh, Demonetization, Healthcare, Private, Utilization.

Introduction

Healthcare is one of the most vulnerable sectors which is adversely affected by economic policies and crisis¹. In India private sector plays a key role in healthcare. Today it accounts for 82% of outpatient visits, 58% of inpatient expenditure, and 40% of births in institutions. India ranks among the top 20 of the world's

countries in its private spending, at 4.2% of GDP². At least 7% of the population in India fall below poverty line each year due to Out of Pocket Health Expenditure³.

The Government of India has enacted demonetization of Rs.500 and Rs.1000 currency on 08-11-2016. The total value of these notes in the economy at that time was Rs.15.41 lakh crores. New notes of Rs.2000 first and Rs.500 later were introduced in their place⁴.

There has been a widely varied response to demonetization. The academicians were skeptical about the role of this exercise in achieving its intended purpose⁵. It was reported that there was a decline in the outpatients of around one-third in peripheral hospitals. The media cited that persons on daily wages had difficulty in obtaining money for their treatment. Apparently

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several hospitals refused treatment in exchange for the demonetized INR 500 and INR 1000 currencies. Reports of people suffering due to cash shortage and long queues in banks and ATMs^{6,7}.

However public welcomed this move and were patient enough to endure the hardships for the sake of perceived overall benefit. There were no reports of widespread unrest^{8,9}. In wake of this, the present study was undertaken to study the impact of demonetization on utilization of private healthcare services in Eluru city, the district headquarters of West Godavari, Andhra Pradesh.

Objectives:

1. To understand the overall experience of the patients regarding health care, in wake of demonetisation.
2. To see the effect on different socio-economic groups and their utilization of health services.
3. To study the implementation of cashless economy in private health care in wake of demonetisation.

Method

Study Setting: The study was done among patients attending various private health facilities in Eluru city, West Godavari.

Study Period: The study was done for a period of two weeks, beginning one month after demonetization (10th to 25th December 2016).

Study Sample: All the private health facilities in Eluru town were approached for permission to do the study. Among them the facilities who have given consent were included. One medical college hospital, four clinics, two nursing homes, and one each of dental, physiotherapy and RMP (registered medical practitioner) clinics have consented to be involved in this study.

Sample Size: At the time of study, to the best of our knowledge, there was no quantitative evidence on the effect of demonetization on utilization of healthcare services in private sector. Hence it was assumed that the proportion affected is 50. Taking $p=50$ and an absolute precision (d) of 7, the sample size was calculated using the formula, $n = (Z_{\alpha/2})^2 \times p \times (1-p) / d^2$. Since the confidence level of this two-tailed study was set at 95pc, the $Z_{\alpha/2}$ was taken as 1.96. Thus a sample size of 196 was obtained, which was rounded to 200. Since a total of ten health facilities were involved in the study, the total

sample was divided by ten, and from each health facility twenty patients were involved.

Interview of study subjects: Each of the health facility was visited either during 10 AM-1PM slot or from 6 PM-9PM slot. The doctor running the facility was met the previous day and briefed about the study. The study subjects were selected from all the people present in the health facility during that particular slot. Patients in out-patient division, wards and casualty were uniformly included. In case the patients were financially dependent, i.e., children, students, elderly or housewives, their attendants who take care of their expenses were interviewed.

Study Tools: A semi-structured questionnaire was designed to interview the patients. It was tested and validated before the actual study. The patients were interviewed in Telugu as per the questionnaire.

Components of the Questionnaire: The general data comprised of the patient's income, occupation, nature of visit to hospital and their health insurance status.

Next set of questions were about the patient's healthcare related experience. They included the number of visits made to health facility in last one month, and whether they have postponed any visits to health facility due to shortage of cash. They were asked whether they had postponed getting routine laboratory investigations done or procuring routine medications due to shortage of cash. Impact on health due to waiting in queues in banks and ATMs was also assessed.

To understand the spending priorities of the respondents, they were asked how much of the newly withdrawn money was spent on health-related expenses, and if they had any other priorities in spending over health-related expenses. To understand the penetration of banking system and cashless payments, the subjects were asked if they were ready to make health-care related payments through digital transactions.

The last component of the study was about the direct effect of cash shortage on their healthcare utilization. The subjects were asked which part of healthcare did they have the biggest difficulty with, namely, billing, consultation, pharmacy, laboratory, transportation. To assess the adverse impact, the subjects were asked if there was any death or aggravation of illness among their family or friends due to shortage of cash and waiting

in queues. Finally the subjects were asked to grade their overall experience in healthcare utilization after demonetization as “no effect” or “effected but tolerable” or “severely affected”.

Data Entry & Analysis: The data from the questionnaires was compiled in Microsoft Excel 13 and analyzed in SPSS Version 20.

The frequencies of various input characteristics were tabulated and expressed as percentages. The patients’ income and amount of money spent were expressed as medians, to avoid getting affected by extreme values. Since the study was limited to private health facilities, all the sections of population were not likely to be covered. So to avoid bias, instead of taking standard classifications for socio-economic status, the patients were divided into four income-groups based on the inter-quartile ranges. The lowest income group was Category 1 and highest was Category 4.

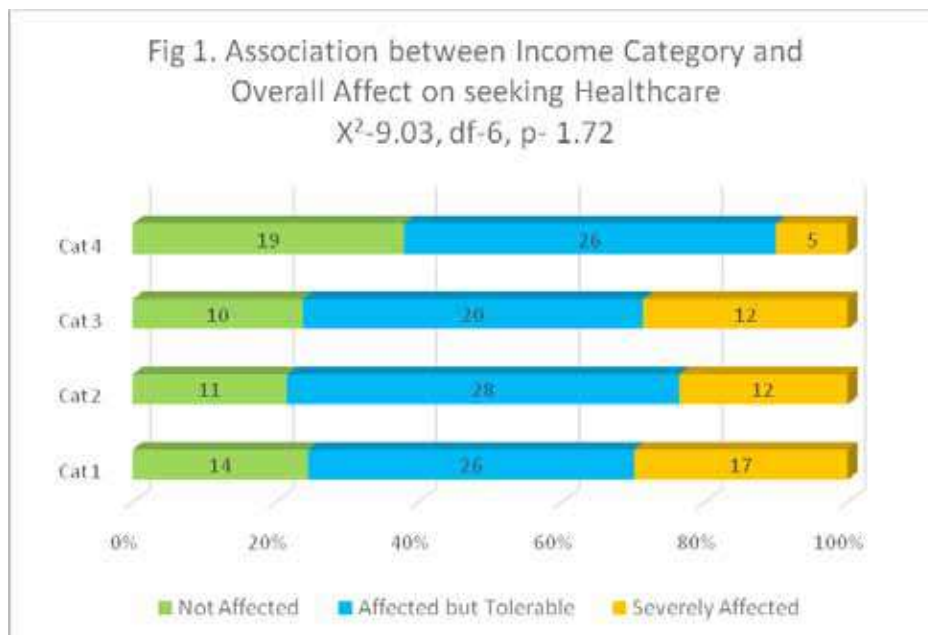
The internal consistency of the questionnaire was checked using Cronbach’s alpha. The output variables were the subjects’ overall experience, the healthcare component where they had the biggest difficulty, and postponement of visit due to cash shortage. The study subjects’ characteristics and experiences were seen for any significant association with the outcome variables using chi-square test. If there was any significant association, the influence of that factor would be measured by logistic regression.

Results

Data of the Respondents: Out of a total of 200 respondents, 88 (44pc) were patients and 112 (56pc) were attendants. Among the respondents, 79(38.5pc) were daily wagers, 72(36pc) were salaried, 38(19pc) were businessmen and land-owners and 11(5.5pc) were pensioners. Regarding the nature of visit, 117 (58.5pc) were out-patients, 29(14.5pc) were admitted on advice, 23(11.5pc) were admitted for elective surgery and 31(15.5pc) presented as an emergency. Regarding the number of visits, 71(35.5pc) respondents are on their first visit to a health facility, whereas 79(39.5pc) have visited more than 3 times in the last one month. Only 52(26pc) of the patients had their visits covered under insurance. The median monthly income was Rs 12000 (95pc CI 10000-15000).

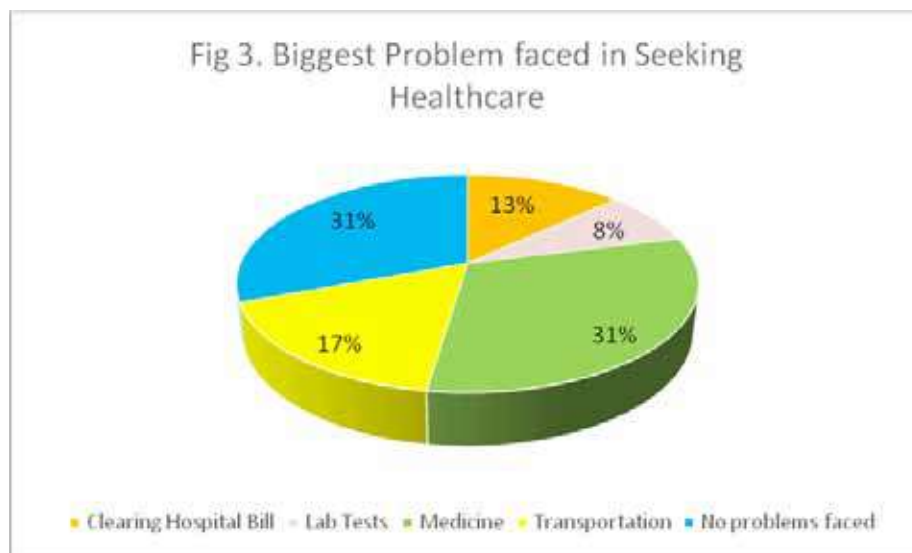
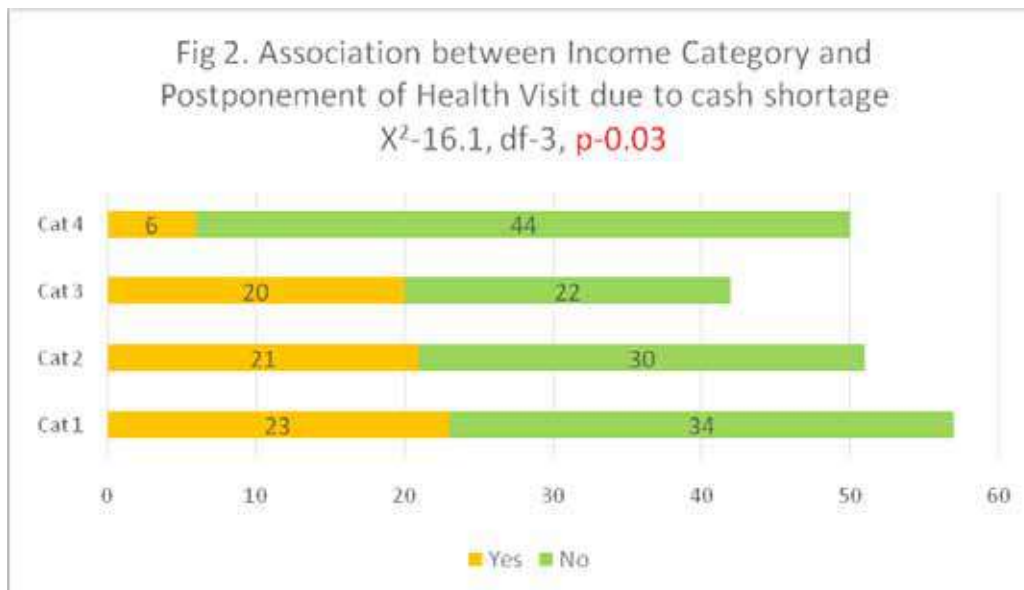
Findings of the Study: When asked about overall experience regarding health care due to demonetization, 27pc of respondents said they were not affected, 49.5pc said they were affected but felt this tolerable, and 23pc said they were severely affected and suffered. There was no statistically significant difference among various income groups, type of visit or insurance status.

There was reluctance to use cards for payment in 64pc of the respondents. This is significantly higher in low income groups. The reasons for this reluctance ranged from ignorance to mistrust. Out of the 36pc ready to use cards, only 2pc could use them for payment as many health facilities were not accepting payments through cards.



Regarding the visits to healthcare facility, 33.5pc had postponed their visit if it was not urgent, particularly due to cash shortage. This was significantly lower in high income groups. This is the only significant statistical association found in the study. 15pc reported their relatives or neighbors had to postpone visits. About 4.5pc reported aggravation in health issues due to postponement. This did not have any significant association with the income category or nature of visit.

The median amount of money spent on healthcare post-demonetization was Rs 4000 (95pc CI 3000-5000). Majority of the people had problem with buying medicines (33.5pc), followed by transportation (15.5pc) and billing (14.5pc). 55pc had difficulty in changing old notes and 46pc with new notes. 15pc postponed buying medicines or getting routine investigations done, due to lack of change. One third (33.5pc) of the respondents felt their plans to visit health-care facilities were affected by waiting for cash in banks and ATMs.



Discussion

Almost half (49.5pc) of the respondents felt their healthcare utilization was impacted by demonetization, but it was tolerable. This was in tune with the findings of

the PHD Bureau, which found that 58% of the population were stressed due to demonetization¹⁰.

In the present study, 33.5pc of the respondents stated that they have postponed their visits to health facilities

if it was not urgent. This is consistent with the findings of Kumar et al that there was one-third reduction in out-patients across the country⁶. However the doctors running the health facilities stated that it was because the period from late November, leading up to Christmas and Sankranti was “off-season”.

Over half of the respondents had difficulty in changing demonetized notes at healthcare facilities. This was in spite of the government allowing essential services to accept demonetized notes for a certain period. Similarly using the newly issues Rs 2000 notes proved difficult as it was difficult to obtain change. It was during the time of study that new Rs 500 notes were announced to tide over this problem. This was in contrast with the findings of Hariharan et al where over 64pc of respondents were satisfied with the flow of new currency after demonetisation⁹. In the present study, 4.5pc of respondents have mentioned aggravation of health issues due to waiting in queues for cash in banks and ATMs.

The government’s intention to boost cashless transactions did not find much takers in the present study. Only 36pc of the respondents were ready to use cards for swiping. This was similar to the findings of Hariharan et al, where 30pc of the respondents were using debit cards and online transactions. Unfortunately, at the time of the study, none of the health facilities were accepting cashless payments. The lone medical college hospital in the city started card swiping six weeks after demonetization. This was in contrast to the study by Rao et al in Lucknow where there was significant use of cashless payments at hospitals¹¹. This calls for a serious re-look on peoples’ attitude about using banking sector and cashless economy in smaller towns and cities.

Conclusion

Most of the people felt their health care was affected due to demonetisation, but it was tolerable. Nearly a third of the respondents have postponed seeking health care if it was not urgent.

Though the health care facilities were asked to accept old notes for an extended period, it could not be done. This was due to the overall difficulty in providing change to the higher notes.

Another crucial finding is the near-total absence of cashless payments in private health care in the study field. This is lacking on both sides. Majority of the

patients are not willing to use cards or operate bank accounts on a regular basis, in spite of having Jan Dhan accounts. Similarly, many health care facilities are not encouraging cashless payments. Since the government is pushing for digital economy, private health care is one crucial area it should focus on, in this endeavor.

It is hoped that the cash crunch subsides soon enough to restore the normality in utilization of private health care facilities.

Conflict of Interest: The authors belong to the medical college, which was one of the ten health facilities included in this study.

Source of Funding: Self

Ethical Issues: The respondents and health facilities were assured of complete confidentiality. Informed consent was taken from all the respondents. This study was approved by Institutional Ethical Committee.

References

1. Chan M. Impact of Financial Crisis on Health: a Truly Global Solution is Needed. World Health Organization. 2009. [Last accessed on 2017 Nov 26]. Available from: http://www.who.int/mediacentre/news/statements/2009/financial_crisis_20090401/en/
2. Sengupta A, Nundy S. The private health sector in India. *BMJ (Clinical research ed.)*, 331(7526), 1157–1158. doi:10.1136/bmj.331.7526.1157
3. Kumar K, Singh A, Kumar S, Ram F, Singh A, Ram U, Negin J, Kowal PR. Socio-economic differentials in impoverishment effects of out-of-pocket health expenditure in China and India: evidence from WHO SAGE. *PloS one*. 2015 Aug 13; 10(8):e0135051.
4. Reserve Bank of India. Annual Report 2015-16. Available at https://www.rbi.org.in/scripts/annual_report. Accessed on 20 January 2019.
5. Indian Express. Amartya Sen on demonatisation. 28th January 2017. Available from <https://indian-express.com/article/india/amartya-sen-on-demonetisation-note-ban-an-undemocratic-move-akin-to-unguided-missile-4495942/>. Last accessed on 10th January 2019.
6. Kumar VD. The missing pieces of the big picture: Unaddressed healthcare conundrums during demonetization. *Journal of Family Medicine and Pri-*

- primary Care. 2018; 7(5):1150-1.
7. Nagarajan K. India's demonetisation drive is affecting access to medical care. *The Lancet*. 2017 Jan 7; 389(10064):32-3.
 8. Pati S, Mahapatra P, Sinha R. Health at the time of demonetization. *Journal of family medicine and primary care*. 2018 May; 7(3):495.
 9. Hariharan S, Krishnakumar J, Stephen T. A cross-sectional study on the assessment of impact of demonetization of Rs. 500 and Rs. 1000 currency notes on the socio-economic and health status of the people residing in an urban area of Kanchipuram district. *International Journal of Community Medicine and Public Health*. 2018 Apr 24; 5(5):1951-5.
 10. PHD Research Bureau. Impact of Demonetization on Economy, Businesses and People. Available at <http://phdcci.in/image/data/Research%20Bureau2014/Economic%20Developments/paper/Study%20on%20Impact.pdf>. Accessed on 9 February 2018.
 11. Rao BV, Rai R, Mehra A, Harsvardhan R, Bhara-dwaj S, Chandra H. Impact of demonetization on patients and finances in a tertiary care teaching hospital in India: Case study of Sanjay Gandhi Post-graduate Institute of Medical Sciences: Lucknow, India. *Journal of Financial Management & Analysis*. 2017;30(1):25-33.

Impact of Learning Opportunities in Preparing Dental Students for Their Profession

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Abstract

Introduction: The emphasis in outcome-based education is on the outcomes or the products, and in the context of a medical or dental school, the kind of doctors and dentists it produces becomes the outcome. The young doctors and dentists coming out of these schools need to possess the competencies to practice in an increasingly complex healthcare scenario with changing patient and public expectations. The choice of learning opportunities (teaching-learning method) should be aligned and oriented towards achieving the expected learning outcomes. The current study established the links between learning opportunities and the expected learning outcomes in dental physiology curriculum through curriculum mapping.

Method: Learning opportunities were linked to expected learning outcomes by examining the conduct of each of them. Moreover, students' and teachers' views were obtained through focus group discussions and interviews.

Results: It was found that learning opportunities provided to students in the form of lectures, problem-based learning and practical sessions served its purpose of achievement of expected learning outcomes. Furthermore, valuable suggestions on the improvement of the existing learning opportunities were obtained.

Conclusions: The study, therefore, confirmed the link between the learning opportunities and expected learning outcomes.

Keywords: Learning opportunity; dental physiology curriculum; expected learning outcomes; curriculum mapping.

Introduction

Reforms in education have led to the advent of outcome-based education (OBE), with the focus

shifting from inputs and processes to outcomes. The emphasis in OBE is on the outcomes or the products, and in the context of a medical or dental school, the kind of doctors and dentists it produces becomes the outcome¹⁻³. The young doctors and dentists coming out of these schools need to possess the competencies to practice in an increasingly complex healthcare scenario with changing patient and public expectations^{2,3}. This being the primary objective, the expected learning outcomes (ELOs) will have to be defined accordingly. ELOs are the culminating demonstration of abilities the learner will be able to do at the end of the learning period^{3,4}. OBE in its structure and composition, has to facilitate achievement of these outcomes by students

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and hence need to be equipped with appropriate content, learning opportunities (teaching-learning method), and assessments, which are selected based on the outcomes chosen³⁻⁵. The choice of teaching method, including lectures, small group work, and independent study, should be aligned and oriented towards achieving the learning outcomes⁵. This requires use of suitable tools to find out the links between learning opportunities and ELOs.

Curriculum mapping is a method employed to know the links between the curricular components, such as learning opportunities, assessments, content, ELOs, etc., and thereby making the curriculum transparent. Or in other words, curriculum map displays the components of the curriculum and relations between them. Curriculum mapping enables the researchers to find out the gaps in the curriculum by assessing the extent to which the curricular components are linked among themselves⁶.

Researchers have used curriculum map to determine contribution of learning events to the medical school's core competencies⁷, coverage of competencies in a dental curriculum⁸, and to explore alignment between the components of the curriculum⁹. Links or relations between the components are the very essence of a curriculum map, as reported by Harden⁶. However, there is a lack of literature from India on curriculum mapping. Moreover, studies from India seldom attempted to find any influence of curricular components on attainment of the ELOs in students. Hence, the current study was conducted to establish links between learning opportunities and ELOs in physiology through curriculum mapping.

The research question formulated was

- Are the various learning opportunities facilitating students to achieve the ELOs?

Method

The undergraduate Bachelor of Dental Surgery (BDS) program at Melaka Manipal Medical College (MMMC), Manipal Campus, Manipal Academy of Higher Education, Manipal, India, is a five year academic program in twin campuses. The first two years of study are done at Manipal, India, and the latter three years at Melaka, Malaysia. During the first year, students learn anatomy, physiology, biochemistry and oral biology. The current study was conducted in the department of physiology, MMMC, Manipal Campus.

The study subjects were students of BDS batches 4, 5, and 6 (September 2012, September 2013, October 2014 admissions) of MMMC and physiology teachers of MMMC.

The ELOs of the physiology curriculum which students must attain at the end of the year are knowledge of basic physiological principles and mechanisms, critical thinking skills, self-directed learning (SDL) skills, collaborative learning skills, communication skills, and practical skills. These ELOs were derived from the BDS program outcomes.

MMMC follows a hybrid curriculum where the learning opportunities available for students are didactic lectures, problem-based learning (PBL) sessions, and practical sessions. Every week, two didactic lectures are conducted. Practical sessions are scheduled for three weeks per block (one slot of two hours duration), which includes both demonstration and hands-on experiments. One PBL session is conducted in each block in the traditional way, consisting of brainstorming and presentation sessions. During the study period in between brainstorming and presentation sessions, students are encouraged to involve in collaborative learning.

Lectures, PBL, and practical sessions were linked to ELOs by examining the conduct of each of them. In addition, students' and teachers' views were obtained through focus group discussions (FGD), and interviews to establish the link between learning opportunities and ELOs.

Two FGDs were conducted with every batch of students at the end of first year to explore the effectiveness of learning opportunities in attaining ELOs. The teachers of the physiology department at MMMC were interviewed individually at the end of the year to explore how useful the learning opportunities were in achieving ELOs. Qualitative data analysis was done using constant comparative analysis¹⁰.

Results

It was found that appropriate learning opportunities were provided in the curriculum for the attainment of ELOs by the students (Table 1). Analysis of qualitative data revealed that lectures helped in acquiring knowledge, critical thinking, and SDL skills; PBL helped to achieve knowledge, critical thinking, SDL, collaborative learning, and communication skills; practical session helped in attaining knowledge, critical

thinking, collaborative learning, communication, and practical skills. The themes that emerged from the qualitative data analysis were a) reasons for achieving ELOs through learning opportunities and b) reasons for not achieving the ELOs through learning opportunities c) suggestions to improve the learning opportunities.

Lectures:

Reasons for achieving ELOs: Students and teachers opined that the scope for increased student-teacher interaction in class, explaining concepts effectively, and teaching using relevant multimedia helped in achieving the required knowledge.

Please change the following sentence 'We guide students in learning by explaining the concepts in an easy way' (Teacher)

Students mentioned that discussion of sample questions also benefited them to develop knowledge. The participants expressed that teaching with case scenarios and teachers asking thought provoking questions made students think critically. Also, students opined that lectures incorporated discussion of content by students and teachers, which made lectures interesting and encouraged students to search for additional information. This, in turn, helped them to attain SDL skills.

Reasons for not achieving the ELOs/suggestions for improvement: Students felt that lectures of some teachers could be improved by providing scope for more interaction with students, improving teachers' communication skills, and in some cases, presentation slides. Students mentioned that lecture handouts could be provided to them so that during the class, they need not have to spend time in noting down the content; instead they could focus more on listening in the class. Students opined that they require more time to take down the notes if handouts are not provided to them. Teachers suggested that to facilitate achievement of learning outcomes through lectures; active learning strategies could be used; students could ask more questions and interact with the teacher during class.

PBL sessions:

Reasons for achieving ELOs: The study participants felt that the thought provoking and interesting PBL cases, assessment during the PBL, and peer interaction during the sessions helped them to attain the knowledge and skills.

'Because we have to present and it is assessed, we search for information, and we understand the topic' (Student)

Also, the mandatory presentation included in PBL, helped them to hone their communication skills besides acquiring additional knowledge in the topic as they had to prepare for their presentation. The challenge involved in arriving at the relevant learning objectives helped them to improve their critical thinking skills. Moreover, students also felt that they could integrate the topics in a better way through PBL.

Reasons for not achieving the ELOs/suggestions for improvement: The respondents commented that in some groups, collaborative learning was less, which was a hindering factor in acquiring knowledge and skills.

'Less group interaction was observed in some groups' (Teacher)

Time constraints, students' preference for studying individually instead of collaboratively, were the reasons given by the participants.

Practical sessions:

Reasons for achieving ELOs: Students and teachers opined that practical sessions were interesting and relevant to the students, which made them acquire knowledge, critical thinking, collaborative learning, communication, and practical skills. They felt that as the practicals were related to theory, it improved their understanding of the theory topics as well.

'Understood some of the theory through practicals' (Student)

The respondents opined that teachers facilitated students in developing practical skills through demonstrations as well as encouraging them to practice. Furthermore, students were made to collaborate with their friends and learn practical skills, as expressed by the participants. Moreover, during clinical examinations, students were taught how to take informed consent from the subjects, which helped them to improve their communication skills. The participants revealed that during practical sessions discussion of renal problems, cases about endocrine disorders helped them to promote their critical thinking skills.

Reasons for not achieving the ELOs/suggestions for improvement: Some students expressed their desire

to learn more about clinical examination practical topics like detailed examination of the cardiovascular system instead of limiting it to auscultation of heart sounds, as per the existing learning objective.

'I feel we need more practicals like palpation of cardiovascular system like MBBS. In future if patient comes to my clinic, I should know' (Student)

Table 1: Links between learning opportunities and expected learning outcomes

Learning opportunities	Expected learning outcomes
Lectures	Knowledge
PBL sessions	Knowledge, critical thinking skills, self-directed learning skills, collaborative learning skills, communication skills
Practical sessions	Knowledge, critical thinking skills, collaborative learning skills, communication skills, practical skills

Discussion

In OBE, the given learning opportunities should facilitate the attainment of the outcomes, and hence selection of proper learning opportunities is crucial⁵. The current study aimed at finding out whether the learning opportunities facilitated achievement of learning outcomes or not, culminated in affirmative results. It is evident from the opinions of majority of the respondents that the learning opportunities helped students to achieve the outcomes.

Lecture is a widely used instructional method in higher education and is one of the key learning opportunities. Lectures continue to play an important role in student learning¹¹ and will be effective, provided, the lecture is planned as per suitable pedagogy, and delivered appropriately¹². It is also necessary that lecture-based teaching employs effective method, such as the active engagement of participants¹³. At MMMC, lectures are used as the main mode of learning opportunity, and it was found that lectures helped in attaining knowledge, critical thinking, and SDL skills. Students mentioned that the use of videos and the interactive mode of teaching helped them to acquire the outcomes and teachers endorsed this opinion. Explaining and questioning are the two important skills in lecturing¹⁴. At MMMC, these techniques were effectively used by teachers to facilitate student learning, as expressed by both teachers and students. Brown¹⁴ pointed out that students value the lectures more if it is well structured, interesting and has

clarity of presentation. Students' opinions obtained in the present study endorse the above fact. Students felt that the interactive sessions, non-monotonous and interesting lectures with appropriate explanations of the topics greatly helped in learning. A lecture could be used to provoke thought, to deepen understanding and to enhance scientific and clinical thinking¹⁴. Students mentioned that thought provoking questions during lecture classes made them think critically. The most important aspect of lecturing appears to be the stimulation of students to become active learners¹⁵. At MMMC, through active learning strategies like conducting quizzes, role-plays, etc., teachers facilitated student learning during the lectures. Students and teachers mentioned that lectures helped to improve SDL skills also. It was reported that students' views about poor lecturing include poor use of audio-visual aids, inaudibility, incoherence, talking too fast, and too much information¹⁴. In the present study also, students mentioned poor use of audio-visual aids, in some cases as one of the reasons for ineffective lecturing.

One must know lectures alone will not be able to nurture the relevant skills needed for dental practitioners. PBL helps facilitate higher order thinking as it is a student-driven process. Moreover, PBL helps arousing curiosity of students, which in turn motivates them to learn even the basics during the process of analyzing cases¹⁶. The success of the PBL depends on the case or problem given to the students, and hence development of an effective case is very important. At MMMC, the case designed is validated at multiple levels. The faculty member in charge of developing the case will design the case, which will be discussed among the members involved in the block for the accuracy and relevance of content. Later it will be scrutinized by heads of departments of first year. The present study revealed that PBL helped students in attaining critical thinking, SDL, collaboration, and communication skills.

Earlier studies reported that medical and biology students found practical sessions in physiology were interesting and also helpful in understanding the theory concepts^{17,18}. The outcome of the current study was also in line with the above observation. Teaching theoretical concepts before practical sessions, practice sessions facilitated by the teacher, and provision of enough time for practicing the skills during routine practical sessions as well as provision of revision classes could have evoked the positive response from students.

Conclusions

Professional education, such as dental education, requires a specific set of competencies to be acquired by the students by the end of their study period. Learning opportunities provided to students in the form of lectures, PBL, and practical sessions served its purpose of acquirement of knowledge as well as practical skills in physiology, facilitation of SDL, critical thinking, and other generic skills in students, as evident from the qualitative data. Some perceptions were found to be similar among students and teachers, which substantiates and reaffirms the authenticity of the responses. The study, therefore, confirmed the links between learning opportunities and ELOs in the dental physiology curriculum at our institution and thereby helping the students to be prepared for their profession. Furthermore, through the study, we obtained valuable suggestions pertaining to the existing learning opportunities from the stakeholders, which helps for continuous quality improvement.

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References

1. Clark JD, Robertson LJ, Harden RM. The specification of learning outcomes in dentistry. *Br Dent J.* 2004a;96:289-294.
2. Clark JD, Robertson LJ, Harden RM. Applying learning outcomes to dental education. *Br Dent J.* 2004b;96:357-359.
3. Harden RM, Crosby JR, Davis MH. AMEE guide no 14: outcome-based education: part 1: *Med Teach.* 1999;21:7-14.
4. Spady WG. Outcome-based education: critical issues and answers. Arlington, VA: American Association of School Administrators, 1994.
5. Harden RM. Outcome-based education - the ostrich, the peacock and the beaver. *Med Teach.* 2007;29:666-671.
6. Harden RM. AMEE guide no. 21: Curriculum mapping: a tool for transparent and authentic teaching and learning. *Med Teach.* 2001;23:123-137.
7. Cottrell S, Hedrick JS, Lama A, Chen B, West CA, Graham L, et al. Curriculum Mapping: a comparative analysis of two medical school models. *Med Sci Educ.* 2016;26:169-174.
8. Mazurat R, Schönwetter DJ. Electronic curriculum mapping: supporting competency-based dental education. *J Can Dent Assoc.* 2008;74:886-889.
9. Balzer F, Hautz WE, Spies C, Bietenbeck A, Dittmar M, Sugiharto F, et al. Development and alignment of undergraduate medical curricula in a web-based, dynamic learning opportunities, objectives and outcome platform (LOOOP). *Med Teach.* 2016;38:369-377.
10. Thorne S. Data analysis in qualitative research. *Evid Based Nurs.* 2000;3:68-70.
11. Gupta A, Saks NS. Exploring medical student decisions regarding attending live lectures and using recorded lectures. *Med Teach.* 2013;35:767-771.
12. Saroyan A, Snell LS. Variations in lecturing styles. *High Educ.* 1997;33:85-104.
13. Lochner L, Gijsselaers WH. Improving lecture skills: a time-efficient 10-step pedagogical consultation method for medical teachers in healthcare professions. *Med Teach.* 2011;33: 131-136.
14. Brown G, Manogue M. AMEE guide no. 22: Refreshing lecturing: a guide for lecturers. *Med Teach.* 2001;23:231-244.
15. Meyers C, Jones TB. Promoting active learning: strategies for the college classroom. San Francisco: Jossey-Bass, 1993.
16. Donner RS, Bickley H. Problem based learning in American medical education: an overview. *Bull Med Libr Assoc.* 1993;81:294-298.
17. Dohn NB, Fago A, Overgaard J, Madsen PT, Malte H. Students' motivation toward laboratory work in physiology teaching. *Adv Physiol Educ.* 2016;40:313-318.
18. Vashe A, Abraham RR, Torke S, Pallath V, Kamath A. Student and faculty perspectives on laboratory based learning (LBL) sessions in physiology. *South East J Med Educ.* 2012;6:1-7.

Home Remedies and Health Care Seeking Behavior among Care Takers of Under-5 Children in Rural Field Practice area of a Medical College: Focus Group Discussion

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Abstract

Background: The health of children has historically been of vital importance to all societies because children are the future of mankind. In developing countries, home remedies are often the only accessible and affordable treatment available.

Materials and Method: The study was conducted in Nagavalli, the rural field practice area of Sri Siddhartha Medical College Tumkur, during January 2019 - March 2019. After getting the clearance from Ethics Committee the data was collected using focus group discussions (FGDs) with purposively selected care takers who were willing to participate and talk freely.

Results: The common home-remedies used for these ailments by majority of the care takers were Tulasi for fever, cough and cold, Garlic for cough and cold, Ginger for cough and cold, Black pepper for cough and cold, Honey for cough, Amulet for bala graha, falls, evil's eye, Crushed pomegranate for diarrhea, Tea decoction for diarrhea, Turmeric for cough and cold, Coffee powder for cuts and injuries, Branding with hot iron rod for pain abdomen and inability to pass stools (Constipation), Hot broken bangle piece: head ache and fever, Hot Castor oil: For earache and for constipation.

Conclusion: Rural population preferred home-remedies for treatment of common ailments in under-5 sick children in the initial phase of the illness. Some of the practices followed by care takers were harmful.

Keywords: Home remedies, Under-five children, Honey, Turmeric, Focal group discussion.

Introduction

The health of children has historically been of vital importance to all societies because children are the future of mankind. Therefore, at each stage of child's growth and development appropriate care is very essential.¹ Minor ailments present in the under-five children such as

fever, diarrhoea and vomiting, ear ache, head ache, nose bleed, sore throat, and common cold etc. can be treated at home with home remedies.

In developing countries, home remedies are often the only accessible and affordable treatment available. Non-availability of doctors and high medicine cost make health care inaccessible to the rural population and consequently home remedies serve as one of the options for immediate care.

Indian Council for Medical Research task force has reported that still in rural parts of India, people follow some home remedies or seek traditional medicine practitioners to get rid of various ailments because they feel that these therapies are time tested and mainly they have no side effects like modern medicine.²

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In focus group discussions there is a tendency that the attitudes and perceptions are developed through interaction with others in the groups.³ Instead of the moderator asking questions, the group members are encouraged to communicate with one another, exchanging ideas and comments on each other's experiences or points of view.⁴ In this sense, focus groups showed dimensions of understanding that often remain untapped or inaccessible by other forms of data collection.⁵ In the context of healthcare and medical research, focus groups are particularly apt due to the fact that most health-related conditions are created by social environments and made within the social context.⁶ Thus, focus groups are a popular method for assessing public experience and understanding of illness,^{7,8} identifying ideas concerning health-risk behaviours and danger,^{8,9} and discovering the public's perception of causes of diseases.¹⁰ They can also be used to gain insights into people's experiences of ill health and health services,^{11,12} and explore the attitudes and needs of healthcare providers.¹³

Objectives:

- To study the use of home remedies during episodes of illnesses among under-5 children.
- To assess health care seeking behaviour among caretakers of under- 5 children.

Materials and Method

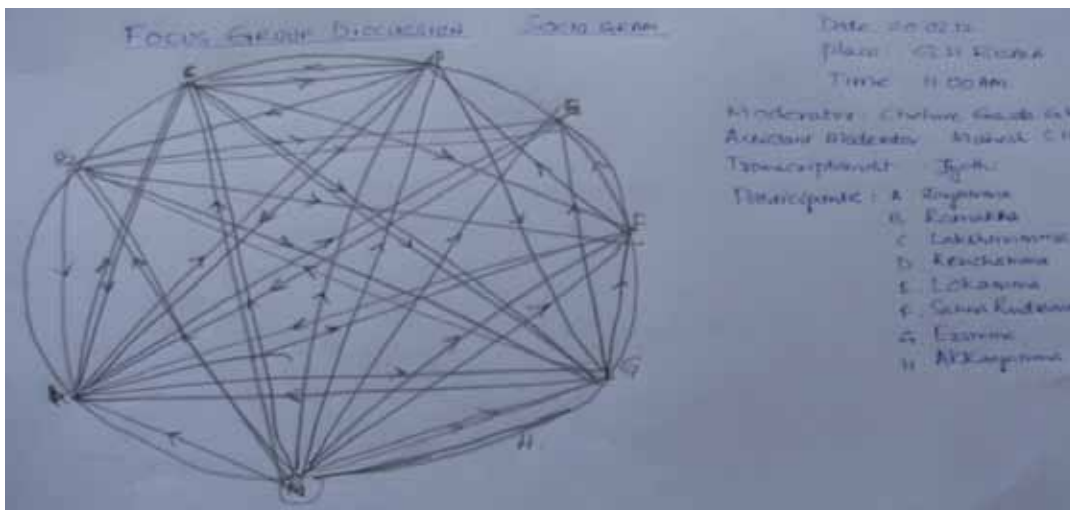
The study was conducted in Nagavalli, the rural field practice area of Sri Siddhartha Medical College Tumkur, during January 2019 - March 2019. After getting the clearance from Ethics Committee, the data was collected

using focus group discussions (FGDs) with purposively selected care takers, who were willing to participate and talk freely.

Focus Group Discussions: Focus Group Discussions (FGDs) were conducted in 19 different villages of field practice area of Sri Siddhartha Medical College. A total of 19 FGDs, each with 8-12 participants, were conducted in the local language Kannada and were recorded on audio. A trained facilitator led each discussion while another person took notes, which were later translated into English. The care takers included mothers and grandparents who were purposively selected from rural field practice area covering different socio-economic strata. The FGDs addressed the various illnesses among under-five children, home remedies for those illnesses and health care seeking behaviour.

The number of FGDs was decided by a saturation point where it stopped yielding new information and after 19 FGDs, saturation point was reached. Statistical analysis was done by Coded key word approach.¹⁴ Coded key word technique allows more precision in identifying comments and does not risk 'losing' a comment merely. The coded key word approach involves reading the focus group notes thoroughly and assigning a code/key word to each comment in order to identify themes or categories within the text. The group (rather than the individual) is the unit of analysis. When constructing tables to classify data or identify themes, a disease is listed in the table, if it is mentioned by a group; however, it is listed only once, no matter how many times respondents in a particular group mention it. The number of groups, not the number of individuals, is used as the denominator.

Sociogram:



The participants were made to sit in a circle, so that each participant is fully visible to all others. The moderator initiated the conversations on the subject and encouraged everyone participate in the discussion and one investigator made notes while the other recorded the conversations. The discussions were continued till all the participants agreed to the relevant and specific home remedy for that particular ailment.

Results

Table 1: Distribution of participants according to religion

Religion	Frequency	Percent
Hindu	186	93.00%
Muslim	14	7.00%
Total	200	100.00%

In the study there were 200 participants of whom 186 were Hindus and 14 were Muslims.

Table 2: Distribution of participants according to Education status

Education	Frequency	Percent
7 th standard	36	18.00%
SSLC	113	56.50%
2 nd PUC	46	23.00%
BA	5	2.50%
Total	200	100.00%

Majority of the participants (113) had studied till SSLC and some of the participants till 2nd PUC (46). Very few (5) had degree qualification.

Table 3: Distribution of participants according to Socio-Economic status

Socio-Economic Status	Frequency	Percent
Lower class	89	44.50%
Lower middle class	98	49.00%
Middle class	8	4.00%
Upper middle class	5	2.50%
Total	200	100.00%

Majority of the participants belonged to lower middle class and lower class according to modified B.G.Prasad's socio-economic status.

Majority of the participants agreed that the most common symptoms among under-5 children were cough, cold, fever, loose stools, pain abdomen,

constipation, cuts and "balagraha" (excessive crying and irritability). A few also mentioned other symptoms like headache, problems of feeding, falls and injuries, difficulty in breathing, ear pain and discharge from ear. The common home remedies used for these ailments by majority of the care takers were

Tulasi, Garlic, Ginger, Black pepper, Honey, Amulet, Crushed pomegranate, Tea decoction, Turmeric, Coffee powder, Branding with hot iron rod, Hot broken bangle piece, Hot Castor oil.

Discussion

The common home-remedies used for these ailments by majority of the care takers were

Tulasi : Fever, cough and cold, Garlic : Cough and cold, Ginger : Cough and cold, Black pepper : Cough and cold, Honey : Cough, Amulet : Bala graha, fall, evil's eye, Crushed pomegranate: diarrhea, Tea decoction: diarrhea, Turmeric; cough and cold, Coffee powder: Injuries, Branding with hot iron rod: for pain abdomen and inability to pass stools (Constipation), Hot broken bangle piece: head ache and fever, Hot Castor oil: For earache and for constipation.

A study conducted by sandy cove et.al showed Comparison of honey with Dexamethasone revealed no significant differences. Honey may be preferable for the treatment for cough and sleep difficulty associated with childhood respiratory tract infection.¹⁵

A quasi experimental study was conducted with 100 parents (27 men, 73 women) enrolled in a prepaid medical health plan to investigate their use of home remedies. A remedy was reported for almost every health problem listed. Substances most frequently used were aloe vera, honey, peppermint, garlic, eucalyptus, and rose hips; health problems most frequently treated were burns, colds, fever, diarrhoea, vomiting, indigestion, insect bites, insomnia and rashes.¹⁶

A study conducted by Cevit Karkaset.al showed honey (25%) and ginger (27%) were the most common home remedies used for the relief of cough. Self-advised medications were used by 24% mothers and majority 58.4% gained knowledge from mass media.¹⁷

It was noticed that majority of the participants preferred home-remedies due to low cost, easy availability and in emergency situations. Few also mentioned that it was recommended by the grand

parents and their neighbors. Majority of them preferred home remedies in the initial phase (i.e. on day 1 and day 2) of the illness irrespective of the availability of health care facilities. Some of the female respondents said they do not use allopathic medicines because of fear of side effects. There was no sex discrimination regarding the use of home-remedies.

When there was no improvement or if the problem aggravated, then majority of the care takers approached clinics or private practitioners in the village or nearby health facility in that area, irrespective of provider's qualification. The reasons for delay in seeking health care by majority of participants were lack of money, faith in home remedies, non-availability of transport, non-availability of doctor and absence of responsible person at home. The socio-economic status of the family played major role in deciding the type of provider to be approached for seeking treatment. Poor families generally approached local practitioners or registered medical practitioners of the area, who provide treatment at low cost. A few care takers approached government health facilities, where treatment is provided at relatively lesser cost.

Bhandari *et al* also reported that 40% of sick neonates did not get medical care in periurban area of Delhi. Various barriers which interfered with the translation of knowledge into action in our respondents in terms of access to medical care were ignorance of parents, lack of money, faith in supernatural causes, non-availability of transport, home remedy, non-availability of doctor and responsible person not at home in descending order.¹⁸

As revealed from many quantitative and qualitative data, there was relatively more preference for government health care services. Hence, improvement in capacity, quality and reach of government health care services and national health programs is crucial for ensuring optimal newborn care in rural area. Kaushal *et al* and Awasthi *et al* also reported similar health seeking behavior for sick children in North India.¹⁹

Health seeking behavior among different populations, particularly in the rural communities, is a complex outcome of many factors operating at individual, family and community level including their bio-social profile, their past experiences with the health services, availability of alternative health care providers including indigenous practitioners and last but not the least their perceptions regarding efficiency and quality of the services.

Conclusion

Rural population preferred home remedies for treatment of common ailments in under-5 sick children in the initial phase of the illness. Some of the practices followed by care takers were harmful. Traditional medicine can contribute and has contributed in various ways to the development and dissemination of good practice. With its centuries-old knowledge of herbal medicines, it has been used to treat or palliate numerous illnesses and has paved the way for discovery of new drugs.

Recommendations: Care takers need to be educated about harmful practices. Improved living conditions, better nutrition, provision of Maternal and Child Health care, immunization and community support will decrease the disease burden. Caretakers should be made to appreciate the need for early diagnosis and start prompt treatment.

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References

1. Deborah E. Bender. Douglas Ewbank. The focus group as a tool for health research: issues in design and analysis. Health transition review vol. 4 no.1 1994.
2. Kombo IP, Dhillon BS, Singh P, Saxena BN, Saxena NC. Self reported gynaecological problems from twenty three districts of India (An ICMR Task Force Study). Indian J. of Commun Med, 2003, 28: 67-73.
3. Keith Tones. Health promotion, health education and the public health. Oxford Textbook of Public Health. Fourth Edition. Oxford University Press. 2004. pp 829-863.
4. Kitzinger J. The methodology of focus groups: the importance of interactions between research participants. Sociol Health Illness 1994; 16:103-21.
5. Kitzinger J. Qualitative research: introducing focus groups. BMJ 1995;311:299-302.

6. Carter S, Henderson L. Approaches to qualitative data collection in social science. In: Bowling A, Ebrahim S, eds. *Handbook of Health Research Method: Investigation, Measurement and Analysis*. Buckingham: Open University Press, 2005: 219-29.
7. Kitzinger J. Understanding AIDS: Researching audience perceptions of acquired immune deficiency syndrome. In: Eldridge J, ed. *Getting the Message: News, Truth And Power*. London: Routledge, 1993:271-305.
8. Ritchie JE, Herscovitch F, Norfor JB. Beliefs of blue collar workers regarding coronary risk behaviours. *Health Edu Res* 1994; 9:95-103.
9. Duke SS, Gordon-Sosby K, Reynolds KD, Gram IT. A study of breast cancer detection practices and beliefs in black women attending public health clinics. *Health Edu Res* 1994; 9:331-42.
10. Trilling JS. Selections from current literature: focus group technique in chronic illness. *Fam Pract* 1999; 16:539-41.
11. Naish J, Brown J, Denton B. Intercultural consultations: investigation of factors that deter non-English speaking women from attending their general practitioners for cervical screening. *BMJ* 1994; 309:1126-8.
12. Murray SA, Tapson J, Turnbull L, McCallum J, Little A. Listening to local voices: adapting rapid appraisal to assess health and social needs in general practice. *BMJ* 1994; 308:698-700.
13. Denning JD, Verschelden C. Using focus group in assessing training needs: empowering child welfare workers. *Child Welfare* 1993;72:569-79.
14. Kreuger RA. *Focus Groups: A Practical Guide for Applied Research*. 1st ed. London: Sage, 1988.
15. Sandy Cove, Gretel H. Pelto. Focused ethnographic studies in the WHO programme for the control of acute respiratory infections.
16. Neemat B. Commonly used home remedies by mothers. *Pakistan Journal Of Biological sciences*. 2008 July 15; 11(14):P.75-77.
17. Cevit Karkas, Behyun. A Multicentre survey of home care remedies. Available from URL: <http://www.wiley.interscience.com>
18. Bhandari N, Bahl R, Taneja S, Martines J, Bhan MK. Pathways to infant mortality in urban slums of Delhi, India: implications for improving the quality of community and hospital based programmes. *J Health Pop Nutr* 2002; 20 : 148-155.
19. Awasthi S, Verma T, Agarwal M. Danger signs of neonatal illnesses: perceptions of caregivers and health workers in northern India. *Bull World Health Organ* 2006; 84 : 819-826.

Breast Cancer Screening: Are 'At Risk Population' Known by Public Health Nurse Practitioners?

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Abstract

Introduction: Health care providers, especially Public Health Nurse who come in regular contact with women, can play an important role in providing the information regarding breast cancer. Hence this study is undertaken to assess the knowledge of risk factors associated with breast cancer and screening for breast cancer among Public Health nurse practitioners.

Method: This is a cross-sectional study designed to assess the Knowledge of risk factors associated with breast cancer and screening for breast cancer among Public Health nurse practitioners working in the Health centres of Dept of Community Medicine of Hassan Institute of Medical Sciences. All (30) Public Health nurse practitioners in the Seven Primary care facilities participated in the study.

Results: Fourteen percent of Public Health Nurse knew that most common cancer among women was breast cancer. However, 43% were aware that the obesity increased the risk of developing breast cancer. Whereas 60% were aware that nulliparity was a risk factor for developing breast cancer and 43% said having 2 or more children decreased the risk of developing breast cancer. However, 33% knew breast feeding was protective against breast cancer. Moreover, early menstruation and late menarche were known to be risk factors by 20% each, and 33% knew physical activity could be a preventive factor for Breast cancer. 96% were aware that a lump in the breast was a sign of breast cancer and 56% said discharge from the nipple was also a sign of cancer in the breast. All 100% knew that Breast Self-Examination was a screening method and only 20% were aware that clinical examination was also a method for identification of breast cancer.

Conclusion: District Health Authorities should periodically train public health nurses to improve their knowledge regarding risk factors, early signs and symptoms of breast cancer and method of cancer screening. This intern would help them to educate, suspect, and detect the breast cancer among the risk population at the earliest.

Keywords: Breast Cancer, Risk factors, Public Health Nurse.

Introduction

Breast cancer is the most common female cancer in the world with an estimated 2.08 million (24.2%) new cancer cases diagnosed in 2018. With age

standardised incidence rate of 46.3/100000 women and age standardised mortality rate of 13/100000 women. While in India also it has now become the most common female cancer with 162 468 (27.7%) new cases reported in 2018. Whereas the age standardised incidence rate was 24/100000 women, 87090 women died from breast cancer in 2018 giving an age adjusted mortality rate of 13 per 100000 of population. And is estimated to increase to 261850 by 2040.¹

Breast cancer risk factors include increased age, early menstrual period, late or no pregnancy, starting

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menopause after age 55, not being physically active, being overweight or obese after menopause, having dense breast, using combination hormone therapy, taking oral contraceptives, personal history of breast cancer, family history of breast cancer, previous treatment using radiation therapy and alcohol consumption.²⁻⁸

Adequate knowledge about the signs and symptoms and early breast cancer detection through breast self-examination (BSE) or clinical breast examination (CBE) or mammogram, is crucial to reducing breast cancer-related morbidity and mortality.⁹ Screening asymptomatic women by means of breast self-examination, clinical examination or mammography can play a significant role in decreasing breast-cancer mortality in developing countries.¹⁰ The Breast Health Global Initiative developed appropriate guidelines that can be used in nations with limited health care resources to improve breast cancer outcomes.¹¹

Health care providers, especially Public Health Nurse who come in regular contact with women, can play an important role in providing the information regarding breast cancer.¹² Empowering nurses with information about early detection method and their related benefits could help in advancing their skills in performing breast self-examination and expanding their role as client educators.¹³ Education and awareness need to be culturally appropriate and targeted towards the relevant risk population, because this may contribute towards an increase in early presentation so that highest benefit can be gained.¹⁴ The information obtained could help to initiate interventions to address the gaps in knowledge of Public Health Nurses towards breast cancer-related risk factors, signs and symptoms and early breast cancer detection through breast self-examination (BSE) or clinical breast examination (CBE). Hence this study is undertaken to assess the knowledge of risk factors associated with breast cancer and screening for breast cancer among Public Health nurse practitioners.

Methodology

This is a cross-sectional study designed to assess the knowledge of, risk factors associated with breast cancer and screening for breast cancer among Public Health nurse practitioner in the Health centres of Dept of Community Medicine of Hassan Institute of Medical Sciences. We have seven Health Centre with following number of Public Health Nurse Practitioners (Salagame PHC (7), Krishna Urban PHC (5), Shantigramma CHC

(5), Masalehosahalli CHC (3), Nitturu PHC (4), Dudda CHC (3), Konanuru PHC (3)). All (30) Public Health nurse practitioners in the selected health facilities participate in the study over a period of 2 months. A pretested questionnaire was used to collect the data. The questionnaire included information on sociodemographic profile of the study subjects, knowledge of breast cancer risk factors, knowledge of breast cancer signs and symptoms, knowledge of Breast Self-Examination, Clinical Examination and Mammography. Data collection on Knowledge of breast cancer among the participants was assessed based on knowledge on risk factors of breast cancer, signs and symptoms of breast cancer and knowledge on BSE and CBE. The assessment is done by scoring breast cancer knowledge computed by giving "1" to the correct answer, and "0" for the wrong and 'do not know' answers. The data obtained was entered excel and analysed using epi info software. The data is display using tables and graphs.

Results

Knowledge about the risk factors for breast cancer among the study participants: Thirteen percent of Public health nurse knew that most common cancer among women was breast cancer and 36% said this cancer was inherited. However, 43% were aware that the obesity increased the risk of developing breast cancer and 30% were aware that the large breast increases the risk of developing breast cancer. Whereas 60% were aware that nulliparity was a risk factor for developing breast cancer and 43% said having 2 or more children decreased the risk of developing breast cancer. However, 33% knew breast feeding was protective against breast cancer. Moreover, early menstruation and late menarche were known to be risk factors by 20% each. However, 60% knew that advancing age was a risk factor for Breast cancer and 66% knew consumption of alcohol can be a risk factor for developing breast cancer but only 33% knew that physical activity could be a preventive factor for Breast cancer. (Table -1)

Knowledge about signs and symptoms of Breast Cancer: 96% were aware that a lump in the breast was a sign of breast cancer and 56% said discharge from the nipple was also a sign of cancer in the breast, whereas 80% of the Public health nurse said pain and swelling in the breast was also a sign of Breast Cancer. Dimpling in the breast was understood to be a sign cancer among 50% of Public health nurse and 46% were aware that ulceration in the breast can be a sign of cancer. Only

30% knew that weight loss can also be a symptom of cancer whereas a majority 63% were aware that the change in the shape of the breast tissue can be a sign of cancer. A minimal 16% of Public health nurse had known that inversion of nipple can be a sign of cancer but 46% were aware that a lump in the arm pit could be a sign of breast cancer. But very few 16% knew that the dry skin on the nipple region can be a symptom of breast cancer. (Table 2).

Knowledge about Screening Method: A large majority 100% knew that Breast Self-Examination was a screening method to appreciate sign of cancer and only 20% were aware that clinical examination was also a method for identification of breast cancer and none of them knew about mammography as a screening method for identification of breast cancer. (Table 3).

Table 1: Knowledge about risk factors of breast cancer among the study Participants

		No (30)	%	Sd
1	Breast cancer is the most common cancers among women	4	13	1.4
2	Breast Cancer is an Inherited Disease	11	36	3.5
3	Being Overweight and Obese increase the risk of developing Breast Cancer	13	43	4.4
4	Breast cancer is more common among Nulliparity increased the risk of developing Breast cancer	18	60	5.9
5	Large Breast increased the risk of Breast Cancer	9	30	2.9
6	Breastfeeding may decrease the risk of breast cancer development	10	33	3.5
7	Bearing two or more children decreases the risk of breast cancer	13	43	4.3
8	Early Menarche may increase the risk of breast cancer	6	20	2.1
9	Late menopause may increase the risk of breast cancer	6	20	2.1
10	Breast cancer risk increase with advancing age	18	60	5.9
11	Smoking and Alcohol consumption increase the risk of breast cancer	20	66	6.8
12	Does physical activity decrease the risk of developing breast cancer?	10	33	3.9

Table 2: Knowledge about Signs and Symptoms of Breast Cancer

		No (30)	%	Sd
1	Lump in the breast	29	96	9.3
2	Discharge from the breast	17	56	5.5
3	Pain and Soreness in the breast	24	80	8
4	Dimpling in the breast	15	50	5.4
5	Ulceration in the breast	14	46	4.6
6	Weight loss	9	30	3.2
7	Change in the shape of the breast	19	63	6.7
8	Inversion in nipple	5	16	2.4
9	Lump Under Armpit	14	46	4.7
10	Dry Skin on Nipple region	5	16	1.8

Table 3: Knowledge about Screening method

		No (30)	%	Sd
1	Brest Self Examination	30	100	9.6
2	Clinical Breast Examination	6	20	2.6
3	Mammography	0	0	0

Discussion

Breast cancer is the most common female cancer in the world as well as in India. Panieri E et al 2012.¹⁵ Opined that screening asymptomatic women by means of breast self-examination, clinical examination or mammography can play a significant role in early detection of breast cancer.¹³.

Knowledge about the risk factors for breast cancer among the study participants: Only thirteen percent of Public health nurses knew that most common cancer among women was breast cancer. The study shows that our public health nurses are not oriented to the problem of Cancer in their population and women cancer in particular. However, factors like multiparity, breast feeding and physical activity as protective factors was not known by many. This shows that the respondents are not informed of the protective factors. Shuyuasa et al¹⁶ in their study found that the risk for breast cancer development among single was 49% more as compared to the married women and also nulliparous woman had 38% more risk as compared to women with 5 or more children. A recent meta-analysis by Zhou Y et al ¹⁷ in 2015 involving twenty-four articles with 13,907 breast cancer cases showed that breastfeeding was inversely associated with the risk of breast cancer. Wherein the relative risk of breast cancer for the ever breastfeeding compared with never was 0.613 and an inverse association was found for the longest as compared with the shortest duration of breastfeeding with the relative risk of 0.471. Also, Pettapiece-Phillips R et al (2015) ¹⁸ in their study reported that physical activity increases the expression of normal BRCA1 or BRCA2 gene and their by mitigating inherited BRCA mutation. Our study shows that the study population are poorly informed about the association of mensuration on breast cancer. This has been documented by shuyuasa et al¹⁶, that relative risks of breast cancer for women reporting menarche prior to the age of 13 years was twice as high as that for those with menarche occurring after 16 years of age. The author also recorded relative risk of 1.40 for women reporting menopause at 50 years of age or over, as compared to those reporting it prior to 50 years. Also 66% knew consumption of alcohol can be a risk factor for developing breast cancer. This association was recorded by Romieu et al 2015 ¹⁹ in their study, wherein it was estimated that, for each 10 g/day increase in alcohol intake the risk increased by 4.2%.

Knowledge about signs and symptoms of Breast Cancer: 96% were aware that a lump in the breast was a sign of breast cancer, which is better than that of a finding reported by Negalign Getahun et al ²⁰ from china where breast lump was the most commonly known symptom of cancer by 61.7% of the respondents. This may be because of the recent experience of the public health nurses with the cases in their field practice areas. Dimpling in the breast was understood to be a sign of cancer among 50% of public health nurse and 46% were aware that ulceration in the breast can be a sign of cancer. Similar observations were reported by Andegiorgish et al ²¹ in their study, where more than 85% of the respondents stated that a lump in the breast, change in the size of the breast and discoloration/dimpling of the breasts are the major signs of breast cancer.

Knowledge about Screening Method: All 100% knew that Breast Self-Examination was a screening method to appreciate sign of cancer and only few were aware that clinical examination was also a method for identification of breast cancer, Santhana krishnan et al²² in their study among nursing staff reported that 73.2% mentioned BSE as a screening test and only 20% mentioned CBE as a diagnostic test. This observation is likely because of the training under non communicable disease programme initiative where predominantly teaching is about the signs and symptoms of breast cancer and about breast self-examination.

Conclusion

Our study revealed minimal awareness of risk factors associated with breast cancer among respondents. The study found that majority of the respondents answered the most common symptom of breast cancer and were aware of breast-self-examination. So, we recommend that District Health Authorities to periodically train public health nurses to improve their knowledge regarding risk factors, early signs and symptoms of breast cancer and method of cancer screening. This intern would help them to educate, examine and detect the breast cancer among the risk population at the earliest.

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References

1. http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx. Source: Globocan 2018
2. <http://www.cancer.org/cancer/breastcancer/detailedguide/breast-cancer-risk-factors>
3. Pharoah PD, Day NE, Duffy S, et al. Family history and the risk of breast cancer: A systematic review and meta-analysis. *Int J Cancer* 1997; 71:800-09
4. Collaborative Group on Hormonal Factors in Breast Cancer. Menarche, menopause, and breast cancer risk: individual participant meta-analysis, including 118,964 women with breast cancer from 117 epidemiological studies. *Lancet Oncol* 2012; 13:1141-51
5. Vrieling A, Buck K, Kaaks R, et al. Adult weight gain in relation to breast cancer risk by estrogen and progesterone receptor status: a meta-analysis. *Breast Cancer Res Treat* 2010; 123:641-49
6. Ewertz M, Duffy SW, Adami HO, et al. Age at first birth, parity and risk of breast cancer: a meta-analysis of 8 studies from the Nordic countries. *Int J Cancer* 1990;15;46:597-603
7. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50,7302 women with breast cancer and 96,973 women without the disease. *Lancet* 2002;360:187-95
8. Rinaldi S, Peeters PHM, Bezemer ID, et al. Relationship of alcohol intake and sex steroid concentrations in blood in pre- and post-menopausal women: the European Prospective Investigation into Cancer and Nutrition. *Cancer Cause Control* 2006;17:1033-43
9. Mitra et al. A cluster randomized, controlled trial of breast and cervix cancer screening in Mumbai, India: methodology and interim results after three rounds of screening. *Int. J. Cancer*: 126, 976–984 (2010)
10. Panieri E¹. Breast cancer screening in developing countries. *Best Pract Res Clin Obstet Gynaecol*. 2012 Apr;26(2):283-90
11. Anderson BO, Shyyan R, Eniu A, Smith RA, Yip CH, Bese NS, et al. Breast cancer in limited-resource countries: an overview of the breast health global initiative 2005 guidelines. *Breast J* 2006;12(Suppl 1):S3–S15
12. Thomas DB, Gao DL, Ray RM, Wang WW, Allison CJ, Chen FL, et al. Randomized trial of breast self-examination in shanghai: final results. *J Natl Cancer Inst* 2002;94(19):1445–1457
13. Collaborative Group on Hormonal Factors in Breast Cancer. Familial breast cancer: collaborative reanalysis of individual data from 52 epidemiological studies including 58,209 women with breast cancer and 101,986 women without the disease. *Lancet*. 2001;358(9291):1389–99
14. Stockton D, Davies T, Day N, McCann J. Retrospective study of reasons for improved survival in patient with breast cancer in east Anglia: earlier diagnosis or better treatment. *BMJ*. 1997;314:472–5.
15. Panieri E¹. Breast cancer screening in developing countries. *Best Pract Res Clin Obstet Gynaecol*. 2012 Apr;26(2):283-90
16. Shyuasa, Bbrian- macmahon. Lactation and Reproductive Histories of Breast Cancer Patients in Tokyo, Japan. *Bull. World Health Org* 1970, 42, 195-204
17. Zhou Y, Chen J, Li Q, Huang W, Lan H, Jiang H. Association between breastfeeding and breast cancer risk: evidence from a meta-analysis. *Breastfeed Med*. 2015 Apr;10(3):175-82
18. Pettapiece-Phillips R¹, Narod SA. The role of body size and physical activity on the risk of breast cancer in BRCA mutation carriers. *Cancer Causes Control*. 2015 Mar;26(3):333-44.
19. Romieu I¹, Scoccianti C¹, Chajès V¹, et al. Alcohol intake and breast cancer in the European prospective investigation into cancer and nutrition. *Int J Cancer*. 2015 Oct 15;137(8):1921-30.
20. Negalign Getahun Dinegedel, Li Xuying. Awareness of Breast Cancer among Female Care Givers in Tertiary Cancer Hospital, China. *Asian Pac J Cancer Prev*, 18 (7), 1977-1983
21. Eritrea Amanuel Kidane Andegiorgish¹, Eyob Azeria Kidane¹, Merhawi Teklezgi Gebrezgi³. Knowledge, attitude, and practice of breast Cancer among nurses in hospitals in Asmara,. *BMC Nursing* (2018) 17:33
22. Santhanakrishnan et al.: KAP regarding breast cancer among nursing staff. *International Journal of Medical Science and Public Health* | 2016 | Vol 5 | Issue

Efficacy and Feasibility of Proprioceptive Neuromuscular Facilitation on Hand Opening in Stroke Individuals: A Case Series

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Abstract

Introduction: Stroke is a leading cause of death all across the globe, and hand impairment after the stroke is inevitable. The hand dysfunctions are the primary cause of disability, and dependency is stroke patients. Thus it is very imperative to address the condition. PNF is a proved treatment to be useful for the weakened muscles and even for the stroke.

Aim/Objective: The purpose of the study was to evaluate the efficacy and feasibility of PNF techniques on hand opening in stroke patients.

Method: Three patients were treated with stroke and inability to open hands, were treated with PNF techniques for four weeks. All three patients recovered with the treatment, and they were able to open their hands fully or partially.

Conclusion: This study concludes that PNF techniques are effective for hand opening in stroke individuals.

Keywords: Stroke, PNF, Hand opening, Hand function.

Introduction

World health organization (WHO) has defined a stroke as rapidly developing clinical signs of focal disturbance of cerebral function lasting more than 24 hours or leading to death with no apparent cause other than a vascular origin.¹ The incidence rate in India is 84-262/100,000 in the countryside and 334-424/100,000 in metropolitan areas.²

Patients suffering from a stroke might have numerous impairments such as weakness, sensory

dysfunction, spasticity, balance issues, in-coordination, gait deviations, perceptual disorders, cognitive deficits, attention deficits, and behavioral changes. The most common impairment following stroke is of the upper limb that is arm, hand, and finger. It is often reported to be incomplete in functional recovery and to regain the motor activities.³

Evidence shows that chronic deficits are very prevalent observant in hand. Finger extension is the motor function very likely to be affected. This distal limb impairment is especially very problematic because proper hand control and hand function are very crucial for manual exploration and manipulation of the environment.⁴

A hand is the last part to be recovered after stroke, and importantly hand opening and wrist extension are very crucial to carry out activities of daily living it becomes very depressing for the patient with this hand impairment.

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Physiotherapy can help immensely for the rehabilitation of the hand with the help of interventions like task-oriented therapy, constraint-induced movement therapy, bio-feedback and robot-assisted therapy, neuromuscular electrical stimulation, functional electrical stimulation.

Even though hand opening is very crucial and essential to carry out hand functions and for the execution the daily activities there is no study done for improving facilitating the hand opening or wrist extension in the stroke population.

PNF is a facilitatory technique which is used to stimulate weakened muscles; weakened muscles will work more efficiently with the enhancement of antagonistic muscle compared to when they operate individually.

PNF patterns are proved to be effective in strengthening the muscles of lower limbs.⁵ PNF techniques such as- rhythmic initiation, repeated stretch, combination of isotonic and percussions are proved to be beneficial for facial palsy patients.⁶ PNF is determined to be helpful for motor recovery on patients with chronic stroke and is useful in restoring functions of stroke survivors.⁷ PNF influences the functional ambulation in stroke individuals.⁸ PNF can decrease the tone abnormality, and muscle stiffness in the lower extremity of chronic stroke patients.⁹ Aquatic PNF patterns is known to improve balance and ADL of stroke patients.¹⁰

Hence, PNF is proved to be useful for facilitating the weakened muscles as well as to gain control for the muscle function. PNF is even proved to be effective for stroke patients when given for facial palsy and lower limbs. Since there is no evidence found to evaluate the effectiveness of proprioceptive neuromuscular facilitation on hand opening in stroke individuals. Therefore, this study was undertaken to evidence the effectiveness of proprioceptive neuromuscular facilitation on hand opening in stroke individuals.

Case Report: There were three participants with hemiparetic stroke aged between 45 and 65 years referred to the physical therapy department. All participants had complained regarding carrying out their daily activities with their affected hands for seven days to 2 months. These participants were screened using inclusion criteria, and the screened participants were given a consent form. Inclusion criteria were having the first episode

of stroke, duration of fewer than three months since onset, age 40-65 years, no significant cognitive deficit (a score >25 points in mini-mental status examination). The participants were not having any deformities of hand, any surgeries of hand affecting hand functions, or diabetic neuropathy.

Case 1: A 63 years old male, who was a retired shopkeeper by profession with a BMI of 22.65. He was suffering from systemic hypertension for around 15 years; he used to have frequent episodes of giddiness and headaches due to hypertension. He experienced weakness of right side of body two months back and was admitted. The participant was great difficulty in doing daily activities as the dominant side of the body was affected by stroke. The physiotherapy examination revealed high blood pressure of 140/90 mm Hg at time of assessment, the higher mental evaluation was normal 30/30 as assessed by mini-mental examination, and reflexes on the right side showed a normal response that is 2+.

The outcome measures used to evaluate the hand opening functionally was BAB and ARAT. The baseline values for BAB was 12, and for ARAT was 2. For assessing the hand opening quantitatively, wrist extension range was taken, which showed 30 degrees at baseline. To evaluate the disability of the participant, the modified Rankin scale was taken, which showed four at baseline. To check the recovery based on Brunnstrom stages, Brunnstrom recovery stages were used, which showed stage 4 when assessing.

Case 2: This was a 57 years old female participant who was a housewife with a BMI of 26.85. She suddenly felt a weakness towards the right side of the body. The participant had difficulty when performing the daily task for seven days as the dominant hand was affected by stroke. When examined physically, the blood pressure came as 138/86 mm Hg, MMSE as normal that is 26/30 and reflexes as exaggerated that is 3+.

The outcome measures at baseline for BAB showed 20, for ARAT showed 16, wrist ROM was 15 degrees, modified Rankin scale was 4, and the stage for Brunnstrom recovery was noted to be 3.

Case 3: This was a 45 years old male participant who was a construction worker with a BMI of 23.82. The participant started experiencing severe headache, and difficulty of speech suddenly one day while working and lost his consciousness and fell. Then he started

experiencing weakness of the left side of the body for 11 days. The participant was right side dominant, and the weakness was on the left side, so the deterioration of hand function was less. The physical examination of the patient depicted the blood pressure of 124/84 mm Hg, the mental examination as normal(30/30) and the reflexes also as normal (2+).

The outcome measures evaluated at the baseline showed the following results, for BAB was 31, for ARAT was 13, active wrist extension was 20 degrees, modified Rankin scale was 3, and the Brunnstrom recovery stage was 4.

Table 1: Characteristics of three patients with hemiparetic stroke having difficulty in hand opening

Characteristics	Case 1	Case 2	Case 3
Age	63	57	45
Gender	Male	Female	Male
Side affected	Right	Right	Left
Hand dominance	Right	Right	Right
SBP	140	138	124
DBP	90	86	84
Duration	2 months	7 days	11 days
MMSE	30/30	26/30	30/30
Reflexes	2+	3+	2+
BMI	22.65	26.85	23.82

Table 2: Descriptions of baseline and post intervention variables

Variables	Case 1		Case 2		Case 3	
	Pre	Post	Pre	post	pre	Post
BAB	12	18	20	24	31	34
ARAT	2	10	16	22	13	19
MRS	4	3	4	4	3	3
Wrist Extention	30 degree	45 degree	15 degree	35 degree	20 degree	33 degree
Brunnstorm Stage	4	5	3	4	4	4

Treatment: The same treatment was given to these three participants. The participants were given conventional physiotherapy as well as two patterns of PNF for the upper limb. The patterns used were facilitating for hand opening that is: flexion-abduction-external rotation and extension-abduction-internal rotation patterns. These patterns were chosen because the end position of these patterns promotes the wrist extension. The techniques used were a combination of isotonic, dynamic reversals, and stabilizing reversals. The participants were made to be supine lying position and fist they were shown the PNF patterns used by passive movement, then they were taught to practice these patterns. For combination of isotonic, they were told to concentric, eccentric and stabilizing contraction of agonist muscle group without relaxation. For dynamic reversals, they were told to do the contraction of agonist and antagonist without pause. For stabilizing reversals, they were told to do alternating isotonic contraction

opposed by therapist’s resistance. Each one of this technique was given for 10 minutes, 5 minutes using flexion-abduction-external rotation pattern and 5 minutes using extension-abduction-internal rotation pattern. The total duration of the PNF treatment was 30 minutes. The conventional treatment given was- passive movement of all joints of upper limb 10 repetitions for each joint, stretching of supinators and wrist flexors 3 repetitions for each, weight bearing on the affected extremity in sitting position for 10 minutes, giving reach outs to the affected extremity in sitting or standing position for 10 minutes, and grip strengthening exercises for 10 minutes. The conventional treatment was given for 45 minutes. The participants were being treated for 4 weeks, for 5 days in a week. Another treatment was given to the participant according to the need of the patient, as strengthening exercises for lower limb, standing, weight shifting, sit to stand, gait training, co-ordination activities.



Figure 1. Treatment given PNF flexion-abduction-external rotation pattern with dynamic reversals



Figure 2. Treatment is given PNF extension-abduction-internal rotation pattern with dynamic reversals

Outcome Measures: The post values were taken after the treatment of affected upper extremity after providing the four weeks of conventional and PNF

therapy. The outcome measures used were BAB, ARAT, MRS, active range of wrist extension, Brunnstrom recovery stages. The post values of all the outcome measures except MRS showed a clinically significant difference. The difference in the pre and post values of BAB in case 1 is 6, case 2 is 4, and in case 3 it is 3. The difference between ARAT scores pre and post was noted to be 8 in case 1, 6 in case 2 and case 3. Wrist extension showed a difference of 15 in case 1, 20 in case 2 and 13 in case 3. Brunnstrom recovery stages also showed an improved response from stage 4 to 5 in case 1. From stage 3 to 4 in case 2, but it didn't show the difference in case 3 where it remained in stage 4 after the treatment. MRS didn't much significant difference in cases 2 and 3, but in case 1 it progressed from 4 to 3.

Discussion

This study was conducted to evaluate the added effects of proprioceptive neuromuscular facilitation on hand opening in hemiparetic stroke individuals to conventional treatment. The conventional treatment for hand opening is passive exercises, stretching exercises, weight-bearing exercises, reach outs, and grip strengthening exercises. These exercises may actively help in gripping activities of hand, but hand opening remains passive in these exercises. So even though the hand gripping will be improved, the hand will remain non-functional as the hand opening is compromised. For the daily activities and the smooth activities of hand, the opening of hand is very imperative. Thus, to evaluate this hand opening with the help of PNF, we selected three patients with hemiparetic stroke. The baseline data of the three patients clearly stated that there was a deterioration in the hand function due to hemiparesis. At the end of the treatment of four weeks, the participants witnessed the improvement in the hand function as assessed by the outcome measures

Our results are in support of Honghun Kim et al. (2011), who suggested that PNF enhances muscle activity. The study proved to be effective in patients with stroke when treated with PNF in improving the functional reach test and muscle activity of lower limb muscles.¹¹ The possible mechanism of PNF affecting the movement of the hand and improving the motor control can be as suggested by K Shimura et al. in 2002, PNF position enhances the range of motion, reduces the time of EMG-RT, and increases the efficiency of muscle contraction.¹²

Conclusion

The objective of this study was to evaluate the efficacy and feasibility of PNF techniques so that this protocol can be used for the rehabilitation of hand opening in stroke individuals. The results show that PNF and conventional therapy is given to all three patients have shown improvement in all the outcome measures compared to the baseline. Also clinically, the patient's hand function is seen to be enhanced after the four weeks of treatment.

Scope of Future Work:

- A randomized controlled trial can be conducted with a larger sample size so that the result can be generalized.
- Long-follow ups can be taken to determine the long term effect of the treatment
- A similar type of study can be done with the combination of other treatment techniques
- Surveys can be done to evaluate the quality of life with the PNF treatment

Conflict of Interest: The authors declare that there is no conflict of interest.

Source of Funding: The project is self-funded.

Ethical Clearance: The study has been approved by the institutional ethics committee.

References

1. Sacco R, Kasner S, Broderick J, Caplan L, Culebras A, Elkind M, et al. An Updated Definition of Stroke for 21st Century A Statement for Health Care Professionals from the American Heart Association/American Stroke association. *Stroke*. 2013;44:2064-89.
2. Pandian J, Sudhan P. Stroke Epidemiology and Stroke Care Services in India. *JOS*. 2013;15(3):128
3. Kumar KV, Joshua AM, Kedambadi R, Mithra PP. Eclectic/mixed model method for upper extremity functional recovery in stroke rehabilitation: A pilot study. *J Nat Sc Biol Med* 2017;8:75-81.
4. Fischer H, Stubblefield K, Kine T, Luo X, Kenyon R, Kamoer D. Hand Rehabilitation Following Stroke: A Pilot Study of Assisted Finger Extension Training in a Virtual Environment. *Topics in Stroke Rehabilitation*. 2007;14(1):1-12.
5. Rhyu H, Kim S, Park H. The effects of band exercise using proprioceptive neuromuscular facilitation on muscular strength in lower extremity. *JER*. 2015;11(1):36-40.
6. D.Sardaru, L. Pendefunda. Neuro-proprioceptive facilitation in the re-education of the functional problems in facial paralysis. A practical approach. *Internal medicine-pediatrics*.2013;(1)117
7. Ribeiro T, Henrique W S S, Alencar Caldas V, Araújo Silva D, Azevedo Costa Cavalcanti F, Lindquist R. Poster 69 Effects of a Training Program Based on the Proprioceptive Neuromuscular Facilitation Method on Post-Stroke Motor Recovery. *Archives of Physical Medicine and Rehabilitation*. 2013;94(10):e35.
8. C0 A, BOA A, OE J, Effect of Proprioceptive Neuromuscular Facilitation technique on functional ambulation of stroke survivors. *Journal of the Nigeria society of physiotherapy*.2011:18-19.
9. Wang J, Lee S, Moon S. The immediate effect of PNF pattern on muscle tone and muscle stiffness in chronic stroke patients. *Journal of Physical Therapy Science*. 2016;28(3):967-970.
10. Kim E, Lee D, Kim Y. Effects of aquatic PNF lower extremity patterns on balance and ADL of stroke patients. *Journal of Physical Therapy Science*.2015;27(1).213-215
11. Kim Y, Kim E, Gong W. The Effects of Trunk Stability Exercise Using PNF on the Functional Reach Test and Muscle Activities of Stroke Patients. *Journal of Physical Therapy Science*. 2011;23(5):699-702.
12. Shimura K, Kasai T. Effects of proprioceptive neuromuscular facilitation on the initiation of voluntary movement and motor evoked potentials in upper limb muscles. *Human Movement Science*. 2002;21(1):101-13.

Knowledge and Perception Regarding Menopause among Married Women

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Abstract

Introduction: Menopause is one of the mile stones in women's life that all women at midlife are expected to experience. **Objectives:** To assess the knowledge and perception of married women regarding menopause, and to find out the association between the knowledge and perception of married women regarding menopause with selected demographic variables.

Methodology: A cross sectional descriptive study was conducted among 140 married women between the age group of 45 – 55 years. The study was conducted in two villages which were selected by simple random sampling from Udupi Taluk, Karnataka. Data were collected by using structured knowledge questionnaire and perception scale towards menopause. Data were analysed by using inferential and descriptive statistics.

Results: Out of 140 married women the data shows that majority of women belongs to the age group of 45-50 years and their mean age was 48.26 years and SD 2.359. Most 106(76.4%) of the women had a history of regular menstrual cycle and 138(98.6%) had no history of any gynaecological illness during the data collection. Majority of the married women 120(85.7%) had average knowledge on menopause. Among 140 married women most 111(79.3%) of them had good perception. There is significant association between knowledge score and education ($\chi^2 = 25.680$, $p = 0.008$) and income ($\chi^2 = 11.071$, $p = 0.027$). There is weak positive correlation between the knowledge and perception was observed ($r = 0.212$, $p = 0.010$).

Conclusion: Awareness regarding menopause is very essential and should not be neglected. Assessing the knowledge and perception regarding menopause will help them to cope up with the changes that take place during this stage.

Keywords: Menopause, knowledge, perception, married women.

Introduction

The menopause refers to the time in every woman's life when menstruation stop and ovaries loss their reproductive function. It is essential to ensure that a

woman understands that the menopause represent a change of life and not an end of life, and that, unless women allows it to do so, it will not result in women suddenly becoming aged and unattractive. Menopause is one of the essential stage in women's life. It is characterized by major physical, psychological and social changes and is currently considered as important public health problem associated with a worse health related to quality of life and it is also very important that all family members should understand and support her during menopausal stage.

Menopause may result many alterations in women's physiological functioning and cause anxiety. It is

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important that women during menopausal period should have adequate knowledge and positive perception regarding menopausal transition that may help them to cope up with the changes in their life and improves the quality of life^[1].

Menopause is not the end of life, but during the menopausal stage women may experience various symptoms. These symptoms may affect their physical as well as psychological activities. Post-menopausal women need better understanding and support from family members especially husband so that they can easily cope up with the postmenopausal life. Study suggested that public health system should continue to educate, counsel and aware about menopause among premenopausal women and their spouses so that they can spend their future life in a better way^[2].

There is a need to identify the problem and create health care facilities for women. With decreased level of oestrogen, the transition to menopause is quite a challenging phase for life of every women. Some women experiencing hot flushes, tiredness and some are experiencing it as losing their energy. Menopausal period of women's life is very crucial where she needs most emotional support and expert guidance. The women's physiological, biochemical and psychological environment altered due to menopause. Thus knowledge and perception of its symptomatology is important to adjust to the normal occurrence. Family members also should aware the changes occur in the women during menopausal stage. Hence the researcher felt to conduct a descriptive study to assess the level of knowledge and perception towards menopause among married women.

Materials and Method

The descriptive survey was carried out in the selected villages of Udupi Taluk among married women. The sample size was calculated as 140 based on the findings of previous study. The Villages were selected by simple random sampling method; subjects were selected by convenient sampling method. Data were collected from the married women aged between 45 – 55 years who did not attained menopause and living with their spouses. The data were collected by administering the demographic proforma, structured knowledge questionnaire and perception scale on menopause to the participants. The tools were validated by 9 experts and the reliability of the tools were, for knowledge questionnaire was 0.71, perception scale was 0.88.

Ethical consideration: Ethical Clearance and administrative permission were obtained before data collection. The data were collected from married women after obtained the consent from the participants who met the inclusion criteria by using structured questionnaire.

Statistical Analysis

The data were analysed by using Statistical Package for the Social Sciences (SPSS) version 16.0. The statistics used for data analysis were, frequency and percentage for distribution of demographic variables, knowledge on menopause, perception towards menopause. The Chi-Square test was performed to find the association between knowledge and perception on menopause with selected demographic variables. Spearman correlation co-efficient was used to analyse the relationship between knowledge and perception regarding menopause. A p-value of < 0.05 was considered to establish the statistical significance.

Results

Result shows that out of 140 participants majority of the married women were belongs to the age group of 45-50 years 118(84.3%), 113(80.7%) were from nuclear family, 130(92.9%) were belongs to Hindu religion, 80(57.1%) of them had their education upto higher secondary and 96(68.6%) of them were house wives. Majority 138(98.6%) of married women had more than 15 years of married life, 49(35%) of them had information from more than one source and 84(60%) of them were having two children. 77(55%) of married women had their monthly income between Rs. 5001 -10000, 107(76.4%) of them had their regular menstrual cycle, 12(8.6%) of them had history of diabetes and 15(10.7%) of them had history of hypertension and 138(98.6%) had no history of any gynec illness at the time of data collection [Table 1,2 & 3].

With regard to knowledge majority of the married women i.e 120(85.7%) had average knowledge, 11(7.9%) of them had poor knowledge and only 9(6%) of them had good knowledge [Fig. 1]. Result further shows that women were know the meaning of menopause [mean 6.30, SD 1.79], they had least knowledge on signs and symptoms present during menopause [mean 3.96, SD 1.351] and women had average knowledge on management [mean 6.34, SD 1.86] and overall maximum knowledge score was 27 and minimum score was 7 and mean and standard deviation was 15.98 and 3.364 respectively [Table 4]. With regard to the

perception on menopause, 111(79.3%) of the married women had good perception, 29(20.7%) of them had average perception[Table 5]. Result also shows that there is significant association between knowledge score and education ($\chi^2 =25.680, p =0.008$) and monthly income of the family($\chi^2 =11.071, p =0.027$). The finding inferred that women those who had good education and socioeconomic background have good knowledge on menopause [Table 6]. Further data shows that there is weak positive correlation between the knowledge and perception on menopause of married women ($r = 0.212, p = 0.010$).

Table 1: Frequency and percentage distribution of sample characteristics N=140

Sample Characteristics	Frequency (f)	Percentage (%)
Age in Years		
45-50	118	84.3
51-55	22	15.7
Type of Family		
Nuclear family	113	80.7
Joint family	27	19.3
Religion		
Hindu	130	92.9
Christian	4	2.9
Muslim	6	4.3
Education		
Primary (1-4)	1	.7
Higher primary (5-7)	16	11.4
High school	80	57.1
PUC	30	21.4
Graduate and above	13	9.3
Occupation		
House wife	96	68.6
Cooli	17	12.1
Beedi roller	21	15
other	6	4.3

Table 2: Frequency and percentage distribution of sample characteristics (Continued): N=140

Sample Characteristics	Frequency (f)	Percentage (%)
Married life in years		
11-15	2	1.4
Above 15	138	98.6
You had any information regarding menopause?		
Yes	73	52.1
No	67	47.9

Sample Characteristics	Frequency (f)	Percentage (%)
If yes mention the source of information		
News paper	11	7.9
TV	9	6.4
Any other	4	2.9
Not received	67	47.9
More than one	49	35
Number of children		
Nil	5	3.6
One	8	5.7
Two	84	60
Three	41	29.3
Four	2	1.4
One	107	33.1
Two	110	34.1
Three and more	95	29.2

Table 3: Frequency and percentage distribution of sample characteristics (Continued) N=140

Sample characteristics	Frequency (f)	Percentage (%)
Monthly income of the family (in Rupees)		
5001-10000	77	55
10001-15000	47	33.6
>15000	16	11.4
Menstrual cycles		
Regular	107	76.4
irregular	33	23.6
History of illness		
Diabetes	12	8.6
Asthma	8	5.7
Hypertension	15	10.7
Hypothyroidism	3	2.1
hyperthyroidism	1	0.7
Nil	101	72.1
History of gynec illness		
Ovarian cyst	2	1.4
Nil	138	98.6



Fig. 1: Distribution of knowledge score on menopause

Table 4: Area wise frequency, percentage, mean, standard deviation of knowledge score of married women: N=140

Area	Total score	Maximum	Minimum	Mean	SD
Introduction and meaning	12	12	2	6.30	1.798
Signs and symptoms	8	8	1	3.96	1.351
Managements	10	10	1	6.34	1.865
Overall total knowledge score	30	7	27	15.98	3.364

Table 5: Frequency and percentage of perception score of married women regarding menopause N=140

Perception score	f	%
Good	111	79.3
Average	29	20.7

Table 6: Association between the level of knowledge and selected demographic variables of married women: N=140

Variables	Knowledge Score			χ^2	P
	Good	Average	Poor		
Age					
45-50	7	103	8	1.614	.535
51-55	3	17	2		
Education					
Primary (1-4)	0	1	0		
Higher primary (5-7)	0	12	4		
High school	4	71	5	25.680	.008*
PUC	1	29	0		
Graduate and above	4	7	2		
Occupation					
House wife	7	81	8		
Cooli	0	16	1	3.028	.852
Beedi roller	2	18	1		
other	0	5	1		
Monthly income of the family (in Rupees)					
5001-10000	3	69	5		
10001-15000	2	40	5	11.071	0.027*
>15000	4	11	1		

*p<0.05 level of significance

Discussion

In the present study majority 118(84.3%) of the married women were belongs to the age group of 45-50 years, 80(57.1%) of them had their education upto higher secondary, and 49(35%) of them had received information from more than one source. Similar findings obtained by Shabana Sultan et al & Neha Mehta et al found that majority 122(81%) of the women were 46-55 years old, 70% had completed their education and

93(62%) of the women received information regarding menopause from friends and relatives [3, 4].

In the present study majority 120(85.7%) of the married women had average knowledge, 11(7.9%) of them had poor knowledge and only 9(6%) of them had good knowledge. Similar findings obtained by a study conducted by Ensieh Noroozirevealed that 32(8%) of the participants had poor knowledge, 272(68%) had moderate knowledge and 154(38.5%) had good

knowledge^[5]. The present study also contradicted by a study done by Prabathi Nepal revealed that majority of the women 90(63.4%) of the respondents had poor level of knowledge, more than one quarter 48(33.8%) had fair and only 4(2.8%) had good level of knowledge on perimenopausal women ^[6]. Similar findings of the study also found by a study done by Marie E Pintoshown that majority of the women 78% in rural area had average knowledge and majority of the women in urban area 62% had satisfactory knowledge ^[1]. The present study shows that the mean + SD score on knowledge was 15.98 + 3.36 and similar findings identified by Kwak et al the mean score on knowledge was 17.93 ± 2.39^[13].

The present study identified that 111(79.3%) of the married women had good perception, 29(20.7%) had average perception on menopause. The study was supported by a cross sectional observational study was conducted among 100 postmenopausal women who visited the outpatient department of Obstetrics and Gynecology, Government Medical College Idukki revealed that 77(77%) had positive perceptions ^[2].

The present study found that majority of the women 96(68.6%) perceived menopause as a normal event in life just as pregnancy and child birth. Similar findings obtained by a study conducted by Sabir GN revealed that 427 (85.4%) of women perceived menopause as a natural condition^[7]. It also supported by a study done by Nisar Nusrat identified that 680 (78.79%) women considered menopause as a natural process^[8].

The present study revealed that most 63(45%) of the women perceived that they should not discuss their experience of menopause to their family members and friends. This was supported by a study conducted by Ibraheem O.M, Oyewole O.E and Olaseha I.O (2015) revealed that women should not discuss about their menopausal experiences with others i.e by 146(60.8%) ^[9]. Women in eastern societies view menopause as a natural process and hold a positive attitude ^[10]. Chen et al^[11] reported that 95.7% midlife Chinese women in Taiwan perceive menopause a natural phenomenon and most of these women could deal with menopause in a positive way. Another population based cross sectional study from south India showed similar results that 57% of women perceive menopause as convenient ^[12]. Majority of women were aware about menopause and most of them were bothered by menopausal symptoms, but very few consulted doctor^[14].

Limitations of the Study: In present study sample size restricts generalization of the study findings and the study finding was limited to married women who did not attained the menopause.

Conclusion

The study concluded that the married women had average knowledge and perception on menopause. So the researcher felt that there is a need to conduct awareness program on menopausal symptoms management. It will help them to cope up with the changes and improve the quality of life of married women during the menopausal period.

Ethical Clearance: From Institutional Ethical Committee (IEC) of Kasturba Hospital, Manipal.

Source of Funding: Self.

Conflict of Interest: Nil.

Reference

1. Marie E Pinto. Knowledge and attitude regarding menopause among urban married women in Mangalore. Journal of South Asian Federation of Obstetrics and Gynecology; 2010; 2(3): 233-235.
2. Leena A. Joseph. Prevalence of menopausal symptoms and perceptions about menopause among postmenopausal women attending Gynecology OPD Kerala. International journal of Reproduction, Contraception, Obstetrics and Gynecology; 2017; 6(2), 413-416.
3. Shabana Sultan, A.S. Knowledge, attitude and practices about menopause and menopausal symptoms among middle life school teachers in Madhya Pradesh India. International journal of Reproduction, Contraception, Obstetrics and Gynecology; 2017; 12(6), 5225-5229.
4. Neha Mehta, DG. Effectiveness of structured teaching program on knowledge regarding menopausal problems and their remedial measures among middle aged women Jaipur, India. International Journal of Advanced Research and Development; 2017. 2(6), 169-174.
5. Ensieh Noroozi, NK. Knowledge and attitude towards menopause phenomenon among women aged 40-50 years in Iran. Journal of Education and Health Promotion. 2013. 2(25), 1-5.

6. Parbati Nepal Paudyal. MN Knowledge on perimenopausal symptom among women attending Lumini Medical College Teaching Hospital Nepal. *Journal of Lumbini Medical College (JLMC)*2014;2(2),41-44.
7. Sabir GN. Perceptions and experiences regarding menopause among menopausal women attending teaching Hospitals in Erbil city Iraq. *Global Journal of Health Sciences*;2012;4(3)170-178.
8. Nisar Nusrat, Z. N. knowledge, attitude and experience of menopause in Pakistan. *Journal of Ayub Medical College Abbottabad*; 2008;20(1), 56-59.
9. Ibraheem OM, OO. Experiences and Perceptions of Menopause among women in Ibadan South East Local Government area, Nigeria. 2014;18(2),81-94.
10. Adler SR, Fosket JR, Kagawa-singer M, Mc Graw SA, Wong kin-Evaon, Gold E, et al. Conceptualizing menopause and midlife: Chinese American and Chinese women in the US. *Maturitas. Journal of Ayub Medical College Abbottabad* 2000;35:11–23.
11. Chen YL, Voda AM, Mansfield PK. Chinese midlife women's perceptions and attitude about menopause. *Menopause (New York)* 1998;5(1):28-34.
12. Aaron R, Muliyeet J. Abrehan S. Medico-social dimension of menopause: a cross national study from rural south India. *Nalt Med J India* 2002;15:14–7.
13. Kwak K E, Park H S, Kang N M. Menopause Knowledge, Attitude, Symptom and Management among Midlife Employed Women; *Journal of Menopausal Medicine* 2014;20:118-125.
14. Khokhar Shazia. Knowledge, Attitude and Experience of Menopause. *Pakistan Journal of Medical Research*; 2013 (April – June) 52(2): 42-46.

Prosthetic Status and Demand for Services in an Adult Rural Population in Relation to Dental Service Infrastructure in Mangalore Taluk, South India

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Abstract

Context: Oral health can be considered as an indicator of general health and quality of life. Planning dental services is therefore the collection of up to date information on the prevalence of oral health status in a given population.

Aims: This study was conducted to assess prosthetic status and demands for services among the rural population in Mangalore Taluk.

Method and Material: A cross sectional survey was carried out on 1312 participants aged 18 years and above. Sixteen gram panchayats were selected and a survey was conducted to determine the prosthetic status and prosthetic need.

Results: Complete denture prosthesis was predominantly high among the age groups above 61. Removable partial denture was predominantly high among the age groups 31-45. Fixed partial denture was high among age groups 46-60.

Conclusions: Irrespective of the age, gender and education the need for Multi unit prosthesis was found to be significantly high.

Keywords: Prosthetic status, prosthetic needs, treatment facilities.

Introduction

Mangalore is one among the five taluks/subdivisions of Dakshina Kannada District of Karnataka State. Mangalore has the highest population of 1048 persons per square kilometer among the taluks of Dakshina Kannada. It is a reputed centre for medical education and health care with five dental schools and a multitude of private dental clinics.¹

Studies reporting the dental prosthetic status and treatment needs of people give an indication of the poor prosthetic status and burden of unmet treatment needs.^{2,3}

Most of the studies done in India to estimate prosthodontic treatment needs are institution based in urban areas in the age groups of 35 years and above and on smaller sample size. Statistics shows a paucity in dental health infrastructure in the rural areas of Mangalore taluk.¹ Therefore this study was conducted to assess prosthetic status and demands for services in Mangalore Taluk.

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Subjects and Method:

A cross sectional survey was carried out to determine the prosthetic status and prosthetic need among the rural population of Mangalore taluk, on 1312 participants.

The sample size was determined based on the prevalence of prosthetic status (22.7%) as determined by the national health survey and fluoride mapping which was carried out in 2002-2003⁴.

The map of Mangalore taluk was divided into North and South zone. Eight gram panchayats each were randomly selected from both zones. Among sixteen gram panchayats selected a house-to-house survey was carried out till a target of 82 individuals were examined in each panchayat. The individuals were interviewed and examined.

Before beginning the data collection, permission was obtained from the Institutional Ethics Committee.

Inclusion criteria: (i) The individual should be a resident of the area (ii) All the population in the age range of 18 years and above.

Patients, who refused for the dental check-up and those with full complement of teeth, were excluded from the study.

A pretested proforma was used for data collection. It consisted of two parts—the 1st part recorded data on sociodemographic factors, while the 2nd part contained a section of the World Health Organization (WHO) Oral Health Assessment Form (1997)⁵ to record the prosthetic status and prosthetic need of the population.

Data collected were analyzed using SPSS version 17.0 and the Chi-squared test. $P < 0.05$ was considered as significant.

Results

This study comprised of 520(40%) males and 792(60%) females. The age and gender distribution as shown in Table 1 shows that among all the age groups females outnumbered males.

Table 2 and 3 revealed that prosthetic status in maxillary arch, complete denture was predominantly high among the age groups above 61 years (58.5%) which was highly expected due to tooth loss. Removable partial denture was predominantly high among the age groups 31-45 years (23.4%). Fixed partial denture was high among age groups 46-60 years (3.8%). Crown was predominantly high among the age groups 18-30 years (8.5%).

Mandibular arch revealed that complete denture

was high among age groups above 61 years (57.4%). Removable partial denture was high among age groups 31-45 years (22.6%). Fixed partial denture was high among age group 31-45 years (1.4%). Crown was high among age group 18-30 years (2.1%).

To quantify based on educational status graduates and post graduates were combined into one group as group A, while those with less qualification formed group B.

Prosthetic status and education in both the arches in Table 4 and 5 showed that, significantly higher number of participants in group B were prosthetic wearers. As the level of education increased the number of prosthesis also increased which infers that influence of education, knowledge and income may have led to an improved prosthetic status.

Distribution of study subjects according to prosthetic status and gender showed that 718(54.7%) in the maxillary arch and 779(59.4%) in the mandibular arch did not present with any prosthesis, 306 (23.3%) in the maxillary arch and 294 (22.4%) in the mandibular arch presented with complete denture prosthesis, in which males presented more than females. 209 (15.9%) in the maxillary arch and 294 (22.4%) in the mandibular arch presented with removable partial denture prosthesis in which females presented more than males. 34(2.6%) and 14(2.6%) presented with fixed prosthesis and crown respectively in the maxillary arch and 13(1.0%) and 14(1.1%) presented with fixed prosthesis and crown respectively in the mandibular arch in which males presented more than females.

Prosthetic need in both arches reveals that majority of the rural adult population required multi unit prosthesis (maxillary 35%, mandibular 46%) followed by full prosthesis (maxillary 26%, mandibular 25%).

Distribution of study subjects according to prosthetic need and age group: while the need for multi unit prosthesis was high among all age groups, the need was alarming among those in the 18-30(57%) and 31-45 year age group (54%). This is an indication of the failure of the health care system where people in productive age group have lost multiple teeth and also have not been able to replace them.

It was found that females had a higher requirement for multi unit prosthesis in both the arches, although the difference was not significant in both genders.

The education level of the population seemed to influence the prosthetic need. Among those with no education and lower levels of literacy the need for multi unit prosthesis was highest, this shows lack of awareness or poor attitude towards oral health resulting in loss of multiple teeth with no replacement.

Table 1: Distribution of study subjects according to age and gender

Age Group	Gender		
	Male	Female	Total
18-30	51(9.8%)	91(11.4%)	142(10.8%)
31-45	158(30.3%)	333(42%)	491(37.4%)
46-60	137(26.3%)	178(22.4%)	315(24%)
>61	174(33.6%)	190(24.2%)	364(27.8%)
Total	520(100%)	792(100%)	1312(100%)

Table 2: Distribution of study subjects according to Prosthetic status and age group (maxillary arch)

Prosthetic Status	Age Group			
	< 44	>45	Total	
Without Prosthesis	Count	421	297	718
	% within Prosthetic status	58.6%	41.4%	100.0%
	% within age group	66.5%	43.7%	54.7%
	% of Total	32.1%	22.6%	54.7%
With Prosthesis	Count	212	382	594
	% within Prosthetic status	35.7%	64.3%	100.0%
	% within age group	33.5%	56.3%	45.3%
	% of Total	16.2%	29.1%	45.3%
Total	Count	633	679	1312
	% within Prosthetic status	48.2%	51.8%	100.0%
	% within age group	100.0%	100.0%	100.0%
	% of Total	48.2%	51.8%	100.0%

$X^2=68.540$ $p<0.001$

Table 3: Distribution of study subjects according to Prosthetic status and age group (mandibular arch)

Prosthetic Status	Age Group			
	< 44	>45	Total	
Without Prosthesis	Count	452	327	779
	% within Prosthetic status	58.0%	42.0%	100.0%
	% within age group	71.4%	48.2%	59.4%
	% of Total	34.5%	24.9%	59.4%
With Prosthesis	Count	181	352	533
	% within Prosthetic status	34.0%	66.0%	100.0%
	% within age group	28.6%	51.8%	40.6%
	% of Total	13.8%	26.8%	40.6%
Total	Count	633	679	1312
	% within Prosthetic status	48.2%	51.8%	100.0%
	% within age group	100.0%	100.0%	100.0%
	% of Total	48.2%	51.8%	100.0%

$X^2=73.396$ $p<0.001$

Table 4: Distribution of study subjects according to Prosthetic status and education (maxillary arch)

Prosthetic Status		Education		
		Group A	Group B	Total
With Prosthesis	Count	624	94	718
	% within Prosthetic status	86.9%	13.1%	100.0%
	% within Education	58.5%	38.4%	54.7%
	% of Total	47.6%	7.2%	54.7%
Without Prosthesis	Count	443	151	594
	% within Prosthetic status	74.6%	25.4%	100.0%
	% within Education	41.5%	61.6%	45.3%
	% of Total	33.8%	11.5%	45.3%
Total	Count	1067	245	1312
	% within Prosthetic status	81.3%	18.7%	100.0%
	% within Education	100.0%	100.0%	100.0%
	% of Total	81.3%	18.7%	100.0%

$\chi^2=32.536$ $p<0.001$

Table 5: Distribution of study subjects according to Prosthetic status and education (mandibular arch)

Prosthetic status		Education		
		Group A	Group B	Total
With prosthesis	Count	672	107	779
	% within Prosthetic status	86.3%	13.7%	100.0%
	% within Education	63.0%	43.7%	59.4%
	% of Total	51.2%	8.2%	59.4%
Without prosthesis	Count	395	138	533
	% within Prosthetic status	74.1%	25.9%	100.0%
	% within Education	37.0%	56.3%	40.6%
	% of Total	30.1%	10.5%	40.6%
Total	Count	1067	245	1312
	% within Prosthetic status	81.3%	18.7%	100.0%
	% within Education	100.0%	100.0%	100.0%
	% of Total	81.3%	18.7%	100.0%

$\chi^2=30.791$ $p<0.001$

Discussion

Data on prosthetic status and need in rural population aged 18 years and above is very scanty. Thereby an attempt was made. In rural areas the standard of living and economic status is low and no importance was given to women's education. Dental treatment is therefore obviously neglected till tooth loss is the final result.⁶ Dentists too are responsible for this state of affairs as for the same population ratio, there are 10 times more dentists in cities than in villages in India.¹

According to the data obtained by Shenoy R (2015)¹

it was found that dental services were not available at any of the 21 PHCs (five urban and 16 rural) in Mangalore taluk. Dental surgeons were posted at both the CHCs and they provided basic dental services such as extractions, minor restorative care and oral prophylaxis to those seeking dental care. Two dentists were rendering services at the District Government Hospital in Mangalore City. They too were providing only basic dental care to patients due to lack of resources.¹

Among private dental clinics 189, were registered with the office of the DHO and the IDA of which 91% (172/189) were located in urban and 9% (17/189) in

rural areas of the taluk. This study found 91% of dental clinics clustered in urban areas. It clearly shows that urban bias exists, with 75% dentists practising in urban areas. Although dental clinics provide a major share of the dental care delivered in India, their inaccessibility forces many rural patients to forgo or delay essential dental treatment. Therefore, although oral health care is accessible in urban areas, it is difficult to obtain in rural areas.¹

Preventive dental care is almost non-existent in rural India⁷. In the present study, when the prosthetic status and age group was evaluated it was found that complete denture was predominantly high among the age groups above 61 in the maxillary (58.5%) and mandibular arches (57.4%). The present study reveals that prosthetic status increased with age, similar results were obtained by Florian, (2003)⁸ showing 23% in 55-64 age group and 69% in 75-79 age group.

In the present study the removable partial denture was predominantly high among the age groups 31-45 in both arches. The prevalence of partial denture decreased with increase in age in the mandibular arch and increased with increase in age in the maxillary arch. According to Shah, (2004)⁹ prevalence of partial denture decreased with age in both arches.

Fixed partial denture was high among age groups 46-60 (3.8%) in the maxillary arch and among 31-45 (1.4%) in the mandibular arch, whereas results obtained by Mojon, (1995)¹⁰ showed 14.4(28.8%) and Prasad, (2001)¹¹ showed (0.89%) of prevalence. Crown was predominantly high among the age groups 18-30 in both arches.

When prosthetic status and gender was evaluated in the maxillary arch, complete denture was predominantly high in both males (26.6%) and females (21.0%) followed by removable partial denture among males (15.1%) and females (16.5%). Similar results were obtained by Galon *et al.*, (1993).¹² In the present study female prosthetic wearers were found to be less than males, the probable reason was that female members usually depend on male members to take them for treatment, which is in agreement with a study by Shah *et al.*, (2012).³

When prosthetic status and education was evaluated in the maxillary arch, majority of the subjects with higher educational level wore fixed prosthesis. Similar results obtained by Florian *et al.*, (2003).⁸ Surprisingly removable partial denture was predominantly high

among graduates and post graduates. The reason was that, they did not want their tooth to be cut in order to fix fixed partial denture.

When Prosthetic Need was evaluated, it was found that among all age groups multi unit prosthesis was needed predominantly in both arches. Study by Prateek *et al.*, (2001)¹³ showed need for removable partial denture among 35-44 year olds for both arches.

In the present study the need for full prosthesis was found to increase as the age increased. The need for Full prosthesis was slightly more in males than females as stated by, Goel *et al.*, (2006)¹⁴ and Shah *et al.*, (2012)³ This may be due to tobacco related habits among males which results in extraction of teeth.

Need for Multi unit prosthesis in mandibular arch was seen most often in subjects of 18-30 years which was in accordance with the study by Prateek *et al.*, (2001)¹³ (18.8%), but in maxillary arch it is seen among subjects of 46-60 years which was contradicting with the results of Prateek *et al.*, (2001)¹³, wherein subjects 25-34 years (12.1%) needed prosthesis.

Need for Multi unit prosthesis was high among females in both the arches whereas according to Shah *et al.*, (2012)³ the need was high among both the genders and according to Prateek *et al.*, (2001)¹³ need was higher among males in maxillary arch and higher among females in mandibular arch. Full and Multi unit prosthesis were needed among all the education levels.

In the present study, the need for multiunit prosthesis was more than the need for single-unit prostheses, but in contrast to this a study by Srivastav A *et al.*, (2011)¹⁵ showed that the need for single-unit prostheses (35%) was more than the need for multi-unit prostheses. Study has evaluated that in comparison with the dental prosthesis used, 45.2% in maxillary and 40.6% in mandibular arch, the need for prosthesis was high, and it was 70.4% in maxillary and 79.2% in mandibular arch. This may be because of low education levels, poor awareness, unavailability of services in rural areas and financial constraints.

Therefore, to improve the prosthetic status and reduce need, it is important to educate and motivate the patients regarding oral health care and provide free dental treatment camps. This is in agreement with Pallegedara and Ekanayake, (2005)¹⁶ who reported that the prevalence of wearing of dentures was low despite

the fact that there was a high prevalence of missing teeth. Lack of perceived need for dentures seemed to be the main reason for this finding.

Conclusion

A large population was found to have complete denture among the study population. Irrespective of the age, gender and education the need for Multi unit prosthesis was found to be significantly high.

Conflict of Interest: Nil

Source of Funding: Self

Ethical Clearance: Taken from University ethics committee.

Reference

- Shenoy R, Panchmal G. An overview of the distribution of dental care facilities in Mangalore taluk, India. *Journal of Contemporary Medicine* 2015; 5:163-66.
- Syed AP, Fuad AS. Dental prosthetic status and treatment needs of adult population in Jizan Saudi Arabia: A survey report. *Eur J Dent* 2016;4:459-463
- Shah VR, Shah DN. Prosthetic status and need among the patients attending various institutes of Ahmedabad and Gandhi Nagar district. *journal of Indian prosthodontic society* 2012; 12:166-167
- National oral health survey and fluoride mapping. New Delhi: Dental Council of India; 2002-03.
- WHO oral health country/area profile .GENEVA World Health Organisation. Available at URL : <http://www.whocollab.od.mah.se/index.html>.
- Parlani S, Tripathi, Singh. Increasing the prosthodontic awareness of an aging Indian rural population. *Indian Journal of Dental Research* 2011; 22:367-70.
- Shah N. Geriatric oral health issues in India. *Int Dent J.* 2001; 51:212-8.
- Florian M, Mundt T et al. Prosthodontic status among old adults in Pomerania, related to income, education level, and general health. *Int J Prosthodont* 2003; 16: 313-18.
- ShahN, Prakash, Sunderam KR. Edentulous, denture wear and denture needs of Indian elderly-a community based study. *J of oral rehabil* 2004; 31:467-76.
- Mojon P, Rentsch A, Budtz-Jorgensen E. Relationship between prosthodontic status, caries, and periodontal disease in a geriatric population. *Int J Prosthodont* 1995; 8: 564-71.
- Prasad KVV, Thanveer K, Javali SB. Denture status and needs of prosthetic treatment in the elderly population of Dharwad district of Karnataka state. *J Ind Dent Asso* 2001: 72; 204-206.
- Galan D, Odlum O. Oral health status of a group of elderly Canadian Inuit (Eskimo). *Community Dent Oral Epidemiol* 1993; 21: 53-56.
- Prateek S, Kashyap B, Goel P, Sahay R. Edentulousness and prosthetic needs of a rural population in southern India. *Journal of Indian Prosthodontic Society* 2001; 1: 20-25.
- Goel P, Singh K, Kaur A, Verma M. Oral health care for elderly: Identifying the needs and feasible strategies for service provision. *Indian J Dent Res.* 2006; 17:11-21.
- Srivastav A, Bhambal A, Reddy V, Jain M. Dental prosthetic status and needs of the residents of geriatric home in Madhya Pradesh, India. *JIOH* 2011; 3: 9-13.
- Pallegedara C, Ekanayake. Tooth loss, the wearing of dentures and associated factors in Sri Lankan older individuals. *Gerodontology* 2005; 22:193-99.

Evaluation of Intrusive Forces Created by ‘V’ Bend, Intrusion Arches at Various Deflections: An Invitro Study

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Abstract

Aim: To evaluate of intrusive forces created by ‘v’ bend, intrusion arches at various deflections- an invitro study.

Objective: The present study is to consider the importance of alloy used as intrusion arches.

Material and Method: We used stainless steel wires, timolium wires, CNA Beta 3. Wires (Libral, USA), blue elgiloy all with rectangular section of dimension 0.017 x 0.025 inch, 15 numbers each. Arch forms are standardized with the help of arch form selector guide. Three distances from vestibule to bracket slot in upper anteriors were marked. Trials were conducted at the CIPET (Central Institute Of Plastic Engineering and Technology, Chennai) and a dynamometer (Autograph, U.K) with 1kgf load cell at 0.01kgf resolution and speed of 10mm/min⁷. The load magnitude at various displacements (5, 10, 15 mm) were recorded.

Statistical Method: The significance level of 5% was taken. ANOVA was used for assessing the force of all the alloys and Tukey test was used for multiple comparisons.

Results: The forces recorded at 5, 10, and 15 mm were all significant between the four alloys when compared except for CNA and timolium between 5 mm and 10 mm and for blue elgiloy between 10 mm and 15 mm were not statistically significant.

Conclusion: The load increments tends to decrease from the first to last increment, and the differences is being more significant from the first increment to the second increment for all the alloys, and more significant in stainless steel and the blue elgiloy. CNA produced the least force.

Keywords: *Intrusion, v-bend, load deflection rate.*

Introduction

Deep bite correction depends on the diagnosis and treatment planning. Orthodontically it can be done either by intrusion of maxillary/mandibular incisors, extrusion of posterior teeth or by a combination of intrusion and extrusion.

Intrusion is the most needed and difficult movement, as it needs a very light and constant force. Forces exceeding the biological limit can damage the supporting tissues. To achieve this proper mechanics is essential.

According to Consolaro(2005) the optimum force established by Schwarz in 1932 was conceptual, because technology for such measurement was not available then.

Force system is determined both by the design and material used in the appliance. Orthodontist must know the role of the wire used including its size and composition.

To achieve intrusion the constancy of the force has

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to be in control. The wire which is more resistant to deflection will release the acquired force at a faster rate. So the wire with low load deflection rate will tend to release the force slower at constant rate.

Due to the recent advancements in metallurgy, the clinician is facing a challenge in selecting an arch wire from a wide range of alloys which are available in a variety of cross sections.

Mulligan prefers constant bends because they are easy to do, readily reproducible, and offer low force ranges when the orthodontist is familiar with the “by - pass” approach to force control.

This study tends to compare intrusive forces in stainless steel, timolium, blue elgiloy and CNA, ‘V’ bend intrusion arches with different magnitudes of deflection. In other words the study tends to identify an alloy at a particular bending magnitude which deliver near ideal force favourable for intrusion.

Aim: To evaluateof intrusive forces created by ‘v’ bend, intrusion arches at various deflections.

Objective: The present study is to consider the importance of alloy used as intrusion arches.

Materials and Method

This study considers Stainless steel wires, timolium wires, CNA Beta 3 wires, Blue elgiloy alloy with rectangular section of dimension 0.017 x 0.025 inch, 15 numbers each. Arch forms are standardized with the help of a arch form selector guide (TP Orthodontic, La Porte, Indiana, USA). Bio-arch IV is selected as the standard arch form, as the arch form of the typhodont coincides with that arch form. Straight length of Blue Elgiloy wire is bent in to arch form with the help of a turret (Morelli, Sorocaba, Sao Paulo, Brazil).

Intraoral rulers are fixed in the phantom upper jaw to record the displacements. Buccal tube(0.22slot) is fixed in the first molar. Stainless steel wire is placed in the centre of upper anteriors to represent bracket slot line, as presence of brackets may interfere during force measurement⁷. A V-bend of 45 degrees for intrusion is made in the second premolar-molar region of the arch wire^{7,22,23,24}. This produced a deflection of 40 mm from the bracket slot line.

Trials were conducted at the CIPET (Central Institute Of Plastic Engineering and Technology, Chennai) and a dynamometer (Autograph, U. K) was used with 1 kgf load and 0.01 kgf resolution. The arch wire was inserted in the auxillary tube and the load is connected to the arch wire in the midline. Trial speed was set at 10 mm/min⁷. The magnitude of the load at 5, 10, 15 mm were recorded.

Statistical Analysis: The significance level of 5% was taken. ANOVA was used for assessing the force of all the alloys and Tukey test (table 3) was used for multiple comparisons.

Table-E enlist the Force values of different alloys at different magnitudes of deflection. On comparing the forces registered at 5, 10, and 15 mm the differences between all the alloys were statistically significant except for CNA and timolium between 5 mm and 10 mm and for blue elgiloy between 10 mm and 15 mm were not statistically not significant as shown by the figures presented in (Table 2).

Result: The Kolmogorov-Smirnoff test identified a normal distribution.

Comparison between the load increments necessary to deflect the arch at every 5 mm (Table 1) identified different forces between nearly all the intervals for stainless steel, CNA, blue elgiloy, timolium.

Table 1: Force Values of different alloys at different magnitudes of deflection

Distance	F	P	Stainless steel		CNA		Blue elgiloy		timolium	
				SD		SD		SD		SD
15-10 mm	12,2955	<0.001	152.70	25.54	101.92	14,81	136.69	30,96	141,18	22,43
LO S mm	26.3513	<0.001	197.51	25.28	117.82	17.50	170.16	30.48	160.32	23.76
5-0 mm	24.0714	<0.001	227.83	30.12	137.87	29.04	197.46	32.87	186.16	25.52

Table 2: Force values at different magnitudes of deflection for different alloys

Alloys	F	P	5 mm	(a)	10 mm (b)		15 mm (c)		Tukey		
		value	x(gf)	SD	x(gf)	SD	x(gf)	SD	ab	ac	bc
Stainless steel	28.5790	<0.001	152.70	25.54	197.51	26.28	227.83	30.12	S	S	s
CAN	10.6654	<0.001	101.92	14.82	117.82	17.50	137.87	29.14	NS	S	s
Blue Elgiloy	14.0475	<0.001	136.69	30.96	170.16	30.48	197.46	32.87	S	s	.NS
Timolium	13.3406	<0,001	141.18	22.43	160.32	23.76	186.16	25.52	NS	s	s

Table 3: Tukey test for multiple comparison

Alloys	F	value	15-10 mm 00		10-5 mm M		5-0 mm (c)		Tukey		
			x(gf)	SD	x(gf)	SD	1(80)	SD	ab	ac	be
Stainless steel	219.3822	<0.001	152.70	25.54	44.81	13.22	30.33	9.51	S	S	NS
CAN	206.0830	<0,001	101.92	14.82	16.64	8.23	19.40	15.02	S	s	NS
Blue Elgiloy	156.5376	<0.001	136.69	30.96	33.48	8.32	27.30	7.60	s	s	NS
Timolium	321.1005	<0,001	141.18	22.43	21.76	5.75	26.62	10.21	s	s	NS

Discussion

At times orthodontist simply placed a V bend in the posterior region for intrusion neglecting proper force measurement. There is no constant angulation which can be placed for all the patients because there are variations in patient’s dental arch length, height of the buccal vestibule, crown height and its angulation. Method error evaluation was not done since the repeatability characteristic could not be assured as the same arch would possibly present some change upon being newly measured.

The observed forces of 227.83 gf for stainless steel, 137. 87 gf for CNA, 197. 46 gf for blue elgiloy, 186. 16 gf for timolium at the same distance of 15mm were different with those of Cristiane Aparecida de Assis Claro et al (2007)⁷, because the arch perimeter of the typhodont used is small and produced only 15mm deflection with a 45 degree V bend.

The CNA wire produced lesser force than stainless steel, blue elgiloy, and timolium when deflected from 15 mm, and presented better spring back than the others. Timolium presented intermediary characteristics between blue elgiloy and CNA. Blue elgiloy presented intermediary characteristics between stainless steel and timolium.

By comparing the load increment at each registered distance of 5 mm, it was possible to identify a higher regularity in the loads necessary to deflect the CNA and Timolium arches, and a higher irregularity in the loads

necessary to deflect the stainless steel and blue elgiloy arches. These are concordant with those of Cristiane Aparecida de Assis Claro et al (2007)⁷ for timolium and stainless steel. Moreover, it was determined that there was a decreasing tendency in load quantity from the first to the last interval.

The load increments necessary to deflect the arches tended to decrease from the first to the last interval, these differences being more significant from the first increment to the second increment for all the alloys. In other words the majority of the load required to deflect the arch wire is spent in the first segment (15-10mm). This is a very important point in a clinical situation, mostly when constant angulation for ‘V’ bends is used. Also, as the tooth starts intruding, the loss of force is minimal as the teeth can never cross the last two segments.

The forces observed in this should not be used as reference and has to be measured when an intrusion arch is tied as the geometry of the teeth and the distance between the point of force application varies from patient to patient.

Conclusion

Based on the analyses conducted in the present study, it was concluded that:

1. The CNA intrusion arches produced the least amount of force followed by timolium, blue elgiloy and stainless steel arches in increasing order at 5,10,15mm of deflection.

2. In all the alloys, an increase in distance of every 5mm entailed a significant increase in force between all registered values.
3. The load increments necessary to deflect the arches tended to decrease from the first to the last interval, these differences being more significant from the first increment to the second increment for all the alloys, more significantly in stainless steel and blue elgiloy.

Conflict of Interest: None.

Ethical Approval: Ethics committee approval obtained from Sree Balaji Dental college & Hospital (SBDCH/IEC/03/2016/5)

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References

1. Burstone, C. J.; Baldwin, J. J. and Lawless, D. T. The Application of Continuous Forces to Orthodontics, *Angle Orthod.*1961; 31:1-14,
2. Burstone CJ. Deep overbite correction by intrusion. *Am J Orthod.* 1977;72:1 -22.
3. Burstone. C. J., and Goldberg, A. J. Beta titanium: A new orthodontic alloy, *Am. J. Orthod.*1980; 77: 121-132.
4. Burstone CJ. Variable-modulus orthodontics. *Am J Orthod* 1981;80: 1 -16.
5. Burstone CJ, Goldberg AJ. Maximum forces and deflections from orthodontic appliances. *Am J Orthod* 1983;84:95-103.
6. Burstone CI, Koenig HA. Creative wire bending-the force system from step and V bends. *Am J Orthod* 1988;93:59-67.
7. Cristiane Aparecida de Assis Claro, Jorge Abrao, Silvia Augusta Braga Reis Forces in stainless steel, Timolium and TMA . intrusion arches, with different bending magnitudes. *Braz Oral Res* 2007;21 (2): 140-145
8. Drake SR, Wayne DM, Powers JM, As gar K. Mechanical properties of orthodontic wires in tension, bending, and torsion. *Am. J. Orthod* 1982;82:206-10.
9. E.van Steenbergena; C. J. Burstoneb; B. Prahlandersenc; I. H. A. Aartmand Influence of Force Magnitude on Intrusion of the Maxillary Segment - *Angle Orthod* 2005;75: 723-729)
10. Genin, P.Laheurte, A.Eberhardt, MP. Filleul. Testing the mechanical properties of titanium molybdenum preformatted orthodontic archwires under tensile stress - A preliminary report. *European Cells and Materials* 2005; Vol. 10. Suppl. 4:11
11. Goldberg AI, BurstoneCJ. An evaluation of beta titanium alloys for use in orthodontic appliances.*J Dent Res* 1979;58:593-600.
12. Goldberg, A.J., and Burstone, C.J:An evaluation of beta titanium alloys for use in orthodontic appliances, *J. Dent. Res.*1979;58: 593-600.
13. Iosif Sifakakis; Nikolaos Pandis; Margarita Makou; Theodore Eliades; C hristoph Bourauel. Forces and Moments Generated with Various Incisor Intrusion Systems on Maxillary and Mandibular Anterior Teeth. *The Angle Orthodontist* 1992;Vol. 79(5):928-33.
14. Material Safety Data Sheet Directive 91/155/EEC
15. Otto RL, Anholm IM, Enge GA. A comparative analysis of intrusion of incisor teeth achieved in adults and children according to facial type. *Am J Orthod* 1980;77: 437-46.
16. Pinandi Sri Pudyani Effects of orthodontic forces on pulp tissue. *Dent. J. Vol.* July-September 2006;39(3)98-101
17. Robert.S. Quinn, D. Ken Yoshikawa. A reassessment of force magnitude in Orthodontics. *Am J Orthod* 1985;88:252-60
18. S. Juvvadi, Evaluation and Comparison of CNA and TMA Wire Properties http://iadr.confex.Com/iadr/2008_toronto/techprogram/session_19417.htm.
19. Sunil Kapila, Rohit Sachdeva, mechanical properties and clinical applications of orthodontic wires *Am J Orthod* 1989;96:100-9.
20. Thomas. F. Mulligan, The Advantages Of Differential Moments *JCO* 2009:379-386.
21. Thomas. F. Mulligan-Commonsense mechanics, Part 5, *JCO*-Jan1980:53-57.
22. Thomas. F. Mulligan-Commonsense mechanics, Part 6, *JCO*- feb1980:98-103.
23. Thomas. F. Mulligan-Understanding and applying wire-bracket angles,*JCO*- Oct 2008: 563-573.
24. Vinod Krishnan, K. Jyothindra Kumar Weld Characteristics of Orthodontic Archwire Materials. *Angle Orthod* 2004;74:533-538.
25. Vinod Krishnan, K. Jyothindra Kumar, Mechanical Properties and Surface Characteristics of Three Archwire Alloys. *Angle Orthod* 2004;74: 825-831.

Autistic Spectrum Disorder- Contextual Paediatric Global Updates

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Abstract

Autistic spectrum disorders are the complex neurological conditions resulting in impaired social interaction, difficulty in understanding verbal and non-verbal communication. Caring for children with autism spectrum disorders (ASDs) is challenging for both children and their caregivers. Paediatric autistic population have restricted stereotyped behavioural conditions thus resulting in psychological distress, depression, anxiety and other physical health problems among caregivers. The Autistic spectrum disorder uplifts its effect in the early 2.5-3years and continues thereafter till the child turns to an adult. Moreover, many caregivers face severe financial crises, given high out-of-pocket health care expenses, unemployment. Certain set of researches conducted reported plethora of psychosocial problems affecting caregivers of children with autism, ranging from stress, depression, anxiety, restrictions of activities, strain in marital relationships and diminished physical health. The paper aims to discuss the prevalence of autistic spectrum disorder that is increasing due to altered environmental changes, genetic pre-disposition and inability to maintain regularity in antenatal services. Further more, altered quality of life of the caregivers will also be discussed along with exploration of their concerns while dealing with special children.

Keywords: *Child Development Disorders, Prevalence, Health Related Quality of Life, Caregivers concerns.*

Introduction

Developmental disorder” or “developmental disability” means a severe, chronic disability of the child that is an attribute to a mental or physical impairment, or combination of both which is manifested and is likely to continue indefinitely. Developmental deficits occur in new-borns due to genetic or chromosome abnormalities, exposure to teratogenic substances, alcohol consumption and certain viral infections during the prenatal period.¹ These abnormalities pose a serious threat to the new-born for the coming ages to develop into a normal child who can be able to co-ordinate between his cognitive and affective area of implementation. The child is self-insufficient which presents with the inability to be receptive and unable to reflect the need for a combination and sequence of self-care activities and capacity for independent living.² Common developmental disorders in paediatric population are namely Conduct disorders, Autism Spectrum Disorders, Attention Deficit Hyperactive disorder (ADHD) and Expressive language disorder. In pace of Attention Deficit Hyperactive disorder (ADHD), Autism Spectrum disorder is one such

developmental condition whose incidence is increasing rapidly across the globe³.

A study regarding Autism Spectrum Disorders funded by the Center for Disease Control and Prevention (CDC) determined the prevalence of ASD in the United States estimated to be about 11.3 per 1,000 (1 in 88) children. Autism Spectrum Disorders among all have an increased prevalence among all developmental disorders which affects nearly 20% paediatric population. It is one of the severe form of developmental disabilities which appear in the first three years of life. Autism spectrum disorder is characterized by the persistent deficits in social communication along with social interaction and nonverbal communication behaviour. Caring for the children suffering with autism is challenging and affects the life of the caregivers. Psychological distress, depression, anxiety and other mental or physical health problems are the common symptoms that the caregivers face while caring for an autistic child. In relation to managing the intellectual inabilities and communicational deficits majority of the caregivers face financial issues during the course of treatment⁹.

Therefore, parenting in the children suffering with Autistic Spectrum Disorder is different and requires necessary structural or technical modifications in both domestic and social environment. Weiss mentioned that the general experiences of the caregivers of the children suffering with Autistic Spectrum Disorders (developmental disabilities) can be either positive (e.g. joyful and happy feelings) or negative (e.g. stress, burden, sorrow, physical exhaustion, etc.) or could be a combination of both, depending on the severity of autistic cases.

Getting insight to the factors causing stress it is necessary to implement corrective measures to enhance the health related quality of life and will idealize the researcher's concept to explore the caregivers concerns among the children diagnosed with autistic spectrum disorder. Since, caregivers are the first point of contact for the children it is necessary to maintain positivity and self-confidence among them to make them resile through the challenging phase of learning, sensory processing problems, speech disabilities, social interaction and repetitive behaviour as well. It is also important to explore the caregivers concerns that can help the researcher to modify the ways the autistic children gain self-esteem and self-confidence to walk in pace with the society.^{14,15}

Need: Autistic spectrum disorder is a developmental disorder characterized by difficulties in social interaction and communication and by restricted or repetitive patterns of thought and behaviour. This restriction in behaviour and thought process of the child poses an emotional threat to the caregivers involved in rendering care and support. Meeting the high care demands of affected children requires much time, effort and patience. This often results in psychological distress, depression, anxiety and other mental or physical health problems among the caregivers.¹⁶ The Autistic spectrum disorder uplifts its effect in the early age of 2.5-3 years and continues thereafter till the child turns to an adult. Specific age for the child to promise better way to face the community with confidence is to start the interventions at the age of three years till the child attains specificity in following the commands. Interventions for children with Autistic spectrum disorder require caregivers involvement thus increasing skills, self-efficacy, knowledge of the disorder, and hence reducing family stress. Assessment of health related quality of life can help gain access to the psychological abilities of the caregivers to provide with necessary required interventions and promote on-

going learning to the child.¹⁷ Furthermore; it is necessary to maintain well-being of the caregivers as it could positively influence the effect the interventions have on children with Autistic spectrum disorder.¹⁹

Caregivers involved in parenting children with Autistic spectrum disorder, usually present themselves with feelings of intense anger, guilt, depression or anxiety most of the time. The lower self-esteem among the caregivers deteriorates the spirit and confidence that is essential for the child to uplift self through the deficits of behavioural, psychological and learning capabilities²⁰.

Review Components:

Prevalence of Autistic Spectrum Disorders and Associated Factors: Supporting an evidence stated by centre for Disease Control and Prevention (CDC) autistic spectrum disorders have jumped a higher prevalence rate since 2014 About 1 in 59 children in the United States have ASD, CDC also generalize the fact that the disorder occur four times more likely in boys than in girls due to genetic related factors.⁸ Earlier, autism was considered to be a rare condition with a prevalence of around 2-4 per 10,000 children. Whereas, in the late 90s and continuing the fact upto present 21st century, an annual rise in incidence of autism in pre-school children is based upon the age of diagnosis and increases in the age-specific prevalence rates in children. Centre of disease prevention and control also reported that at present the prevalence rates have a rise of up to 60 per 10,000.⁹

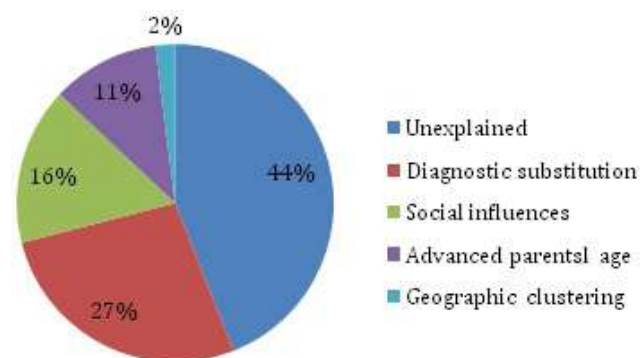


Figure 1: Factors explaining increase in Autistic spectrum disorder prevalence. (Source: Dr. Peter Bearman)²¹

Figure 1 explains the certain factors that have jumped the prevalence rates are changes in the diagnostic criteria, development of the concept of the wide autistic spectrum, different method used in studies, growing awareness and knowledge among parents and

professional workers and the development of specialist services.

Upon a household survey conducted by LR French and KL.Hyde in 2011 it was found that more than 10 million children in India suffer from autism,¹¹ Moreover, it was found that in India about 1 to 1.5 per cent autistic children are between age group from two and nine years. In order to combat the rising prevalence rates it is the prime responsibility of the health care workers to find out an effective way to impart knowledge to practice monthly ante-natal check-ups till last trimester. In addition to it, L.Wing and D Potter focussed on the need of specific care to be undertaken to strengthen the area of diagnostic investigations and hence management of the disorders based upon speech, behaviour and communication strategies. Strong treatment modalities and health care team can help manage an autistic child effectively and can help him/her to gain livelihood and occupational choices.¹²

Quality of Life- Caregivers: Research evidences from the recent years have reported that the parents of the children suffering with an autistic spectrum disorder usually experience heightened stress, overburden and a sense of self blaming. Getting insight to certain factors causing stress it is necessary to measure the health related quality of life .Since, caregivers are the first point of contact for the children, it is necessary to maintain the feeling of positivity and self-confidence among them. Caring for an autistic child is challenging and needs the devotion to balance learning with the practical aspects form the side of the child.¹³

Sharpley, et al. commented on the three most stressful factors among mothers of autistic child namely (a)concern over the permanency of the condition; (b)poor acceptance of autistic behaviours by society and, often, by other family members; and (c) the very low levels of social support received by parents.” Study conducted by KL Hyde revealed the fact that majority of parents of children with autism worry about everything from lifetime dependency to family disharmony.Ciara Padden & Jack E. James in the early 2017 conducted a research study to compare the stress involving Physiological Indicators and Parental Self-Reports. Concludingwith the findings, caregivers of the autistic children reported to experience higher levels of stress and poor physical and psychological health than parents of the normally developing child.

Interesting fact emerged from a research conducted by Ewa pistula and Rafal Kawa in 2015. The study concluded that the parents of children with ASD reported significantly higher levels of parental distress, anxiety, and depression. With the exception that parents of children with ASD had significantly lower cortisol levels 30 min after waking, no other significant group differences were found for physiological measures. Parents of children with ASD reported significantly higher use of a number of adaptive coping strategies (e.g., emotional support) in comparison to parents of the normal children.¹⁵

After concluding the fact that, Quality of life among the caregivers of an autistic child is low based upon the social, physical and physiological roles, Larsson quoted a prime need to assess the quality of life at the care centres in order to resile the caregivers and hence assure the effective care for the special children thereafter. So, talking about World Health Recommendations, the psycho-educational interventions must be inculcated among caregivers to be capable of handling stress and emotions and hence modifying false beliefs and solving daily problems.¹⁹

Caregivers Concerns Involved in Management of Autistic Children: Caregivers are the first point of contact involved in care and management of the autistic child. World Health Organization census denotes the fact that about 94% of the caregivers suffer from physical and psychological distress. Various researchers concluded the related fact that the major concerns evolved while caring for an autistic child are inability to compensate the communication loss and social discrimination. The Primary objective of one of the research conducted by Silvia von Kluge was to identify the cognitive and behavioural profiles that actually affected adjustment, among parents of autistic children. Findings of the study revealed that emotion focussed strategies among caregivers experienced the feeling of guilt and false beliefs. Moreover, Caregivers concerns are often described as the areas involved as the challenges during provisional care in managing significant proportion of children with autism spectrum disorder (ASD). Due to the challenging behaviours in children and adolescents suffering with Autistic spectrum disorder often result to underlying social and communication difficulties and comorbid anxiety. Furthermore, the significant difference can be brought if the families of the children with special needs determine the triggers of behavioural problems and then find out the appropriate interventions

to prevent the identified triggers, before the behaviour becomes habitual.¹⁶

Various researchers qualitatively evolved the basic concerns during the talk exploration with the parents/caregivers of the autistic children. A research conducted by Fletcher-Watson et al in 2015 concluded that the caregivers also experience repetitive behaviour, difficulty in controlling emotional perspectives, performing group activities and activities of daily living. He also quoted that inability towards brain enhancing activities through continuous efforts are also considered as a major factor of worry for the caregivers. Boyd et al. in 2015 did a research study on exploration of the concerned factors and concluded that the caregivers involved in parenting children with Autistic spectrum disorder, usually present themselves with feelings of intense anger, guilt, depression or anxiety most of the time. Researchers from the health and family welfare highlighted that lower self-esteem among the caregivers deteriorates the spirit and confidence that is essential for the child to uplift self through the deficits of behavioural, psychological and learning capabilities.

Effective Management of an Autistic Child: In various areas of developing countries such as India, the prevalence rates are rising due to lack of appropriate resources and health-care related manpower. Moreover, main drawback stands on the part that India as a whole is not practising the interventions on a daily routine,

but implementation is done mainly on Out Patient basis. This stands no longer useful for the child because repetitions in the form of therapies can only be effective if they are given daily on the desired routine. In order to gain effective outcome of the interventions the following process should be followed.¹⁷The findings laid down by Luke T. Curtis and Kalpana Patel indicated that the maintenance of optimum nutrition during ante-natal period can combat the congenital risk of developing Autistic spectrum disorders and ADHD as the nutritional and environmental factors play major roles in disease occurrence.

Recent research focus on the fact that despite having a diagnostic guideline, still the census falls below the normal in order to follow the appropriate diagnostic criteria. The American Academy of Pediatrics and American Psychological Association recommended an approach to the identification of ASD that involves systematic analysis. Besides routine appointments, the approach calls for formal screening in case the behaviours of concern are noted during surveillance. If screening, including any caregiver concern, indicates cause for an attention, this is to be followed by the formal diagnostic assessment thereafter. Lack of appropriate manpower, resources and standardized cognitive and developmental testing are leading to slower management process related to autistic spectrum disorder. As per the American Academy of Pediatrics guidelines following steps need to be undertaken to ensure the early diagnostics of Autism:

Strengthening areas of Genetic counselling.

Systematic diagnostic evaluation to rule out the cause of autistic spectrum disorder.

Start the occupational therapy (Speech+behaviour+symptomatic) by the age of 3 years.

Routine follow-up visits as per psychologist's advice.

Evaluation of every visit.

Assessment of risk factors- Genetic predisposition.

Conclusion

Autistic Spectrum Disorder ranges in severity from a handicap that somewhat limits an otherwise normal life to a devastating disability that may require an appropriate institutional care. It involves various impairments such as social interactions, verbal and nonverbal

communication.¹⁸ Children with an Autistic spectrum disorder have certain restricted behavioural functions, such as stereotype behaviour, inability to adjust to new situations and experience severe tantrums or sleep problems.²⁰ A research study carried out by AP Hill, K P. Zuckerman supported the evidence that about 47%

of the parents deny about being their child to be autistic. Furthermore, parents of children with autistic spectrum disorder experience heightened stress, overburden and sense of self blame. Since, caregivers are the first point of contact for the children getting insight to the factors that are causing stress is of utmost necessity to measure the health related quality of life. Thus, conclusion can be made out by improvising strategies towards the management of developmental deficits necessarily to strengthen the child's capabilities and parental coping comprehensively.²¹

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Conflict of Interest: Nil

References

1. Achenbach TM. Manual for the CBCL/4–18 and Profile. University of Vermont Department of Psychiatry; Burlington: 1991.
2. Achenbach TM, Rescorla LA. Manual for the ASEBA School-Age Forms & Profiles. University of Vermont, Research Center for Children, Youth, & Families; Burlington, VT: 2001.
3. Baker-Ericzen M, Brookman-Frazee L, Stahmer A. Stress levels and adaptability in parents of toddlers with and without autism spectrum disorders. *Research & Practice for Persons with Severe Disabilities*. 2006;30(4):194–204.
4. Bandura A. *Social Learning Theory*. Prentice-Hall; Oxford, England: 1977.
5. Barkley RA. Taking charge of ADHD: The complete authoritative guide for parents, revised edition. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2002;41(1):101–102.
6. Brazier JE, Roberts J. The estimation of a preference-based measure of health from the SF-12. *Medical Care*. 2004;42(9):851–859. [PubMed]
7. Bromley J, Hare DJ, Davison K, Emerson E. Mothers supporting children with autistic spectrum disorders social support, mental health status and satisfaction with services. *Autism*. 2004;8(4):409–423. [PubMed]
8. Brouwer WBF, Van Exel NJA, Tilford MJ. Incorporating caregiver and family effects in economic evaluations of child health. In: Ungar WJ, editor. *Economic evaluation in child health*. Oxford: Oxford University Press; 2010.
9. Brouwer WB, Van Exel NJ, Van den Berg B, Van den Bos GA, Koopmanschap MA. Process utility from providing informal care: The benefit of caring. *Health Policy*. 2005;74(1):85–99. [PubMed]
10. Brouwer WB, Van Exel NJ, Van Gorp B, Redekop WK. The CarerQol instrument: A new instrument to measure care-related quality of life of informal caregivers for use in economic evaluations. *Quality of Life Research*. 2006;15(6):1005–1021. doi: 10.1007/s11136-005-5994-6. [PubMed][CrossRef]
11. Couturier JL, Speechley KN, Steele M, Norman R, Stringer B, Nicolson R. Parental perception of sleep problems in children of normal intelligence with pervasive developmental disorders: Prevalence, severity, and pattern. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2005;44(8):815–822. [PubMed]
12. Chamberlain P, Baldwin DV. Client resistance to parent training: Its therapeutic management. In: Kratochwill TR, editor. *Advances in School Psychology*. Hillsdale, NJ, England: Lawrence Erlbaum Associates, Inc; 1988. pp. 131–171.
13. Chamberlain P, Reid JB. Using a specialized foster care community treatment model for children and adolescents leaving the state mental hospital. *Journal of Community Psychology*. 1991;19(3):266–276.
14. Chandler S, Christie P, Newson E, Prevezer W. Developing a diagnostic and intervention package for 2- to 3-year-olds with autism. *Autism*. 2002;6(1):47–69. [PubMed]

Effectiveness of a Comprehensive Nurse-Patient Strategy in Care of Patients with PIVC and its Clinical Outcomes

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Abstract

Introduction: Peripheral Intra-Venous Cannulation (PIVC) is the second most common invasive procedure performed on in-patients, with an estimated 80% of patients requiring a peripheral cannula and about 69% of PIVC insertions were failed due to occlusion, infiltration, phlebitis and dislodgement.

Aims: To assess the effectiveness of a comprehensive nurse-patient strategy in the care of PIVCs on clinical outcome.

Materials and Method: A quasi-experimental, post-test-only design was used. 30 subjects from each groups, i.e experimental and control group, were observed for development of PIVC complications. Education was provided to nurses and patients in the experimental group regarding how to prevent the early removal of PIVCs. The obtained data were analyzed and interpreted using descriptive and inferential statistics to compare the clinical outcomes among the groups.

Result: The results shows that there is significant difference was observed in duration of PIVCs. Among the experimental group, after implementation of the Nurse-Patient Strategy, 66.66% of the PIVCs stayed more than three days (72 hours) whereas in the control group it was 40%. The pain and swelling were mostly observed complications in PIVC.

Conclusion: A comprehensive nurse-patient strategy has proved effective to increase the practice of flushing PIVCs, which in turn improves their indwelling period.

Keywords: *Infusion, education, thrombosis, duration.*

Introduction

Peripheral Intra - Venous Cannulation (PIVC) is the most common invasive procedure performed on patients who are admitted to hospital, which is the second most requiring procedure during their hospital stay^[1]. PIVCs

increasingly used to save the life of the patients during emergency conditions^[2]. These devices may need to be left in place for days or even weeks; however, it can be associated with complications. Mechanical complications include phlebitis, occlusion, thrombosis, dislodgement, leakage, infiltration, pain and scar formation^[3,4,5,6,7]. PIVC failure rates have been reported as high as 69% and occlusion was observed as the least common complication (0.5%)^[8].

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The identified predictors of phlebitis were females, insertion in the forearm and infusion of medication^[9]. Even though it is an invasive procedure, technically difficult, more prevalent; the most nursing professionals in developing country are not been skilled and receive

little education and opportunity to practice skills until competent^[10]. There is very scarce and little evidence of PIVC insertion, maintenance and removal in country like India.

Methodology

A quasi-experimental, post-test-only design was used to assess the effectiveness of a comprehensive nurse-patient strategy in the care of Peripheral Intra-Venous Catheters (PIVCs) in terms of duration and insertion of I V Catheters at a tertiary care hospital. A total of thirty patients from each of two groups, i.e the experimental and the control group, were observed for development of PIVC complications. Education was provided to nurses and the patients in the experimental group regarding how to prevent the early removal of PIVCs. Sample size was calculated based on the pilot study by using formula: $N = 2*(Z_{1-\alpha/2} + Z_{1-\beta})^2 * \sigma^2 / d^2$ (Comparing two means)^[11] and it was found 30 in each group. After institutional ethics approval data collection was done through observation which began after the implementation of the comprehensive nurse-patient strategy among the experimental group. Thirty patients from the surgical and medical ward were taken by simple random sampling technique for each control and experimental group. Patients who were undergoing PIVC insertion on the upper extremities, between 18 and 65 years of age were included in the study. The patients who receive blood transfusion, parenteral nutrition, chemotherapy; or contrast media (dye); diagnosed with peripheral vascular diseases and already inserted PIVC patients were excluded.

The nurses were assessed for their existing practices through a checklist which covers the areas on IV insertion, maintenance and removal of PIVC. The comprehensive nurse-patient strategy was employed to nurses who were in the experimental group and were as control group received the standard care. The recruited patients who had undergone PIVC procedure were educated in the patient strategy before undergoing PIVC insertion. The event of insertion and removal of PIVC in every participant were observed. The indwelling period was calculated in hours from the time of PIVC insertion until removal. Care of the PIVC (flushing practice) was observed during drug administration through the PIVC. Flushing before and after drug administration was observed and documented with additional details of the solution used for flushing, the reason for not flushing and visible contamination of the PIVC insertion site.

The description of the comprehensive nurse - patient strategy intervention is given below:

Comprehensive nurse-patient strategy was operationally defined as education including practice skills in PIVC insertion, maintenance and removal to nurses and instruction on PIVC maintenance practices to the patients who require venepuncture with cannula placement. Comprehensive nurse-patient strategy was developed based on literature review^[2,4,10] and suggestions from experts; which consisted strategy for nurses and patients. A strategy was accomplished in the form of educational intervention to the nurses in the clinical setting as group discussion and demonstration of practice skills in the skill lab and at the clinical area in real time. Prior to the intervention a need assessment was carried out to understand the context, the need for improvement and existing information on PIVC care. Regarding patient strategy, the practices considered were movement and position of the limb, cleanliness, care of the extension line and complications and at the end a pamphlet was provided to the patients after the instructions.

The obtained data were analysed by using the SPSS package version 16 and were interpreted by using descriptive and inferential statistics on the basis of the objectives and hypotheses of the study.

Results

The data were collected from 60 subjects (30 in the control and 30 in the experimental group). The data shows that 17 (57%) of the patients were in the 51-65 age group in both the control and the experimental group. Males predominated in both groups, with 27 (90%) in the control group and 22 (73%) in experimental group. Most of the patients, i.e., 12 (40%) in the experimental group and 17 (57%) in the control group, had an education up to high school. The data obtained by observation during the insertion of the PIVC show that the majority of the PIVC insertions in the experimental 29 (97%) and the control group 27 (90%) were performed with a 20G cannula. The vein selected among the experimental group was mostly the cephalic vein 14 (47%), whereas 40% in the control group. The type of adhesive used to secure the PIVC was mostly non-transparent in both the experimental 29 (97%) and the control 30 (100%) group. The connectors used among the experimental were mostly 3-way i.e by 19 (63%), whereas 80% of them used in the control group (Table 1).

PIVC maintenance practices were observed, specifically flushing practices during and after drug administration. In the experimental group 16 (53%) and in control group only 3 (10%) IV cannula flushing practices were observed. Coming to noncompliance to the practice of IV cannula flashing before 14 (47%), after 18 (60%) in experimental group and in control group majority 27(80%) were not complaint with flashing practises. The main reason reported for non-compliance in flushing before and after drug administration was ignorance 27(80%) by the groups. (Table 2). Clinical outcomes were reported by the patients were pain and

swelling in both the experimental and the control group (Fig.1). The duration of the time of IV cannula insitu was observed in 20 (67%) patients and it was in place longer than 3 days (72 hours), whereas in the control group for 12(40%) remained longer than 3 days. Further to this a statistically significant difference between the groups ($t_{(58)}=4.245, P<0.05$) was observed on indwelling period. Comparison of flushing practices among the groups was statistically shown difference in flushing practices before drug administration between the groups ($\chi^2=13.01, P<0.05$) and after drug administration between the groups ($\chi^2=19.20, P<0.05$). (Table 3).

Table 1: Frequency and percentage of insertion practices among nurses N: 30+30=6

Insertion practice	Experimental		Control	
	(f)	(%)	(f)	(%)
PIVC site				
Cephalic vein	14	46.6	6	20
Dorsal venous arch	5	16.6	3	10
Dorsal metacarpal vein	6	20	12	40
Basilic vein	2	6.6	3	10
Accessory cephalic	2	6.6	3	10
Intermediate basilic	1	3.3	1	3.3
Type of adhesive				
Transparent	1	3.3	0	0
Non-transparent	29	96.6	30	100
Type of connector				
3-way	19	63.3	24	80
10-cm extension	11	36.6	6	20

Table 2: Frequency and percentage of maintenance practices N: 30+30=60

Practice	Experimental		Control	
	(f)	(%)	(f)	(%)
Flushing before drug administration (N: 30+30=60)				
Done	16	53.33	3	10
Not done	14	46.66	27	90
Reasons for not flushing before drug administration (N: 14+27=41)				
Forgetfulness	7	50	24	80
Ignorance	7	50	3	20
Fluid used to flush before drug administration (N: 16+3=19)				
Heplock	8	50	3	100
NS	8	50	0	0
Flushing after drug administration (N: 30+30=60)				
Done	18	60	2	6.66
Not done	12	40	28	93.33

Practice	Experimental		Control	
	(f)	(%)	(f)	(%)
Reasons for not flushing after drug administration (N: 12+28=40)				
Forgetfulness	7	58.33	3	10.72
Ignorance	5	41.66	25	89.28
Fluid used to flush after drug administration (N: 18+2=20)				
Heplock	3	16.66	1	50
NS	15	83.33	1	50

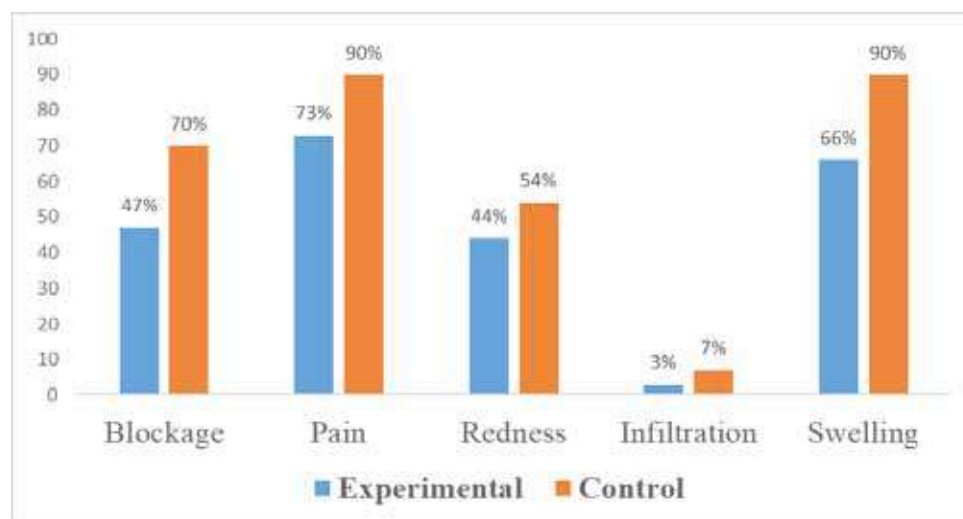


Fig 1: Bar diagram on complications of PIVC

Table 3: Comparison between the experimental and control groups: N=30+30=60

Group	Mean	Standard deviation	Standard error	't' value	Mean difference	df	p value
Comparison of indwelling periods							
Experimental	76.6	22.67	4.14	4.245 (t)	23.73	58	0.001*
Control	52.87	20.57	3.75				
Flushing before drug administration		Experimental	Control	χ^2	df	P value	
Done	16	3	13.01				
Not done	14	27					
Flushing after drug administration							
Done		18	2	19.20	1	0.001*	
Not done		12	28				

*significant at 0.05 level of significance

Discussion

In the present study, patients who underwent PIVC insertion in the cephalic vein were observed to have a longer indwelling period with a 10-cm extension than those who underwent PIVC insertion in the dorsal venous arch. No other studies could be identified that compared a 10-cm extension with a 3-way connector for PIVCs. The complications observed in the study at the

time of PIVC removal were pain and swelling and the appropriate selection of vein is one of the key indicator for longer indwelling period and which supplemented by implementation of nurse patient strategy.

These findings were supported by an experimental study conducted in Queensland, Australia, which found that phlebitis occurred in 7% of patients from each group, while occlusion, accidental removal and other

complications were equivalent between the routine and clinically indicated PIVC removal groups [12]. Other few studies were done to assess the incidence and predictors of PIVC-induced complications. The top observed complication were phlebitis (17.6%) followed by pain (7.6%), and occlusion among all patients (0.5%) [13,14,15,16].

In the present study, the onset of phlebitis was found to be deferred in the experimental group (36.66% within 72 hours and 63.3% after 72 hours of PIVC insertion) compared to the control group (76.6% within 72 hours and 23.3% after 72 hours of PIVC insertion). These findings were supported by a study results, where the incidence of phlebitis was 11.09% and patients who had PIVCs in an upper limb were at high risk of phlebitis. Further study results recommended that the correct selection of PIVC sites is an important factor in the prevention of phlebitis [17,18,19].

When considering the study limitation the researcher could not ensure the use of transparent dressings to secure PIVCs, though it was part of the nurse education strategy, owing to non-availability due to the cost in the pharmacy stores. This study sheds light on infusion safety and the routine PIVC changing protocols that exist in various hospitals around the world. It shows that a combined educational strategy can improve the indwelling period and care of PIVCs. Thus, it is recommended that the nurse-patient strategy be implemented for PIVCs to ensure fewer complications and longer indwelling periods. The developed strategy should be used by nurses in general and specifically with the selected patients for better outcomes of PIVC. It reinforces the knowledge acquired by nurses during their training and adds to the weight of a continuous nursing education. Nurse administrators can arrange training similar to this strategy where PIVC-related problems are prevalent and can update policies related to PIVC removal and replacement.

The study results recommended improved insertion techniques to reduce the incidence of PIVC associated complications, thus extending the onset of such complications beyond 72 hours^[6]. The predictors for PIVC failure are studied in greater perspective [2,5,20,21]. The practices related to the periodic replacement of PIVCs are still not clear and there is a weak evidence from developing country. There is a need to train the nurses to improve the practices [10,17, 22]. This study demonstrated improvement in skill of nurses and patient

outcome from putting into practice the comprehensive nurse-patient strategy in clinical nursing care. The Peripheral Intra-Venous Catheter (PIVC) insertion poses a challenge for nurses in clinical practice. The evidence contributes the literature which should be considered to improve the patient care outcome on PIVC maintenance. Comprehensive nurse – patient strategy will facilitate nurses abilities in PIVC management and further improves clinical outcomes and patient satisfaction. Ongoing education to the clinical nurse, patient/family will enhance the standard of care and improve the outcome.

Conclusion

Pain associated with PIVCs is a common problem in hospitals around the world. A comprehensive nurse-patient strategy has proved effective to increase the practice of flushing PIVCs, which in turn improves their indwelling period. This study suggests that the selection of the cephalic vein for PIVC insertion also may increase the indwelling period.

Ethical Clearance: From Institutional Ethical Committee (IEC) of Kasturba Hospital, Manipal.

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Conflict of Interest: Nil.

References

1. Fernandez -Ruiz M, Carretero A, Diaz D, Fuentes C, Gonzalez J, Garcia-Reyne A, Lopeza-Medrano F. Hospital-wide survey of the adequacy in the number of vascular catheters and catheter lumens. *Journal of Hospital Medicine*. 2014;9(1):35-41.
2. Denton A. Royal College of Nursing (2016) Standards for Infusion Therapy (online) (Vol. 4). London: Retrieved March 2018; from <https://www.rcn.org.uk/professional-development/publications/pub-005704>.
3. Marnejon T, Anjelo D, Abu Abdou A, & Gemmel D. Risk factors for upper extremity venous thrombosis associated with peripherally inserted central venous catheters. *The Journal of Vascular Access*. 2012; 13(2): 231-238. doi:10.5301/jva.5000039
4. Vizcarra C, Cassutt C, Corbitt N, Richardson D, Runde D, & Stafford K. Recommendations for improving safety practices with short peripheral catheters. *Journal of Infusion Nursing*. 2014;37(2): 121-124.

5. Keogh S & Flynn J. Maintenance of intravascular device patency: a survey of nursing and midwifery flushing practice. *The Queensland Nurse*. 2014;33(2):30-31.
6. Abolfotouh M, Salam M, Bani-Mustafa A, White D, & Balkhy H. Prospective study of incidence and predictors of peripheral intravenous catheter-induced complications. *Therapeutics and Clinical Risk Management*. 2014;8(10): 993 -1001.
7. Aziz A. Variations in aseptic technique and implications for infection control. *British Journal of Nursing*. 2009; 18(1): 26-31. doi:10.12968/bjon.2009.18.1.32073
8. Keogh S, Flynn J, Marsh N, Higgins N, Davies K, & Rickard C. Nursing and midwifery practice for maintenance of vascular access device patency. A cross-sectional survey. *International Journal of Nursing Studies*. 2015; 52(11): 1678-1685. doi:10.1016/j.ijnurstu.2015.07.001
9. Balton D. Improving peripheral cannulation practice at an NHS Trust. *British Journal of Nursing*. 2010;19(21): 1346-1350. doi: 10.12968/bjon.2010.19.21.79998
10. Qamar Z, Afzal M, Kousar R, Waqas A, & Gilani S. A. Assess Nurses Knowledge and Practices towards Care and Maintenance of Peripheral Intravenous Cannulation in Services Hospital Lahore, Pakistan. *Saudi Journal of Medical and Pharmaceutical Sciences*. 2017; 3(6B): 608-614. doi: 10.21276/sjmps
11. Antonisamy B, Christopher S, Samuel P P. *Biostatistics Principles and Practice*. Tata McGraw Hill Education Private Limited; NewDelhi.
12. Ullman A, Keogh S, Marsh N, & Rickard C. Routine versus clinically indicated replacement of peripheral catheters. *British Journal of Nursing*. 2015; 24(2): S14. doi:10.12968/bjon.2015.24.Sup2.S14.
13. Milutinović D, Simin D, & Zec D. Risk factor for phlebitis: a questionnaire study of nurses' perception. *Rev. Latino-Am. Enfermagem*. 2015; 23(4): 677-684.
14. González López J, Arribi Vilela A, Fernández, E. d, Olivares, JC, Herrera, PP, & Benedicto CM. Indwell times, complications and costs of open vs closed safety peripheral intravenous catheters: a randomized study. *Journal of Hospital Infection*. 2014; 86(2): 117-126..
15. Webster J, Osborne S, Rickard C, & Hall J. Clinically-indicated replacement versus routine replacement of peripheral venous catheters. *The Cochrane Database Systematic Reviews*. 2010;17(3): CD007798.
16. Webster J, Osborne S, Rickard C, & New K. Clinically-indicated replacement versus routine replacement of peripheral venous catheters. *The Cochrane Database Systematic Reviews*. 2013; 30(4)
17. Keogh S, Flynn J, Marsh N, Mihala G, Davies K, & Rickard C. Varied flushing frequency and volume to prevent peripheral intravenous catheter failure: a pilot. *Bio Med Central*. 2016;17: 1-10. doi:10.1186/s13063-016-1470-6
18. Chiu P C, Lee Ya Hui, Hsu H T, Feng Y T, Lu I C, Chiu S L, Cheng K I. Establish a perioperative check forum for peripheral intravenous access to prevent the occurrence of phlebitis. *Kaohsiung Journal of Medical Sciences*. 2015; 31: 215 - 221.
19. Laudenbach N, Carie A B, Klaverkamp L, & Hedman-Dennis S. Peripheral IV stabilization and the rate of complications in children: An exploratory study. *Journal of Pediatric Nursing*. 2014; 29(4): 348 - 353.
20. Marsh N, Webster J, Larsen E, Cooke M, Mihala G, & Rickard C. Observational study of peripheral intravenous catheter outcomes in adult hospitalized patients. *Journal of Hospital Medicine*. 2017;12(1):E1-E7.
21. Carr PJ, Rippey JC, Cooke M, Bharat C, Murray K, Higgins N, Rickard C. Development of a clinical prediction rule to improve peripheral intravenous cannulae: the vascular access decisions in the emergency room (VADER) study protocol. *BMJ Open*. 2016;6:009196:1-7. doi:10.1136/bmjopen-2015-009196.
22. Helm R, Klausner J, Klemperer J, Flint L, & Huang E. Accepted but unacceptable: peripheral IV catheter failure. *Journal of Infusion Nursing*. 2015;38(3):189-203. doi:10.1097/NAN.000000000000100.

Healthcare Rights of the Mentally Ill: Awareness among Healthcare Providers

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Abstract

Background: Enjoyment of the human right to health is vital to all aspects of a person's life and well-being. Since the origin of human civilization, mentally ill patients have received the scant amount of care and concern for the community. For centuries, as a result of this, the rights of mentally ill have been abused and ignored. Psychiatric hospitals, informal healing centre and family homes reported that low-income countries neglect the mentally ill patient. Various initiatives exemplify a top down approach to promoting human rights which historically has had limited impact at the level of those living with mental illness and their families. Human rights are an important component for effectiveness in care. The health caregivers and the medical and nursing interns must know the rights of a mentally ill person; and should support, protect and meet their health needs. So, there is need to know whether the health caregivers are aware of the human rights of the patients who are mentally ill.

Objectives: To assess the awareness regarding the Healthcare Rights and General rights of the mentally ill among health care providers.

Method: The study was conducted in a medical college and hospital in Mangalore. The Survey method was used to collect the data. The study population was professionals and medical and nursing interns taking care of mentally ill. The Sample size was 154. Purposive sampling technique was used. The data were collected using structured questionnaires after which it was analysed using frequency, percentage, chi-square test, fishers exact test.

Result and Conclusions: Results show moderate awareness. Hence, it is recommended that the health care providers should be given more awareness regarding the human rights of the mentally ill.

Keywords: *Healthcare rights, healthcare providers, mentally ill, awareness.*

Introduction

Mental disorders represent four of the ten leading causes of disability worldwide¹. People with mental illness may be experiencing a wide range of human rights violations². The majority of the mentally ill may be excluded from community life and denied basic rights

such as shelter, food and clothing. This could be due to stigma and misconceptions associated with mental illness³. Mentally ill are also discriminated against in the field of employment, education and housing⁴.

The United Nations has defined Human Rights as "Those rights which are inherent in our nature and without which we cannot live as human beings"⁵. People with mental disorders are particularly vulnerable to abuse and violation of their rights. If a protective mechanism is not in place, they are susceptible to abuse by society, which includes family members, caregivers, professionals, friends, fellow citizen etc.⁶. Human rights are also connected to mental health in two distinct ways as mental health policy affects human rights

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and human rights violations affects mental health⁷. Therefore, positive promotion of mental health laws and human rights are an essential means of promoting and protecting their rights. Despite this, countries all over the world fail to legislate effectively⁸. Indeed, it is important to improve the quality of life and mutually reinforce one on another.

The Constitution of India assures equal treatment and equality of opportunity and status to all the citizens. Every person with a mental illness has the same basic rights as every other person, specifically including the rights set out in the International Covenant on Civil and Political Rights (ICCPR) and the rights recognized in the Declaration on the Rights of Disabled Persons; that discrimination on the basis of mental illness is not permitted and that people being treated for a mental illness must be accorded the right to recognition as a person before the law⁹. Despite the adequate legislations, we often come across horrendous stories about the way people with mental illness are treated in the community and various psychiatric institutions¹⁰. As evident by the National Human Rights Commission report¹¹ which highlighted the gross inadequacies and subhuman living conditions in mental hospitals. Furthermore, India's dismal record of rights violations of the mentally ill was glaringly exposed with the grotesque death of 25 patients at an "asylum" in Tamil Nadu¹². The lack of human rights or their violations, as seen in the Erwadi tragedy and similar cases, does not stem from a shortcoming in existing Indian or international law per se; but is the result of social stigma, prejudice, and other social and economic factors linked with mental illness¹³.

Many countries are facing challenges regarding the adequacy of human resource which is needed in delivering evidenced based care for mentally ill. At present, human resources for mental health in countries of low and middle income show a serious shortfall that is likely to grow unless effective steps are taken. It proved that through primary health care setting, community-based protocols and task based approaches stand the best way in delivering mental health care. Non-specialist health professionals, lay workers, affected individuals, and caregivers with brief training and appropriate supervision by mental health specialists are able to detect, diagnose, treat, and monitor individuals with mental disorders and reduce caregiver burden¹⁴.

Lack of knowledge and awareness among the students is associated with the negative attitudes

towards mental illness in the community. Medical health professionals have to conduct awareness camps at initiative levels like schools, universities. Educating the students at the training level leads to the change in the attitude of the students towards the mental patients¹⁵. A study assessing the students attitude on stigma towards the mentally ill showed that the attitude was poor towards the mentally ill. They suggested that the improvement in the role of teachers in educating their students regarding the mental health is important in building up the attitude of students towards the mentally ill¹⁶. Information regarding the rights of the mentally ill is disseminated by mental health professionals and mass media. The society can be misguided when the information delivered to them through the healthcare professionals and the mass media is inadequate. Supporting this fact, a study was conducted to assess the knowledge about human rights of the mentally ill among the mental health professionals and the health journalists, which showed through both the groups have good knowledge about the human right of persons with mental illness (approximately 86.3% right responses); there was a trend towards Mental Health Professionals(MHP) having better knowledge compared to Health journalists(HJ)¹⁷.

The human right frameworks have both normative and legal backing and have substantial overlapping with medical ethics. Being inclusive in all the aspects of mental health care, human rights have provided a base to the guidance in the care of mentally ill patients eliminating the past indifferences regarding the worth and dignity of the mentally ill patients¹⁸. There has been a dynamic relationship between the concept of mental illness, the treatment of the mentally ill and the law. The mental health professional especially nurses should know the basic legal and ethical aspects of psychiatry. The descriptive study was thus undertaken with the objective to identify the knowledge of the staff nurses regarding legal and ethical responsibilities in the field of psychiatric nursing at selected psychiatric centre. The findings of the study revealed that majority (90%) of the nurses possess a moderate level of knowledge¹⁹.

Therefore, it is an urgent need to take necessary steps to protect, promote and fulfil human rights of people with mental illness through providing care, education to the community and strengthening the legislations. Hence this study was conducted with a twofold objective of assessing the awareness regarding healthcare rights of mentally ill and general rights of the mentally ill among healthcare providers.

Methodology

The present study was a cross sectional based descriptive study. All the professionals taking care of mentally ill and medical and nursing interns who were undergoing training to care for mentally ill were taken as the subjects for the study from a medical college and hospital in Mangalore for a period of One-month study. Data from the subjects was obtained by a structured questionnaire in a medical college and hospital Mangalore. The sample size included the doctors, staff nurses, medical interns, nursing interns and clinical counsellors from the medical college and hospital. A total of 154 samples were included in the study, ethical clearance was taken from the institutional ethics committee before starting the study. After obtaining the consent from the subjects, the data was collected using a structured questionnaire, the questionnaire was adapted and modified from the study of Yang, 2013²⁰ which included the demographic factors, awareness and human rights of mentally ill. The data thus obtained was compiled and tabulated using frequency, percentage along with the use of SPSS software.

Results and Discussion

The questionnaire was distributed among the 154 selected samples of the study. Those consenting to participate were taken for the data collection. The questionnaire was administered in an anonymous form and no identifiable information was collected from the participants. Conditions of anonymity and confidentiality were observed throughout the course of the study.

The majority of the sample were females than males with an age <30 years. Educational background was also considered in the study in which it was found that the medical and nursing interns were in the majority of 67.5% and also it was observed that they didn't have much experience in the care of the mentally ill. The respondents being in the early stage of their healthcare profession and working in a general hospital with psychiatric set up emphasise on the need for inclusion of mental health in their curriculum and training.

Insert Fig 1: Section 1: This section was about the awareness regarding the healthcare rights of mentally ill. The association between demographics and healthcare rights is also presented below.

Healthcare professionals have high awareness regarding seclusion and restraint (87.2%) followed by

treatment and planning (82.6%) and moderate awareness regarding occupational therapy (78.1%) followed by social responsibility (74.6%) and admission and discharge (51.3%) and have low awareness regarding privacy (37.65%). The findings are not in accordance to a study in Bangalore²¹ which revealed that awareness regarding seclusion and restraint was 70% (less than present study) and privacy was 44% (more than present study).

Insert Table 1: Table 1 shows that there is no significant difference between occupation and awareness of healthcare rights ($p=0.3 >0.05$). There is a significant difference between age and awareness ($p=0.004 <0.05$). This indicates that the awareness among age <30 was good (65.6%) than above 30 years. Younger individuals had more awareness and it could be due to more media exposure by the younger generation. There is a significant difference between gender and awareness of healthcare rights ($p=0.18 <0.05$). This indicates that the awareness among female (65.7%) was good compared to males. These findings do not coincide with the study by Ananthapriya, 2014 where results revealed that male caregivers had relatively more awareness than the female caregivers. The findings of this study coincide with study conducted among the ayurvedic doctors revealed that among 30, majority of participants i.e. 25 were not aware of the rights of mentally ill person only 2 of them are having highly adequate level of knowledge (Nagarajaiah & Vijayarani, 2009)²².

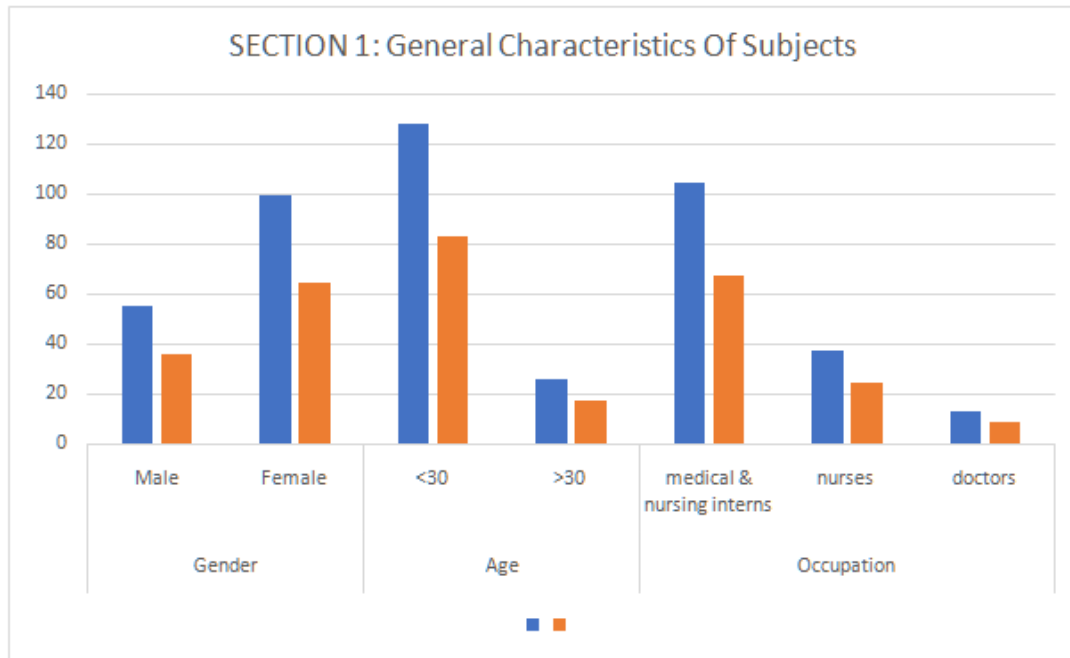
Section 2: The respondents were assessed on their awareness regarding the general rights of the mentally ill. The association between demographics and awareness is also presented below.

The respondents had 65.09% of awareness of the existing human rights for the mentally ill in place and this also is seen in contrast with the studies by Jagannathan and Rao, 2015 whose results showed though knowledge was satisfactory, it was not comprehensive enough to propagate it to others. Mainly in the domains like personal needs, communication, hospital stay and violation practices needed to be improved.

Insert Table 2: The above table shows that there is no significant difference between age and awareness of general rights ($p=0.5 >0.05$); gender and awareness of general rights ($p=0.1 >0.05$). There is a significant difference between occupation and awareness ($p=0.00 <0.05$). This indicates that the awareness among doctors

was good (84.6%) than nurses, medical and nursing interns. In relation to this finding a study conducted on nurses in Karad, by Chendake et.al,²³ showed that 85%

of the nursing students had average knowledge and 15% had poor knowledge regarding the human rights of mentally ill.



(blue: count, red: %)

Fig 1: General Characteristics of Subjects

Table 1: Association of demographics with awareness of healthcare rights of mentally ill

Demographic variables		Awareness of healthcare rights of mentally ill			
		Poor	Moderate	Good	
Occupation	Medical & Nursing interns	6.7%	31.7%	61.5%	Fisher's Exact test p=0.300
	Nurses	0.0%	35.1%	64.9%	
	Doctors	0.0%	53.8%	46.2%	
Age	<30	5.5%	28.9%	65.6%	Chi square test p=0.004
	>30	0.0%	61.5%	38.5%	
Gender	Male	10.9%	36.4%	52.7%	Fisher's Exact test p=0.018
	Female	1.0%	33.3%	65.7%	

Table 2: Association between demographics & awareness of general rights of mentally ill

Demographic variables		Awareness of rights of mentally ill			
		Poor	Moderate	Good	
Occupation	Medical & Nursing interns	7.7%	57.7%	34.6%	Fisher's Exact test p=0.00
	Nurses	13.5%	78.4%	8.1%	
	Doctors	0.0%	15.4%	84.6%	
Age	<30	8.6%	60.9%	30.5%	Chi square test p=0.532
	>30	7.7%	50.0%	42.3%	
Gender	Male	9.1%	49.1%	41.8%	Chi square test p=0.149
	Female	8.1%	64.6%	27.3%	

Conclusion

This study emphasis on educating the healthcare providers about human rights of mentally ill by investigating the awareness of human rights among them. As per the study findings. the level of awareness of the different aspects pertaining to the human rights of mentally ill was less than 80%. Indeed, there is a strong need to educate the healthcare professionals by conducting training programs about the human rights of mentally ill and their protection. So, that the stigma towards the mentally ill from the society can be removed with making it even more imperative to treat all humans equally regardless of the disease condition.

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References

- World Health Organization. Investing in mental health. 2003. WHO, Geneva. [cited 2017 Jan 15] Available from: http://www.who.int/mental_health/media/i_nvestingmnh.pdf
- Channabasavanna SM, Murthy P. The national human rights commission report 1999: a defining moment. *Mental health: An Indian perspective 1946–2003*. 1946:108-12.
- World Health Organization. Mental Health, Human Rights & Legislation. WHO Geneva. [cited 2017 Jan 15]. Available from: http://www.who.int/mental_health/policy/legislation/policy/en/
- Vijayalakshmi P, Ramachandra, Reddemma K, Math SB. Perceived human rights violation in persons with mental illness: Role of education. *International journal of social psychiatry*. 2013 Jun;59(4):351-64.
- Prasad MN, Theodore DD. Knowledge of nursing students regarding human rights of mentally ill. *Asian Journal of Nursing Education and Research*. 2016 Apr 1;6(2):151.
- Nagaraja D. Chairpersons desk. Sovenir: second international conference of ISPN, NIMHANS, Bangalore, Human Rights in Mental Health Nursing Practice, (2009) 4
- Sharma S, Chadda RK. Mental hospitals in India: Current status and role in mental health care. Institute of Human Behaviour and Allied Sciences; 1996.
- Freeman M, Pathare S. WHO resource book on mental health, human rights and legislation. World Health Organization; 2005.
- Human Rights of Mentally Ill Persons. [Last accessed on jan 22, 2017]. Available www.LegalServiceIndia.com. database on the Internet.
- Gadit, A. A. M. Abuse of mentally ill patients: Are we ignoring the human rights principle? *Journal of the Pakistan Medical Association*, (2008). 58(9), 523–524.
- NIMHANS, Nagaraja, D., & Murthy, P. *Mental Health Care and Human Rights*, (2008) 470.
- IANS. In India, mentally ill are treated as prisoners, not as patients. *The New Indian Express*. [Last accessed on January 22, 2017]. Available at [http://www.wcsarchive.org:8081/MediaArchive/libertynsf/\(docid\)/17E050063CFFC470E5256B5900184A8E](http://www.wcsarchive.org:8081/MediaArchive/libertynsf/(docid)/17E050063CFFC470E5256B5900184A8E).
- Sharma S. The Indian institutional mental care experience. *Curr Opin Psychiatry*. 2003;16:547.
- Kakuma R, Minas H, van Ginneken N, Dal Poz MR, Desiraju K, Morris JE, Saxena S, Scheffler RM. Human resources for mental health care: current situation and strategies for action. *The Lancet*. 2011 Nov 11;378(9803):1654-63.
- LundvikGyllensten A, Svensson B, Björkman T, Eklund M, Hansson L, Östman M, Leufstadius K, Bejerholm U, Brunt D, Markström U, Sandlund M. Attitudes in healthcare students towards mental illness-A pre-and post multicenter university program survey.
- Jyothi, N. U., Bollu, M., Ali, S. F., Chaitanya, D. S., & Mounika, S. A Questionnaire Survey on Student's Attitudes towards Individuals with Mental Illness, (2015). 7(7), 393–396.
- Jagannathan, A., & Vn, R. Knowledge about Human Rights of Persons with Mental Illness in India: A Pilot Cross-Sectional Study, (2015). 2(1), 7–9.
- Bradley VJ, Sahakian BJ. Human Rights-Based Approaches to Mental Health: A Review of Programs. *Health and human rights*. 2016 Jun;18(1):263-76.
- Ananthapriya. Compare the awareness about Human rights of mentally ill among the Male and Female caregivers of patients diagnosed with psychiatric disorders

20. Yang, A. J. Human rights awareness of people with mental disorders among mental health workers, (2013).7(1), 83–94.
21. Thapa K, Samson VW. A study to assess the knowledge and attitude of staff nurses regarding human rights of mentally ill patients at selected hospitals of Bangalore, India. *Journal of Kathmandu Medical College*, 2017 Jan.-Mar., Vol. 6, No. 1, Issue 19, 27-31
22. Nagarajaiah, M Vijayarani. (2009). Issues and concerns in human rights of mentally ill person-nursing perspective. *SOUVENIR: Human rights in mental health nursing*. October 66.
23. Chendake, M., Mohite, V. R., Gholap, M., Naregal, P. M., & Hiremath, P. (2014). A Study to Assess the Knowledge Regarding Human Rights of Mentally Ill among Post Basic B. Sc. Nursing Students in Krishna Institute of Nursing Sciences, Karad. *International Journal of Health Sciences and Research (IJHSR)*, 4(10), 164-171.

Added Effect of Deep Breathing and Diaphragmatic Breathing Exercise in Upper Abdominal Surgery Patients: A Randomised Clinical Trial

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Abstract

“Added Effect of Deep Breathing and Diaphragmatic Breathing Exercise in Upper Abdominal Surgery Patients: A Randomised Clinical Trial”

Background: PPC complication like atelectasis is, reduced lung capacity, secretions, etc. are the most common complications seen in the patients undergoing upper abdominal surgery patients. Literature suggests that deep breathing and diaphragmatic breathing exercise is effective in reducing these complications.

Aim: To evaluate the added effect of deep breathing and diaphragmatic breathing exercise in upper abdominal surgery patients.

Method/Design: Thirty six patients with upper abdominal surgery were randomised into 3 groups by block randomization opaque sealed envelope method. Group A, B and C were given diaphragmatic breathing, deep breathing and combined deep and diaphragmatic breathing exercises respectively. Outcomes were taken on post-operative day 2 and day 7 for pulmonary function test (FVC, FEV1), chest expansion measurement with inch tape, and AMPAC6-click scale.

Results: Between the groups analysis using ANOVA showed that there was no significant difference between the groups in pre-and post-values (>0.05). Within the group analysis using paired t- test showed a significant difference ($p<0.05$) in the pre-and post-values of chest expansion measurement and AMPAC scale but not in pulmonary function test.

Conclusion: We concluded that combine application of diaphragmatic breathing and deep breathing exercise did not yield a statistically significant improvement but diaphragmatic breathing and the deep breathing exercise can be given individually. This gave a significant improvement in the post-operative pulmonary complication in the upper abdominal surgery.

Keywords: *Respiratory physiotherapy, abdominal surgery, pulmonary function, deep breathing, pulmonary complications, physiotherapy.*

Introduction

Globally 234 million patients undergo surgery yearly. [1-3] The world bank in 2002 reported 164 million disability-adjusted life years, out of which 11% disease has to be treated surgically. Surgery is performed in all aspects of the body. [2,4] “Surgical removal of mass or masses from the abdomen by the abdominal incision is called as laparotomy.” [1] Exploratory laparotomy is a method of opening of the abdominal cavity and

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examining of its contents, for example, to obtain a source of bleeding or injury, etc.^[1]

Post-operative pulmonary complication (PPCs) can be defined as “pulmonary abnormalities occurring in the post-operative period, producing clinically significant identifiable disease and dysfunction that adversely affect the clinical course.”^[1,5] Incidence of PPC is 35%. General anaesthesia directly affect the respiratory system causing PPC.^[6-8] It causes temporary Phrenic nerve dysfunctions^[9] and shallow monotonous breathing pattern. Which will decrease in ventilation in the lower zone of the lungs.^[5] The incision pain further reduces the ventilation.^[4] All these factors will contribute to impaired respiratory function, exacerbate mucociliary clearance, depresses cough reflexes thus causing secretion retention resulting in atelectasis, which will lead to reduced lung functions and lung volumes.^[7,8,10]

Breathing exercise is defined as “the therapeutic intervention by which purposeful alteration of a given breathing pattern is categorized as breathing exercises outcomes.” Different techniques of treatments were percussion, clapping, vibration, diaphragmatic breathing exercise, incentive spirometry and so on. They include different forms of breathing exercise like diaphragmatic breathing exercise, deep breathing exercise (DBE), ACBT, etc.^[9-13]

Anaesthesia will significantly reduce vital capacity, the expiratory flow rate which will lead to decrease pulmonary reserve. Thus, Diaphragmatic breathing is used to regulate the movement of the diaphragm while inhalation and exhalation^[14] causing reduction in work of breathing, improve alveolar ventilation, improve airway clearance by improving cough and also improves the strength of the respiratory muscle. An RCT study done by Alaparathi GK et al. found that volume IS and diaphragmatic breathing exercise can be given as an intervention for all patients in the management of laparoscopic abdominal surgery.^[11]

Thoren et al. conducted the first study showing the effects of DBE on PPC in abdominal surgery patients. DBE with end-inspiration hold concentrates on reducing atelectasis, increases lung volume and facilitates secretion elimination and improving the gaseous exchange.^[15] Slow inspiration helps in improving basal ventilation by proper distributions of air to the lower lobes of the lungs, end inspiration hold for 2-6 sec may help to reduce airway collapse and revert atelectasis.^[16,17]

From the literature, as mentioned earlier, it is clear that the conclusion of these studies has been conflicting, and this may contribute to a varied pattern of practices and the use of breathing exercise for the patient with upper abdominal surgery. Hence there is a scarcity of literature on the combined effect of diaphragmatic breathing and DBE. Therefore, this study has been taken up to find out the combined effect of diaphragmatic breathing and DBE on upper abdominal surgery patients.

Materials and Method

Current study was a prospective randomised clinical trial carried out in the Surgery department of Tertiary Hospital of India between May 2018 to April 2019. Thirty-six patients, 23 males and 13 females undergone upper abdominal surgery were recruited. After obtaining the ethical clearance from the Institutional Ethical Committee (figure 1), the trial was registered in the Clinical Trial Registry of India (CTRI/2018/06/014443) and an informed consent was taken from the patients. Patients who were above the age of 18 years, undergoing any upper abdominal surgery were included with VAS score <5, no previous history of cardiac and pulmonary complications and non-obese individual (body mass index > 27 kg/m²). The patients were excluded if they have hemodynamic instability, required ICU care for more than 48 hours, require mechanical ventilation.

Procedure: The patient allotment was done by block randomisation with opaque sealed envelope method into 3 groups Group A, Group B, Group C.

- **Group A** was given diaphragmatic breathing
- **Group B** was given DBE
- **Group C** was given the combine of both

All the groups were given 4-6 cycles of the breathing exercise per hourly for 8 working hours a day for 7 days of the week and early mobilisation exercises which included ankle toe movements, heel slides, bed side sitting, ambulation and stair climbing.^[11]

Outcome: Blinded assessor took the outcome measures pre-treatment on POD 2 and post treatment on POD 7. The outcome measures were pulmonary function test (PFT) values forced vital capacity (FVC) and forced expiratory volume at first sec (FEV1). The FVC evaluate the vital capacity of the lungs on forceful expiration and FEV1 will help to evaluate the volume of air breath out during the first second of the expiration,^[18] chest

expansion measurement with inch tape for upper lobe at axillary level, middle lobe at 4th intercostal and xiphoid process for lower lobe, [1] Activity Measure for Post-Acute Care (AM-PAC) “6-Clicks”. It has 2 short forms

- Inpatient Daily Activity Short Form
- Inpatient Basic Mobility Short Forms.

It measures 2 functional domains that are essential mobility, daily activities. [19]

Statistical Analysis: Statistical analyses were performed using SPSS version 16.0. The test of ANOVA was used to compare pre-test and post-test values of the outcome measures for between the group analysis. Within the group analysis was performed using paired t-test. The p value < 0.05 was considered to be statistically significant.

Results

There was no significant difference ($p > 0.05$) seen in all three groups when they were analysed for the baseline data (Table 1) which showed that the groups were homogeneous.

When all the three outcome measures pre-and post-values were compared for between the groups analysis, there was no significant improvement seen between the groups. All the groups showed equally better improvement which was observed when intergroup comparison was performed (Table 2).

On comparison of within the group analysis of each group showed statistically significant improvement in the chest expansion measurement and the AMPAC scale ($p < 0.05$). But there was no improvement observed in the pulmonary function test outcome (Table 3).

Table 1: Baseline data of age and gender of all the groups

Groups		(Group A)	(Group B)	(Group C)	P-Value
Age		49.16 ± 19.06	48.16 ± 11.13	56.33 ± 16.90	0.407
Gender	Male	7	8	8	0.887
	Female	5	4	4	

Table 2: Between the group comparison of all the groups for each outcome measures

Outcome	Groups	(Group A)	(Group B)	(Group C)	P-Value
PFT	FVC - PRE	2.4650 ± 0.20487	2.4842 ± 0.16373	2.4842 ± 0.16279	0.33
	FVC_POST	2.4791 ± 0.23	2.5142 ± 0.16	2.5245 ± 0.17	
	FEV1 – PRE	2.4 ± 0.2	2.4 ± 0.16	2.3 ± 0.16	0.36
	FEV1-POST	1.58 ± 0.30	1.61 ± 0.16	16.6 ± 50.18	
Chest Expansion Measurement	At Axillary Level Pre	0.80 ± 0.23	0.94 ± 0.44	0.88 ± 0.19	0.88
	At Axillary Level Post	1.46 ± 0.36	1.67 ± 0.41	1.50 ± 0.33	
	At 4 th Ntercostal Pre	1.4 ± 0.61	1.53 ± 0.57	1.50 ± 0.47	0.44
	At 4 th Intercostal Level Post	2.18 ± 0.57	2.29 ± 0.44	2.15 ± 0.44	
	At Xiphisternal Level Pre	2.08 ± 0.29	2.10 ± 0.69	2.15 ± 0.68	0.76
	At Xiphisternal Level Post	2.79 ± 0.62	3.14 ± 0.56	3.02 ± 0.73	
AMPAC 6 CLICK	AMPAC – IDA PRE	6.00 ± 0.00	6.25 ± 0.85	6.08 ± 0.28	0.76
	AMPAC – IDA POST	18.90 ± 2.07	19.50 ± 2.23	19.36 ± 2.01	
	AMPAC – IBM PRE	6.08 ± 0.28	6.00 ± 0.00	6.05 ± 0.23	0.6
	AMPAC – IBM POST	19.63 ± 2.37	20.50 ± 2.93	20.54 ± 2.73	

Table 3: Within the group comparison of all the three groups for all the outcome measures

Outcome	Group A		Group B		Group C	
	Mean & Std. Deviation	P-Value	Mean & Standard Deviation	P-Value	Mean & Std. Deviation	P-Value
AMPAC IDA PRE	6.0 ± .00	.047	6.25 ±.86	.003	6.09 ±.30	.045
AMPAC IDA POST	18.90 ± 2.07		19.50 ±2.23		19.63±2.01	
AMPAC IBM PRE	6.090 9 ± 0.30	.047	6.0 ±.00	.003	6.09±.30	.043
AMPAC IBM POST	19.63 64 ±2.37		20.50 ± 2.93		20.54±2.73	
XIPHISTERNAL_ LEVEL PRE	2.045 5 ±.61	.000	2.10 ±.65	.015	2.33±.84	.000
XIPHISTERNAL_ LEVEL POST	2.790 9 ±.62		3.14 ±.56		3.02±.73	
NIPPLE LEVEL PRE	1.427 3 ±.62	.000	1.53 ±.57	.003	1.52±.50	.000
NIPPLE_ LEVEL POST	2.181 8 ±.57		2.29 ±.44		2.15±.44	
AXILLA LEVEL PRE	.7727 ±.21	.000	.94 ±.44	.008	.81±.19	.008
AXILLA_ LEVEL POST	1.463 6 ±.36		1.67 ±.41		1.50±.33	
FVC PRE	2.460 0 ±.21	.153	2.48 ±.16	.339	2.37±.16	.042
FVC_ POST	2.479 1 ±.23		2.51 ±.16		2.52±.17	
FEV1 PRE	1.470 9 ±.21	.113	1.51 ±.15	.283	1.47±.30	.961
FEV1_ POST	1.584 ±.30		1.61 ±.16		16.68±50.18	

Discussion

This randomised clinical trial was designed to evaluate the added effect of deep breathing and diaphragmatic breathing exercise in the upper abdominal surgery patients. Between the group analysis showed no significant difference. These findings were rationalised by a systematic review and meta-analysis done by T. Samantha et al.^[8] Different studies evaluated the outcome measures which included pulmonary function test values. On analysing their between the group comparison showed no difference in 3 studies, 2 studies showed improvement in only few of the parameters out of 6. The FVC values only showed significant improvement. The possible reason given by the author is the methodological limitation, lack of well-defined studies which hindered their results. Another systematic review by Pasquina P. et al.^[9] included 35 trials, out of which 13 trials gave no intervention to the control group from which 9 studies did not show significant difference between the groups in PFT. This study states an unclear use of PFT and also no evidence of improvement in their parameters with any of the tested physiotherapy treatment.

In the present study, there was no significant improvement found in the PFT when within the group analysis was done. This finding correlates with the findings of the Manzano RM. et al.^[7] who evaluated the

PFT values and found no significant difference in the groups suggesting that the results were not achieving because the patients were not able to produce the best or even moderate efforts to fulfil their pulmonary capacity and produce maximum forced expiration and the post-operative pain in the suture site which hinders them to breathe to their maximum capacity.

A RCT done by Alaparthi GK. et al.^[11] proved controversial where 260 patients were randomised into 4 groups. The outcome measures used were PFT, diaphragm excursion with ultrasound. The FVC, FEV1, PEFR and diaphragm excursion within the groups showed a significant improvement in all the groups and on between the group comparison, diaphragm excursion and FVC showed less significant difference than the control group. The possible reason for the decrease is the post-operative pain, the anaesthesia and analgesic usage. This improvement was visible in the present study when diaphragmatic breathing exercise was given individually to the patients.

Another study done by Tripathi S. et al.^[17] showed a significant improvement in the respiratory rate and values of the PFT. The practice of the deep breathing exercise increases the lungs capacity which was depicted by the results in the study. The result of the current study is in accordance with the study stated above when individual DBE was given and showed significant improvement.

Conclusion

From the study conducted we draw a conclusion that the breathing exercise like diaphragmatic breathing and DBE can be given individually with the conventional early mobilisation technique. This will yield a significant improvement in the post-operative pulmonary complication following the upper abdominal surgery.

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Source of Funding: Self

References

- Shingavi S, Kazi A, Gunjal S, Lamuvell M. Effects of Active Cycle of Breathing Technique and Autogenic Drainage in Patient with Abdominal Surgery. *International Journal of Applied Research*. 2017;3(2):373-376.
- Bhasin S, Roy R, Agrawal S, Sharma R. An Epidemiological Study of Major Surgical Procedures in an Urban Population of East Delhi. *Indian Journal of Surgery*. 2010;73(2):131-135.
- Patel K, Hadian F, Ali A, Broadley G, Evans K, Horder C, et al. Postoperative pulmonary complications following major elective abdominal surgery: a cohort study. *Perioperative Medicine*. 2016;5(1):1-7.
- Tadyanemhandu C, Mukombachoto R, Nhunzvi C, Kaseke F, Chikwasha V, Chengetanai S, et al. The prevalence of pulmonary complications after thoracic and abdominal surgery and associated risk factors in patients admitted at a government hospital in Harare, Zimbabwe-a retrospective study. *Perioperative Medicine*. 2017;6(1):1-8.
- Nascimento P, Módolo N, Andrade S, Guimaraes MMF, Braz LG, Dib RE. Incentive spirometry for prevention of postoperative pulmonary complications in upper abdominal surgery. *Cochrane Database of Systematic Review* 2014, Issue 2. Art. No.: CD006058. DOI: 10.1002/14651858.CD006058.pub3.
- Kodra N, Shpata V, Ohri I. Risk Factors for Postoperative Pulmonary Complications after Abdominal Surgery. *Open Access Maced J Med Sci*. 2016;4(2):259-263.
- Manzano R, Carvalho C, Saraiva-Romanholo B, Vieira J. Chest physiotherapy during immediate postoperative period among patients undergoing upper abdominal surgery: randomized clinical trial. *Sao Paulo Med J*. 2008;126(5):269273.
- Grams S, Ono L, Noronha M, Schivinski C, Paulin E. Breathing exercises in upper abdominal surgery: a systematic review and meta-analysis. *Rev Bras Fisioter*. 2012;16(5):345-353.
- Pasquina P, Tramér M, Granier J, Walder B. Respiratory Physiotherapy To Prevent Pulmonary Complications After Abdominal Surgery. *Chest*. 2006;130(6):1887-1899.
- Patman S, Bartley A, Ferraz A, Bunting C. Physiotherapy in upper abdominal surgery – what is current practice in Australia?. *Archives of Physiotherapy*. 2017;7(1):1-11.
- Alaparathi G, Augustine A, Anand R, Mahale A. Comparison of Diaphragmatic Breathing Exercise, Volume and Flow Incentive Spirometry, on Diaphragm Excursion and Pulmonary Function in Patients Undergoing Laparoscopic Surgery: A Randomized Controlled Trial. *Minimally Invasive Surgery*. 2016;2016:1-12.
- Dias CM, Placido TR, Ferreria MF, Guimarães FS, Menezes SLS. Incentive Spirometry and Breath Staking: Effects on the Inspiratory Capacity of Individuals Submitted to Abdominal Surgery. *Rev Bras Fisioter*. 2008;12(2):94-99.
- Solomen S, Aaron P. Breathing techniques- A review. *International Journal of Physical Education, Sports and Health*. 2015;2(2):237-241.
- Frownfelter D, Dean E. Principles and practice of cardiopulmonary physical therapy. 4th ed. St. Louis: Mosby-Year Book;1996.
- Tripathi S, Sharma R. Deep Breathing Exercise and its Outcome among Patient with Abdominal Surgery: A Pilot Study. *International Journal of Nursing Science*. 2017;7(5):103-106.
- Westerdahl E. Optimal technique for deep breathing exercises after cardiac surgery. *Minerva Anesthesiol*. 2015;81:678-683.
- Thomas J, McIntosh J. Are Incentive Spirometry, Intermittent Positive Pressure Breathing, and Deep Breathing Exercises Effective in the Prevention of Postoperative Pulmonary Complications After Upper Abdominal Surgery? A Systematic Overview and Meta-analysis. *Physical Therapy*. 1994;74(1):3-10.

18. Miller M, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. *European Respiratory Journal*. 2005; 26(2):319-338.
19. Jette D, Stilphen M, Ranganathan V, Passek SD, Frost FS, Jette AM. Validity of the AMPAC “6-Clicks” Inpatient Daily Activity and Basic Mobility Short Forms. *Physical Therapy*. 2013; 94(3):379-391.

A Review Study on Pharmaceutical Inventory Management & Store Keeping Practices of Pharmacy in Rural Hospitals

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Abstract

Background: In pharmacy operations, inventory is referred to as the stock of pharmaceutical products retained to meet future demand. Inventory represents the largest asset in pharmacy practice, and its value continues to rise because of the growth in variety and cost pharmaceutical products. From both financial and operational perspectives, efficient inventory management plays a great role in pharmacy practice.

Ensuring medicines availability is an important goal for health system as medicines are an important building block in the health system. Essential medicines are defined by the WHO as those medicines which respond to the most pertinent health needs of a population. These medicines are the foundation for most public health programmes that are aimed at reducing morbidity and mortality. WHO states that essential medicines should be available at all times. The consequences of medicine unavailability are widespread and can have detrimental effects on individual and public. Unplanned treatment interruptions could lead to an increase in resistance for example to antimicrobials and antivirals which can have the ripple effect of switching to more costly treatment and interventions. Patients may have to travel to alternative facilities including the private sector facilities to source medicines. This may be costly and becomes a barrier to accessing medicines. Therefore to ensure uninterrupted availability of medicines, inventory management system of medicines has been upgraded from paper based to computer and web-based system.

Keywords: Inventory control, Pharmacy security, Drug procurement, Inventory management, Drug tracking, Drug storage, ABC and VED.

Introduction

Pharmacy inventory management is a complex but critical process within the healthcare delivery system. Without adequate pharmacy inventory management practices, hospitals run the risk of not being able to provide patients with the most appropriate medication when it is most needed. Additionally, pharmacies

dispensing patterns and drug selection choices may have a direct effect on the affordability of care¹. In addition to patient safety & financial considerations, stringent regulatory requirements pertaining to drug traceability, inventory management elevate the importance of maintaining effective control over drug inventories in today's ever expanding healthcare compliance environment. Pharmacies can control a number of factors within the pharmacy inventory management & pharmacy revenue cycles that can support better outcomes for patients and enhance the bottom line for facilities. This provides perspectives on leading practices & internal controls pertaining to :- procurement, tracking system, traceability, storage, disposal of drugs etc.³. These control mechanisms can provide a basis for consistent quality, better financial performance & improved regulatory compliance when implemented appropriately and adhered to during day-to-day operations.

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Pharmacy Revenue Cycle: It typically includes the following areas: pharmacy purchasing data, dispensing transactions, charge description master(CDM), pharmacy charges & patient billing. The amount of inventory a pharmacy carries may have a significant financial impact given that a drug resting in inventory has minimal payment(reimbursement value until it is dispensed. Mismanagement & discarding of expired medications has a potentially costly impact . An inventory tracking system that interfaces appropriately with the billing system facilitates an effective pharmacy revenue cycle & revenue integrity program⁵.

Pharmacy Security: A pharmacological as well as the location of the drugs it houses should be restricted through physical access controls. Entrances to pharmacies should now be restricted by either badge access readers or biometric readers. Individuals who are able to enter the pharmacy should be limited to only licensed professionals who acquire access such as pharmacists, technicians, pharmacy & pharmacy director. Cameras & alarm system should exist in order to monitor the access in & out of the pharmacy on a continual basis⁸.

Drug Procurement:- Drug costs make up an increasing percentage of healthcare expenses. Proper management of drug procurement is essential for addressing cost & promoting patient safety & quality care. To ensure pharmacy procurement activities are operating appropriately, formal procurement procedures are to be followed. They should be designed to promote safety & efficacy for drug purchases & should include cost containment techniques such as practicing competitive bidding to secure optimal drug pricing⁴.

Drug receipt & storage:- Drugs received & stored in a pharmacy can be placed in inventory through a no. of avenues when drugs are received, before placing them in to inventory. Pharmacy personnel should perform appropriate receipt procedures such as reconciling drugs received to drugs ordered, to ensure that discrepancies between quantity & drug type don't exist. Once the drugs received have been verified, they should be physically maintained in secure storage areas or active dispensing areas of the pharmacy. Drug storage should include the use of automated dispensing devices. Controlled substances require additional storage security to prevent any unauthorized access. Temperature can be important factor in maintaining & storing drugs to ensure their quality & integrity. Many drugs (eg.vaccines) require storage in climate controlled environments such as a

refrigerator with specific temperature ranges²⁹.

Drug tracking & inventory management:- Effective & tracking systems that allow pharmacies to accurately record inventory components such as medication expiration dates & physical quantities also have the potential to reduce adverse patient outcomes. The “real time” tracking ability offered through these systems includes recommending items & quantities to be ordered based on par levels set by the pharmacy in the system, providing limits on excessive orders & electronically placing orders after a manual authorization when setting the par levels for the automated ordering, it is important to set appropriate levels to maximize the ordering process & minimize excessive supplies⁸.

A pharmacy's inventory represents its single, largest investment .Consequently no other asset has the potential to devastate a pharmacy as much as poorly controlled inventory .In an average pharmacy, cost of goods sold account for approximately 68% of total expenditures .For every 1% change in an average pharmacy's cost of goods, profits may increase or decrease by slightly more than 20%. Thus, the inventory control matters of great importance to both cashflow & profitability⁶.

The objective of inventory control system is to make inventory decisions that minimize the total cost of inventory. This is not to beconfusive with minimizing inventory. It is often more expensive in a pharmacy to run out of an item than to simply keep more units in stock.

For example, in a retail pharmacy if a customer is unable to obtain their medication, they may go somewhere else and the pharmacy may lose future purchases. In a hospital pharmacy if we run out of an item, we might be required to obtain it by a more expensive method (over-night deliverey). Most pharmacy inventory decisions involve replenishment system i.e. how much to order & when to order. In this course, we will look at several models for minimizing the total cost of inventory,including the popular method of Economic Order Quantity(EOQ). This particular method attempts to balance the carrying cost inventory with the cost of running out²⁸.

Purchasing Concepts:

ABC classification system: The ABC classification system group items according to annual sales volume, in an attempt to identify the small number of items that

will account for most of the sales volume & that are the most important ones to control for effective inventory management³².

VED Analysis: It stands for Vital Essential Desirable, takes a qualitative approach. VED analysis encourages us to divide inventory in to three groups: vital items, essential items are those without which healthcare set-up can function but the quality, speed or cost of service will be damaged. Unavailability of desirable items will not affect the functioning of the healthcare set-up but may incur minor costs or short-term disruption²⁰.

Five steps to do VED Analysis:

- i. First draw up a list of every non-trivial item our healthcare centre has ordered multiple times in the past 1-5 year.
- ii. Assemble a panel of experts from the healthcare centre. It's absolutely critical that this panel is representative of every area and every level of your organization. Which inventory is vital is dependent on perspective, so there needs to be someone present who can make a fair case for each department.
- iii. Set an agreement threshold -50% is generally a good starting point. That means if 50% of votes agree, the item is placed in that.
- iv. Have the panel discussion and vote on a category for each item.
- v. If any items fail to reach the 50% threshold then they will require further discussion until an agreement is reached. We might also want to define a failure option, which will usually be an executive decision by senior management, if a category simply can't be agreed upon⁵.

Method

Peer reviewed articles published in English were searched for on the availability & inventory control techniques of medicines and medicine stock management common used databases for public health and medicine which include PubMed, EBSCOHost, Google Scholar, Scopus and Cochrane. Articles from the past three decades were considered. The identified articles were analysed for relevance. This was identified by searching through websites WHO, IPHS and google. A review template was developed to extract information from the literature identified for the structured literature review.

Discussion

Compared to the set-up of the health-care located at the urban areas, the condition of PHCs in the rural areas are compromised. Every PHC should have a separate location for storing drugs & other medical supplies and it is called the main drug store. The main purpose of managing a store is to cater the needs of receiving, holding & dispatch stock. With the advent of essential drug concepts, essential medicines defined by WHO as well as by IPHS need to be dispensable at the PHCs. Therefore, drugs need to be available and accessible whenever required in all appropriate dosage forms. Medicine supply management in health systems occur at more than one level and the factors that influence this at the health facility may not always stem from the health facility itself. However, studies have reported that some health facilities may have medicine shortages even though the stock is available at the central level which supplies them with medicines. There is a lack of research that has been carried out at health facility levels such as PHC clinics exploring the processes at the facility and how these may be linked to the occurrence of medicine stock outs levels especially in the lower income settings. The absence of medicines i.e. stock-outs at these levels should be prioritized. The factors that contribute the most of the occurrence of stock-outs of medicines at the facility level include inadequate health workforce particularly pharmacy personnel. Poor medicine stock management and inefficient communication between suppliers, depots and health facilities.

Conclusion

A considerable amount of research has been conducted in the area of medicines availability particularly to determine what the likely causes of unavailability are. It is known that the causes of medicines unavailability are mostly embedded in the medical supply systems, particularly in the procurement and distribution of medicines. Non-existent or poor stock control including poor forecasting are the major causes of stock-outs and shortages reported in literature at the health facility level when stock is available at the central or depot level and it is very important to continually assess and improve medicine stock management at the health facility level to ensure uninterrupted access medicines for patients at these facilities. This involves incorporation of standardized strategic methodology with Information and Communication Technology interventions in processes dealing with pharmaceutical purchasing,

selection, quantification, distribution, management of human resource and inventory management.

Ethical Clearance: Not Applicable as secondary data analysis was carried out.

Source of Funding: Self-funding.

Conflict of Interest: Nil.

References

1. Monica Balakrishnan Kokilam, Harish Ganesh Joshi, Veena Ganesh Kamath. Assessment of Pharmaceutical Store and Inventory Management in Rural Public Health Facilities:- a study with reference to Udupi District, Karnataka. *Pharm Method*,2015;53-9.
2. Geetha Mani, Kalaivani Annaduri, Raja Danasekera, Jagadeesh Ramasamy D. Drug Inventory control analysis in a Primary level Health care facility in Rural Tamil Nadu, India. *Healthlinep* ISSN December 2014; 5(2): 2320-1525.
3. Bhatnagar A. Textbook of Public Health and Community Medicine. First edition. Pune. Department of Community Medicine, Armed Forces Medical Colleges, Pune in collaboration with WHO, India Office, New Delhi, 2009; p335.
4. Devnani M. Gupta AK, Nigah R. ABC and VED Analysis of the Pharmacy Store of a Tertiary Care Teaching, Research and Referral Healthcare Institute of India. *J Young Pharm*.2010;2(2):201-205.
5. Gupta R, Gupta KK, Jain BR, Garg RK, ABC and VED Analysis in Medical Stores Inventory; *MJAFI*; 2007;63:325-327.
6. Khurana S, Chillar N, Gautam VKS. Inventory control techniques in medical stores of a Tertiary care neuropsychiatry hospital in Delhi. *Health* 2013;5(1):8-13.
7. Junita I, Sari RK. ABC-VED Analysis and Economic Order Interval (EOI)- Multiple items for Medicines Inventory Control in Hospital. Presented in The 2012 International Conference on Business and Management, 2012, September 6-7.
8. USAID Deliver Project. (2013). Addressing Procuring Bottlenecks: A Review of procurement Bottlenecks in Public Sector Medicine Supply Chains and Practical Approaches Taken to Resolve Them. U.S. agency for International Development.
9. A.T. Kearney Inc. (2004). Improving the Medicine Supply Chain. An Imperative for public Health care.
10. Management Sciences for Health.(2012).MDS-3:Managing Access to Medicine and Health Technologies.
11. L. Kohn, J Corrigan and M. Donaldson, To err is human: building a safer health system: National Academy Pr.,2000.
12. P.S. Landry and R. Philippe, 4U2C or how logistics can service healthcare. *Ecole des Hautes Commerciales, Montreal, Quebec*,2002.
13. N.H Mustaffa and A. Potter, "Healthcare supply chain management in Malaysia: a case study", *Supply Chain Management: An International Journal*, Vol. 14, No. 3, pp.234-243,2009.
14. F.J.Beier, "The management of the supply chain for the hospital pharmacies: a focus on inventory management practices", *Journal of Business Logistics*, Vol 16, No.2, pp.153-173,1995.
15. Kant S, Pandaw CS, Nath LM. A management technique for effective management of medical store in hospitals. *Medical store management technique. J Acad Hosp Adm*. 1996 and 1997;8 and 9:41-7.
16. Kunders GD, Gopinath S, Katakam A. In: *Hospitals: Planning, Design and Management*. New Delhi: Tata McGraw-Hill Publishing Company Limited; 2000. Planning and designing supportive services- Pharmacy; pp. 273-81.
17. Kidwai M. A report of inter-country course. New Delhi: National Institute of Health and Family Welfare; 1992. Inaugural address. Logistics and supply management for health and family planning programme; pp.66-70.
18. Pillans PI, Conry I, Gie BE. Drug cost containment at a large teaching hospital. *Pharmacoeconomics*. 1992;1:377-82.
19. Gupta S, Kant S. In: *Hospital stores management- An integral approach*. New Delhi: Jaypee Brothers Medical Publishers(P) Ltd; 2000. Inventory control; p. 60-72.
20. Ramanathan R. ABC inventory classification with multiple-criteria using weighted linear optimization. *Comput Oper Res*. 2006;33:695-700.
21. Das JK. Inventory Control. In: Kaushik M, Agarwal AK, Arora SB, editors. *Essentials of Logistics and Equipment Management, Manual of Post Graduate*

- Diploma in Hospital and Health Management. New Delhi: Indira Gandhi National Open University, School of Health Sciences; 2001.
22. Gopalakrishnan P, Sundaresan M. An integrated approach. New Delhi: Prentice Hall; 1985. Material management.
 23. Thawani VR, Turankar AV, Sontakke SD, Pimpalkhute SV, Dakhale GN, Jaiswal KS, et al. Economic analysis of drug expenditure in Government Medical College Hospital, Nagpur. *Indian J Pharmacol.* 2004;36: 15-9.
 24. Beier FJ. The Management of the supply chain for hospital pharmacies: A focus on Inventory management practices. *J Business Logistic.* 1995;16:153–77.
 25. Anonymous Anonymous. Supply Chain: Cost of goods grab executives' attention. *Health Facil Manage.* 2008;21 26-8,30,32.
 26. Duclos LK. Hospital inventory management for emergency demand. *J Supply Chain Manage.* 1993;29:29–38.
 27. Brown RB. New York: John Wiley and Sons; 1977. Materials management systems.
 28. Bhushan B, Gupta RS, Bharat B. Materials management system in central drug stores under Delhi Municipal Committee. *Health Popul Perspect Issues.* 1996;19:96–106.
 28. Gandhi P, Basur A. Application of ABC analysis in medical store of ESIC, Delhi. *Health Administrator.* 2000;9 and 10:90–5.
 29. Doshi RP, Patel N, Jani N, Basu M, Mathew S. ABC and VED analyses of drug management in a government tertiary care hospital in Kerala. *iHEA 2007, 6th World Congress: Explorations in Health Economics Paper.* 2007.
 30. Vaz FS, Ferreira AM, Kulkarni MS, Motghare DD, Pereira-Antao I. A Study of Drug Expenditure at a Tertiary Care Hospital: An ABC-VED Analysis. *J Health Manag.* 2008;10:119–27.
 31. Ammer DS. Bombay: D.B. Taraporevala Sons and Co. Pvt. Ltd; 1982. Materials management and purchasing.
 32. Sikdar SK, Agarwal AK, Das JK. Inventory analysis by ABC and VED analysis in medical stores depot of CGHS, New Delhi. *Health Popul Perspect Issues.* 1996;19:165–72.
 33. Gupta R, Gupta KK, Jain BR, Garg RK. ABC and VED analysis in medical stores inventory control. *Med J Armed Forces India.* 2007;63:325-7.
 34. Ramanathan R. ABC inventory classification with multiple-criteria using weighted linear optimization. *ComputOper Res.* 2006; 33(3): 695–700.
 35. Das JK. Inventory Control. In: Kaushik M, Agarwal AK, Arora SB, editors. *Essentials of Logistics and Equipment Managemnt, Manual of Post Graduate Diploma in Hospital and Health Management.* New Delhi: Indira Gandhi National Open University, School of Health Sciences; 2001.

The Effect of Circuit Training and Weight Training on Selected Physiological Variables and Running Performances among University Athletes

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Abstract

The purpose of the study was to find out the effect of circuit training and weight training on selected physiological variable among university athletes. To achieve the purpose of the present study, forty five (n=45) University athletes from Chennai, Tamilnadu, India were selected as subjects at random and their ages ranged from 18 to 21 years. The experimental group endured the training activities for 12 weeks with a schedule of six days whereas the control group remained with no activities. The subjects were tested prior to and after the experimentation on vo2 max. The obtained data from the experimental and control groups of initial and final readings were statistically analyzed with analysis of covariance (ANCOVA). To find out difference between experimental and control group at the level of significance was set at 0.05. It was proved that there was a significant difference existing on circuit training group on selected physiological variable among university athletes.

Keywords: *Circuit training, Weight training, Physiological, Experimental group, Control group.*

Introduction

Athletics is mostly an individual sport, with the exception of relay races and competitions which combine athletes performances for a team score, such as cross country. Organized athletics are traced back to the Ancient Olympic Games from 776 BC. The rules and format of the modern events in athletics were defined in Western Europe and North America in the 19th and early 20th century, and were then spread to other parts of the world. Most modern top level meetings are conducted by the International Association of Athletics Federations and its member federations. A variety of running events are held on the track which fall into three broad distance categories: sprints, middle-distance, and long-distance track events.¹ Relay races feature teams comprising four runners each, who must pass a baton to their teammate after a specified distance with the aim of being the first team to finish. Hurdling events and the steeplechase are a variation upon the flat running theme in that athletes must clear obstacles on the track during the race. The field events come in two types jumping and throwing

competitions. In throwing events, athletes are measured by how far they hurl an implement, with the common events being the shot put, discus, javelin, and hammer throw.² There are four common jumping events: the long jump and triple jump are contests measuring the horizontal distance an athlete can jump, while the high jump and pole vault are decided on the height achieved.³

Circuit training is a practical method entailing some preliminary planning, but beyond that, it needs co-ordination. Athletes find it motivating since it makes conditioning fun and challenging through competition against team mates.⁴ Circuit training is a continuous series of exercises attempting to improve as many components of physical fitness as possible especially endurance.

Weight training improves the muscle strength, power and endurance. Weight training mostly increases the size of muscle fibers. During this training the muscle protein content increases rapidly which involves in metabolic reactions. Strength training can be resulted in

hypertrophy of the muscle, partly through an enlargement of muscle fibers. In addition, training with high weight can change the fiber type distribution in the direction of faster twitch fibers. An improvement in muscular strength training through isolated movements seems closely related to training speeds.⁵ It was well established that weight training can enhance the force production capabilities of an older adult by increasing muscle mass or improving muscle quality (i.e., the force-generating capacity of individual muscle fibers). It was recommended that beginners start with 8 to 10 exercises for the major muscle groups with more repetitions thrice in a week. Before the weight training the doctor's suggestion for people who have overweight. This type of training needs the selection of right equipment and must be conditioned before the weights. Weight training can be used without recourse to the devices.⁶

Muscle strengthening is critically important for injury prevention, rehabilitation, and performance enhancement. Strength is the ability of the body, to withstand force. The development of strength involves exercising at various loads, modes, speeds, angles and frequencies. The combination of these variables dictates the outcome of the weight training programme.

Statement of the problem: The purpose of the study was to find out the effect of circuit training and weight training on selected physiological variables among university athletes.

Methodology

The purpose of the study was to find out the effect of circuit training and weight training on selected physiological variables among university athletes. To achieve the purpose of the present study, forty five University athletes from Chennai, Tamilnadu, India were selected as subjects at random and their ages ranged

from 18 to 21 years. The experimental groups endured the training activities for 12 weeks with a schedule of six days whereas the control group remained with no activities.

Test Administration of VO2 max

VO2 Max

Purpose: To measure the VO2 max level of the university athletes.

Equipment Required: Flat, non-slip surface, marking cones, 20m measuring tape, beep test audio, music player, recording sheets.

Procedure: This test involves continuous running between two lines 20m apart into the recorded beeps. For this reason, the test is also often called the 'beep & beep' or 'beep & beep' test. The participants stand behind one of the lines facing the second line, and begin running when instructed by the recording. The speed at the start is quite slow. The subject continues running between the two lines, turning when signaled by the recorded beeps. After about one minute, a sound indicates an increase in speed, and the beeps will be closer together. This continues each minute (level). If the line is reached before the beep sounds, the subject must wait until the beep sounds before continuing. If the line is not reached before the beep sounds, the subject is given a warning and must continue to run to the line, then turn and try to catch up with the pace within two more 'beeps'. The test is stopped if the subject fails to reach the line (within 2 meters) for two consecutive ends after a warning.

Scoring: The athlete's score is the level and number of shuttles (20m) reached before they were unable to keep up with the recording.

Results and Discussions

Table 1: computation of mean and analysis of covariance of VO2 max of circuit training, weight training and control groups

Tests	CTG	WTG	Control Group	Source of Variance	Sum of Squares	df	Mean Square	F
Pre Test Mean	47.00	46.66	46.13	BG	5.733	2	2.867	0.89
				WG	135.067	42	3.216	
Post Test Mean	52.93	54.06	46.80	BG	458.533	2	229.267	69.64*
				WG	138.267	42	3.292	
Adjusted Post Test Mean	52.97	54.07	46.75	BG	453.099	2	226.549	67.81*

* Significant at 0.05 level Table value for df 2, 42 was 3.21 and 2, 41 was 3.22

The above table 1 indicates the adjusted mean value of vo2 max of circuit training group, weight training group and control groups were 52.97, 54.07 and 46.75 respectively. The obtained F-ratio of 67.81 for adjusted mean was greater than the table value 3.22 for the degrees of freedom 2 and 41 required for significance

at 0.05 level of confidence. The result of the study indicates that there was a significant difference among experimental and control groups on vo2 max. The above table also indicates that both pre and post test means of experimental and control groups differ significantly.

Table 2: Adjusted mean and differences between the means of circuit training, weight training and control groups on VO2 max

CTG	WTG	Control Group	Mean Difference	CI value
52.97	54.07	---	1.10	1.69
52.97	---	46.75	6.22*	
---	54.07	46.75	7.32*	

Table 2 shows the adjusted means on vo2 max and difference between the means of the circuit training group, weight training group and control group. The mean differences of circuit training group and control group, weight training group and control group were 6.22 and 7.32 respectively was greater than the CI value 1.69. Hence there exists significant difference.

The mean difference between circuit training group and weight training group was 1.10 lesser than the CI value 1.69. Hence there exists no significant difference.

Discussing on Findings: The result of the study reveals that the experimental groups produced significant improvement on selected physiological variables when compared to the control group after the completion of twelve weeks of circuit training and weight training.

Discussion on Hypotheses: The hypothesis stated the circuit training programme would show significant difference on selected physiological variables and running performances among university athletes. From the analysis of data it was proved that there was a significant difference existing on circuit training group on selected physiological variables among university athletes. Hence the formulated hypothesis was accepted at 0.05 level of confidence.

Conclusions

From the analysis of data it was proved that there was a significant difference existing on circuit training

group on selected physiological variables among university athletes.

Ethical Clearance: Nil

Source of Funding: Self

Conflict of Interest: Nil

References

1. Duffield R, Dawson B, Goodman C. Energy system contribution to 400-metre and 800-metre track running. Journal of sports sciences. 2005 Mar 1;23(3):299-307.
2. Santos J, Shannon K. Track: The Field Events. Sports illustrated; 1989 Aug 1.
3. Frohlich C. Effect of wind and altitude on record performance in foot races, pole vault, and long jump. American Journal of Physics. 1985 Aug; 53(8):726-30.
4. Curry TJ, Weiss O. Sport identity and motivation for sport participation: A comparison between American college athletes and Austrian student sport club members. Sociology of Sport Journal. 1989 Sep;6(3):257-68.
5. Bangsbo J, Mohr M, Poulsen A, Perez-Gomez J, Krstrup P. Training and testing the elite athlete. J ExercSci Fit. 2006;4(1):1-4.
6. Schnell J, inventor. Training apparatus. United States patent US 4,635,933. 1987 Jan 13.

The Assessment of Suppression in Anisometropia

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ABSTRACT

Anisometropia is dissimilarity between the power between the two eyes that occurs in one or both principal meridian.^[1] This becomes clinically significant when its magnitude reaches approximately 1D in either or both of the principal meridians.^[3] When two eyes forms two non uniform images due to differences in power of both eye which leads to retinal rivalry. Suppression is an active inhibitory mechanism from the brain to reduce retinal rivalry.^[18] Total 50 subjects of age groups 5-19 yrs were undergone both objective and subjective refraction with anterior and posterior segment evaluation. After that worth four dot test was done on each patient from near to far. (40cm- 4m). For evaluation Log Marchart, Heine retinoscope, worth four- dot torch, slit-lamp was used. Analysis of subjects showed that suppression is lesser in myopic group than hyperopic. The degree of suppression in anisometropia, their mean and SD in NA(0.57±0.62) and AA(1.2±1.18) respectively (P<0.01) be statistically significant. The mean and SD of angle of suppression in hyperopia (1±0.9), myopia (1.02±1.25) degree respectively(p>0.001) was statistically non significant. The mean and SD of differences in refractive error (DRE) in hyperopia (3.1±1.23), myopia (-2.72±1.03) and angle of suppression in each groups hyperopic(0.99±.91) and myopic groups (1.04±1.24) respectively (p<0.001) was statistically significant. However suppression is found in Amblyopia cases with greater visual acuity than refractive error. Difference in refractive power show Statistical significance in suppression as their degree of anisometropia increases.

Keywords: *Non amblyopia (NA), amblyopia (AA), Difference in refractive power of both eye (DRE), refractive error (RE), angle of suppression (AOS).*

Introduction:

The prevalence rate of anisometropia in children is 7%^[7] which also make it considerable factor for refractive error management in optometric field. “Anisometropia is inter eye asymmetry of refractive status of an individual’s”.^[3] To some extent changes in size and shape of objects causes asymmetric astigmatism, asymmetric hyperopia and asymmetric myopia.^[1] Due to difference in images of both eye brain is unable to fuse both image to form a binocular single image to perceive which leads confusion in the brain. Due to conflict & confusion created by dissimilar stimuli on corresponding points, the phenomenon of retinal rivalry takes place.^[9,10] The dominance of the eye rather than the attention value of the stimulus is responsible for it. To maintain the uniformity of viewing single image from both eye brain starts to suppress the one eye image also known as

neurophysiological process.^[8,17] The suppression of eye leads to deprivation of growth of that eye development in binocular skills like accommodation and vergences. Children mostly develop unilateral amblyopia or sometime bilateral amblyopia due to suppression.^[18] in some cases often strabismus is also found due to suppression of one eye.^[5,6]

Effects of Suppression in Anisometric Groups:

The level of suppression in anisometropia, strabismus and mixed amblyopia was evaluate in study done by shows that the most important role of suppression is in amblyopia and its impact while treating amblyopia.^[2] To assess the depth of stereopsis and fusion in patients with anisometropia with presence of amblyopia study done by Hyun Sun Jeo et, al shows that depth of stereopsis and fusion were significantly lower in case of non amblyopic anisometropia (NA) than amblyopic amblyopia (AA).

There were no statistical significance in comparison of NA and isometropic groups.^[4] The level of stereopsis in the NA group, however, did not differ significantly from that in the isometropic control, while the rate of fusion was significantly lower. Dadeya S study on the effect of anisometropia in binocular vision shows that small amount of anisometropes shows fusion whereas greater power was unable to fuse. While prescribing glasses to anisometropia with binocular vision, the most considered factor is amblyopia.^[3]

Material and Methodology

50 subjects were undergone comprehensive eye evaluation in which vision with Log Marchart, refraction both objective and subjective with Heine retinoscope^[19] Topcon autorefractometer. Anterior segments and posterior segment were evaluated with slit lamp (Topcon) and direct ophthalmoscopes(Heine).^[12,20] After that worth four dot test was done on each patient using worth four dot torch and red green filter at room illumination from 40cm to 4m with increasing steps. Subjects with BCVA with refractive power were added filters, red filter in OD(right eye) and left filter in OS (left eye). After that subject were asking to look straight ahead at the torch from 40cm. First right eye is covered and ask "how many lights do you see?" Now the left eye is cover and asks, "How many lights do you see?" After that both eyes open asked, "How many lights do you see?" This process is repeated each step in increasing way till 4m.^[11]

Results

The statistical analysis was done by qimacros and quick pad calculator using t test to compare two groups mean values. Worth four -dots test was obtained on 50 children in age from 5 to 19 from near to distance (40 cm to 4m). Total subjects of age groups of 5 to 19 (12.16±4.08) were participated in study in which mean values of hyperopia (4.5±1.67), myopia (-5.8±3.36), amblyopia(-0.7±6.5) and non amblyopia(0.8±.8). 26% of the participants had no suppression, 8% of the participants had suppression from 40cm, 32% had suppression from 1m, 16% had suppression from 2m, and 18% had suppression from 3m. The mean values of refractive error with angle of suppression shows statistically significance in both amblyopic, non amblyopic groups (p=0.05) and myopic and hyperopic groups are not statistically significant. (p>0.0001). Differences of refractive error in both eye shows

statistically significant compare to angle of suppression. (p=0.0001) in both myopic and hyperopic groups.

Discussion

The principle of our study was to evaluate the suppression in anisometropic children between two groups myopia, hyperopia and amblyopic, non amblyopic patient in age group of 0-19 yrs. Initial result show that myopic groups had less suppression compare to hyperopic groups. 23% of the participants had no suppression, 4% of the participants had suppression from 40cm, 37% had suppression from 1m, 17% had suppression from 2m, 19% had suppression from 3m. 52% of participants were hyperopic and 24% were myopic. The primary finding is that the majority of myopic patient having less suppression compare to hyperopic patient. Non amblyopic patient were having less suppression compare to amblyopic groups. As vision decreases suppression of group's increases shows statistically significant result. But difference of refractive error as increases doesn't show statistically significant result comparing to suppression. Our study shows similar result as Hyun Sun Jeo et, al study depth of suppression in stereopsis and fusion in presence of amblyopic in anisometropia shows that depth of stereopsis and fusion were significantly lower in case of non amblyopic anisometropia (NA) than amblyopic amblyopia (AA). there were no statistical significance in comparison of NA and isometropic groups. S dadeya et, al, the effect of anisometropia on binocular visual function shows that small amount of anisometropes shows fusion whereas greater power were unable to fuse similar to our study lower groups of myopia and hyperopia shows no suppression, with increases of re suppression increases.

Conclusion

Our goals of the study were to find out the suppression in anisometropic children. Hence in our study, we concluded that suppression presence in anisometropia is more significant with decreased of vision. However differences of refractive error in both eye compare to suppression doesn't show any significant results. In amblyopic and non amblyopic groups as the refractive error increases, suppression increases. However most of participant had suppression from 1m despite of different ranges of refractive error. This should be taken in consideration while prescribing or evaluating any anisometropic children to control their suppression.

Conflicts of Interest: No

Ethical Clearance: Non-invasive study that's why ethical clearance was not required.

Funding: No as study used the instruments and procedure which is done regularly on clinical basis.

References

1. Benjamin W, Borish I. Borish's Clinical Refraction. St. Louis, Mo.: Butterworth-Heinemann/Elsevier; 2006.23-25
2. Sd Gupta, Sc Sood, Is Jain. Anisometropia and Amblyopia in Straight Eyes, Indian Journal of Ophthalmology. 1978;21(2):59-62
3. Dadeya S, Kamlesh, Shibal F. The Effect Of Anisometropia on Binocular Visual Function, Indian Journal of Ophthalmology, 2001;49(4):261-3
4. Jeon H, Choi D. Stereopsis and Fusion in Anisometropia according to the Presence of Amblyopia. Graefe's Archive for Clinical and Experimental Ophthalmology. 2017; 255(12):2487-2492.
5. Barrett B, Panesar G, Scally A, Pacey I. A Limited Role for Suppression in the Central Field of Individuals with Strabismic Amblyopia. Plos One. 2012;7(5):E36611
6. Karen Holopigian et.,al, Clinical Suppression And Amblyopia, Investigative Ophthalmology & Visual Science, Vol. 29, No. 3, March 1988
7. Hu Y, Wu J, Lu T, Wu H, Sun W, Guo D. Prevalence And Associations Of Anisometropia In Children. Investigative Ophthalmology & Visual Science. 2016; 57(3):979.
8. Li J, Thompson B, Lam C, Chan L, Maehara G, Woo G. The Role of Suppression in Amblyopia. Acta Ophthalmologica. 2011; 89:0-0.
9. Steele A, Bradfield Y, Kushner B, France T, Struck M, Gangnon R. Successful Treatment of Anisometropic Amblyopia with Spectacles Alone. American Journal of Ophthalmology. 2006;141(6): 1174.
10. Lee J, Seo J, Baek S. The Effects of Glasses for Anisometropia on Stereopsis. American Journal of Ophthalmology. 2013; 156(6):1261-1266.E1.
11. O'donoghue L, Breslin K, Saunders K. The Changing Profile of Astigmatism in Childhood: The Nicer Study. Investigative Ophthalmology & Visual Science. 2015; 56(5):2917.
12. Grosvenor T. Primary Care Optometry. Oxford: Butterworth-Heinemann; 1986.576-577
- 10 Eugene M, Helveston, Andrea Molinari, Visvvaraja Subrayan, Radhika Chawela. Vision and Refraction; Orbis. 2014;.13-20
- 11 Scheiman M, Wick B. Clinical Management Of Binocular Vision, 3rd Edition, 2008,
- 12 Kivlin Jd, Flynn Jt. Therapy of Anisometropic Amblyopia. Journal of Pediatric Ophthalmology and Strabismus 1981; 18:47-56.
- 13 Helveston Em. Relationship between Degree of Anisometropia and Depth of Amblyopia; American Journal of Ophthalmology. 1966;62
- 14 Fink Wh. The Dominant Eye; Its Clinical Significance. Arch Ophthalmology. 1938;4:555-582.
- 15 Porac C, Coren S. The Dominant Eye. Psychol Bull. 1976; 83:880-897.
- 16 Mapp Ap, Ono H, Barbeito R. What Does The Dominant Eye Dominate? A Brief and Somewhat Contentious Review. Percept Psychophysics. 2003;65:310-317
- 17 Gunter K. Von Noorden, Emilio C. Campos, Hermann M. Burian. Binocular Vision And Ocular Motility. 2002; 6th Edition; 19-22
- 18 Kristina Tarczy-Hornoch, Modified Bell Retinoscopy: Measuring Accommodative Lag In Children, Optom Vision And Science; 2009 December; 86(12): 1337-1345
- 19 Lindy Dubois. Clinical Skills For Ophthalmic Examination; 2nd edition: 2006:56

Proficiency, Perspective and Practice Regarding Plagiarism among Dental Professionals of Three Dental Colleges of Western Chhattisgarh: A Cross Sectional Study

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Abstract

Aim & Objectives: To determine and compare knowledge, attitude and practice regarding plagiarism among faculties and postgraduates of dental colleges of Western Chhattisgarh.

Material and Method: A descriptive cross-sectional questionnaire study was conducted among 198 dental professionals of 3 dental colleges in Western Chhattisgarh. The study was conducted for a duration of 1 month using self- structured close ended questionnaire consisting 43 items, assessing knowledge, attitude and practice to collect data regarding plagiarism. Descriptive statistics, ANOVA and Kruskawallis test were applied to analyse data.

Results: In the present study out of 198 study participants 87 were males and 111 were females. The Mean knowledge of postgraduates, BDS and MDS faculties were 9.38 ± 3.9 , 9.64 ± 3.9 and 12.8 ± 3.6 respectively. The mean attitude of postgraduates, BDS and MDS faculties were 0.95 ± 2.0 , 1.78 ± 3.2 and 1.91 ± 3.0 while mean practice of postgraduates, BDS and MDS faculties were 3.9 ± 1.6 , 4.9 ± 0.9 and 4.91 ± 1.3 respectively. Intergroup comparison of knowledge among faculties in different specialities was found to be significant ($p \leq 0.05$).

Conclusion: This study concluded that knowledge, attitude and practices regarding plagiarism among the postgraduates was found to be less as compared to faculties.

Keywords: Dental professionals, Plagiarism, Western Chhattisgarh.

Introduction

Scientific research work is as important as taking good care of the patients.¹ High standards of scientific and medical research practice is expected from the researchers. To bag the confidence of the public, it is essential to maintain the probity, uprightness, prowess and truthfulness of the scientific researches.² There

is a rising concern in academia regarding the increase in scientific misconduct that is occurring among the students.³ Plagiarism constitute a severe educational challenge which is intensely faced by universities, research institutions and even schools.⁴ Scientific misconduct includes fabrication, falsification, plagiarism and other unethical behaviour in scientific researches.⁵ Plagiarism is a form of academic misconduct which is derived from the Latin word *plagiare* or *kidnapper*; which refers to presenting the ideas of somebody else without acknowledging or giving credit to the original.⁶ Self-plagiarism is defined as the inappropriate presentation of one's own published data or text as new and original.⁷ There are various types of plagiarism including taking data, tables or figures from previous publications and using it without citation, publish similar documents

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repeatedly, publish similar article in a local and also in an international journal with different or same authorship.⁸ Plagiarism may be intentional or unintentional. The first and leading reason is the accessibility of elephantine information at our fingertips through the internet facility.⁹ Internet facilitates with the plagiarism detection software; an initiative to terminate the degradation of the scientific writing. The main consequences of plagiarism are penalties that can range from warnings to various forms of legal actions.¹⁰ Since the dental postgraduates and faculties are always under pressure for the publication for which certain ethics should be followed for the scientific writings; they neglect the consequences of such academic theft. Previous studies indicate lack of knowledge about plagiarism, students aptness towards such behaviour and not understanding the seriousness of such violations increase plagiarism frequency especially when the internet is the source of plagiarism.^{11,12,13} Thus this study was conducted with an aim to assess knowledge, attitude and practice regarding plagiarism among postgraduates and faculties of dental colleges of Western Chhattisgarh.

Methodology

This present cross-sectional questionnaire study was carried out on 275 participants (faculties and postgraduates) enrolled in 3 dental colleges of Western Chhattisgarh.^{14, 15} The close-ended questionnaire containing 24 knowledge, 10 attitude and 9 practice related questions was developed by modifying the questions from previous similar studies¹⁶⁻¹⁹. Only those subjects who gave the written consent were considered to be the part of the study.

Pilot Study: A self structured, close-ended questionnaire was prepared in English language. The questionnaire content and face validation were carried out among 10 experts in the subject of Public Health Dentistry. The reliability of the questionnaire was assessed in a pilot study conducted among 30 participants who were not included in the main study. The reliability of the questionnaire was 0.76 (Cronbach's alpha) which was considered good. The knowledge questions were assigned score of one for the correct answer and zero for the wrong answer. The partially filled or incomplete questionnaires were excluded. Similarly for attitude score one was assigned for the correct answer and zero for incorrect answer. The option of don't know was assigned zero score.

Questionnaire: The questionnaire was divided into 4 parts with close ended questions.

1. First part of the questionnaire recorded the demographic details.
2. The second part included 24 questions for the assessment of the knowledge towards plagiarism.
3. The third part constituted of 10 questions to assess the attitude of the participants.
4. The fourth part comprised of 9 questions to assess the practice of the study participants.

Total 239 questionnaires were distributed (68 MDS faculties, 26 BDS faculties and 145 P.G students). Six dental professionals were excluded from the study as they expressed inability to spare time and didn't provide consent. One ninety eight study participants returned the filled questionnaire. Questionnaire were distributed among all the dental professionals in all specialities. On the day of data collection, the study subjects were explained verbally about the study before filling of the questionnaire. The filled questionnaire was collected on the next day.

Statistical Analysis: The data was entered in Microsoft Excel sheet and the data analysis was done using statistical software SPSS version 19.0 (IBM Corporation, SPSS Inc, Chicago, IL, USA). Descriptive statistics were derived. ANOVA test was used for the comparison of knowledge and practice between dental professionals in different subject specialities, whereas Kruskal Wallis test was used for the comparison of attitude between them. $P \leq 0.05$ was considered to be statistically significant. Kolmogorov-smirnov test was used to check the normality of the data.

Results

This cross sectional questionnaire study was conducted to assess the knowledge, attitude and practice regarding plagiarism among the postgraduate students and faculties of dental colleges of Western Chhattisgarh. The response rate was 82% with the total of 198 dental professionals returning the filled questionnaire. The mean age of 198 study participants was 30.57 ± 6.02 . Out of total participants 122 were post graduate students, 62 and 14 were MDS and BDS faculties respectively.

Table 1: Distribution of study participants according to their knowledge, attitude and practice.

Designation	Knowledge (Mean±SD)	Attitude (Mean±SD)	Practice (Mean±SD)
BDS Faculty	9.64 ± 3.97	1.78 ± 3.21	4.9± 0.92
Postgraduates	9.38 ± 3.90	0.95 ± 2.10	3.9 ± 1.61
1 st Year	9.25±2.51	0.8±2.12	4.5±1.25
2 nd Year	9.46±3.96	1.05±2.04	3.6±1.73
3 rd Year	9.37±4.52	0.88±2.12	4.0±1.64
MDS Faculty	12.81 ± 3.67	1.91 ± 3.06	4.9 ± 1.34

Table 1 showed higher mean score of knowledge among MDS faculties as compared to others. A statistical significant difference was present between the knowledge of the dental professionals of different specialties ($p < 0.001$).

Practice when assessed among the dental professionals, BDS faculties had a mean practice of 4.9 ± 0.92 , postgraduates had 3.9 ± 1.61 whereas MDS faculties had a mean practice of 4.9 ± 1.34 . Out of total

participants, 55% of dental professionals have sometimes plagiarised, 52.5% of study participants believe that a person can always write a scientific paper without plagiarizing, 73.7% of study participants answered that they sometimes copy a sentence or just two to take an inspiration for further writing,

There was a highly statistically significance found in knowledge between BDS and MDS faculties ($p = 0.006$) & MDS and postgraduate students ($p = 0.000$). (Table 2).

Table 2: Comparison of knowledge and practice regarding plagiarism between BDS faculty, MDS faculty & postgraduate students.

	Designation		Mean Difference	f-Value	p-Value
	BDS Faculty	MDS Faculty			
Knowledge	BDS Faculty	MDS Faculty	-3.16	16.73	0.001***
	P.G. Students	BDS Faculty	-0.25		
	MDS Faculty	P.G Students	3.42		
Practice	BDS Faculty	P.G Students	-0.93	2.41	0.09
	P.G. Students	MDS Faculty	-0.95		
	MDS Faculty	BDS Faculty	-0.23		

Statistical test – ANOVA. $p \leq 0.05$

Attitude when assessed among the study participants, it was found that 32.7% had uncertain attitude followed by 40.15% with positive attitude and 27.0% with negative attitude. The mean attitude among the BDS

faculties were 1.78 ± 3.21 , among postgraduates were 0.95 ± 2.10 whereas MDS faculties had a mean attitude 1.91 ± 3.06 . (Table 3).

Table 3: Comparison of attitude regarding plagiarism between BDS faculty, MDS faculty & postgraduate students.

Attitude	Designation	N	Mean±S.D.	X ² -Value	P-Value
	BDS Faculty	14	1.78 ± 3.2		
	Postgraduates	122	0.95 ± 2.0		
	MDS Faculty	62	1.91 ± 3.0		

Test applied- kruskal-wallis H test, $p \leq 0.05$

There was no statistically significant difference found in knowledge, attitude and practice regarding plagiarism between the study years of postgraduate students. (Table. 4 & 5).

Table 4: Comparison of knowledge and practice regarding plagiarism between the study years of the postgraduate students.

	Study Year		Mean Difference	f-value	p-value
Knowledge	First Year	Second Year	-0.03	6.56	0.001***
	Second Year	Third Year	0.11		
	Third Year	First Year	-0.08		
Practice	First Year	Second Year	1.66	2.37	0.07
	Second Year	Third Year	-0.41		
	Third Year	First Year	-0.44		

Statistical test – ANOVA. $p \leq 0.05$

Table 5: Comparison of attitude regarding plagiarism between the study years of the postgraduate students.

	Designation	N	Mean±S.D.	X ² Value	p-value
Attitude	1 st year postgraduate	27	0.8±2.1	1.26	0.53*
	2 nd year postgraduate	52	1.05±2.04		
	3 rd year postgraduate	43	0.88±2.12		

Test applied- kruskal-wallis H test, $p \leq 0.05$

There was statistically significance found in knowledge between the faculties with a teaching experience of 10 years and above and less than 4 years with a mean difference of 2.52 ($p= 0.04$) whereas no statistically significance found in attitude and practice.

Discussion

In the present study, the mean knowledge regarding plagiarism was categorized as below average<10, average = 10.1-15, good = 15.1- 20 and excellent = 20.1-24. The mean knowledge of the postgraduate is 9.38 ± 3.90 , which was lesser than the mean knowledge score of the faculty (12.81 ± 3.61). The reason could be that the MDS faculties are more updated with plagiarism in their due course as faculty. Similar results was found in the studies conducted by Poorolajal et al.²⁰

Our study found that overall (93.9%) dental professionals knew what plagiarism is which was in accordance with the study conducted by Singh et al²¹. The study population of the present study stated that the reason for indulging in plagiarism was mainly due to pressure to complete the task in short time and easy to cut and paste. This was in accordance with study conducted by Zulle et al ²². The reason for this could be that the

pressure of appraisal and promotions were dependent on their research work and publication, hence they could have indulged into plagiarism. Thirty two percent of the study subjects knew that plagiarism was a punishable offence. Surprisingly a study conducted by Singh et al ²¹, only 5% of the population were aware for that. As per the section 57 of the Indian copyright Act (ICA), 1957 ²³ has stated that plagiarism attracts punishment in the form of warning and penalty. This striking difference in the awareness could be lack of noteworthiness of the consequences of plagiarism among researchers and also the due prominence towards learning of such ethical issues in the under graduate curriculum is not asserted.

In the present study 40.15% had positive attitude, 32.7% with uncertain attitude followed by 27.0% with negative attitude. The reason may be because of the ignorance regarding the impact of plagiarism in research and plagiarism is not been a part of undergraduate curriculum. Our study showed that (58.2%) postgraduates and (80.6%) faculties agreed that plagiarism is an ethical issue in scientific writing which was in accordance with study conducted by Kirthiet al¹⁷. This study result showed that (48.4%) postgraduate students and (69.4%) faculty members agreed that plagiarized paper does

harm to science. As per the study conducted by Gomez et al² (3.5%) postgraduate students and (9.8%) faculties, as per Jain et al⁷(22.6%) dental professionals disagreed to the statement that plagiarized paper does no harm to science.

In our study 40.15% of dental professionals showed positive attitude towards question related to plagiarism. This was in accordance with the study conducted by Rathore et al²³ which had high ATPQ (attitude towards plagiarism questions) 51.6%.

In the present study (48.4%) faculties agreed that it is necessary to plagiarize sometimes which was contradicting to the study conducted by Gomez et al²(27.4%) and Kirthi et al¹⁷ (15.9%) agreed to the statement sometimes it is necessary to plagiarize. This is a highly concern raising issue as most of the study subjects don't find it wrong to copy a sentence. Cognizance regarding the ICA 1957 needs to be ameliorated. In the present study (23.8%) postgraduate students and (43.5%) faculties always have made an attempt to write an article without plagiarizing. This kind of practices need to be encouraged and highlighted among all the researchers as it increases the quality of scientific writing.

Conclusion

Though the postgraduate students are the rising buds as a future professionals, they need a proper guidance from their faculty members while writing the scientific paper for the first time, then only the chances of plagiarizing of a paper will be carved out. To maintain the originality of the scientific writing, scientific writing courses program should be carried out among the postgraduate students as they are in the budding stage as our future professionals.

Ethical Clearance: It was obtained from the institutional ethical committee of Rungta College of Dental Sciences & Research, Bhilai, Chhattisgarh.

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References

1. Lynoe N, Jacobsson L and Lundgren E. Fraud, misconduct or normal science in medical research— an empirical study of demarcation. *J Med Ethics* 1999;25:501-506.
2. Gomez M.S, Nagesh L and Sujatha B.K. Assessment of the attitude towards plagiarism among dental postgraduate students and faculty members in Bapuji Dental College and Hospital, Davangere—a cross sectional survey. *IOSR Journal of Dental and Medical Sciences*. 2014; 13(5):1-6.
3. Bhakta P.G.H, Muzzin B.K, Dewald P.J, Campbell P.R and Buschang P.H. Attitudes towards students who plagiarize: A dental hygiene faculty perspective: *Journal of dental education*. 2014;79(1):131- 145
4. Al-Dabbagh M, Salim N, Rehman A, Alkawaz M. H, Saba T, Al-Rodhaan M and et al. Intelligent Bar Chart Plagiarism Detection in Documents: *The Scientific World Journal*; 2014
5. Mavrinac M, Brumini G, Billic- Zulle L and Petrovecki M. Construction and Validation of Attitudes towards Plagiarism Questionnaire. *Croat Med J*. 2010;51:195-201.
6. Oxford English Dictionary. Plagiarism 2017. Available from: <http://www.oed.com/view/Entry/144939> [accessed 15 September 2017; 10:00 am]
7. Jain S, Saxena V, Hongal S, Jain M, Torwane N and Sharva V. Comparison of Opinion Referendum of Medical and Dental Postgraduates Towards Plagiarism in Bhopal-Central India. *Journal of the College of Physicians and Surgeons-Pakistan*: 2015;25(7):514-518.
8. Mansour S.S, Abusaad S.F, Dosuky A.M and Ibrahim A.W. Improving knowledge, skills, and attitudes of the nursing faculty members and postgraduate students towards plagiarism in academic writing. *Journal of Nursing Education and Practice*: 2017;7(9):107-120.
9. Naveen N, Raveendran N, Vanishree N, Prasad K, Narayan R.R, Vignesh D. An effectual analytics and cross sectional study on plagiarism among dental post graduates of Bangalore city. *International Journal of Applied Dental Sciences* 2017; 3(3): 23-26.
10. Berlinck R.G.S. The academic plagiarism and its punishments: a review. *Brazilian Journal of Pharmacognosy*. 2011; 21(3): 365-372.
11. Ryan G, Bonanno H, Krass I, Scouller K and Smith L. Undergraduate and postgraduate pharmacy students perceptions of plagiarism and academic honesty. *Am J Pharm Educ*. 2009;73:105.

12. Comas R and Sureda J. Academic cyber plagiarism: tracing the causes to reach solutions. *Digithum*.2008;10;1-7.
13. Pupovac V, Bilic- Zulle L and Petrovecki M. On academic plagiarism in Europe. An analytical approach based on four studies. *Digithum*.2008;10:13-19.
14. Kumar PM, Priya NS, Musalaliah SV, Nagasree M. Knowing and avoiding plagiarism during scientific writing. *Annals of medical and health sciences research*. 2014; 1;4(3):193-8.
15. Couzin-Frankel J, Grom J. Scientific publishing. *Plagiarism sleuths*. *Science*. 2009; 324:1004-7.
16. Howard S, Ehrich J and Tognolini J. Measuring Attitudes Toward Plagiarism. Issues and Psychometric Solutions. *Journal of Applied Research in Higher Education*.2015;7 (2): 243-257.
17. Kirthi P.B, Pratap. K, Padma T.M and Kalyan V.S. Attitudes towards Plagiarism among Post-Graduate Students and Faculty Members of a Teaching Health Care Institution in Telangana - A cross-sectional questionnaire based study. *International Journal of Advanced Research* .2015;3(8):1257 – 1263.
18. Smedley A, Crawford T and Cloete L. An intervention aimed at reducing plagiarism in undergraduate nursing students. *Nurse Education in Practice*. 2015 :1-6.
19. Shirazi B, Jafarey A.M and Moazam F. Plagiarism and the medical fraternity: a study of knowledge and attitudes. *The Journal of the Pakistan Medical Association*. 2010;60(4):269 .
20. Poorolajal J, Cheraghi P, Irani A.D, Cheraghi Z and Mirfakhraei M. Construction of knowledge, attitude and practice questionnaire for assessing plagiarism. *Iranian journal of public health*. 2012;41(11):54-58.
21. Singh P.H and Guram M. Knowledge and Attitude of Dental Professionals of North India toward Plagiarism. *North American Journal of Medical Sciences*.2014;6(1):6-11.
22. Zulle B.L, Mavrinac M and Petrovecki M. Attitudes toward plagiarism among pharmacy and medical biochemistry students –crosssectional survey study. *Biochemia Medica*. 2010;20(3):307-13.
23. Rathore F. A, Waqas A and Farooq F. Exploring the attitudes of medical faculty members and students in Pakistan towards plagiarism: A cross sectional survey. *PeerJ*.2015.

Palateless Complete Denture: A Minimally Invasive Approach to Preventive Case

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Abstract

Background: Tooth loss due to caries and various other consequences, can cause simple loss of function to long term deleterious effects on the remaining residual bone, oral proprioception, temporomandibular joints and facial appearance.

Case Description: A 33 year old female patient with Kennedy's class I edentulism in both the arches with just three teeth remaining in maxilla has been treated with attachment retained maxillary palateless overdenture and mandibular removable partial denture. The maxillary teeth 11 21 23 were endodontically treated and a short coping with rhin 83 attachment were cemented and a maxillary overdenture over this was fabricated. This was opposed by mandibular partial denture. This case report attempts to prevent the remaining teeth in the oral cavity and gives a cost effective treatment option to the patient considering her financial status.

Conclusion: This case report emphasizes the use of preventive prosthodontics helping enhance the quality of life of patient

Keywords: *Overdenture, Tooth-supported overdenture, Attachments, combination syndrome, preventive prosthodontics.*

Introduction

Overdentures have always offered a prudent appeal and sensible approach to prosthodontists and numerous patients have been benefitted by it. The applied ingenuity of this technique has mitigated much time dependent risk inherent in complete denture service. It has been successfully used for ages, however the emphasis on preventive dentistry has popularized its use. This case report presents a similar case of preventive prosthodontics.¹

Case Report: Patient details: A 33 year old female patient reported to Department of Prosthodontics, Manipal College of Dental Sciences, Manipal with a chief complaint of missing teeth in upper and lower arches and wanted them to be replaced. The patient reported with a history of uneventful extractions of maxillary and mandibular posterior teeth. The medical and family history were not relevant.

Examination: Extra oral examination exhibited apparently bilaterally symmetrical face and normal temporomandibular joints.

Intra oral examination revealed partially edentulous arches with only three teeth in maxilla. 11, 21 23. The Retained teeth were having good periodontal support. The mandibular arch had Kennedy's class 1 partial edentulism with 32, 32 41, 42, 43 present. Oral mucosa and tongue were normal (Figure 1). The residual alveolar ridges were high well rounded.

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Figure 1: Pre Treatment

Diagnostic mounting: After diagnostic mounting, various treatment options available were discussed and the treatment plan was decided. The available treatment options were either extraction of remaining maxillary teeth and fabrication of conventional complete denture or implant supported overdenture, or to retain the maxillary teeth and fabrication of tooth supported overdenture. The patient rejected the option of implants due to additional surgery involved, more expenditure and prolonged duration of treatment. So, tooth supported overdenture was chosen as treatment option. All the maxillary teeth were chosen as Overdenture abutments and they were endodontically treated. The diagnostic mounting helped us evaluate the interarch space and it was found adequate for overdentures with short copings.

Treatment: The Overdenture abutments were then prepared to fabricate copings with attachments. A post space of 5mm length was prepared [Mani peeso reamers #1, #2, 28 mm] and a definite chamfer finish line [Shofu Inc. crown and bridge preparation kit] around the abutments (Figure 2).



Figure 2: Abutment preparation

Polyvinyl silicone elastomeric impression [Reprosil® heavy body and light body Dentsply caulk,

Germany] was made using a J shaped wire loop snugly fitting the post space (Figure 3).



Figure 3: Polyvinylsiloxane impression

Indirect method was used to fabricate the post and wire was coated with tray adhesive [Caulk tray adhesive, Dentsply, Germany] to make impression of the post space and Master cast was poured [Type IV die stone, Ultrarock, Kalabhai Karson Pvt. Ltd., Mumbai, India] and custom cast copings were fabricated with male component of Rhein 83 attachments (Figure 4).



Figure 4: Wax pattern

The parallelism of all the three attachments was maintained and they were casted using co-cr alloys. The

finished and polished copings with male component of attachments were tried in the patient's oral cavity and cemented (Figure 5) with GIC [GC Fuji PLUS™ GC America].



Figure 5: Copings cemented

An irreversible hydrocolloid impression [Zelgan 2002 Dentsply] was made and a stone cast [Type III dental stone, Kalstone, Kalabhai Karson Pvt. Ltd., Mumbai, India] was poured. A custom tray was fabricated using self cure acrylic resin [Trevalon, Dentsply India Private Limited, Gurgaon Haryana], and was used for border molding light body polyvinyl siloxane was used for final impression (figure 6).



Figure 6: Wash impression

The cast was then poured and trial denture bases were fabricated. Jaw relations were recorded and teeth arrangement was done using Acryrock teeth (Acryrock Ruthinium dental products). After a satisfactory try in, the dentures were fabricated using Trevalon HI heat cure denture base resin with palateless maxillary denture reinforced with metal mesh and female components of the attachments incorporated in it during denture curing using lab analogue, and mandibular removable partial denture with wrought wire clasps. The dentures were inserted (Figure 7) and patient was instructed

about the care and maintenance of the denture and the abutments. The periodic recall of the patient (Figure 8) and periodontal health of the abutments and remaining natural teeth was taken care.



Figure 7: Maxillary and Mandibular Dentures in place



Figure 8: Pre and post treatment views

Discussion

Various treatment options were given to patient including implants, overdentures, partial denture or complete denture. Financial constraints of the patient excluded the option for implants. The treatment of choice for the patient was overdenture for maxilla and removable partial denture for mandible. A reasonably right choice due to various reasons explained here. Complete dentures present many problems related to mastication and phonation, which may be eluded by retention of some natural teeth, and their supporting structures, which serve useful function for long periods of time. The biologic maintenance of temporomandibular articulation, neuromuscular mechanism, and the supporting structures of a denture can be accomplished by teeth than the mucoperiosteum. In this case the preservation of the remaining teeth prevented the impending complications of an edentulous maxilla opposed by a partially edentulous mandible which could have led to a classic case of combination syndrome.^{3, 4} The preservation of anterior teeth helps preventing the proprioception⁵, dimensional perception⁶ and directional sensitivity.⁷ Retention of these teeth made

possible a denture which provided support, retention, stability, ability to bear more occlusal load and comfort superior to that of a conventional complete denture. Various advantages such as the preservation of alveolar bone and the maintenance of occlusal vertical dimension and centric relation. It increases patients' manipulative skills in handling the denture. Facial and lip changes are minimized and the masticatory performance is maximized. The teeth selected as abutments were based on the number of teeth remaining, leading to one tooth per quadrant and a tripod approach for the support due to position of teeth in the arch gave us the mechanical advantage. Canine being the best abutment due to longest root, more surface area, strategic position in the arch and more proprioceptive nerve endings around it gives us the best choice for the abutment.¹The use of short copings was decided according to the amount of inter arch space available and to increase the retention and support from the natural tooth, the radicular extension of 5mm was decided. Among the various options available for Overdentures the attachment retained have proven to be the best and provide better retention and stability when compared to Overdentures with only copings. This type of stud attachments are easier for the patient to maintain his hygiene. Since there was adequate retention and stability with the maxillary denture a decision for palateless denture was made considering patient's concern regarding discomfort caused by the palatal coverage and the denture was reinforced with metal mesh to combat flexural fatigue likely to develop in this type of denture. The patient benefits psychological, functional as well as biologic advantages.

Conclusion

The old age concept of over dentures helps prevent the vicious cycle of residual ridge resorption and combination syndrome to a great extent. With innovative approaches, and identifying possibilities rather than limitations, it has enthralled the field of preventive prosthodontics. Doing justice to every minute detail

of treatment can be the only key to achieve success in prosthetic rehabilitation of patients.

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References

1. Brewer AA, Morrow RM; OVERDENTURES. 2nded. The C.V. Mosby Co. 1975.
2. Preiskel HW. Overdentures made easy: a guide to implant and root supported prostheses. 1. Chicago: Quintessence; 1996. pp. 184–193.
3. Winkler S. Essentials of Complete Denture Prosthodontics. 2nded .2009.
4. Rahn A.O, Heartwell C.M, Textbook of complete dentures. 5th ed. Philadelphia, 1993.
5. Crum RJ, Louiselle RJ: Oral Perception and Proprioception: A Review of Literature and its Significance to Prosthodontics, J Prosthet Dent 28: 215-230, 1972
6. Kapur KK, Collister T: A Study of Food Textural Discrimination in Persons with Natural & Artificial Dentitions. 2nd Symposium of Oral Sensations & Perception, 1970
7. Kawamura Y, Watanabe M: Studies on Oral Sensory Threshold, Med. J Osaka Univ. 10:291-301, 1960
8. Fenton AH. The decade of overdentures: 1970–1980. J Prosthet Dent. 1998;79:31–36. doi: 10.1016/S0022-3913(98)70190-8. [PubMed] [Cross Ref]
9. Morrow RM, Powell JM, Jameson WS, Jewson CG, Rudd KD. Tooth supported complete dentures: an approach to preventive prosthodontics. J Prosthet Dent. 1969; 21:513–522. doi: 10.1016/0022-3913(69)90073-0.

Effectiveness of Pelvic Proprioceptive Neuromuscular Facilitation on Trunk Control in Children with Spastic Diplegia: A Randomized Controlled Trial

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Abstract

Background: One of the most prevalent neurodevelopmental disorder seen in children is Cerebral palsy and it is associated with lifelong disability. Impaired trunk control effects performances of daily life such as sitting, reaching and walking. It is evidenced from studies that pelvic asymmetry is common in children with CP. The PNF patterns of pelvis not only exercises the pelvic motion and stability, but also facilitates trunk motion and stability.

Objective: To investigate the effectiveness of pelvic PNF techniques on trunk control in children with spastic diplegia.

Method/Design: 36 diplegic children irrespective of gender, age group between 8-15 years were recruited for the study. The intervention group received pelvic PNF along with the conventional therapy for 4 weeks. The control group received conventional physiotherapy in form of truncal exercises for 4 weeks. The primary outcomes used were TCMS and PALM.

Results: The results showed that there is an improvement in the TCMS score after the application of pelvic PNF techniques on children with spastic diplegia.

Conclusion: Application of PNF along with conventional therapy helps in improving trunk control and reducing disability in children with spastic diplegia.

Keywords: Cerebral palsy, Pelvic asymmetry, PNF, Trunk impairment.

Introduction

Spastic diplegia is the predominant type of cerebral palsy (CP), in which both lower limb is manifested with spastic muscle weakness¹. It is commonly seen among 64% to 75% of preterm infants, especially those children's birth weights below 1000gm². In India

3 (out of 1000) in every live birth manifest CP which is considered to be a higher incidence rate than the incidence rate of developed countries (2/1000)³.

Apart from perceptual, cognitive and special sensory deficits, children with spastic diplegia develops impaired trunk control, pelvic asymmetry, balance and gait abnormality etc^{4,5,6}. Further, mal-adaptation of neuromusculoskeletal structural components can lead to abnormal pelvic tilts which causes a reduction in the trunk control and normal functioning of the lower limb⁵.

Evidence shows that children with CP frequently show impaired trunk control, which can affect performances of daily life such as sitting, reaching and walking etc⁷. It is also proved that pelvic asymmetry is

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common and it influence the functions of trunk and lower limb⁸. Pelvis is an integral part of trunk that supports lower extremity and provide base for the lower limb motions. Since the trunk muscles helps in the motion of pelvis, the range of motion in pelvis depends on the quality and quantity of motion in the lower spine.

The relationship among the movements of pelvis, trunk and lower limb is evidenced, where the altered pelvic symmetry reduce the effective functioning of trunk and lower limb. In order to address the all three components collectively or individually various rehabilitation protocols are used. In the treatment of cerebral palsy especially in the case of spastic diplegia, the clinicians focusses on training the muscle strength, task manipulation, sensory-motor integration, balance, core muscle strength, muscle flexibility, trunk stability, postural control, co-ordination and gait pattern to improve the quality of life⁹.

Since the pelvis is a prime structural and functional component, and its influence on trunk control during static and dynamic activities, it is important to focus on trunk control by treating the pelvic asymmetry if it is identified. Evidence also strongly supports the positive relationship between the pelvic asymmetry and its associated dysfunctions such as poor trunk control and gait pattern manifested in spastic diplegic children⁹. The impaired trunk proprioception can also be considered as a contributing factor for the poor trunk control and pelvic mal-alignment.

Even though there are various interventions applied for the management of pelvic asymmetry, there is no study been done focusing on the training of multi segmental sensory motor integration in order to improve the pelvic symmetry and trunk control in children with spastic diplegia. According to the physiological mechanisms of proprioceptive neuromuscular facilitation, it can facilitate the normal functional movement pattern by activating the muscles of pelvis, trunk and lower limb when applied over the pelvic segment. Therefore collaborating PNF with conventional physiotherapy can help in improving the trunk control as well as to correct the pelvic malalignment in children with spastic diplegia.

PNF is a technique used to facilitate the response of neuromuscular processing through a proprioceptive stimuli. PNF deploys a distinctive diagonal pattern which in turn stimulates the proprioceptive sensation⁸.

This technique not only stimulates the proprioceptors

(muscle spindle and golgi tendon organ) and it also stimulates other deep sensory receptors for vibration, pressure, tactile discrimination and kinaesthetic sensation¹⁰. So it may collectively improve muscle strength, flexibility, inter and intramuscular coordination, balance and other functional activities. The principles and techniques of PNF are predominantly beneficial when consolidated along with the proper selection and implementation of joint and soft tissue mobilization techniques¹⁰. Since there is a no study evidenced the effectiveness of pelvic PNF on trunk control in children with spastic diplegia, this study was conducted to evaluate the effectiveness of pelvic proprioceptive neuromuscular facilitation on Trunk control in children with spastic diplegia.

Methodology

Trial Setting: A prospective, parallel group and assessor blinded randomized controlled trial was conducted during the period between March 2018 to March 2019 in the Department of Paediatric Physiotherapy of Justice K.S. Hegde Charitable Hospital, Mangalore, Karnataka state of India.

The ethical approval was attained from the Institutional Ethics Committee of Nitte Institute of Physiotherapy, and trial was registered in CTRI. This trial followed the ethics of research in humans (Helsinki convention norms) and prior to the participation, all the participants and their parents were informed about the study and consent was obtained. The participants were also made known about their rights to withdraw their participation during the study.

Participants: The participants diagnosed with spastic diplegia by the Paediatrician and Neurologist of the Justice K. S. Hegde Charitable Hospital, According to the selection criteria, an independent Physiotherapist assessed the patient and included the participant to undergo the study interventions. Inclusion criteria were, either Gender between 8 to 15 years, children diagnosed with spastic diplegia, children having pelvic asymmetry, children who can sit independently, children who are able to follow commands (Paediatric MMSE greater than or equal to 22) and children with GMFCS level 1 to 3. Exclusion criteria's were, children undertaking Botox injection since 6 months, children who underwent any surgery involving spine and lower limb in past 6 months, children having uncontrolled seizure since past 6 months. Children with fixed deformities in spine,

children with any fractures and dislocation of spine and lower extremity.

These participants once screened by inclusion criteria, were given consent and assent forms, and were divided into 2 groups, experimental and control group. Both group participants pre-post pelvic tilt was assessed using PALM device and trunk control was assessed using TCMS by the blinded assessor.

Interventions: The experimental group received both conventional and Pelvic PNF for 30 minutes each, once in a day, 5 days per week for 4 weeks. The experimental received anterior elevation-Posterior depression pattern with the techniques of Rhythmic initiation, Slow reversal and Stabilising reversal¹⁷. Each side of the pelvis were given these techniques for 15 minute each, and total 30 minutes of pelvic PNF in one session with rest periods in between. Participants were positioned into side lying with both hip flexion 100⁰ and knee flexion 45⁰, neck supported by a pillow with flexion of 30⁰. The position of the therapist was behind the child to face the direction of the pelvic movement, the hand of the therapist placement for anterior elevation

over the crest of the ilium one hand overlaps other for posterior depression heel of the one hand hold with other hand on the ischial tuberosity. “Pull up” and “Push down” command were given along with the techniques of rhythmic initiation, slow reversal and stabilizing reversal¹¹.

Control group received conventional physiotherapy in form of truncal exercises, which consist of upper and lower part of trunk for total 30 minutes including rest periods in between, once in a day for 5 days for 4 week duration.

Results

Baseline Outcome: 36 children diagnosed of spastic diplegia (72.2 % male and 27.7 % females) with a mean age of 11 years homogeneously distributed among the two groups in this study. We found that there is no statistically significant difference between the baselines mean scores of PALM device and TCMS. This also indicate that there is indication for abnormal pelvic alignment and trunk control ability among the children with spastic diplegia who are participated in this study.

Table 1: Baseline characteristics (PALM: Palpation Meter Device, TCMS: Trunk Control Measurement Scale)

Variables		Experimental group	Control group	p.value
Age (Years)		10.56 ± 2.45	11.44± 2.28	0.268
Gender	Male	83%	61%	0.137
	Female	17%	39%	
PALM score		2.21± 0.95	2.34± 0.89	0.684
TCMS score		25.39 ± 8.69	26.44± 10.12	0.739

Table 2. Within group comparison of TCMS and PALM

Groups	Outcome measures		Mean± S.D	p.value
Experimental	PALM	Pre	2.15 ± 0.87	<0.001
		Post	1.75 ± 0.72	
	TCMS	Pre	24.79 ± 9.33	<0.001
		Post	31.50 ± 8.84	
Control	PALM	Pre	2.46 ± 0.76	<0.001
		Post	2.15 ± 0.75	
	TCMS	Pre	25.54 ± 10.30	<0.001
		Post	27.77 ± 10.58	

Table 3. Between group comparison

Outcome measure		Mean± S.D	p. value
PALM	Experimental	.40 ±0.25	0.323
	Control	.31 ±0.23	
TCMS	Experimental	-6.71 ±4.94	0.004
	Control	-2.23 ±1.42	

Pelvic Symmetry: After the 4 weeks of pelvic PNF with conventional treatment among the 18 patients of intervention group and 18 patients of control group which was treated with conventional treatment alone proved to be effective in reducing the pelvic asymmetry. Similarly, the mean difference between the change score of PALM device indicate the addition of pelvic PNF into the conventional treatment have not produced any significant effect on pelvic asymmetry among the children with spastic diplegia.

Trunk Control: In the case of trunk control the children treated with pelvic PNF along with conventional treatment and standalone conventional treatment have significantly improved after the 4 weeks of treatment. However, the children who received Pelvic PNF in addition improved better (meandifference = -4.48) compared to conventional treatment which was applied in the control group.

Dropout: During the first two weeks of intervention there were 3 subjects in the experimental group and 2 subjects in the control discontinued (overall dropout percentage = 13.88%) the treatment due to the long travel distance and other personal reasons.



Figure 1: The patient receiving Pelvic PNF.



Figure 2: The patient receiving conventional treatment.

Discussion

According to the data basis searched, this would be the first study addressing the effect of Pelvic PNF for improving trunk control in cerebral palsy children. This study was used to evaluate the effectiveness of Pelvic Proprioceptive Neuromuscular Facilitation on Trunk control in children with spastic diplegia. The primary outcome measure TCMS showed a significant improvement in comparison with the control group. That is the group treated with PNF combined with conventional treatment has improved better in TCMS score compared to conventional treatment.

In a study conducted by Khanal D et.al to find out the effect of Pelvic PNF techniques on facilitating trunk movement in stroke population, the study came with a conclusion that both the control and intervention group showed improvement on trunk performance, range of motion, balance and gait after the intervention¹⁰.

PNF deploys a distinctive helical or diagonal pattern which in turn stimulates the proprioceptive sensation and promotes nerve root response, thus enhancing functional movements, and stimulating weakened muscles. The weakened muscles, thus functions more constructively and beneficially with the action of the antagonistic muscle when compared to their individual action alone. PNF

also stimulates proprioceptors within the tendons and muscle, thus improving strength of muscle, flexibility, function and balance. Hence improving proprioceptive sensation is a key component for trunk stability and thus PNF exercises helps in improving trunk stability^{10,11}.

There are few studies quoting the need of focusing on pelvic asymmetry in children with cerebral palsy. In a study done by De Moraes Filho et.al on identifying the factors affecting pelvic asymmetry during gait in children with cerebral palsy, it was observed that pelvic retraction and internal hip rotation are the strongest contributors for asymmetric pelvic tilt. Since the trunk muscles helps in the motion of pelvis, the range of motion in pelvic pattern depends on the amount of motion in lower spine¹².

Another study conducted by Sebastian Wolf et.al, it was found out that anterior pelvic tilt is the main factor for the functional impairment in spastic diplegic children¹³.

Hence, from the retrieved literature, it can be shown that, correcting the pelvic malalignment, and thus improving trunk control can help in making a child with poor trunk control functionally independent.

In a systematic review done by Anttila et.al to find out the effectiveness of Physical therapy interventions for children with cerebral palsy, they focused on interventions such as Neuro Developmental Therapy (NDT), strength training, conductive education, and various Physical therapy interventions such as Constrained Induced Movement Therapy (CIMT), postural control, passive stretching, hydrotherapy and orthotic devices⁹.

Though many studies have addressed various such therapeutic interventions, there are no studies done in cerebral palsy children focusing on correcting the pelvic asymmetry and thus improving trunk control. Since pelvis is the framework which connects the trunk and lower extremity, correcting the pelvic malalignment by means of giving pelvic PNF could improve trunk control^{12,13,14,15}. Once the trunk control is improved, it can also act as a contributing factor for improving gait as well as balance.

Hence incorporating pelvic PNF along with the conventional physical therapy can also benefit in improving trunk control and thus making a child functionally independent.

Conclusion

The conclusion of this study is that use of proprioceptive neuromuscular facilitation technique for the pelvis has shown an improvement in trunk control among children with spastic diplegia. The four week intervention programme shows an improvement in trunk control as seen in the TCMS outcome measure thereby reducing disability among children with spastic diplegia. Hence, incorporating pelvic PNF along with conventional physical therapy can also benefit in improving trunk control thus making the child functionally independent.

Limitations and future scope: Small sample size were included and there was no follow up present. Hence similar type of study can be conducted in a larger population and in future studies could include certain other components such as the effect of PNF on balance, gait, functional independence, quality of life and caregiver burden.

Conflict of Interest: The authors had declared that there is no conflict of interest

Source of Funding: Self

Ethical Clearance: The study has been approved by the institutional ethics committee.

References

1. Leppert M. Developmental-behavioral pediatrics. 4th ed. Philadelphia, Pa: Saunders, Elsevier; 2009.
2. Fenichel G. Clinical pediatric neurology. 6th ed. Philadelphia, Pa: Saunders/Elsevier; 2009.
3. Karthy J. Incidence of cerebral palsy remains constant in India Health news [Internet]:Medindia; 2010 Oct 4 [updated on 2015 Jun 22; [cited on 2017 Oct 10].
4. Shepherd R. Physiotherapy in paediatrics. 3rd ed. London, Pa: Elsevier/Butterworth Heinemann; 1995.
5. ElBasatiny H, Abdelaziem A. Effect of Trunk Exercises on Trunk control, Balance and Mobility Function in Children with Hemiparetic Cerebral Palsy. International IJTRR. 2015;4(5):236-43.
6. Niklasch M, Döderlein L, Klotz M, Braatz F, Wolf S, Dreher T. Asymmetric pelvic and hip rotation in children with bilateral cerebral palsy: Uni- or bilateral femoral derotation osteotomy?. Gait & Posture. 2015;41(2):670-75.

7. Gnat R, Saulicz E, Biały M, Kłaptocz P. Does Pelvic Asymmetry always Mean Pathology? Analysis of Mechanical Factors Leading to the Asymmetry. *J Hum Kinet.* 2009;21(1):23-35.
8. Levangie P, Norkin C. Joint structure and function. 5thed. Philadelphia, Pa: F A Davis company;2011.
9. Anttila H, Autti-Rämö I, Suoranta J, Mäkelä M, Malmivaara A. Effectiveness of physical therapy interventions for children with cerebral palsy: A systematic review. *BMC Pediatr.* 2008;8(1).
10. Khanal D, Singaravelan R, M. Khatri S. Effectiveness of Pelvic Proprioceptive Neuromuscular Facilitation Technique on Facilitation of Trunk Movement in Hemiparetic Stroke Patients. *IOSR-JDMS.* 2013;3(6):29-37.
11. Adler S, Becker D, Buck M. PNF in practice. Heidelberg: Fourth ed. Springer Medizin Verlag; 2014.
12. de Moraes Filho M, Kawamura C, Andrade P, dos Santos M, Pickel M, Neto R. Factors associated with pelvic asymmetry in transverse plane during gait in patients with cerebral palsy. *J Pediatr Orthop B.* 2009;18(6):320-4.
13. Wolf S, Mikut R, Kranzl A, Dreher T. Which functional impairments are the main contributors to pelvic anterior tilt during gait in individuals with cerebral palsy?. *Gait & Posture.* 2014;39(1):350-364.
14. Suriyaamarit D, Boonyong S. Mechanical work, kinematics and kinetics during sit-to-stand in children with and without spastic diplegic cerebral palsy. *Gait & Posture.* 2019; 67:85-90.
15. Timgren J, Soynila S. Reversible Pelvic Asymmetry: An Overlooked Syndrome Manifesting as scoliosis, Apparent Leg-Length Difference, and neurologic Symptoms. *J Manipulative Physiol Ther.* 2006; 29(7):561-5.

A Quasi Experimental Study to Evaluate the Effectiveness of Revised Nursing Care Standard Operative Procedures on Knowledge & Practice Regarding Infant Feeding among Students of Selected Nursing College, Vadodara

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Abstract

Background: Malnutrition has been responsible, directly or indirectly, for 60% of the 10.9 million deaths annually among children under 5. Well over two-thirds of these deaths, which are often associated with inappropriate feeding practices, occur during the first year of life. No more than 35% of infants worldwide are exclusively breastfed during the first four months of life; complementary feeding frequently begins too early or too late, and foods are often nutritionally inadequate and unsafe. Malnourished children who survive are more frequently sick and suffer the life-long consequences of impaired development.

Method and Materials: Quantitative evaluatory approach with quasi experimental non randomized control group design including 40 students from BSc nursing in which 20 experimental and 20 control were selected as a sample with use of purposive sampling technique. To collect data self-structured questionnaire and practice checklist were administered.

Results: The pre-test score of the experimental group the knowledge score mean % is 34.60% and the practice score mean % is 34.03% & that in control group the knowledge score mean % is 38.33% and practice score mean % is 30.57%. In respondents 45% were having inadequate knowledge, 55% were having adequate knowledge & no one were having excellent knowledge while in practice 80% were having poor practice, 20% were having adequate practice & no one having good practice in providing infant feeding. The post test score of the experimental group the knowledge score mean percentage is 85.19% and the practice score mean % is 88.46% & that in control group the knowledge score mean % is 36.91% and practice score mean % is 37.5. In respondents 27.5% were having inadequate knowledge, 22.5% were having adequate knowledge & 55% were having excellent knowledge. And in practice 32.5% were having poor practice, 17.5% were having adequate practice & 50% were having good practice in providing infant feeding. **Conclusion:** Administration of procedure regarding Standard operative procedure on infant feeding was effective as there is a significant difference in pre-test and post-test knowledge & practice score.

Keywords: *Infant Feeding, Standard Operative Procedure.*

Introduction

“Formula feeding is the longest lasting uncontrolled experiment lacking informed consent in the history of society”

Infant means age between 0 and <12 months (and also sometimes referred to as 0-11 months) that is 12 completed months of life. A young infant is referred

as an infant aged between 0 and <6 months, that is six completed months of life. A very young infant is defined as an infant aged between 0 and <2 months (sometimes referred to as 0-1 months) that is two completed months of life.¹

Infant feeding plays a major role in promotion of infant health by reducing and preventing malnutrition.

Breastfeeding, especially if given exclusively up to first six months of life can make a major contribution to an infant's development and health and also associated with mother's better health. Infant feeding is also associated with reducing healthcare costs as well as having a positive impact on health of an infant in the society.²

Feeding baby with Katori spoon plays a specific & useful role. It helps Babies for better lip development, control and movement as they suck feed off a spoon. And also helps to limits the amount of food so baby will spit out and gets more food into baby's stomach. However, probably persons (i.e. nurses, parents) place the spoon in child's mouth and then scrape the food off on the top of infants lip as they remove the spoon. Instead of these they have to teach infant to suck the food off the spoon.⁴

Bottle feeding is a way to provide breast milk or formula feed to a baby who is not willing or not able to breastfeed directly from the breast. Bottle feeding is best alternative used for mother who is not able to breastfeed via breast or in the absence of breastfeeding.⁴

Need for the study: Directly or indirectly, 60% of the 10.9 million deaths occur annually among children under five due to Malnutrition. And two-thirds of these deaths are often related with inappropriate feeding practices; occur during the first year of life. Worldwide Only 35% of infants are exclusively breastfed during the first 4 months of their life. And also provides complementary feeding either too early or too late. Foods which are provided in weaning are frequently nutritionally unsafe & inadequate. The children who survive in malnutrition are more frequently suffer from the life-long consequences of impaired development.⁶

Appropriate feeding practices for infants and young children can increase their survival chances. It also helps to promote optimal growth and development, especially from birth to 2 years of age in the critical window. As per recommendation, breastfeed should be started within one hour of birth in infants, and continue breastfeed exclusively up to first six months of life. After six months continue to be breastfed up to 2 years of age with appropriate complementary feeding (age-appropriate feeding can be solid, semi-solid and soft foods.)

As infants growing, their nutrient needs also grown up with them. An infant's nutrient demands start to exceed after the first six months of life, what breast milk

alone can provide. To satisfied these growing demands, WHO recommends to begin eating solid, semi-solid or soft foods at age after 6 months to make sure that infants nutrient intake is sufficient to fuel their developing brains and bodies and thus it become increasingly important to track indicators related to consumption of solid, semi-solid and soft foods.⁸

Thus, adequate, appropriate knowledge & true knowledge along with the good skill practices are required to be imparted among the nursing students & nurses & the community should be made aware of providing infant feeding.

Material and Method

Research Design: In this study, the research design was studywas Quasi experimental research (Non-randomized control group) design.

Setting: The study was conducted in the Sumandeep Nursing College, Piparia, Vadodara.

Sample: 40 Students of 3rd year B.Sc. Nursing of Sumandeep Nursing College, Piparia, Vadodara.

Inclusion criteria:

1. Nursing students studying in 3rd year BSC. Nursing of Sumandeep Nursing College.
2. Nursing students who are willing to participate in the study.

Exclusion Criteria:

1. Nursing students who are not available during the time of data collection

Tool for data collection:

This consists of two parts:

Section 1: Self-Structured questionnaire to assess the knowledge regarding procedure of infant feeding.

Section 2: Check list to assess the practice of infant feeding.

Scoring procedure: For knowledge assessment

If answer is right then give 1

If the answer is wrong then give 0.

Scoring interpretation:

Category	Knowledge Score
Inadequate knowledge	0-8
Adequate knowledge	9-17
Excellent knowledge	18 – 25

For practice checklist 1 mark given for each correct step and 0 mark was given for wrong practice and partial step Scoring interpretation:

Category	Practice Score
Poor practice	0-10
Adequate practice	11-18
Good practice	19 – 26

Reliability: The reliability of tool established by using split half method Spearman Brown Prophecy formula ($r=0.87$) reliability test.

Data collection procedure:

1st & 2nd Day: Study subjects were selected from the population of the Study with use of purposive sampling technique and the purpose of the study was explained to the study subjects and the necessary information was provided to them regarding the research and the collection of the information. Thereafter, Informed consent was taken from each subject before implementing the data collection process, The subjects were explained about the tool and then pre-test was conducted for all the 40 subjects. After the pre-test whole sample were divided into two groups i.e. experimental (20) and control (20) group respectively using non-randomization process. Then, administered an infant feeding procedure to the experimental group by keeping control group blind.

8th and 9th day: The post test was conducted for all 40 selected study samples by administering same knowledge questionnaire and practice checklist to test hypothesis.

Statistical Design: Data were verified prior to computerized entry. The Statistical Package for Social Sciences (SPSS version 20.0) was used. Descriptive statistics were applied (e.g., mean, standard deviation, frequency and percentages). Test of significance (unpaired t test) was applied to test the study hypothesis.

Findings:

Section-I: Overall Distribution Of Respondent To Knowledge Level In Pre-Test

Table:1 Overall distribution of knowledge level in pre-test

Category	Knowledge	
	Frequency	%
Inadequate	18	45
Adequate	22	55
Excellent	00	00

Above table reveals that out of 40, total numbers of 18 with 45% of respondents were having inadequate knowledge, total number of 22 with 55% were having adequate knowledge but no one were having excellent knowledge regarding standard operative procedure on infant feeding.

Overall Distribution Of Respondent To Knowledge Level In Post-Test

Table:2 Overall distribution of knowledge in post-test

Category	Knowledge	
	Frequency	%
Inadequate	11	27.5
Adequate	9	22.5
Excellent	20	50

Above table reveals that out of 40, total numbers of 11 with 27.5% of respondents were having inadequate knowledge, total number of 9 with 22.5% were having adequate knowledge and total number of 20 with 50% were having excellent knowledge regarding standard operative procedure on infant feeding.

Section-II: Overall Distribution of Respondent to Practice in Pre- Test

Table:3 Overall distribution of practice score in pre-test

Category	Practice	
	Frequency	%
Poor Practice	32	80
Adequate Practice	8	20
Good Practice	00	00

Above table reveals that out of 40, total numbers of 32 with 80% of respondents were having poor practice, total numbers of 8 with 20% were having adequate practice and 00% were having good practice regarding standard operative procedures on infant feeding.

Overall Distribution Of Respondent To Practice In Post-Test

Table: 4 Overall distribution of practice score in post-test

Category	Practice	
	Frequency	%
Poor Practice	13	32.5
Adequate Practice	7	17.5
Good Practice	20	50

Above table reveals that out of total 40, 13 numbers with 32.5% of respondents were having poor practice, 7 numbers with 17.5% were having adequate practice and 20 numbers with 50% were having good practice regarding standard operative procedure on infant feeding

Section-III: Effectiveness Of The Knowledge Level In The Post Test Score

Distribution of mean percentage and “t” – value of post test knowledge score in experimental and control group.

Table 5: Mean % and t value of post-test knowledge score in both group

Post- Test Knowledge	Mean %	Mean Difference	t- Value	Significance
Experimental	85.19	48.28	15.18	S
Control	36.91			

At df = 38 and significant level 0.05 the obtained p value =15.18 is found to be more than the table value (2.02) which suggest the significant difference between experimental and control post-test knowledge score.

Effectiveness Of The Practice In The Post Test Score: Distribution of mean percentage and “t” – value of post test practice score in experimental and control group

Table 6: Mean % and t value of post-test practice score in both group

Post- Test Practice	Mean %	Mean Difference	t- Value	Significance
Experimental	88.46	50.96	14.31	S
Control	37.5			

At df= 38 and significant level 0.05 the obtained p value =14.31 is found to be more than the table value(2.02) which suggest the significant difference between experimental and control post-test knowledge score.

so there is no correlation between the knowledge and practice.

Thus, here the H1 is tested and as the above analysis reveals that there is a significant difference between post test score of knowledge and practice in the experimental and control group H1 IS ACCEPTED.

Discussion

Section-IV: Correlation Between The Knowledge And Practice Regarding The Revised Standard Operative Procedureon Infant Feeding

The aim of the study was conducted to evaluate the effectiveness of SOP on knowledge and practice regarding infant feeding among nursing students. It was found that nursing students had inadequate knowledge and practice regarding infant feeding and sop is effective to improve the knowledge and bring a good practice related to infant feeding.

The correlation co-efficient value(r) obtained by using Karl Pearson’s correlation co-efficient is -0.04

Various evidences how the effectiveness of SOP in improving knowledge and practice regarding infant feeding. The B.Sc. nursing students are having lack of knowledge regarding infant feeding, so it is important

that health care provider should provide the knowledge related to infant feeding.

Conclusion

The analysis shows that the total mean of post-test knowledge and practice score was observed to be significantly higher than the total mean of pretest knowledge and practice score after providing SOP to the nursing students regarding infant feeding. Hence, it is concluded that the SOP was effective to increase the knowledge regarding the infant feeding among nursing students. Demonstration regarding infant feeding should be given to all nursing students to improve their knowledge and practice of procedure which may aid in reducing rate of malnutrition and feeding problems.

Conflicts of Interest: The authors declare that there is no conflict of interest statement

Source of Funding: Fund for this research is researcher own.

Ethical Clearance: Ethical Clearance for this dissertation was obtained from the ethical committee SVIEC of Sumandeep Vidyapeeth University.

Reffernce

1. "Breastfeeding and Breast Milk: Condition Information". 19 December 2013. Archived from the original on 27 July 2015. Retrieved 27 July 2015.
2. American Academy of Paediatrics. American Academy of Paediatrics. Committee on Nutrition. Soy protein-based formulas: recommendations for use in infant feeding. Paediatrics. 1998 Jan;101(1 Pt 1):148.
3. Dykes F, Hall-Moran V, editors. Infant and young child feeding. John Wiley & Sons; 2009 Aug 14.
4. Lang S, Lawrence CJ, Orme RL. Cup feeding: an alternative method of infant feeding. Archives of disease in childhood. 1994 Oct;71(4):365.
5. Standard Operative procedures, clinical research resource HUB [Internet]. Hub.ucsf.edu. 2016 [cited 27 March 2016]. available from: <http://hub.ucsf.edu/sops>
6. World Health Organization, UNICEF.. Global strategy for infant and young child feeding. World Health Organization; 2003.
7. Organisation mondiale de la santé. Département santé et développement, World Health Organisation Staff, World Health Organization, UNICEF.. Global strategy for infant and young child feeding. World Health Organization; 2003.
8. Rommel N, De Meyer AM, Feenstra L, Veereman-Wauters G. The complexity of feeding problems in 700 infants and young children presenting to a tertiary care institution. Journal of paediatric gastroenterology and nutrition. 2003 Jul 1; 37(1):75-84.
9. Definition of ASSESS [Internet]. Merriam-webster.com. 2016 [cited 27 March 2016]. Available from: <http://www.merriam-webster.com/dictionary/assess>
10. What is effectiveness? Definition and meaning [Internet]. Business Dictionary.com. 2016 [cited 27 march 2016]. Available from: <http://www.businessdictionary.com/definition/effectiveness.html#ixzz43gfk000>

Knowledge, Attitude and Practice of Biomedical Waste Management in Nursing Staff of a Private and a Government Tertiary Care Teaching Hospital: A Comparative Study

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Abstract

Introduction: Biomedical waste is “Any waste which is generated in the diagnosis, treatment or immunization of human beings or animals or during research” in a hospital. Improper disposal of hospital waste poses a major threat to the environment. Lack of proper management, awareness, insufficient resources and poor control of disposal of waste are the most pressing problems faced.

Objective: To compare the knowledge, attitude and practice of hospital waste management in nursing staffs and nursing assistants of a private and government tertiary care hospital in Chennai, Tamil Nadu.

Methodology: This is a cross sectional study done in a private and a government tertiary care teaching institute on 300 nursing staff (150 from each) using an orally administered structured questionnaire. The data were entered into excel and analysis was done.

Result: Of the 150 participants from government hospital 71% had training in BMW management, 82% knew where to report in case of a needle stick injury, 61% perceived that they have adequate knowledge regarding BMW management, 98% were willing to attend programmes regarding BMW. 73% had good knowledge regarding BMW management. 90% practice good management of BMW.

Of the 150 participants from private hospital 81% had training in BMW management, 79% knew where to report in case of needle stick injury, 67% perceived that they have adequate knowledge regarding BMW management, 95% were willing to attend programs regarding BMW management. 74% had good knowledge. 85% practice good management of BMW.

Conclusion: The knowledge, attitude and practice of BMW management among nurses and nursing assistants of the private and the government hospital are found to be satisfactory. There is no significant difference (at $p < 0.05$) in the knowledge, attitude and practice of BMW management among the nurses and nursing assistants of both the hospitals.

Keywords: *Biomedical waste management, knowledge, attitude, practice, nursing staff.*

Introduction:

Biomedical waste (BMW) is the waste that is generated in hospitals and health care centres during diagnosis, treatment or immunisation of human beings, mainly consists of needles, syringes, ampoules, dressing materials, disposable plastics and microbiological wastes⁽¹⁾. With the aim of reducing health problems and

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treating the sick, health care services inevitably produce wastes that may be hazardous to health. According to the World Health Organisation (WHO), 10-25% of the biomedical waste are estimated to be hazardous⁽²⁾. Improper handling of biomedical waste increases the airborne pathogenic microbes, adversely affecting the hospital environment and community at large. Apart from polluting water, air & soil, it also has considerable impact on human health due to aesthetic effects.

BMW management (BMWM) means the management of waste produced by hospitals using techniques that will check the spread of diseases. The objectives of biomedical waste management are to reduce waste generation, to ensure its efficient collection, handling, as well as safe disposal in such a way that it controls infection as these wastes need a special attention for their proper disposal. Adequate knowledge, attitude and practices regarding biomedical waste management is lacking in developing countries⁽³⁾. The volume of the health care wastes have also increased over the last 30 years. The World Health Organisation has hence prepared biomedical waste management guidelines to ensure proper handling of these wastes.

This study was done to assess and compare the knowledge, attitude and practice of biomedical waste management among the nursing staff working in a private tertiary care hospital and a government tertiary care hospital in Chennai.

Materials and Method

This was an observational cross-sectional study done from January 2019 to May 2019. This study was conducted in a private tertiary care hospital and in a government tertiary care hospital situated in Chennai, capital city of Tamil Nadu in South India. The study included the nurses and nursing assistants working in the above mentioned institutions.

The sample size of the study is $n=300$, 150 from each of the above mentioned institutions. The sample size was measured using the formula $\{(Z_{\alpha}-Z_1-b)^2 * [P_1(100-P_1)+P_2(100-P_2)]\} / (P_1-P_2)^2$, where $P_1 = 35\%$, $P_2=20\%$ ⁽⁴⁾, expected difference of 15%, alpha error of 5% at 95% confidence interval.

After obtaining permission from the human resource department, a list of all the nurses and nursing assistants working in the above mentioned institutions was obtained and the participants were selected randomly using

random numbers table. Nurses and nursing assistants not willing to participate in the study were excluded.

The study tool used was an orally administered structured questionnaire containing questions regarding the knowledge, attitude and practice of Biomedical waste management (BMWM) respectively. Questions related to demographic details like the participants name, age, sex, department they are currently working in, total years of experience, years worked in the current hospital, their training in biomedical waste management, years of experience, vaccination against Hepatitis, needle stick injury were also included. It included eleven questions to assess their knowledge, which included questions regarding where they would dispose certain wastes like anatomical wastes, contaminated gauze, disposable intravenous tubes and catheters, broken glass vials, discarded disinfectants, contaminated mattresses and linens. The six attitude questions were regarding whether they thought biomedical waste management as a financial burden on the setup, do they find it as a burden to report a needle stick injury, whether they are interested in attending programs to enhance and upgrade their knowledge on biomedical waste management and if they think it is important to dispose health care wastes in a proper manner. Six questions regarding their practice of biomedical waste management was also included (Table 2). One point was awarded to each correct answer and the wrong answers weren't given any point. Each of the three aspects were assessed separately and a score of more than 60% was considered that the participant had good knowledge, attitude and practice of biomedical waste management. The data was entered in MS-Excel spreadsheet and analysis was done using SPSS software. Qualitative data was expressed as frequencies and proportions, quantitative data were summarised as mean (standard deviation). Bivariate analysis was done using chi square.

Results

A total of 300 nurses and nursing assistants took part in this study, of which 150 were from the private institute and 150 were from the government institute.

The mean age of the participants from the government institute was 32.9 years whereas the that of participants from the private institute was 25.17 years. Of the participants, 81% from the government institute and 75% from the private institute were nurses. The mean years of experience was higher in the government,

which is 8.29 years compared to 3.06 mean years in the private institute (Table 1).

Significantly more percent of the participants (90%) from the government institute separate biomedical waste during collection and they also collect liquid waste in leakage proof bags (77%) when compared to the participants from the private institute. Significantly more participants from the private institute collect liquid and other wastes together (43%) whereas more percent (23%) of participants from the government institute store infectious waste together with the other wastes. 83% of the participants from the government institute use personal protection while handling biomedical waste whereas only 77% of the participants from the private institute do so which is significantly less when compared. (Table 2)

Only 71% of the participants from the government institute and 81% of the participants from the private institute have had training in biomedical waste management. (figure 1).

Although the difference is not statistically significant, it was found out that increased percentage of the participants from the government institute had a good knowledge, attitude regarding biomedical waste management and a good practice of biomedical waste management when compared with the participants from the private institute (Table 3).

All the participants from the private institute had been vaccinated against Hepatitis B compared to the 73% from the government institute and 82% of the government institute participants knew to whom they

were supposed to report an incident of needle stick injury compared to the 79% from the private institute. 25% of the participants from the private institute have had a needle stick injury in the past and 90% of them had reported the incident to appropriate authority, whereas 33% of the participants from the government institute have had a needle stick injury and all of them had reported the incident to the authority.

61% of the participants from the government institute showed a positive attitude towards biomedical waste management but only 48% of the private institute participants showed positive attitude. 98% of the participants from the government institute and 95% of the participants from the private institute were willing to attend programs regarding biomedical waste management.

70% of the participants from the private institute and 62% of the participants from the government institute think that there is an increased risk of injury if the health care waste is segregated at the source. 45% of the participants from the private institute and 33% of the participants from the government institute think BMW setup as a financial burden on the institute. 31% of the total study population consider it as a burden to report needle stick injury.

Table 1: General profile of the participants

General Profile	Government	Private
Mean age	32.89 years	25.17 years
Mean years of experience	8.29 years	3.06 years
Nurses	122 (81%)	112 (75%)
Nursing assistants	28 (19%)	38 (25%)

Table 2: Comparison between the various practice habits of the participants from the two institutes .

Practice Habits	Government	Private	P-Value
Sort BMW during collection	135(90%)	120(80%)	0.015293*
Separate sharps from blunt waste	140(93%)	137(91%)	0.515049
Use personal protection tools while handling BMW	125(83%)	116(77%)	0.191118
Collect liquid waste in leakage proof bags	115(77%)	91(61%)	0.002815*
Collect liquid and other wastes together	44(29%)	64(43%)	0.016145*
Store infectious wastes together with other wastes	35(23%)	14(9%)	0.001039*

(* - Significant at $P < 0.05$)

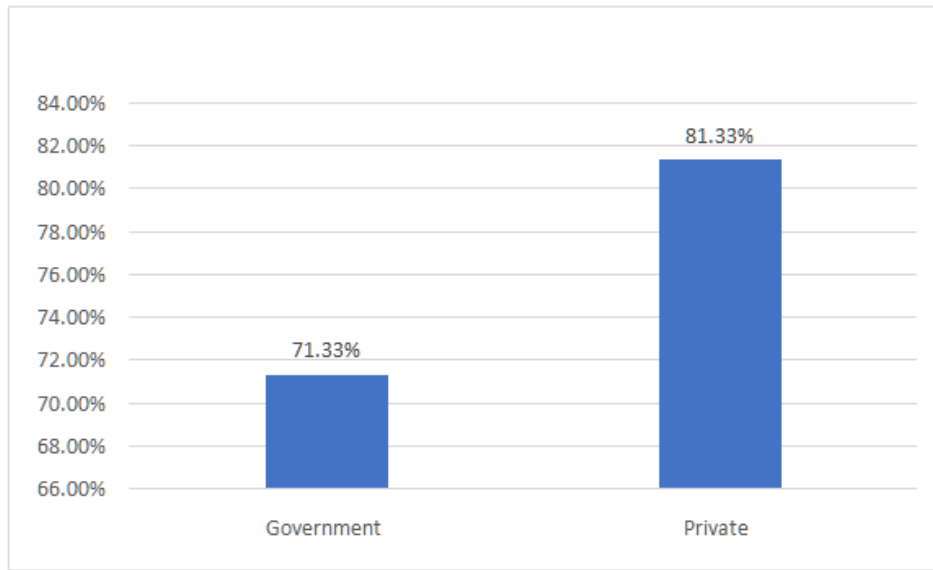


Figure 1: Participants with training in BMW.

Table 3 Comparison between the percentage of participants having good knowledge, practicing good management of BMW and having a good attitude regarding the same

	Government	Private	P- Value
Good knowledge	73.33%	74%	0.872707
Good attitude	61.33%	48.33%	0.076136
Good practice	90%	85.33%	0.285049

Discussion

This is a cross sectional study conducted in a private and a government tertiary care hospitals regarding the knowledge, attitude and practice of BMW among their nurses and nursing assistants.

In this study it was found that 71% of the participants from the government institute and 81% of the participants from the private institute had training in biomedical waste management, compared to 68% of the nurses who participated in a study done by Lohani N et al⁽⁵⁾.

All the participants from the private institute had been vaccinated against Hepatitis B compared to the seventy three percent (73%) from the government institute. Only 20% of the nurses who participated in the study done by Soyam GC et al⁽⁶⁾ had been vaccinated against Hepatitis. Reporting of an incident of needle stick injury was high in both the study groups (100% in the government and 90 % in the private institutions) when compared to a study done by Stein et al⁽⁷⁾ which showed only 37% reporting .

83% of the participants from the government institute use personal protection while handling biomedical waste whereas only 77% of the participants from the private institute do so. In a study by Madhu Kumar et al⁽⁸⁾ all the participants wore personal protective equipments while handling biomedical waste

98% of the study population knew about the different biomedical waste categories compared to 56% of the participants in a study done by Basu et al⁽⁹⁾, 45% of nurses of a study by Anand P et al⁽¹⁰⁾ and 90% of the study population consisting of doctors and nurses in a study conducted by Mathur et al⁽¹¹⁾.

Sixty one percent (61%) of the participants from the government institute and only forty eight percent (48%) of the private institute participants showed a positive attitude towards biomedical waste management. In a study done by Adekunle Olalfa et al⁽¹²⁾ 54% of the staff who participated showed a positive attitude towards biomedical waste management.

70% of the participants from the private institute and 62% of the participants from the government institute

think that there is an increased risk of injury if the health care waste is segregated at the source, whereas in a study by Adekunle Olalifa⁽¹²⁾ et al 24% of the participants had the same idea. 31% of the participants consider it as a burden to report needle stick injury, while 44% of the nurses who participated in a study by Anand P et al⁽¹⁰⁾ thought the same. But in a study by Malini et al⁽¹³⁾, the participants did not consider it as a burden to report an incident of needle stick injury. 45% of the participants from the private institute and 33% of the participants from the government institute think biomedical waste management setup as a financial burden on the institute. In a study done by Khan MJ et al⁽¹⁴⁾, 53% of the physicians who took part thought BMWM setup as a financial burden on the institute.

Conclusion

In this study it has been found that the difference in the knowledge, attitude and practice of biomedical waste management was not significant. But certain aspects in the practice of biomedical waste management like segregation of waste during collection and collection of liquid and other wastes separately were better among the participants from the government institute, whereas more percent of participants from the private institute stored infective and other wastes separately. The attitude regarding biomedical waste management was better in the participants from the government institute than that of the participants from the private institute and more participants from the government institute were willing to attend programs to improve their knowledge and practice of biomedical waste management.

Even though the knowledge, attitude and practice of biomedical waste management are not poor among the participants of this study, it can be further improved by conducting programs stressing not only on the knowledge and practice but also should stress about the attitude of the workers towards biomedical waste management by educating them about the importance of it and by enlightening them about the hazardous effects of improper management of biomedical waste management on the environment, public health and also on health of the health care workers themselves.

Conflict of Interest: Nil

Source of Funding: Nil

Ethical Clearance: Approval was obtained from Institutional Research Board of Saveetha Medical College and Hospital, Thandalam, Chennai.

References:

- Ola-Adisa EO, Mangden YPE, Sati YC, Adisa JO. Knowledge, Attitudes/Beliefs and Practices in Medical Waste Management-An Appraisal of Jos North LGA, Plateau State, Nigeria. *Int J Res Humanit Soc Stud.* 2015;2:43.
- Y. Chartier, J. Emmanuel, U. Pieper, A. Prüss, P. Rushbrook and R. Stringer, *Safe Management of Wastes from Healthcare Activities*, World Health Organization (WHO), Geneva, Switzerland, 2nd edition, 2014.
- Ehrampoush MH, Baghiani Moghadam MH. Survey of Knowledge, Attitude and Practice of Yazd University of Medical Sciences Students about Solid Wastes Disposal and Recycling. *Iranian J Environ Health Sci Eng.* 2005;2(2):26.
- Mehta TK, Shah PD, Tiwari KD. A Knowledge, Attitude and Practice Study of Biomedical Waste Management and Bio-safety among Healthcare Workers in a Tertiary Care Government Hospital in Western India [Internet]. Vol. 9, *National Journal of Community Medicine* | Volume. Available from: www.njcmindia.org
- Lohani N, Dixit S. Biomedical waste management practices in a tertiary care hospital: a descriptive study in Srinagar, Garhwal, India. *Int J Community Med Public Heal.* 2017 Jan 25;4(2):465.
- Soyam GC, Hiwarkar PA, Kawalkar UG, Soyam VC, Gupta VK. KAP study of bio-medical waste management among health care workers in Delhi. *Int J Community Med Public Heal.* 2017 Aug 23;4(9):3332.
- Stein AD, Makarawo TP, Ahmad MF. A survey of doctors' and nurses' knowledge, attitudes and compliance with infection control guidelines in Birmingham teaching hospitals. *J Hosp Infect.* 2003;54:68-73.
- Madhukumar S, Ramesh G. Study about awareness and practices about health care wastes management among hospital staff in a medical college hospital, Bangalore. *Intern J Basic Med Sci.* 2012;3(1):7-11.
- Basu M, Das P. PRA of future physicians on biomedical waste management in a tertiary care hospital of WBJSBM 2012 J-42. doi: 10.4103/097.-9668.95945. P 22690049; PP Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3361776/>
- Anand P, Jain R, Dhyani A. Knowledge, attitude and

- practice of biomedical waste management among health care personnel in a teaching institution in Haryana, India. *Int J Res Med Sci.* 2016;4246–50.
11. Mathur V, Dwivedi S, Hassan MA, Misra RP. Knowledge, attitude, and practices about biomedical waste management among healthcare personnel: A cross-sectional study. *Indian J Comm Med.* 2011;36:143-5.
 12. Olaifa A, Govender RD, Ross AJ. Knowledge, attitudes and practices of healthcare workers about healthcare waste management at a district hospital in KwaZulu-Natal. *South African Fam Pract.* 2018 Sep 3;60(5):137–45.
 13. Malini A, Eshwar B. International Journal of Biomedical Research Knowledge, Attitude and Practice of Biomedical waste management among health care personnel in a tertiary care hospital in Puducherry. *Int J Biomed Res [Internet].* 2015;6(03):6. Available from: www.ssjournals.com
 14. Khan MJ, Hamza MA, Zafar B, Mehmod R, Mushtaq S. Knowledge, attitude and practices of health care staff regarding hospital waste handling in tertiary care hospitals of Muzaffarabad, AJK, Pakistan. *Int J Sci Reports.* 2017 Jun 30;3(7):220.

A Study to Find Out Strongest Predictive Factor for Functional Outcome After Stroke: An Exploratory Study

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Abstract

Background: Stroke is second commonest cause of death and fourth leading cause of disability worldwide. Its recovery makes an important concern not only for the physiotherapists but for the entire rehabilitation team.

Aim/Purpose: Stroke affects each patient variably and differently. All stroke patients who receive physiotherapy services may improve in function, rate and quality may vary. At present, there is no any objective method which tells expected prediction for recovery after stroke. So it becomes very important that there should be identification of different factors to predict recovery after stroke.

Objective: To find out strength of association between different predictive factors and functional outcome of stroke patients.

Setting: Different physiotherapy centres of Surat city.

Method: Exploratory study was done in Surat city. Selection of stroke patients was done as per selection criteria. After ethical clearance, subjects were explained about the study. Informed consent forms were signed by the patient and/or relatives. Subjects selected by convenient sampling were assessed for different 21 factors and functional outcome by Modified Barthel Index Score was recorded for all patients.

Participants: Total 125 male and female stroke patients.

Main Outcome Measure: Modified Barthel Index Score.

Results: Linear regression at confidence interval 95% was applied to find out strength of association between different predictive factors and post stroke functional outcome. Length of hospitalization was found as strongest predictive factor for functional outcome.

Conclusion: These findings may suggest that length of hospitalization is strongest factor for prediction of post stroke recovery.

Keywords: Stroke, Predictive factors, Modified Barthel Index, Post stroke functional outcome, Length of hospitalization.

Introduction

World Health Organization (WHO) defines stroke as a clinical syndrome characterized by rapidly developing clinical symptoms and/or signs of focal and at times global loss of cerebral function, with symptoms lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin.^{1,2}

Stroke is classified into two types. Ischemic stroke is the most common type affecting about 67-80% of individuals with stroke.^{2,3} and results when a clot or block impairs blood flow, depriving the brain of essential oxygen and nutrients, leading to disruption of cellular metabolism, injury and death of tissues. Hemorrhagic stroke occurs when blood vessels rupture, causing

leakage of blood in and around brain. It may occur due to increase in intracranial pressure or restriction of distal blood flow.¹ Stroke is a global health problem. It is second commonest cause of death and fourth leading cause of disability worldwide.⁴

The incidence of stroke rises rapidly with increasing age. In India, the overall prevalence rate for stroke lies between 84 – 262 per 100,000 in rural area⁵ and between 334 – 424 per 100,000 in urban areas.⁵ After the age of 55 years, the risk of stroke doubles every 10 years; two thirds of all strokes occurring in people older than the age of 65 years.⁶ The incidence of stroke is about 1.25 times greater for males than female.⁷

Major risk factors for stroke are hypertension, heart disease, atherosclerosis, diabetes and elevated total blood cholesterol level. All these factors are not only responsible for occurrence of stroke but they are also affecting post stroke recovery. Recovery from stroke is generally fastest in the first weeks after onset, with measurable neurological and functional recovery occurring in the first month after stroke. Much of early recovery can be attributed to the resolution of diachesis, or transient inhibition of function, that accompanies acute stroke. Thus the reduction of edema, absorption of damaged tissue, and improved local circulation and cellular metabolism allows intact neurons that were previously inhibited to regain function.⁸ Patients can continue to make measurable functional gains generally at a reduced rate for months or years after insult. Late recovery of function has been demonstrated for patients with chronic stroke (defined as greater than 1 year post-stroke) who undergo extensive functional training.⁹⁻¹⁴ These changes are due largely to function-induced plasticity. A functional training approach that emphasizes use of the more involved extremities and an enriched environment effectively stimulates neural reorganization of the brain. Prolonged recovery with improvements occurring over a period of years is especially apparent in the areas of language and visuospatial function.¹⁵ Predictor on activity limitation and participation restriction are found the effect of age, gender, stroke type, stroke severity, pre stroke disability and post stroke disability remains highly prevalent on activity limitation and participation restriction after 4 years of stroke¹⁶

Stroke affects each patient variably and differently.¹⁷ All stroke patients who receive physiotherapy services may improve in function, rate and quality of improvement

may vary.¹⁸ Some stroke patients may show very good recovery in short period where some may show minimal improvement. This leads to variation in financial cost of treatment.¹⁹ In this fast growing world of health science at present, there is no formula or scale which tells time prediction for recovery after stroke. Era of evidence based practice and clinical reasoning is emerging day by day. Health insurance coverage also needs some objective data for prediction for recovery after stroke. So it becomes of utmost importance that there should be some objective criteria to predict recovery of stroke. Information of factor responsible for good recovery after stroke is mandatory for patient evaluation, treatment planning, guidance to patient and relatives and also for searching new therapeutic regime.²⁰ For the same, association should be found between different predictive factors and functional recovery in stroke patients. So objective of study is to find out strength of association of different predictive factors with post stroke functional outcome.

Materials and Method

The present study is an exploratory study which is a cross-sectional observational design; where each subject was assessed one time only for physical assessment and was assessed for past history, records of hospitalization and demographic data etc. The Ethical Committee recognized by the Central Drug Standard Control Organization (CDSCO), Govt. of India had approved this search protocol. The patients of Surat, those coming to different Physiotherapy clinics with a clinical diagnosis of stroke by general physician or neurophysician and who are discharged from hospital due to stable medical condition and having less than 6 months post stroke duration, during the period of September 2017 to October 2018 were considered as the study population.

Few different hospitals and physiotherapy centres of Surat city were visited frequently, at least once a week, to reach to new stroke patients. In the present research, a Convenient Sampling was used to select stroke patients. The purpose of this study was explained and a written informed consent was taken from all the patients &/or relatives. Patients were preliminary screened based on the inclusion and exclusion criteria.

Inclusion Criteria:

1. All stroke patients who are willing to participate
2. Both male & female stroke patients

3. Mini mental scale examination score ≥ 24 ²¹
4. Duration of stroke varies from discharge from hospital up to 6 months²²
5. Patients who are taking medical treatment as per guidelines of Neurophysician or General Physician & physiotherapy treatment as per guidelines of Physiotherapist.
15. Duration of Diabetes
16. Duration of Atrial Fibrillation
17. Duration of Cardiomyopathy
18. Duration of Renal dysfunction
19. Socioeconomic condition
20. Education
21. Post Stroke Duration

Exclusion Criteria:

1. Stroke patients who are not cooperative.
2. Stroke patients who have auditory &/or visual deficits.
3. Stroke patients who do not have proper medical records.
4. Patients having another neurological deficit with stroke.
5. Patients who have been Discharged Against Medical Advice (DAMA) from initial hospitalization due to request of patients &/or relatives or extended hospitalization due to any other medical &/or surgical condition with stroke or who are not hospitalized.

Patients were assessed as per assessment form which includes patient's demographic data, stroke history, addiction history, family history and presence of co-morbidities etc. List of the factors are as follows:

1. Age
2. Gender: Male/Female
3. Hand dominancy: Right/Left
4. Body Mass Index (BMI)
5. Side affected: Right/Left
6. Type of Stroke: Hemorrhagic/Ischemic
7. Length of Coma (LOC)
8. Length of Stay in Hospital (LOS)
9. Family History: Present/Absent
10. Duration of Smoking History
11. Duration of Alcohol History
12. Duration of Tobacco History
13. Transient Ischemic Attack/Stroke History: Present/Absent
14. Duration of Hypertension

All these factors were decided by review of literature and consensus among eleven subject experts who are dealing with stroke patients with experience of more than five years which included one neurophysician and ten senior physiotherapists and neurophysiotherapists.

Additionally all the patients were assessed by Modified Barthel Index for post stroke recovery and by Revised Kuppaswami Scale for socio economic status of them.

All the subjects passed for assessment for demographic details and physical examination performed by there searcher. On the day of the study, all subjects underwent a baseline assessment using Mini Mental Examination Scale Examination. All the measurements were taken by there searcher of the study. All the patients included in study were under Physiotherapy treatment. Goal of Physiotherapy treatment was an attempt to meet the individual needs of the patients, incorporating re-education of lost movement, facilitation method and was aimed at enhancing patient's independence for activity of daily life. Patients were allowed to speech therapy requiring their services.²³

Outcome Measure: The Mini-Mental Status Examination (MMSE) provides a valid and reliable quick screen of cognitive function.¹⁸ Functional outcome was assessed by means of the Modified Barthel Index (MBI).²⁴

Human and Animal Research: This study is approved and registered in Clinical Trial Registry of India with registration number CTRI/2018/10/015992

Statistical Analysis: In 125 stroke patients, from discharge to upto 6 months, Modified Barthel Index (for post stroke recovery as dependent variable) was checked for multivariate linear regression with all predictive factors (as independent variables)with confidence interval set at 95% by SPSS version 20 for Microsoft Windows.

Result

Results by for multivariate linear regression with all predictive factors is shown in following table 1.

Table 1: Strength of association of different predictive factors on post stroke recovery

Sr. No.	Factor	R Square	Adjusted R Square	Strength of Association
1	Side of body	0	-0.008	0.8
2	Age	0.023	0.015	1.5
3	Gender	0.035	0.027	2.7
4	Hand dominancy	0.005	-0.003	0.3
5	Type of stroke	0	-0.008	0.8
6	Length of coma	0.092	0.085	8.5
7	Length of hospitalization	0.146	0.139	13.9
8	Body Mass Index	0.042	0.031	3.1
9	Family History	0.005	-0.003	0.3
10	Smoking history	0	-0.008	0.8
11	Alcohol history	0	-0.008	0.8
12	Tobacco	0.004	-0.004	0.4
13	TIA	0.02	0.012	1.2
14	Diabetes	0.002	-0.006	0.6
15	Hypertension	0.006	-0.003	0.3
16	Atrial fibrillation	0.003	-0.005	0.5
17	Cardiomyopathy	0.003	-0.005	0.5
18	Renal dysfunction*	-	-	-
19	Socioeconomic condition	0.007	-0.001	0.1
20	Education	0.037	0.029	2.9
21	Post stroke duration	0.023	0.015	1.5

*In study, no patient with renal dysfunction was found.

Bar diagram showing strength of association of different predictive factors in post stroke functional outcome

Discussion

From the results, it is seen that different factors affect post stroke functional outcome variably. Out of all these factors, length of hospital stay is most significant as well as strongest predictive factor. Literature has found more than 60 predictors those affect post stroke recovery. Length of hospitalization is contributing 13.9% alone in predicting post stroke functional outcome. Length of hospitalization shows time taken by physician to make vitals stable. Many studies aimed to see the

outcome/recovery of patient with respect to all factors (age, gender, body mass index, diabetes, hypertension, smoking addiction, tobacco addiction, alcohol addiction, family history of stroke, previous history of transient ischemic attack) on recovery after stroke.

Other studies of Simic-Panic S Dusica et al. (2015) also showed that length of stay in hospital is also considered predictive factors which are decided by functional status at the time of admission in hospital and it shows time taken for vitals to be stable.^{25, 26} Jon Erik Ween et al (2000) concluded that length of stay was significantly prolonged in patients with poor outcomes.²⁷ Stephen Bagg (2002) concluded that it is one of the strongest predictor for stroke outcome.²⁵ All these studies support findings of present study.

Additionally it was found during study that few patients had taken discharge against medical advice and few patients have not hospitalised themselves and taken treatment at home by frequent visit of doctor to avoid financial burden of hospital stay. These types of patients were not included in study. So for these types of patients, significant factor for recovery is questionable.

Limitations of present study were small sample size, un-cooperative patients may not respond well for some examination, weight of patient cannot be measured accurately in few patients for those who are not able to stand without assistance and undiagnosed co-morbidities like hypertension and diabetes etc may affect the results.

Future studies can be done with more sample size as per prevalence rate and follow-up for more than 6 months.

Conclusion

Length of hospital stay is the strongest factor to predict post stroke functional outcome. So it should be considered for prognosis of stroke recovery.

Ethical Clearance: Yes

From Ethics Committee, School of Physiotherapy, RK University (ECR/259/Indt/2016)

Funding: Self

Conflict of Interest: None

References

1. Carr J, Shepherd R. Neurological rehabilitation. Edinburgh: Churchill Livingstone/Elsevier; 2010

2. Implications of the AHA/ASA Updated Definition of Stroke for the 21st Century [Internet]. Worldneurologyonline.com. 2019 [cited 13 November 2019]. Available from: <https://worldneurologyonline.com/article/implications-of-the-ahaasa-updated-definition-of-stroke-for-the-21st-century/>
3. O'Sullivan S, Schmitz T. Physical rehabilitation. Philadelphia: Davis; 2007.
4. Tripathi M, Vibha D. Stroke in Young. India. Stroke Research and Treatment. 2011; 2011:1-6
5. Pandian J, Sudhan P. Stroke Epidemiology and Stroke Care Services in India. Journal of Stroke. 2013;15(3):128.
6. Umphred D. Neurological rehabilitation. Saint Louis [etc.]: Mosby/Elsevier; 2013.
7. Heart Disease and Stroke Statistics—2014 Update | Circulation [Internet]. Ahajournals.org. 2019 [cited 13 November 2019]. Available from: <https://www.ahajournals.org/doi/abs/10.1161/01.cir.0000441139.02102.80>
8. Stein D, Brailowsky S, Will B. Brain repair. New York: Oxford University Press; 1997.
9. Wolf S, Lecraw D, Barton L, Jann B. Forced use of hemiplegic upper extremities to reverse the effect of learned nonuse among chronic stroke and head-injured patients. Experimental Neurology. 1989;104(2):125-132.
10. Liepert J, Miltner W, Bauder H, Sommer M, Dettmers C, Taub E et al. Motor cortex plasticity during constraint-induced movement therapy in stroke patients. Neuroscience Letters. 1998;250(1):5-8.
11. Miltner W, Bauder H, Sommer M, Dettmers C, Taub E. Effects of Constraint-Induced Movement Therapy on Patients With Chronic Motor Deficits After Stroke. Stroke. 1999;30(3):586-592.
12. Kunkel A, Kopp B, Müller G, Villringer K, Villringer A, Taub E et al. Constraint-induced movement therapy for motor recovery in chronic stroke patients. Archives of Physical Medicine and Rehabilitation. 1999;80(6):624-628.
13. Taub E, Miller NE, Novack TA, Cook EW, Fleming WC et al: Technique to improve chronic motor deficit after stroke. Archives of Physical Medicine and Rehabilitation. 1993; 74(4):347-354
14. Visintin M, Barbeau H, Korner-Bitensky N, Mayo N. A New Approach to Retrain Gait in Stroke Patients Through Body Weight Support and Treadmill Stimulation. Stroke. 1998;29(6):1122-1128.
15. Post-Stroke Rehabilitation Guideline Panel: Post-Stroke Rehabilitation Clinical Practice Guideline. Aspen, Gaithersburg, MD, 1996 (formerly published as AHCPR Publication No. 95-0662, May 1995).
16. Gadidi V, Katz-Leurer M, Carmeli E, Bornstein N. Long-Term Outcome Poststroke: Predictors of Activity Limitation and Participation Restriction. Archives of Physical Medicine and Rehabilitation. 2011;92(11):1802-1808.
17. Nazzal M, Saadah M, Trebinjac S, A Al-Awadi O, A Al-Shamsi K. Effect of risk factors on functional outcome after stroke rehabilitation. Neurosciences. 2006;11(1):15-20.
18. Lin J, Tsai A, Lo S, Chang J, Huang M. Predicting the Grade of Disability 1 Year After Stroke Following Rehabilitation. The Kaohsiung Journal of Medical Sciences. 2005;21(5):212-219.
19. Ones K, Yalcinkaya EY, Toklu BC, Caglar N. Y, BC T, N C. Effects of age, gender, and cognitive, functional and motor status on functional outcomes of stroke rehabilitation. NeuroRehabilitation. 2009;25(4):241-249.
20. Jorgensen H, Reith J, Nakayama H, Kammersgaard L, Raaschou H, Olsen T. What Determines Good Recovery in Patients With the Most Severe Strokes?. Stroke. 1999;30(10):2008-2012.
21. Tombaugh T, McIntyre N. The Mini-Mental State Examination: A Comprehensive Review. Journal of the American Geriatrics Society. 1992;40(9):922-935.
22. Takeuchi N, Izumi S. Noninvasive Brain Stimulation for Motor Recovery after Stroke: Mechanisms and Future Views. Stroke Research and Treatment. 2012;2012:1-10.
23. Loewen S, Anderson B. Predictors of stroke outcome using objective measurement scales. Stroke. 1990;21(1):78-81.
24. Gauthier L, Dehaut F, Joanne Y. The Bells test: a quantitative and qualitative test for visual neglect. International Journal of Clinical Neuropsychology. 1989;11: 49-54.

25. Bagg S, Pombo A, Hopman W. Effect of Age on Functional Outcomes After Stroke Rehabilitation. *Stroke*. 2002;33(1):179-185.
26. Dusica S, Gordana D, Mirjana J, Nedeljko P. Stroke rehabilitation: Which factors influence the outcome? *Annals of Indian Academy of Neurology*. 2015;0(0):0.
27. Jon EW, Stephen T, Mernoff, Michael P. Recovery Rates After Stroke and Their Impact on Outcome Prediction. *Neurorehabilitation and Neural Repair* 2000;14:229-235

Impact of Demographic Factors on the Ethical Conduct of Physicians in India

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Abstract

The study focus on the various demographic characteristics related to physician's practice related code of ethics in the healthcare sector which might help in upgrading the ethical standards to promote healthy medical care. The demographic characteristics of the physicians includes gender, age groups, work experience and education qualification. The target population was full time physicians from the with a sample size of 114, comprising of 56 male and 58 female respondents with age group 25-29 years, 30-34 years and above 34 years. To accomplish the objectives stratified random sampling technique was used. A standardized questionnaire was used to identify the practice related code of ethics of the physicians. The results revealed that there was a significant difference among various work experience and education qualification. Whereas, age and gender were found to have no significant difference regarding practice code of ethics. Therefore it is vital to change the attitude of physicians and have adequate knowledge and awareness about the ethical codes among all the stage of the medical process.

Keywords: Healthcare sector, Hospitals, Physicians, Practice code of ethics, Demographic characteristics, Healthcare ethics.

Introduction

Health care sector is one of the largest growing sectors in India. According to Indian Brand Equity Foundation, 2017 Indian health care sectors became the fifth largest employer with a total of 4,713,061 employers¹. To cater the various requests of the patients in the medical field, the physicians are expected not only to have the skills and knowledge relevant to their particular field but also with the ethical and legal perspective which needs to be followed on the regular practices².

But what does ethics means? The word *Ethics* originally is derived from the Greek word *ethikos* or *ethos*-meaning *custom, habit or character*. However, ethics has been defined in a range of diverse forms³. Medical ethics has been framed into four moral principles: a. Autonomy, is the respect for the patient's decision making capacity b. Beneficence, is the obligation to remove harm and contribute for the welfare of others c. Non malfesance, is not to impose adverse effects on the patients d. Justice, implies equitable and fair distribution of benefits, risk, cost and resources⁴. Conversely in the recent years, there has been increasing

concern regarding the ethical behavior of the health care professionals. This is frequently indicated as complains against the physicians for the illegal medical practices such as re-using syringe, unnecessary prescription and health care fraud^{5,6,7}.

Gender, Age, Work experience and Education on ethical practice at workplace: Gender differences in the work environment are initiated from psychological, social or physical features⁸. According to the social role theory, men and women hold different place in workplace as well as in the family⁹. Furthermore, men and women are genetically programmed differently to behave since birth¹⁰. Therefore gender role attitudes may lead to differences in the perception of unethical behaviour among the men and women.

Age can be a factor related with practice code of ethics among the physicians. A study was conducted regarding practice code of ethics among 500 medical doctors, revealing that the doctors of age group 25-29 follow strict ethical behaviour than the senior doctors¹¹. Another study tried to understand the knowledge of medical ethics among the senior and junior doctors¹².

Practice code of ethics is influenced by the work experience of the doctors in their particular field. A study conducted on medical professionals of Rajasthan showed that best practice was found among those with 10-20 years of work experience¹³. Moreover, medical doctors with work experience more than 8 years were likely to have favorable attitude towards code of ethics as they might recognize the importance of code of ethics¹⁴.

Doctors working in government health sector showed healthy practice of ethical principles than those of the private health facilities. This might be because government health facilities have ethical committee that oversees the medical doctors working according to the ethical codes¹⁵. For medical doctors to practice health ethics, a proper training and education qualification with respect to clinical expertise and knowledge about the subject matter is necessary¹⁶.

Need of the Study:

1. The study aims to give an insight about the various medical care practices which are being adopted in hospitals by the physicians.
2. The study aims to offer a valuable framework for establishing standard ethical norms for medical care.
3. The study will help in finding out the differences regarding the demographic factors of the physicians.

Objectives:

1. To find out the significant differences between male and female physicians on practice code of ethics.
2. To find out the significant differences between the three age groups (25-29), (30-34) (34 and above) of the physicians on practice code of ethics.
3. To find out the significant differences between work experience of physicians on practice code of ethics.
4. To find out the significant differences between general practitioner and specialist on practice code of ethics.

Hypotheses:

1. There will be significant difference between male and female on practice code of ethics among the physicians

2. There will be significant difference between age groups of the physicians on practice code of ethics
3. There will be significant differences between work experiences of physicians on practice code of ethics.
4. There will be significant differences between general practitioner and specialist on practice code of ethics.

Methodology: For the present study, the targeted respondents were the general practitioners and the specialist in the medical ground from the selected district of Assam. 114 samples comprising of male (56) and female (58) respondents were selected. Ages of the participants were grouped accordingly 25-29 years, 30-34 years and above 34 years. To accomplish the objectives stratified random sampling technique was used.

Tools Used:

1. Socio-demographic data sheet (self, 2019): Socio-demographic data sheet consist of the personal records of the respondents like age, gender, education level and work experience
2. Practice related code of ethics: Practice related code of ethics is a questionnaire developed, based on the Ethiopia's health professional code of ethics¹⁷. Practice related code of ethics is assessed using 16 practice based questions related to medical practice. Scoring is done on a 5-point likert scale.

Result and Discussion

Demographic Profile of Respondents: To portray the sample, demographic profile of the respondents such as sex, age, education, work experience and level of satisfaction were assessed. Sex (M=1.51, S.D. = .50) was coded as male and female. Age (M= 35.07, S.D. = 10.89) of the participants was coded with the following levels: 25-29 years, 30-34 years and above 35 years. Education (M= 1.46, S.D. = .50) was coded as general practitioner and specialist. Work experience (M= 8.1, S.D. = 8.6) was coded as less than 4 years, 4-8 years and more than 8 years.

Table 1: Demographic characteristics of the sample

Characteristics	Categories	Frequency	Percentage %
Sex	Male	56	49.1 %
	Female	58	50.9 %
Age	25-29 yrs	44	38.6 %
	30-34 yrs	30	26.3 %
	>34 yrs	40	35.1 %
Work experience	<4 yrs	67	58.8 %
	4-8 yrs	4	3.5 %
	>8 yrs	43	37.7 %
Education	General practitioner	61	53.5 %
	Specialist	53	46.5%

Source: Self

Gender wise, 49.1% respondents working in the hospitals were male, followed by 50.9% female. As far the age of the physicians is concerned, majority (38.6%) of respondents were from the age group 25-29 years, followed by 34 years and above (35.1%). Only 26.3% respondents were from 30-34 years. Work experience of the respondents is concerned; majority (58.8%) of

the respondents with work experience was less than 4 years, followed by 37.7 % more than 8 years. Only 3.5 % of the respondents were found to have work experience between 4 – 8 years. Education wise, 53.5% respondents working in the hospitals were general practitioners, followed by 46.5% specialist.

Testing of Hypothesis:

Table II: Mean, SD and t- test of male and female physicians on practice code of ethics

Gender	N	Mean	SD	t-value	Non- Sig
Male	56	47.40	10.45	.23	0.16
Female	58	50.47	7.9		

* Correlation is significant at the 0.05 level (2-tailed), **Correlation is significant at the 0.01 level (2-tailed)

Table II shows the mean score of male and female physicians, which are 47.40 and 50.47 respectively. The t value of both male and female is .23 (not significant). The first hypothesis of the study “There will be significant difference between male and female on practice code of ethics among the physicians” is rejected. The result goes in parallel to the previous studies where no difference between male and female on ethical behaviour was found¹⁸. However, in the present era females are getting more dynamic and outgoing rather than keeping themselves intact to their emotions and family duties. Moreover females might have higher expectation about

jobs, and place more significance on promotion, leading to greater satisfaction in the job. This might facilitate both men and women to move in a parallel platform, equally fighting for their rights on competitiveness, success and status. Another study reveals that males are more prone to conformity pressure than female¹⁹. This means that peer pressure impacts males due to their vulnerability to conformity pressure. This finding can be supported by a strong argument, if there would have been a difference, which might show males to have a stronger career orientation than females, due to which men are at risk for ethical decision making.

Table III: Mean, SD and F value of three age groups among physicians on practice code of ethics

Age	N	Mean	SD	F	Non-Sig
25-29	44	50.75	5.49	2.16	0.12
30-34	29	48.27	9.57		
>34	41	47.47	10.71		

* Correlation is significant at the 0.05 level (2-tailed), **Correlation is significant at the 0.01 level (2-tailed)

Table III shows the mean score of ages 25-29, 30-34 and >34 among the physicians, which are 50.75, 48.27 and 47.47 respectively. The F value of the three age groups is 2.16 (not significant). The second hypothesis of the study “There will be significant difference between age groups of the physicians on practice code of ethics” is rejected. This means that there is no significant difference between the age groups of the physicians on practice code of ethics. The result shows that the mean of the physicians of age group 25-29 years are greater than the others age group. This might indicate that ethical practice might be greater in age group 25-29 years in compared to the other groups. This might be due to the fact that younger physicians are new in the healthcare field and are eager to practice appropriately

what they have been trained and educated in the medical school. Moreover, the older practitioners, due to heavily involved in various medical organizations with increases burnout might lead to involve in breakdown of ethical behaviour. As the physicians spent enough time with the co-workers or supervisors, witnessing them might make them experience confusions about ethical principle²⁰. However, a study conducted in Rajasthan found no age difference to be associated with ethical behaviour²¹. Another study showed no differences on age group regarding issues such as whether patients should be informed if the doctors were wrong, whether consent should be taken from the children or if it was acceptable for the doctors to conduct illegal actions without prior permissions²².

Table IV: Mean, SD and F value of three groups of work experience among physicians on practice code of ethics

Work experience	N	Mean	SD	F	Sig
<4 yrs	64	48.93	9.27	9.43	.000
4-8 yrs	5	31.75	11.50		
>8 yrs	45	50.22	5.83		

*Correlation is significant at the 0.05 level (2-tailed), **Correlation is significant at the 0.01 level (2-tailed)

Table IV shows the mean score of work experiences <4 years, 4-8 years and >8 years among the physicians, which are 48.93, 31.75 and 50.22 respectively. The F value of the three age groups is 9.43 (significant at .000 level). The third hypothesis of the study “There will be significant difference between work experiences of the physicians on practice code of ethics” is accepted. This means that there is a significant difference between the work experiences of the physicians on practice code of ethics. Medical doctors with work experience above 8 years are likely to have favorable attitude towards ethical

code of conduct than doctors with 4-8 years of experience. Possible explanation supporting the differences of work experience might be the commitment and interest of physicians for their work with work experience greater than 8 years. Doctors with more experience in work might be able to identify the importance of the ethical code of behaviour. Moreover physicians can gather more knowledge with the increase of work experience, which might facilitate to understand what is right and what is wrong to practice code of ethics²³.

Table V: Mean, SD and F value of level of education among physicians on practice code of ethics

Level of education	N	Mean	SD	t value	Sig
General practitioner	56	48.51	10.30	1.75	0.01
Specialist	58	50.1	6.72		

*Correlation is significant at the 0.05 level (2-tailed), **Correlation is significant at the 0.01 level (2-tailed)

Table V shows the mean score of level of education i.e. general practitioner and specialist which are 48.51 and 50.1 respectively. The t value is 1.75 (significant at .01 level). The fourth hypothesis of the study “There will be significant difference between levels of education on practice code of ethics” is accepted. This means that there is a significant difference between the levels of education of the physicians on practice code of ethics. However, since the mean value of specialist is higher than the general practitioner, the specialist practices ethical codes of conduct. As the specialist physicians are expected to be more careful and cautious while dealing with a specific illness they need to communicate properly with the clients. This might make obligatory for the specialist to behave ethically than the general physicians.

Conclusion

Education level, and work experience, was found to be significantly different on practice of code of ethics. Whereas, age and gender were found to have no significant difference regarding practice code of ethics. Therefore it is vital to change the attitude of physicians and have adequate knowledge and awareness about the ethical codes among all the stage of the medical process. This can be done through training programs, increasing public awareness about the health care deliverance, client/patient rights, establishing ethical committee in the institution, strengthening practical based education, proper medical ethics course and reporting of unethical conducts.

Ethical Clearance: No Ethical Considerations Apply.

Source of Funding: Self

Conflict of Interest: Nil

References

1. Indian Brand Equity Foundation. 2017. Retrieved from www.ibef.org
2. Unnikrishnan B, Kanchan T, Kulkarni V, et al. Perceptions and Practices of Medical Practitioners towards Ethics in Medical Practice - a study from coastal South India. *Journal of Forensic Legal Medicine*.2014; 22:51-6.
3. Kumar S, Rai K A. *Business Ethics*.Cengage Publisher; 2019.p.6.
4. Kehinde F M, Tajudeen O, et al.Medical Ethics in sub-Saharan Africa: Closing the gaps. *African Health Science*. 2015; 15(2): 673-781.
5. Nye County Comments. Nevada’s Medical Scandal’ Nye-Gateway to Nevada’s Rurals. 2008. Access at <http://nyenevada.blogspot.com/2008/03/nevadas-medical-scandal.html>
6. Patrick R. Doctor Convicted in fraud, drug case’ McClatchy. *Tribune Business News*.2008 Access at <http://gowmu.wmich.edu/cp/render.UserLayoutRootNode.uP>
7. Truesdell CJ. Pooler Physician Hung Thien Ly Convicted of 129 Felony Counts of Dispensing Drugs Illegally’. *US Fed News Service, Including US State News*. 2008. Access at http://gowmu.wmich.edu/cp/render.UserLayoutRootNode.uP?uP_tparam=utf & utf=http%3A%2F%2Fwww.wmich.edu%2Flibrary%2F
8. Nadler J T, Stockdale M S. Workplace Gender Bias: Not just between strangers. *North American Journal of Psychology*. 2012; 14(2): 281-292.
9. Diekman A B, Schneider M C. A social role theory perspective on Gender gaps in Political Attitudes. *Psychology of Women Quarterly*. 2010; 34(4): 486-497.
10. Tiruneh A M,Ayele T B.Practice of code of Ethics and Associated factors among Medical doctors in Addis Ababa, Ethiopia. *PLoS ONE*.2018; 13(8).
11. Tiruneh A M,Ayele T B.Practice of code of Ethics and Associated factors among Medical doctors in Addis Ababa, Ethiopia. *PLoS ONE*.2018; 13(8).
12. BrogenA, Rajkumari B, Laishram J, Joy A.Knowledge and Attitudes of doctors on Medical

- Ethics in a teaching hospital, Manipur. *Indian Journal of Medical Ethics*. 2009; 6-4.
13. Jana W, Tibor S, Wolfgang S, et al. Medical Ethical knowledge and Moral Attitudes among Physicians in Bavaria. *DtschArztebl Int*.2012; 109(8): 141–147.
 14. Anup N, Himanshu K, Gautam B, Sonia P, Swasti T. Knowledge, attitude & practices regarding Ethics & Law amongst medical and dental professionals in Rajasthan. *Journal of Dental and Medical Sciences*2014;13(5): 102-109.
 15. Anup N, Himanshu K, Gautam B, Sonia P, Swasti T. Knowledge, attitude & practices regarding Ethics & Law amongst medical and dental professionals in Rajasthan. *Journal of Dental and Medical Sciences*2014;13(5): 102-109.
 16. Kehinde F M, Tajudeen O O, et al. Medical Ethics in sub-Sahara Africa: Closing the gaps. *African Health Science*. 2015; 15(2): 673-781.
 17. Jalal H, Buchanich M J, Robert S M, et al. Changing dynamics of drug overdose epidemic in United States from 1979 through 2016. *National Library of Medical National Institute of Health*.2018;361.
 18. Sloane P J, Williams H. Job satisfaction Comparing Earnings and Gender Labour. 2000; 14(3): 473-505.
 19. Cull J G. The Relationship between Sex Role and Modification of Judgments. *The Journal of Psychology*. 1976; 93: 316.
 20. Gabel S. Ethics and value in Clinical practice. Whom do they help? *Mayo Clinical Practicing* 2011;86(5):421-424.
 21. Anup N, Himanshu K, Gautam B, Sonia P, Swasti T. Knowledge, attitude & practices regarding Ethics & Law amongst medical and dental professionals in Rajasthan. *Journal of Dental and Medical Sciences*. 2014;13(5): 102-109.
 22. Brogen A, Rajkumari B, Laishram J, Joy A. Knowledge and Attitudes of doctors on Medical Ethics in a teaching hospital, Manipur. *Indian Journal of Medical Ethics*.2009; 6-4.
 23. Roxas ML, Stoneback JY. The Importance of Gender Across Cultures in Ethical Decision. 2004.

Issues in India's Healthcare System

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Abstract

India as the second most populous country of the world where more than 60% of its population rely on Agriculture and allied occupations, healthcare has remained the matter of concern. With a weak primary health sector, lack of skilled medical professionals, inadequacy of regulation for private hospitals, low public spending on health, fragmented health information system, rising cost of medical treatment in India, medical research in India having very little application and weak governance and accountability of the sector are the matters of great concern from the perspective of service delivery. The Supreme Court of India held healthcare as the fundamental right under article 21 of the constitution, but in practice, it has not been fundamentally right in India. Though Ayushman Bharat, is a well thought out project, intending healthcare for the masses, its delivery and sustainability is questionable. The paper is an attempt to discuss the problems inherent in the India's healthcare system.

Keywords: Health, Hospital, Medical Treatment, Ayushman Bharat.

Introduction

India, as one of the World's fastest growing economies and second most populous nation, faces a lot of challenges and unprecedented opportunities as far as access to quality health services is concerned. India has witnessed record-breaking economic growth over a decade which has brought down poverty significantly.¹ According to a report published by the World Bank, infant mortality rate has come down from 66 to 38 per 1000 in India from 2000 to 2015. Life expectancy rate has gone up from 63 to 68 years. Maternal mortality rate has been decreased from 374 to 172 per lakh live births during the said period.² Over the period, India has developed the world-class scientists in health sector, leading hospitals and the dynamic pharmaceutical and biotechnology industries which has attracted foreign patients for treatment. India, nevertheless, faces

persistent and daunting challenges, particularly for the poor as far as access to health services are concerned. In Odisha, a tribal man was forced to shoulder the dead body of his wife due to denial of mortuary van by the medical authority.³ Another Odisha man was also forced to carry daughter's dead body for 6 km after ambulance dropped them midway.⁴ Many such incidents are being reported and published in newspapers over the years.

Some of the other challenges that health sector in India is facing are low birth weights and child undernutrition which often result in premature death of the child, neonatal mortality, life long health problems; growth in noncommunicable diseases such as diabetes, obesity and tobacco use, resulting in cancer and other diseases; injuries and deaths due to high rates of road traffic accidents. Though the Government of India is providing comprehensive health coverage for all through the schemes like *Ayushman Bharat*, nevertheless, the nation's rapidly developing healthcare system remains an area of concern. Health sector is often seen to be underfunded, in many cases, funded amounts are underutilized. In many cases, it is also found to be underregulated. Odisha Sum Hospital Tragedy that killed around 20 patients in fire due to non-compliance

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of safety issues is a case in point.⁵As a result of which many hospitals are having reported to have safety issues of the patients. There are disparities in health and health care systems between rich and poor states. The present government is increasing coverage, but insurance remains limited.

Structural Problems in Indian Health Care System: Despite several recorded improvements in Indian health care system, the country is reported to have lagged behind many health indicators. The country comprises of around 18% of the World land areas, but accounts for 20% of the world burden of diseases, 21% of all child deaths (less than 5 years) and 27% of the all neonatal deaths.⁶ Indian healthcare system is facing many structural problems today which are summarized below:

(a) A Weak Primary Health Sector: In 2015, one government hospital bed was available for every 1833 persons as compared with 2336 persons a decade earlier. However, the study found that the availability of the beds in government hospitals across the states of India is inequitably distributed. For example, one government hospital bed was available for 614 persons as compared with 8789 persons in Bihar^[7]. The care facilities were also quite inadequate. Figure 1 represent the sorry state.

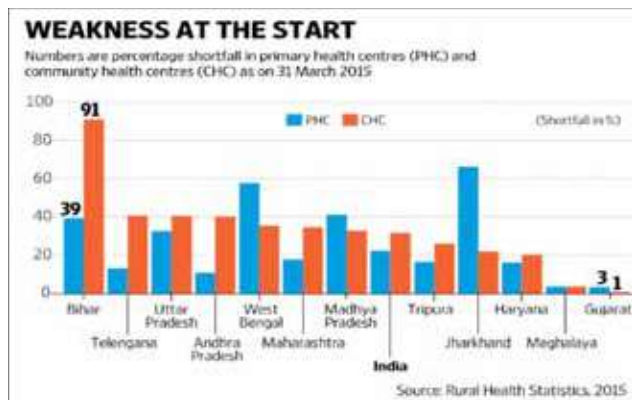


Figure 1:

(b) Unequally Distributed Skilled Manpower: Despite increase of seats in MBBS and nursing programs, India still suffers from paucity of skilled health professionals. In many states such as Gujarat

and West Bengal, the shortfalls of skilled health professionals exceed 80%. The Lancet study said:

“India does not have an overarching national policy for human resources for health. The dominance of medical lobbies such as the Medical Council of India has hindered adequate task sharing and, consequently, development of nurses and other health cadres, even in a state like Kerala that has historically encouraged nurse education and has been providing trained nurses to other parts of India and other countries.”⁷

(c) Large Unregulated Private Sector

The National Sample Survey Office (NSSO) number found that there has been decrease in the use of public hospitals over the period of past 2 decades- only 32% of urban Indians use them compared to 43% in 1956-96. The study also found that many of the private practitioners don't have requisite qualification or are underqualified. Lancet stated: “the many new institutions set up in the past decade... encouraged by commercial incentives, have often fuelled corrupt practices and failed to offer quality education.”⁷

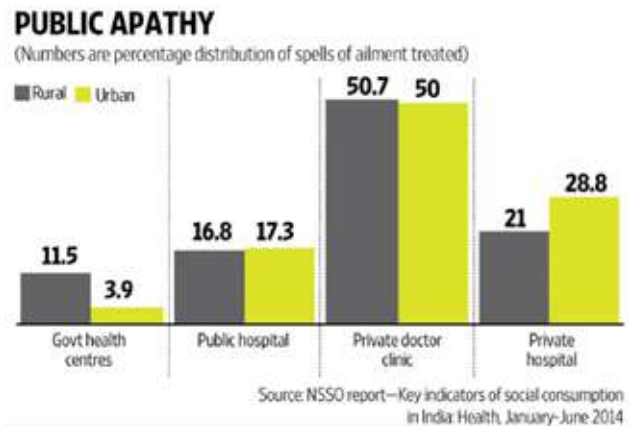


Figure 2

(d) Low Public Spending on Health: Expenditure on public health remains meagre in India. Even though, there has been 7% annual increase of expenditure in recent years, central government expenditure has plateaued. Many state governments fail to use the allotted funds which reflects the structural weaknesses in the system which need to be addressed.

Table 1: Year-wise Projected Demand, Actual Allocation and Expenditure of Department of Health Research (Including ICMR)

Financial Year	Projected Demand (Rs in crore)	Actual Allocation (Rs in crore)	Actual Expenditure (Rs in crore)	% Increase of expenditure over previous year
2013-14	2283	726	461.84	
2014-15	2581.5	726	569.61	23.33%
2015-16	2817.91	713.17	590.65	3.70%
2016-17	1689.43	750	647.82	9.67%
2017-18	2933	1500	911.07	40.66%

*Expenditure upto February, 2017

Source: <https://health.economictimes.indiatimes.com/news/industry/the-sorry-state-of-medical-research-in-india/58241623>

(e) **Fragmented Health Information System:** Clean and up-to-date health data is not available. Though many agencies such as NSSO to the Registrar General of India to disease specific programme-based systems are working for maintenance of

health data, yet still, data is missing in many cases as they exclude private sector. In many cases, data is also duplicated. And agencies don't talk to the parties concerned.

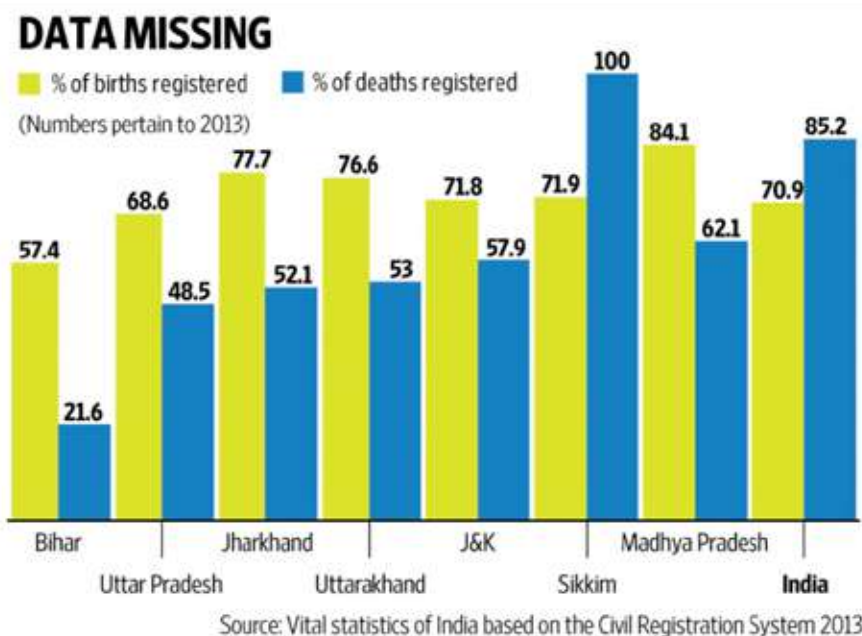


Figure 3

Figure 3 exhibits the % of births and deaths registered. As in states, health data is missing, its is difficult to forecast the health facilities requirement.

(f) **Rising cost of Medical Treatment:** Rising cost of medical treatment is one of the reasons attributed to poverty. Though, government of India has introduced *Jan Aushadhi* campaign to provide 361

generic medicines at affordable prices and different price regulation policies, but in reality, these have not been fully effective. Corruption in healthcare system has increased irrational use of drugs and technology. The nexus between the doctors, medicine stores, pharmaceutical and device companies compel the patients to follow unnecessary procedures such as CT scans, caesarean sections and stent insertions.

THE COST OF FALLING ILL

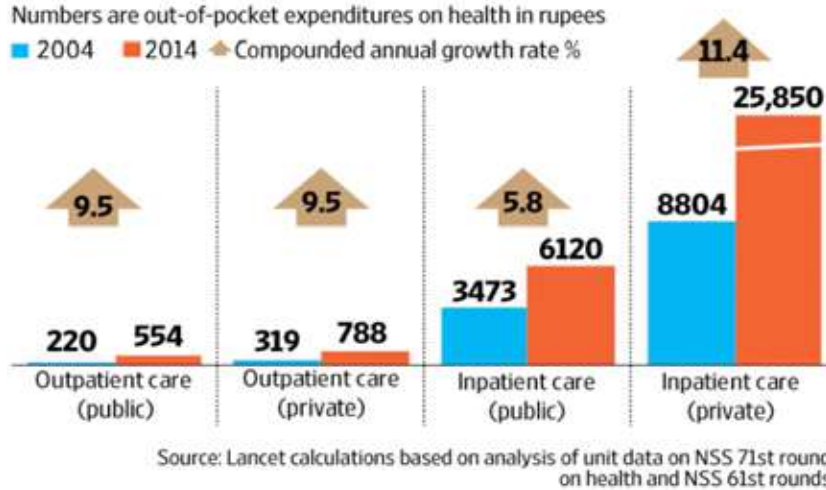


Figure 5

(g) **Sorry State of Medical Research in India:** The Indian Council of Medical Research (ICMR) has 800 scientists working across 32 institutes in India, but failed to list even a new intervention in terms of

vaccine, new drugs, diagnostic test or treatment procedure developed by hundreds of scientists over a period of last two years.⁸

Table 2: Research Output of ICMR

Years	Published Papers	Patent filed	Patent granted	Research Project funded
2015	965	33	2	1745
2016	720	12	1	

Source: <https://health.economicstimes.indiatimes.com/news/industry/the-sorry-state-of-medical-research-in-india/58241623>

7. **Weak governance and accountability:** “In the past 5 years, the government has introduced several new laws to strengthen governance of the health system, but many of these laws have not been widely implemented,” said Lancet. In some cases, the “scope of (some) regulations is still unclear, and there are fears that these laws have hindered public

health trials led by non-commercial entities.”⁷ Inadequate public investment in health, lack of trust and engagement between various healthcare sectors and poor coordination between central and state governments are some of the impediments to assure universal health care in India.

Table 3: Health Law and their status of implementation

Law	Status
Clinical Establishments Act 2010 (provides for registration and regulation of clinical establishments and prescribes minimum standard of facilities and services)	Enacted only in 9 states
National Mental Health Care Bill (mandates right to care)	Cleared by cabinet, awaiting passage in Parliament
Medical Devices Regulation Bill, 2006 (provides for quality standards of biomedical equipment manufacturing and marketing)	Yet to be passed

Source: Lancet, **Note:** These are just examples and not an exhaustive list

Critique of Ayusman Bharat Scheme: There are two types of health schemes of government of India. Majority of them are well thought out schemes, but these are poorly implemented. As a result of which these don't reach out to the intended beneficiaries fully. But there are some schemes which are drafted at policy stage. These have very little possibility of working and if these worked, would be very difficult to sustain. *Ayusman Bharat* falls in the second category.

Free universal healthcare is already available in India. In India, Most of the government hospitals charge no fees or a very nominal fee. But accessibility and quality of service delivery remain a matter of concern. Secondary and tertiary care are in scarce supply in many states. But on paper, free healthcare exists. Therefore, *Ayusman Bharat* does the more or less the same things. As the government hospitals lack adequate healthcare facilities, the government use private hospitals which would reinforce the impression that private hospitals are better than government hospitals.

There are issues when private hospitals provide healthcare services free of fees. Their infrastructure will benefit the poor patients. But there is no regulatory mechanism to monitor the quality of their services. As the fee under the scheme is low, hospital may not be able to sustain the services without the revision of fee rates. Poor patients' lives may be put at risk at the mercy of private hospitals due to unavailability of appropriate regulations.

Budget allocation for the year Rs. 3200 crore under the scheme in 2018 which is quite meagre to cover a small subset of the 10 crore families enrolled. If we assume that 5 per cent of those enrolled claims 20 per cent of those eligible Rs. 5 lakh, the scheme would need Rs 50000 crore. It's doubtful whether Government will be able to cover 10 crore families. An if this happens if it will be able to sustain it will be a matter of concern because of the high operating costs. The IT infrastructure needed for this scheme is also enormous and it is dubious if government will be able to maintain the data privacy and security when the patients use their Aadhar information to access this scheme.

Conclusion:

The Supreme Court of India held healthcare as the fundamental right under article 21 of the constitution, but in practice, it has not been fundamentally right in India. For every 51000 people, there is only one

healthcare centre often managed by one doctor. But this is where 90% health needs can be met. The health sector has attracted good investments, but delivery remains contentious. Though private players have entered the health sector and increased competition, nevertheless, improved quality and efficiency in the healthcare delivery has remained a question mark. Lack of penetration, opaqueness in diagnosis, exorbitant billing and poor quality of service indicates that Indians get treated below the standards prescribed by World Health Organization. Although Indian healthcare system services are among cheapest in the world, yet, it has become unaffordable for many locally. It's high time to introspect the feasibility of the schemes like *Ayusman Bharat*. But it's roll-out is very much like GST. Public and private health systems are placing huge demands on the capacity of the nation's health leaders and professionals. Rising to meet these challenges, the citizens of India have an opportunity to have a major influence on their own health on the future of public health and medical research globally.

Ethical Clearance: Not Applicable

Source Funding: Self

Conflict of Interest: Nil

References

1. World Bank Report, Press Release, India's Growth Story since the 1990s remarkably stable and resilient, 2018 March 14, available at <https://www.worldbank.org/en/news/press-release/2018/03/14/india-growth-story-since-1990s-remarkably-stable-resilient>.
2. The World Bank IBRD.IDA Data, World Development Indicators, 2015, available at <https://data.worldbank.org/indicator/SP.DYN.LE00.IN?end=2017&start=1960&view=chart>.
3. India Today Report. Tribal man in Odisha has to walk 10 km carrying wife's dead body after being denied govt help. 2016 May 25, available at <https://www.indiatoday.in/india/story/odisha-tribal-man-carrying-wife-dead-body-with-daughter-337142-2016-08-25>.
4. India Today Report. Another Odisha man forced to carry daughter's dead body for 6 km after ambulance dropped them midway. 2016 Dec 23, available at <https://www.indiatoday.in/india/story/odisha-father-daughter-dead-body-walk-ambulance-dropped-338868-1999-11-30>.

5. The Hindu Report. 22 killed in Bhubaneswar Sum Hospital, 2016 Oct 17, available at <https://www.thehindu.com/news/national/22-killed-in-Bhubaneswars-SUM-Hospital-fire/article16074835.ece>
6. Krishnan R. Seven charts that show why India's healthcare system needs an overhaul, 2019 Dec 15, available at <https://www.livemint.com/Opinion/qXD81719wXXDQVpGyyARrO/Seven-charts-that-show-why-Indias-healthcare-system-needs-a.html>.
7. Patel. V., Parikh. R., Nandraj. S. & Balasubramaniam. Assuring Health Coverage for All in India, 2015 Dec 12, available at [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(15\)00955-1/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(15)00955-1/fulltext).
8. ET Health World News. The sorry state of Medical Research in India, 2017 April 18, available at <https://health.economictimes.indiatimes.com/news/industry/the-sorry-state-of-medical-research-in-india/58241623>.

A Pre-experimental Study to Assess the Effect of Planned Teaching Programme on Knowledge of Staff Nurses Regarding Hemodialysis in Selected Hospitals at Jaipur

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Abstract

The word dialysis derived from Greek word “dialysis”, meaning dissolution, “dia” meaning through, and “lysis” meaning loosening. Dialysis is a process for removing waste and excess water from the blood, and is primarily used to provide an artificial replacement for lost kidney function in people with renal failure. Dialysis may be used for those with an acute disturbance in kidney function or for those with progressive but chronically worsening kidney function¹.

Purpose: Sometimes nurses fail to adopt modern or recent nursing care for the hemodialysis due to the lack of knowledge and ignorance for learning therefore, the investigators is challenged to explore the knowledge level of staff nurses is relation to hemodialysis with a view to develop a planned structured teaching. The investigator during his training period and clinical experience observed. Lack of desirable knowledge and any standardized protocols in the dialysis and related units. So, the need to develop a planned teaching programme on hemodialysis was felt for nursing staffs in selected hospital. Objectives: 1. To determine the level of knowledge of the staff nurses regarding haemodialysis measured by structured knowledge questionnaire. 2. To evaluate the effectiveness of structured teaching programme by comparing the pre and post knowledge score. 3. To determine the association between the pre-test knowledge score with selected demographic variable on hemodialysis among staff nurses.

Methodology: The research design was Pre-experimental one group pre-test and post-test design, the setting chosen to conduct study was SMS Hospital, Jaipur, Rajasthan 203012. Sample size was 60; the sampling technique used was purposive sample technique. The staff nurses who fulfilled the inclusion criteria were selected as samples. The tool was submitted to seven experts of department of Medical Surgical Nursing and statistician and doctors. Experts were asked to give their opinions and suggestions about the content of tools. The interpretation of the score cut-off; Poor 0-40, Average 41-60, Good- 61-74 and very good 75 and above. The data gathered and analyzed by using descriptive and inferential statistics method and interpretation is made on the basis of objectives of the study.

Major Findings: The analysis of the study findings revealed that the pre-test mean was 16.02 with a standard deviation of 2.86 and the post-test mean was 23.88 with a standard deviation of 3.06. The tabulated value of score at 5% level of significance and 59 degrees of freedom is 2 and the table value was less than the calculated value (7.86).

Conclusion: This study represents the significant gain in knowledge through the planned teaching Program. Thus it suggests that the STP has been effective in increasing the knowledge of staff nurses about hemodialysis.

Keywords: *Assessment, Effectiveness, Hemodialysis, Planned Teaching Programme, Staff Nurses, Knowledge.*

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Introduction

The word dialysis derived from Greek word “dialusis”, meaning dissolution, “dia” meaning through, and “lysis” meaning loosening. Dialysis is a process for removing waste and excess water from the blood, and is primarily used to provide an artificial replacement for lost kidney function in people with renal failure. Dialysis may be used for those with an acute disturbance in kidney function or for those with progressive but chronically worsening kidney function¹.

Absolute indications for dialysis include: severe volume overload refractory to diuretic agents, severe hyperkalemia and/or acidosis, encephalopathy not otherwise explained, and pericarditis or other serositis. Additional indications for dialysis include symptomatic uremia (e.g., intractable fatigue, anorexia, nausea, vomiting, pruritus, difficulty maintaining attention and concentration) and protein-energy malnutrition/failure to thrive without other overt cause. No absolute serum creatinine, BUN, creatinine or urea clearance, or glomerular filtration rate (GFR) is used as an absolute cut-off for requiring dialysis, although most individuals experience, or will soon develop, symptoms and complications when the GFR is below <10 mL/min¹.

Nurses must take on important contribution towards maintenance of health in all aspects due to scientific changes in medical science and technology. Those expanding responsibilities of nursing based on growing demands of more knowledge and raise the need for critical evaluation of the educational programs that prepares the nurses to entire in to the skilful nursing profession.

The majority of nurses 53.9% had very high level of educational needs 33.8% had high level and 12.3% had moderate level of educational needs³.

Nurses have been identified as being more enthusiastic in constantly working in a hospitals nephrology nursing and renal dialysis is a highly specialized field because the health team member are giving special care to fulfil the basic needs such as elimination of waste from the blood products and to maintain the electrolyte balance. The renal patients care being treated with Hi-Tech equipments⁴.

The nurses’ responsibilities for the haemodialysis patients are to maintain the patency of the vascular access site and keep it free from infection, to monitor

the patient before, during, after treatment, to teach the patient and family about dialysis treatment and often home treatment and to assist the patient and family to cope with necessary life style changes and problems⁹.

Materials and Method

Research approach: Quantitative Research approach

Research design: Pre experimental research design

Setting of the study: SMS Hospital, Jaipur, Rajasthan, 302012

Population: Staff Nurses

Sample: Staff nurses

Sample size: 60

Sampling techniques: Purposive sampling techniques⁷

Criteria for sample selection

Inclusion criteria

Staff Nurses who

- Staff nurses who are present during data collection.
- Staff nurses who are willing to participate.
- Staff nurses who are working in nephrology units.

Exclusion criteria

1. Student Nurses.

Development and Description of the Tool:

Section A: Assessment of Demographic Variables: Personal data sheet on the demographic characteristics of elderly includes such as age in years, gender, professional qualification, years of experience, areas of working and previous information.

Section B: It Includes Structured Knowledge Questionnaire: The related literature was reviewed for the construction of the structured knowledge questionnaire. It consisted of 30 items divided into 3 areas. They are:

- Dialysis : 5 items
- Haemodialysis : 10 items
- Management before, during and post haemodialysis: 15 items

All the items were multiple choice questions, which had 3 alternative responses. A score value of 1 was allotted to each correct response and for wrong response zero was awarded. Thus there were 30 maximum obtainable scores. The level of knowledge was categorized based on the scores obtained.

Findings: The data analysis was done using descriptive and inferential statistics.

Descriptive Statistics:

1. Frequency and percentage distribution was used to analyse the demographic variables of staff nurses.

2. Mean and standard deviation to assess the level of knowledge among staff nurses.

Inferential Statistics

1. The calculated paired t-test to compare pre-test and post-test level of knowledge among staff nurses after planned teaching programme.
2. Chi square test was used to associate the post- test level of knowledge among staff nurses with their selected demographic variables⁷

Organisation of the Data

Section I:	• Description of socio-demographic characteristics of samples.
Section II:	• Percentage distribution of overall knowledge levels and knowledge in Specific areas related to haemodialysis among staff nurses in pre Test and post-test. • Mean, mean% and standard deviation of pre-test and post- test knowledge scores
Section III:	• Effectiveness of planned teaching programme among staff nurses on haemodialysis knowledge by comparing the pre-test and post-test assessment. • Significance difference between pre-test and post-test knowledge scores
Section D:	• Association between the knowledge of staff nurses on haemodialysis with selected demographic variables.

Effectiveness of planned teaching programme on level of knowledge among staff nurses. N=60

Depression	Mean	S.D.	Paired ‘t’ value
Pre-test	16.02	2.86	t = 14.3
Post test	23.88	3.06	P<0.05

P<0.05 S-Significant

The table shows that the pre-test mean score of depression among geriatrics was 16.02 with S.D 2.86 and the post-test mean score of depression was 23.88 with S.D 3.06. The calculated paired’ value of t=14.3 was found to be highly statically significant at p<0.05 level. This clearly indicates that after providing planned teaching on haemodialysis to the staff nurses, their post-test level of knowledge hasincreased and this clearly indicates that planned teaching programme on haemodialysis was found to be highly effective in increasing the level of knowledge regarding haemodialysis among staff nurses.

Section D: Association of post test level of knowledge among staff nurses with their selected demographic variables: The post-test level of knowledge among staff nurses at p<0.05 level all the

demographic variables had not shown statistically significant association with the post- test level of knowledge among staff nurses.

Discussion

The analysis shows that in the pre-test, majority 54(90%) of staff nurses had average level of knowledge, 4(6.67%) had good level of knowledge and only 2(3.33%) were poor, whereas in the post test after providing the planned teaching on haemodialysis, majority 58(96.67%) were very good and 2(3.33%) had good level of knowledge and no one had average and poorknowledge. The calculated paired’ value of t=14.3 was found to be highly statically significant at p<0.05 level. Hence H₁ hypothesis stated earlier that “there will be a highly statistically significant association between the pre-test level of depression score and post-test level of depression score. The post-test level of depression among geriatrics at p<0.02 level all the demographic variables had not shown statistically significant association with the post- test level of depression among geriatrics. Hence H₂ hypothesis stated earlier that “there will not be a statistically significant association between

the post-test levels of depression score with selected demographic variables.

Conclusion

Majority of staff nurses have average and good knowledge level before administration of PTP. The hypothesis H₁ was accepted suggesting that there will be significant difference between pre and post-test knowledge score of staff nurses regarding haemodialysis and H₂ was rejected suggesting that there will be no significant association between the knowledge of haemodialysis and selected demographic variables.

Source of Funding: Self

Ethical Considerations:

- Formal permission was obtained from dean of Jaipur Hospital College of Nursing, Jaipur
- Written consent was obtained from the Medical Superintendent of SMS Hospital.
- Consents from the participants were obtained

Conflict of Interest: Nil

References

1. Rakshakamel. Educational needs nurses regarding AIDS. Abstract of nursing Thesis. tabriz University of medical science; 200I.
2. Rowland and Rowland. Nursing administration hand book. 2nd edition. Oспен system. Corporation may land; 1985.
3. Arena and page. The imposter phenomenon in the clinical nurse specialist role. Journal of nursing scholarship. 1992; 24:2 P121-125.
4. Chuck cheingkaipeter. Clinical nurse specialist and quality patient care. Journal of advanced nursing. Black well science Ltd. vol. 26.1997; P501- 506.
5. Lewis heistkemperdirksen. Medical surgical nursing. 6th edition. Mosby publication. Missouri. 2000; P1232-1236.
6. Suddarth and Brunner. Medical surgical nursing. 10th edition Lippincott. Philadelphia. 2004; P1285-1290.
7. Polaski A.L, Tatro S.E, LuckMann's core principles and practice of medical-surgical nursing. Saunders publications; p.958, 889-890
8. Suzanne C.S, Brenda.B. Text book of Medical Surgical Nursing. 10th ed. Philadelphia: Lippincott Williams and Wilkins publications; p.1515-1520
9. Lewis S.M, Heitkemper M.M. Dirksen S.R. Medical Surgical Nursing-Assessment and Management of Clinical problems, 6th ed. Mosby publications; p.1191, 1199, 1210.
10. Delormo et al., varying heparin requirement is hemodialysis patient receiving or thropoiat. American nursing association journal. 1997; 19:41. P367-372.

A Study on Consumers' Satisfaction Level towards Select Organic Food Products in Salem District of Tamil Nadu

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Abstract

The Organic Farming is carried out in 178 countries across the world at present. More than 90% of sales took place in North America and Europe. USA, Germany and France hold the highest share and Switzerland, Denmark and Luxembourg are the top three countries where the consumption per capita is the highest pertaining to organic foods as per the report given by the IFOAM. On the other hand, Asia Pacific market is growing rapidly at 29% and Projected as the fastest growing market. According to IFBL report, India has the largest number of organic food producers in the world. Increased health consciousness among people, food safety, environmental protection, and increase in the usage of organic and natural products are some of the key reasons for the expansion of this organic food markets. Organic food products are focused in developed countries because, the purchasing power of consumers are very high. Consumer satisfaction is a key indicator used to measure the customer loyalty and retention. So the researcher focused on the Consumers' Satisfaction towards Select Organic Food Products in Salem District of Tamil Nadu. The population size of the study was 100 respondents from Salem district by using convenience sampling technique. The percentage analysis and chi-square analysis were applied for testing the data. Finally the researcher providing suitable suggestions and conclusion based on their results and findings from study.

Keywords: *Organic Food Products, Farming, Health and Environmental Friendly.*

Introduction

Agriculture is the primary sector and backbone of the Indian economy. The people are getting food and food products from the agriculture sector. The drastic growth of population is creates more demand for food and food products. Due to increasing population in the world the exploitation of natural resources was started. To meet the more demand for foods, the farmers are applying the chemicals based fertilizers and pesticides at the time of cultivation and to getting more yields and profitable. This resulted not only in undesirable side effects in the agro-ecosystems and also affects the human health. After the long period of time the people are turned to think about the healthy food and back to organic farming. The consumption of organic food products provides the high nutritional value for human health. The organic food products are grown naturally without use of chemicals, pesticides and fertilizers. The organic farming works at gross root level preserving the reproductive and regenerative capacity of the soil, good plant nutrition, sound soil management and produces

nutritious food in rich vitality which has resistance to disease¹. India have lot of potential to produce all varieties of products due to the agro climatic region. The organic producers to tap the market which growing steadily in domestic and export market. The government of India has implemented many schemes to promote organic farming like Paramparagat Krishi Vikas Yojana (PKVY), National Project for Organic Farming (NPOF), National Mission for Sustainable Agriculture (NMSA), etc., all the schemes are running successfully in many states especially PKVY is more successful one. The farmers are more benefited from these schemes². The organic food market is large distance spread and the consumers are becoming more intended to buy organic food products. The adoption of organic products and processing is highly depends by market demand. Now a days the food consumption pattern are changing rapidly for the reason of health and environmental issues. The reason for purchasing organic food products is the consumers are feel these products is healthier and environmental friendly. The previous studies are found

that the consumers are got more awareness on organic food products and started buying and utilizing for their regular consumption³. Hence, the organic food becomes a most important food in the emerging life of every human beings.

Importance of the Study: India has the largest number of organic producers in the world, according to the World of Organic Agriculture report 2018 has published more than 835000 certified organic producers in India. Organic food industry has nascent stage and steadfast growth in the fast few years. India has ranked 9th place in terms of world organic agricultural land and in terms of total number of producers at 1st place as per the data given by FiBL report 2018⁴. Sikkim has become first fully organic state in India. The consumption of organic food products is significantly increasing in the world. The consumers are prefer organic food products, because these are the promoted as superior and better option for the development of our human health. Looking demand side of organic food market there are several factors are influencing the consumer to prefer organic food products like certification, health benefits, environmental friendly and price etc. The consumer satisfaction plays a vital role in every business⁵. The satisfaction level of the consumers are most important for repurchasing the organic food products. Hence, the researcher to study the satisfaction level of the consumer towards select organic food products in Salem District of Tamil Nadu. The organic food markets is spread to move on from Tier I cities to Tier II cities and Metro cities. The Salem District is one of the Tier II and also Metro cities one. So, the research select the Salem District and to conduct the study from the Salem District organic food consumers⁶.

Statement of the Problem: Organic farming is not new one. It is started 1000 years of ago, the people have been growing food by natural and organic method. The quality of food and food products have greater demand in the market, but increasing population in the world to meet the high demand of food the agriculture industries are adding numerous chemicals, fertilizers and pesticides at the time of cultivation and getting more yields. These type of conventional food products are neatly packaged and reached to the consumers in the marketplace. The consumer are consuming these products and its affects the various illness like nausea, diarrhea, anxiety, cramps, chronic diseases etc⁷. In this situation the negative impact of contemporary food industries turned the people to think about the chemical

free food products. The organic food products are not processes using irradiation, industrial solvents or chemical food additives. The prevention from many illness, thus increasing our quality of life by the way of using organic food products. The population of organic food consuming is increasing trend and consuming varieties of organic food products. When the consumer are attract and satisfied after using the organic food products, he or she buy again and again, so the marketers to know the satisfaction level of the consumers. The consumer satisfaction plays a very important role in any business. At this juncture the researcher intended to study the Consumer's Satisfaction Level towards Select Organic Food Products in Salem District of Tamil Nadu.

Objectives of the Study:

1. To study the demographic profile of the respondents in the study area.
2. To examine the consumer's attitude towards organic food products.
3. To measure the satisfaction level towards select organic food products in Salem District.
4. To offer suitable suggestions and conclusion.

Material and Method

The descriptive research design was adopted. The study was covered both primary and secondary data. The primary data was collected through well-structured interview schedule from 100 respondents in the study area by using convenient sampling technique has been used. The secondary data were collected from various websites, magazines & journals and government reports. In order to analyze the data percentage analysis and chi-square analysis was used to testing the data.

Findings of the Study:

Age: 10% of the respondents are age group of up to 25 years, 39% of the respondents are 26-35 years, 30% of the respondents are 36-45 years, and 11% of the respondents are 46-55 years and remaining 10% are 56 and above.

Gender: 56% of the respondents are Male and remaining 44% of the respondents are Female.

Educational Qualification: 6% of respondents are illiterate, 20% & 46% of the respondents are Up to H.Sc. & Graduates, 23 of the respondents are Post Graduates and rest of 5% under others category.

Employment Status: 15%, 34%, 19%, 09% of the respondents are belongs to Govt & Private employee, Business, Professional and remaining 23% of the respondents are belongs to Others category.

Monthly Income: 15% of the respondents are belongs to the income level of Upto Rs.10000, 45%, 21%, 09% and 10% of the respondents are belongs to the income level of Rs.10001-20000, Rs.20001-30000, Rs. 30001- 40000 and above Rs.40000.

Marital Status: 76% of the respondents are married, 24% of the respondents are unmarried.

Family Pattern: 53% of the respondents are Nuclear Family and remaining 47% of the respondents are Joint Family.

No. of Family Members: 37%, 54%, 09% of the respondents are upto 3 members, 4-6 members, and above 7 members.

Residence: 28% of the respondents are belongs to Rural Area, 17% of the respondents are Semi-urban, and remaining 55% of the respondents are belongs to Urban area.

Findings Related Consumer’s Attitude towards Organic Food Products: The above table shows that, the consumers are mostly to know the organic food products through self, friends and relatives, and Magazines. The purchase decision of consumers made by self and friends. The more number of the consumers to purchase OFP for the past 1-2 years. The consumer’s spending amount to purchase OFP is Rs. 1001-2000 per month. The majority of the consumers to preferred millet, jiggery & sugar, and oil items, because these product are most essential commodities in daily usage foods.

Satisfaction Level towards Organic Food Products:

Variables	Chi-square	df	Significance
Nutrition value of the product	84.200 ^a	4	.000
Hygienic value of the product	57.600 ^b	3	.000
Freshness of the products	1.014E2 ^a	4	.000
Taste of the organic food products	82.800 ^a	4	.000
Packaging of the OFP	67.900 ^a	4	.000
Quality of the product	65.200 ^b	3	.000
Price of the organic food products	1.052E2 ^a	4	.000
Availability of product and Shops	84.300 ^a	4	.000
Originality of the organic food products	51.440 ^b	3	.000
Health improvement by using Organic food products	1.094E2 ^a	4	.000
More number of varieties	1.040 ^c	2	.595
Atmosphere on organic shops	33.840 ^b	3	.000
Customer service on the shops	26.000 ^b	3	.000
Product Advertisement	67.500 ^a	4	.089
Brands of the organic food products	62.500 ^a	4	.000
Satisfaction on label	65.200 ^a	4	.000
Pleasant texture	49.040 ^b	3	.000

Source: Primary Data, **Note:** a. 0 cells (.0%) have expected frequencies less than 5. The minimum expected cell frequency is 20.0., b. 0 cells (.0%) have expected frequencies less than 5. The minimum expected cell frequency is 25.0c. 0 cells (.0%) have expected frequencies less than 5. The minimum expected cell frequency is 33.3.

The above variables were used to measure the satisfaction level of the consumers. Out of seventeen variables only two variables are not significant at

5% level. The result indicates that consumers are not satisfied with more number of varieties of the products and product advertisement in the market.

Discussion

- The availability organic food products are very low and more number of varieties are lacking in the market. The consumer tastes are differing from person to person. The consumers are expected more number of varieties, because when the conventional foods are lot of varieties in the market. They are also expecting more varieties in organic food products. So, the marketers and farmers focus to satisfy the consumers' expectation.
- The most of the consumers are know about the organic food products only through the family members, friends and relatives. The advertisement strategy is adopted by the marketers are very low in market. So, the retailers are focused the advertisement campaign to improve the strategy in marketing of the products. The government also arrange the publicity and to create awareness about the organic food advantages among the peoples in the society.

Conclusion

The health and environmental benefits are emerged as the most important determinants to prefer organic food products. Organic foods are having more benefits like better quality, good for health, free from chemical residues which resulting no side effects and do not cause the harmful to the consumers' health etc. The consumers are aware about the benefits of organic food products. The nutritional value, hygienic, quality of products and many terms are to measure the satisfaction level of the consumers towards organic food products. So, the marketers to measure the consumer expectation and satisfaction level is important to increase the market shares. The competitive market place where the business are constantly competing for customers. The study of consumer satisfaction has made a number of benefits to the marketers for inviting customers to express their

opinion and also opportunities to invite the customers to learn new information about the products and services. Once the consumers are satisfied in purchasing, he or she buys again and again. Satisfaction is only determined the future markets. The government to create awareness and encouraging sustainable purchase with organic products.

Ethical Clearance: My research entitled "A Study on Consumers' Satisfaction Level towards Select Organic Food Products in Salem District of Tamil Nadu". My research aims and methodologies to make sure that the research will be conducted in a way that protects the dignity, rights and safety of the research participants, and that the research design is ethically sound.

Sources of Funding: Self

Conflict Interest: No

References

1. Mohana Soundari R. and Sathya N. A Study on customer preference towards natural organic products in tirupur city, Vol.2(1) ed. : International Journal of Current Research and Modern Education; 2017.
2. Sangeetha R. . A Study on Consumer Preference towards Organic Products in Tirupur, Vol.V, Issue 1(4) ed. : International Journal of Management Studies; 2018.
3. Savithri N and Lavanya B. A Organic Food Products: A Study on perception of Indian consumers, Vol.6(1) ed. : International Journal of Research and Analytical Reviews; 2019.
4. FiBL & IFOAM year book 2018.
5. Mohana Soundari R. and Sathya N. A Study on customer preference towards natural organic products in tirupur city, Vol.2(1) ed. : International Journal of Current Research and Modern Education; 2017.
6. India Organic Food Market Forecast and Opportunities 2017.

An Empirical Relationship between Stress and Time Management of School Students

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Abstract

Time management is the main factor to reduce stress among the students. The main aim of this study is to find the factors causing stress among the students and impact of time management on stress. The researcher used regression analysis to find the result. Time management and stress are negatively correlated. Poor time management increase stress level to the students. The results shows that pressure of parents and pressure of teachers increase stress level than the other factors.

Keywords: *Stress, Time Management, Academic Performance.*

Introduction

Time Management has been defined as a “combination of time assessment, goal setting, planning, and monitoring activities” (Hafner & Stock, 2010, p. 430)⁹ or a “self-controlled attempt to use time in a subjectively efficient way to achieve outcomes” (Koch & Kleinmann, 2002, p. 201)¹⁰, while others do away with the need to define time management altogether (e.g., Barling, Cheung, & Kelloway, 1996; Trueman & Hartley, 1996)⁴.

Good time management such as setting goals and priorities as well as monitoring the use of time can facilitate productivity and minimize stress, contributing to work effectiveness, maintaining balance and academic success. From this broadened perspective, people can see that the real value of time management is that it enhances their lives in all dimensions. What people gain from time management, in essence, is not more time, but a better life (Britton & Tesser, 1991; Misra & McKean, 2000)⁶.

Time management is essentially to the students and this will be trained by the teachers how they managed

the time to provide high performance and to reduce stress. Most of the time students face problems like task aversion and uncertainty, so they start to procrastinate because they lack organizational skills. As a result, students will not be able to organize duties according to their priorities, so they get distracted easily, ending up procrastinating. Effective time management is associated with greater academic performance and lower levels of anxiety in students; however many students find it hard to find a balance between their studies and their day-to-day lives.

Time management skill is one of the criteria that are used by students which results in an academically successful performance; the attempt for success is called academic motivation. Academic motivation means internal tendency of the learner that leads them to learning, skill acquirement and academic achievement. Academic motivation is very important for nursing students. Reduction of motivation has adverse effects on nurses, health of patients and society, and it diminishes many assets.

The students know to manage the time wisely make them calmly to do the work and complete the portions on time without any stress. This will useful to the students to achieve high in their academic performance.

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Review of Literature: Alexander Hafner et al (2014) Decreasing students’ stress through time management training: an intervention study. The purpose of this study

was to observe the effects of a time management training program on perceived control of time and perceived stress in the context of higher education. As expected, perceived stress decreased and perceived control of time increased after training, whereas demands did not change. Therefore, time management training might be beneficial for undergraduate students' well-being¹.

Ahmad Saleh Al Khatib (2014) Time Management and Its Relation to Students' Stress, Gender and Academic Achievement among Sample of Students at Al Ain University of Science and Technology, UAE. The objective of the present study was to investigate the relationship between time management, perceived stress, gender and academic achievement among United Arab Emirates college students. Time management was measured by Time Management Questionnaire" developed by Britton and Tesser (1991), while perceived stress was measured by The Perceived Stress Scale developed by Cohen (1985). The findings of the study showed that there was statistically significant negative relationship between time management and perceived stress².

Faisal Z. Miqdadi, Abdulla et al(2014) The Relationship between Time Management and the Academic Performance of Students from the Petroleum Institute in Abu Dhabi, the UAE. ASEE 2014 Zone I Conference, April 3-5, 2014, University of Bridgeport, Bridgeport, CT, USA. This research study is about time management and how it is related to academic performance the Petroleum institute (PI) in Abu Dhabi, the UAE. The study was made by surveying male freshmen and sophomore students regarding problems of procrastination, disorganization, interruptions and work load stress. The results obtained showed that time management is highly related to academic performance. Finally, by discussing the results, we came up with recommendations that can lead the PI students to a better level of time management⁷.

Dr. Ghada Abd Elasm Eldeeb, Dr. Entisar Kamel Eldosoky (2016). Relationship between Effectiveness of Time Management and Stress levels among Nursing Students. The aim of the study is to compare time management and stress among 3rd and 8th levels nursing students. No students in both groups have high levels of time management. Regarding stress 3rd level students have higher mean scores of stress than 8th level students. There is non statistical significant positive correlation between time management and stress. The

objective of the present study was to investigate the relationship between time management, perceived stress, gender and academic achievement among United Arab Emirates college students. The respondents were 352 college students from Al Ain University of Science and Technology. The findings of the study showed that there was statistically significant negative relationship between time management and perceived stress. Females reported higher time management compared to their males counter mates. Higher time management and lower perceived stress were associated with high levels of academic achievement⁸.

Brad Aeon, Herman Aguinis (2017) It's About Time: New Perspectives And Insights On Time Management. Time management has helped people organize their professional lives for centuries. This study illustrate how time structures and time norms operate at the team, organizational, and national levels of analysis in influencing time management outcomes. It rely on the behavioral economics literature to describe how cognitive biases influence individual time management decisions. Integrating insights from a diverse set of fields results in a better understanding of past research and allows us to reinterpret conflicting results prevalent in the time management literature⁵.

Arezoo Mohamadkhani Ghiasv and et al(2017) Relationship between time management skills and anxiety and academic motivation of nursing students in Tehran. Time management skills are essential for nursing students' success, and development of clinical competence. The purpose of this study was to determine the relationship between time management skills and anxiety and academic motivation of nursing students in Tehran medical sciences universities in 2015. Most participants had a moderate level of time Management skills (49%), State Anxiety (58%), Trait Anxiety (60%) and Academic Motivation (58%). The results also showed a statistically significant negative correlation between the students³

Richelle V. Athoms (2019) Impact of Time Management Behaviors on Undergraduate Engineering Students' Performance. This article examines the self-reported time management behaviors of undergraduate engineering students using the Correlation analysis, regression analysis, and model reduction are used to attempt to determine which aspects of time management the students practiced, which time management behaviors were more strongly associated with higher grades within

the program, and whether or not those students who self-identified with specific time management behaviors achieved better grades in the program. It was found that students' perceived control of time was the factor that correlated significantly with cumulative grade point average. On average, it was found that time management behaviors were not significantly different across gender, age, entry qualification, and time already spent in the program¹¹.

Objectives of the Study:

1. To find the factors causing stress on school students
2. To Evaluate impact on time management on stress
3. To study the relationship between stress and time management

Hypotheses of the Study:

1. There is significant difference among the factors causing stress on school students
2. There is significant influence of time management on stress
3. There is significant relationship between stress and time management

Analysis and Discussion: There are lot of factors causing stress among school students whereas heavy portions, deadlines to complete the portions, examinations, competition, pressure of parents, pressure of teachers and to attain the desired goal. These are all the factors causing stress among the school students. The regression analysis shows the relationship between these factors and how this factors affects their academic performance. The results are presented below:

Table 1: Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.996 ^a	.993	.992	.63350

a. Predictors: (Constant), S1,S2,S3,S4,S5,S6,S7

Source: Computed data

From the above table it is found that R=.996 R square = .993 and adjusted R square .992. This implies the stress create 99% variance over the students' performance. The cumulative influence of eight variables of stress over students' performance is ascertained through the following one way analysis of variance.

Table 2: ANOVA^a

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	26277.140	7	3753.877	9353.721	.000 ^b
	Residual	197.452	492	.401		
	Total	26474.592	499			

a. Dependent Variable: Academic Performance

Table 3: Coefficients^a

Model B	Unstandardized Coefficients		Standardized Coefficients	t	Sig.	
	Std. Error	Beta				
1	(Constant)	-.129	.113		-1.148	.252
	Examination	1.269	.099	.202	12.875	.000
	Pressure of teachers	1.063	.101	.165	10.484	.000
	Pressure of Parents	1.162	.082	.207	14.174	.000
	Attain the desired goal	.356	.091	.070	3.913	.000
	Heavy Portion	1.089	.107	.181	10.206	.000
	Competition	.614	.103	.109	5.981	.000
	Health issues	.498	.117	.090	4.271	.000

Dependent Variable: Academic Performance, **Source:** Computed data, It illustrates that Examination (Beta = .202, t = 12.875, p = .000), Pressure of teachers (Beta = .165, t = 10.484, p = .000), Pressure of parents (Beta = .207, t = 14.174, p = .000), Attain the desired goal (Beta = .070, t = 3.913, p = .000) Heavy portions (Beta = .181, t = 10.2016, p = .000), Competition (Beta = .109, t = 5.981, p = .000), Health Issues (Beta = .090, t = 4.271, p = .000) are statistically significant at 5% level. This specifies that pressure of parents and pressure of teachers creates stress among the students and they measure them during the realization of academic performance.

Findings and Conclusions

The factors affecting stress among the school students are Examination, Pressure of teachers, Pressure of parents, attain the desired goal, heavy portions, competition, and health issues of the students. Pressure of teachers and pressure of parents are create more stress among the students than other factors.

Time Management is the main factor to reduce stress among the students. This will reflects in their academic performance. The teachers should have to provide the time management chart to the students to attain the desired goals in their academic performance effectively. Effective time management produce good academic performance to the students. Time management and stress are negatively correlated. Poor time management increase the stress level.

Finally the study concludes that management should teach time management to the students and this will lead to produce good results to the students as well as the management.

Conflict of Interest: Nil

Ethical Clearance: Taken from UGC Committee.

Source of Funding: Self

References

- Alexander Hafner et al .Decreasing students' stress through time management training: an intervention study. *European Journal of Psychology of Education*. 2014. Volume 30. Issue (1).
- Ahmad Saleh Al Khatib. Time Management and Its Relation to Students' Stress, Gender and Academic Achievement among Sample of Students at Al Ain University of Science and Technology, UAE. *International Journal of Business and Social Research (IJBSR)*, 2014 Volume -4, No.- 5.
- Arezoo Mohamadkhani Ghiasvand et al Relationship between time management skills and anxiety and academic motivation of nursing students in Tehran. *Electronic Physician*. 2017. Volume 9 Issue 1
- Barling, Cheung, & Kelloway, 1996; Trueman & Hartley, 1996.
- Brad Aeon, Herman Aguinis. It's About Time: New Perspectives And Insights On Time Management. *Academy Of Management Perspectives* 2017, Vol. 31, No. 4, 309–330.
- Britton & Tesser, 1991; Misra & McKean, 2000.
- Faisal Z. Miqdadi, Abdulla et al. The Relationship between Time Management and the Academic Performance of Students from the Petroleum Institute in Abu Dhabi, the UAE. *ASEE 2014 Zone I Conference*, April 3-5, 2014, University of Bridgeport, Bridgeport, CT, USA.
- Dr.Ghada Abd Elaslalm Eldeeb, Dr. Entisar Kamel Eldosoky. Relationship between Effectiveness of Time Management and Stress levels among Nursing Students. *IOSR Journal of Nursing and Health Science* 2016. (IOSR-JNHS) e-ISSN: 2320–1959.p- ISSN: 2320–1940 Volume 5, Issue 2, PP 95-100.
- Hafner & Stock, *Stress*. 2010, p. 430.
- Koch & Kleinmann, *Time Management* 2002, p. 201
- Richelle V. Athoms Impact of Time Management Behaviors on Undergraduate Engineering Students' Performance. *Sage Journals* 2019 Volume: 9 issue: 1.

Prevalence of Anemia among Higher Primary School Girls in Selected Urban and Rural Schools

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Abstract

Introduction: Anemia is one of the world's most wide spread health problem having major consequences for human health as well as social and economic development and affecting both developing and developed countries¹. The body required increased amount of iron when growing rapidly and when frequent blood loss occurs through menstruation, hence adolescent girls are significantly high risk of developing iron deficiency. This is especially true for some adolescent girls who experience heavy blood loss during menstruation².

Objective: To determine and compare the prevalence of anemia among higher primary school girls between urban and rural schools.

Methodology: A descriptive comparative study was conducted among 450 (urban) and 450 (rural) school girls at higher primary schools, Belgaum, Karnataka. Stratified random sampling technique was used to select the school girl children. Haemoglobin estimation was done by using Sahli's method to determine anemia.

Results: Higher prevalence of anemia was observed to be (90%) among rural higher primary school girl children compared to the urban (79.8%) counterpart. The occurrence of anemia reported through the study, was associated with age, class, religion of the child, parents' occupation (p value<0.05) in urban and rural higher primary school. In addition, there was also significant association was found between prevalence of anemia and type of diet, previous source of information, parents' education, family income of participants (p value <0.05) in rural school.

Conclusion: Present study showed higher anemia prevalence in rural school girl children compared to urban. Early intervention is utmost required by considering these factors along with the existing programs will help directly to overcome this issue.

Keywords: Anemia; higher primary school girls; knowledge; prevalence; rural; urban.

Introduction

Anemia is one of the world's most widespread health problem having major consequences for human health as well as social and economic development and affecting both developing and developed countries¹.

In developing and developed countries the prevalence of anemia among adolescent is estimated to be 27% and 6% respectively³.

India is one of the country tagged with highest anemia prevalence according to estimates from WHO, which estimates that, in developing countries 27%

of adolescents were anemic⁴ the high incidence of low birth weight babies, high prenatal mortality and the consequent high fertility rates. Objective was to determine the prevalence of anaemia among school going adolescent girls. The present study included 320 adolescent girls from selected Government Secondary Schools of district Rohtak (Haryana).

Today, the country is suffering from most wide spread disorder of nutritional deficiency mainly due to anemia occurring primarily due to iron deficiency. More than 39% girls of age 15–19 years which fall under adolescent group were mildly anemic, while 15% were

moderately anemic and 2% severely anemic⁵. A cross-sectional study carried out in four villages of Wardha among 630 adolescent girls, the prevalence of anemia was found to be 59.8% and the prevalence of severe, moderate and mild anemia was 0.6%, 20.8% & 38.4% respectively⁶. Thus, this anemia still remained as a serious public health problem.

Objectives:

1. Compare the prevalence of anemia among higher primary school girls between urban and rural schools.
2. Find out the association between prevalence of anemia and socio demographic variables of higher primary school girls in urban and rural schools.

Null Hypothesis:

H₀₁: There will be no difference between the prevalence of anemia among higher primary school girls in selected urban and rural schools.

H₀₂: There will be no association between the prevalence of anemia and socio demographic variables among higher primary school girls in selected urban and rural schools.

Materials and Method

Research approach: Quantitative research approach.

Research design: A descriptive comparative research design

Setting: The present study was conducted in 7 Urban and 6 Rural higher primary schools in Belgaum district.

Population:

- Target population: girls studying in selected urban and rural higher primary schools of Belgaum district.
- **Accessible population:** girls who are studying in 6th, 7th and 8th standard, who are fulfilling the selection criteria in selected 7 urban and 6 rural higher primary schools of Belgaum district.

Sampling Procedure: In the present study, Out of 129 urban higher primary schools, 7 were selected and out of 659 rural higher primary schools, 6 were selected randomly. Among 7 Urban schools 226 students (girls) were studying in 6th standard, 370 in 7th and 401 in 8th

standard. Using the stratified random sampling method according to different classes, picked 102 school girl children (samples) in the 6th standard, 167 samples in 7th standard and 181 samples in 8th standard proportionately. Further, using the method of simple random sampling, girls from each class were selected who were fulfilling the sampling criteria.

The same sampling procedure was used for selecting samples from the rural area.

Sample and sample size: 450 urban and 450 rural girls studying in higher primary schools.

Inclusion Criteria:

- School girls studying in VI, VII and VIII standards.
- Girls who are present in the school at the time of data collections.
- Girls willing and their parents' consent to withdraw blood sample for haemoglobin estimation.

Exclusion criteria:

- School girls who were seriously ill & Psychiatric problems as reported by their teacher.

Demographic Variables: Child's data: The items included were hemoglobin level, age, class, type of diet and residence.

Parent's Data: The items included were educational status of father and mother, occupational status of father and mother, religion, type of family, monthly income of family and number of siblings.

Data Collection Procedure: Before collecting the data prior permission was obtained from the Health and family Welfare Officer, Belgaum, Block education officer and the Principals of selected schools. The concerned authority of institution had given dates and timings to conduct the research study. Keeping in mind the ethical aspect of research, consent form was sent along with the child to home to get the parents signature (consent). The researcher collected the data after the respondents were assured the anonymity and confidentiality of the information provided by them. The Hemoglobin estimation of selected girls was done by using Sahli's method under the supervision of principal investigator, the laboratory technicians checked the haemoglobin level.

The process adopted for haemoglobin estimation was as follows:

Blood was mixed with N/10 HCl resulting in the conversion of Hb to acid hematin which is in color brown. The solution was diluted till it's color matches with the brown colored glass of the comparator box. The concentration of Hb was read directly.

Data Analysis:

1. **Descriptive Statistics:** Frequency distribution, percentage, mean, was used to assess the demographic variables.
2. **Inferential Statistics:** Chi-square test and Fisher's Exact test was used to determine the association of prevalence of anemia with the selected demographic variables.

Findings:

Part I: Description of demographic characteristics of urban and rural school girl children.

- In Urban schools, out of 450, 180 (40.00%) participants were age of 13 years, 132 (29.3%) were 14 years, 126 (28.0%) were 12 years, 7 (1.6%) were 11 years and remaining only 5(1.1%) were 15 years. Almost similar was observed in rural area.
- In urban schools, out of 450, 181 (40.2%) participants were belongs class VIII, 167 (37.1%) were class VII and remaining 102(22.7%) participants were class VI. The same was observed in rural area.
- In urban area, out of 450, more than 85% participants belongs to urban residence and in rural area almost all the participants belongs to rural residence.
- In urban schools, more than 50% participants had mixed dietary habit, 186 (41.30%) had vegetarian. In rural area around 70.00% participants had vegetarian, 143 (34%) had mixed food habit.
- Majority 91.1% fathers of participants qualified with secondary, under graduate and pre-university education in urban, whereas in rural area about 91.3% were studied primary, secondary and pre-university but no one has done post graduation.
- In urban area, around 50% fathers were self employed, 148(32.9%) were working in private

sector and 84(18.7%) fathers were government employee and none them were unemployed. In rural area around 85% of fathers were self employed, 51(11.3%) were working private sector, 15(3.3%) were in government sector and only 3 fathers were unemployed.

- In urban area, more than 80% mothers were housewives, 53 (11.8%) were working in private sector and 22 (4.9%) mothers were government employee. In rural area almost all the mothers were housewives.
- Out of 450 participants in urban area majority them belongs to Hindu religion, followed by 82 (18.2%) belongs to Muslim and 42 (9.3%) belongs to Chirstian and in rural area more than 80% participants belongs to Hindu religion 51 (11.3%) belongs to Muslim and only 6 belongs to Chirstian.
- In urban area majority of participants belongs to nuclear family whereas in rural area majority participants belongs to joint family.
- Regarding family income, in urban area 182 (40.4%) participants has more than 15000 rupees, 140 (31.1%) participants was 10001 to 15000 rupees, 125 (27.8%) participants was 5001-10000 rupees and only 3 (0.7%) participants was less than 5000 rupees. Where as in rural area almost three-fourth participants family income was 5001-10000, followed by 57 (12.7%) participants was 10001-15000, followed by 30 (6.7%) participants was less than 5000 rupees and 27 (6.0%) participants was more than 15000 rupees.
- In urban area, out of 450, around 50% participants had only one sibling, 120 (26.7%) had two siblings, 71 (15.8%) had no siblings and 51 (11.3%) participants had three and more siblings. In case of rural area, 159 (35.3%) participants had two siblings, 148 (32.9%) had three and more siblings, 136 (30.2%) had only one sibling and only 7 (1.6%) participants had no siblings.

Part II: Anemia Prevalence and its comparison between urban and rural higher primary school girls.

Table 1: Prevalence of anemia and its comparison

Type of Anemia	Group		Total	χ^2 Calculated value
	Urban	Rural		
No anemia (>12g/dl)	91	45	136	35.56 S
	20.2%	10.0%	15.1%	
Mild anemia (10-11.9g/dl)	268	245	513	
	59.6%	54.4%	57.0%	
Moderate anemia (07-09.9g/dl)	91	160	251	
	20.2%	35.6%	27.9%	
Total	450	450	900	
	100.0%	100.0%	100.0%	

S: Significant, χ^2 Table value = 5.99, p<0.05

The data shows that out of 900 participants, majority of 513 (57.0%) in urban and rural area had mild anemia. In urban, 91 (20.2%) and rural area 160 (35.5%) had moderate anemia. Remaining 20.2% and 10.0% participants had no anemia in urban and rural area respectively. The prevalence of anemia among higher primary school girls in urban and rural area was 79.8% and 90% respectively.

The above table shows that the calculated chi-square (χ^2) value (35.56) is more than the table value (5.99) hence the null hypothesis is rejected. Therefore, concluded that there was significant difference between the prevalence of anemia among higher primary school girls in urban and rural schools (p<0.05).

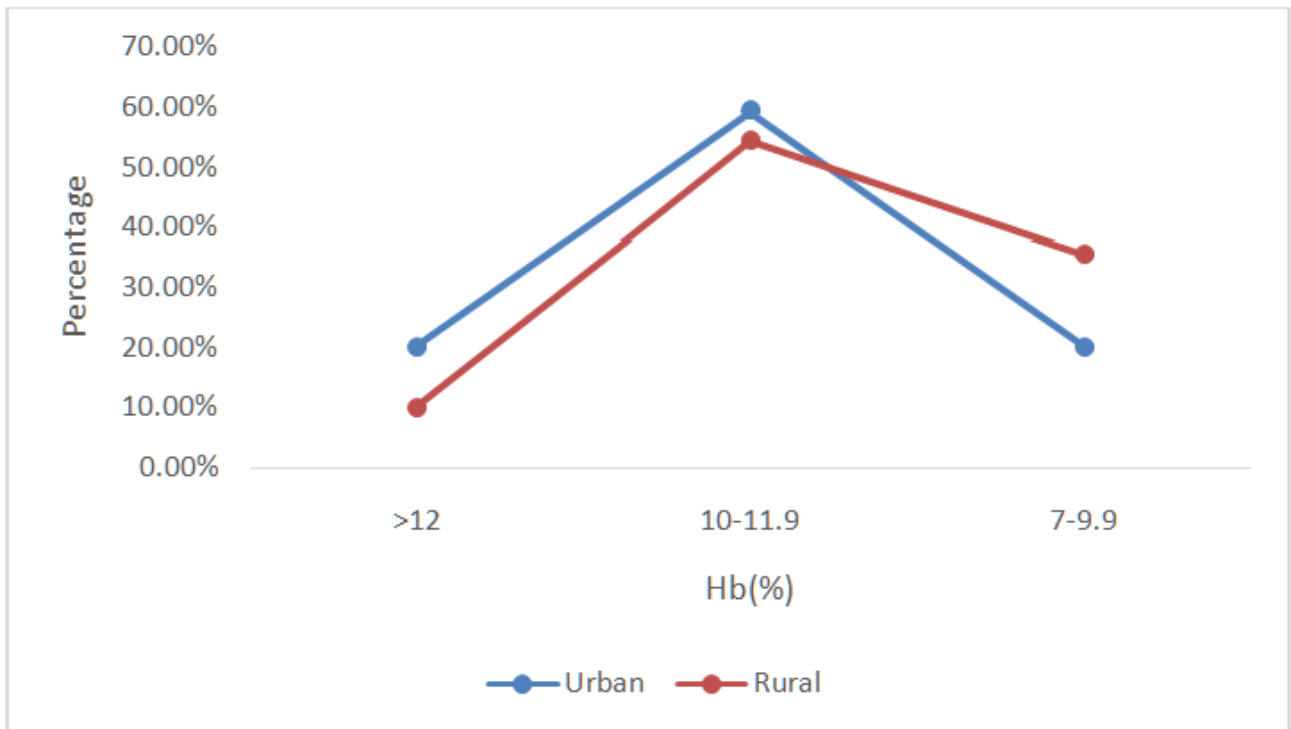


Fig. 1 Prevalence of anemia and comparison between urban and rural schools.

Part II: Association between the anemia prevalence & socio-demographic variables in urban higher primary schools.

The demographic variables of age, class, father occupation, mother occupation and religion, the calculated value of Fisher-Exact test and chi-square is greater compared to table value. Hence the null hypothesis is rejected at 5% significance level. Therefore, concludes a significant association between age of the participants and anemia (p value < 0.05).

Regarding residence, type of diet, father education, Type of Family, family income and No. of siblings, the calculated value of Fisher-Exact test and chi-square is less compared to table value. Hence the null hypothesis is not excluded at 5% significance level. Therefore, there was no significant association between type of residence of the participants and anemia (p value < 0.05).

Part III: Association between anemia prevalence & socio demographics variables in Rural higher primary schools

The calculated chi-square value is greater than table value in class, previous source of information, religion except type of family. Hence the null hypothesis is rejected at 5% level of significance. Therefore, the results of Chi-Square test for rural school girl children show that there is significant association between class, previous source of information, religion and prevalence of anemia (p value < 0.05).

The calculated Fisher-Exact test value is greater than table value in age, type of diet, father & mothers' education and occupation, family income, number of siblings. Hence the null hypothesis is rejected at 5% level of significance. Therefore, the results of Fisher-Exact test for rural school girl children shows that there is significant association between age, type of diet, father & mothers' education & occupation, family income, number of siblings and prevalence of anemia (p value < 0.05).

Discussion

In India, anemia prevalence among adolescent girls was comprehensively demonstrated in rural and urban differentials in the present study. While there are different causes that are connected with the anemia prevalence, our study highlighted socioeconomic factors which are responsible for anemia. Factors like age,

education, family size, religion, economic status and region of residence were the significant determinants of anemia.

Almost two fold of anemia prevalence was observed among children residing in rural areas when compared to that of children of urban area. Statistical analysis of the present study revealed that majority of the participants in urban and rural area had mild anemia. But in rural area moderate mild was observed as high when compared with the urban area. No anemia was observed in very few participants of urban area when compared to rural area.

The difference seen was mainly due to poor accessibility to health care facility, lacking awareness, defecation in open air, poverty & illiteracy which is commonly more observed in rural parts of India. Addition to this, most of the children in rural area was deprived of nutrition which is also one of the factor the increased anemia prevalence. A study conducted in Belagavi, Karnataka showed that the prevalence of anaemia among school children was found to be 47.9%. A high prevalence of 57% was seen among girls. Prevalence was more in rural area i.e. 52.7% compared to that of urban i.e. 43%. Mild anaemia was found to be more prevalent in both urban and rural children i.e. 28.7% and 29.7% respectively⁷. In rural Hassan, a study reported of moderate (40.1%) and severe (4.9%) anemia in girls⁸.

Pattnaik et al., 2012, in their study described about the anemia prevalence in girls at their adolescence age residing in parts of rural area of Khordha District, Odisha. Around 78.8% anemia prevalence rate in girls at their adolescence age. Of the total 119 girls who were anaemic, 75.6% were suffering from mild degree of anemia and 24.4% girls were having moderate degree of anemia and also reported that anemia was significantly higher with H/O excessive menstrual bleeding ($P=0.001$), no H/O intake of IFA in last 6 months ($P=0.001$)⁹.

Chant. et. al., study reported that the. Prevalence of anaemia was significantly high (80%) in the adolescent girls who already attained menarche. A statistically significant relation exists between family size and anaemia. Percentage of anaemia was high among labour class (85%) than business class (61.7%). Prevalence of anaemia was to be found high in vegetarian (78.13%) than non-vegetarian (75.29%)¹⁰ poor dietary intake of iron, prolonged menstrual period, and worm infestation.

A study was conducted with the objective to determine the associated risk factors of anaemia among adolescent girls. **METHOD** A cross-section study was conducted among 202 adolescent girls in rural area of Katihar. Information was collected on a predesigned and pretested proforma about contributory factors in relation to anaemia, by oral questionnaire method. Sahli's haemoglobinometer was used for the haemoglobin estimation. **RESULTS** Prevalence of anaemia and severity of anaemia was found to be high in the age group 17 to 19. Prevalence of anaemia was significantly high (80%).

In the present study, school children of adolescence age with family size of more than five & five are more prone to anemia prevalence in comparison to school going adolescents with small size family having less than five members. The reason behind this could be because large family size results in less care for each individual of the family also constrain of income in intake of a sufficient diet that includes food varieties that is micro-nutrient rich as that of iron.

Conclusion

This study concludes that anemia prevalence among girls during adolescence were very high in India which requires concerted efforts by all the stakeholders, policy maker, planners involved in National Health Policy. Results clearly indicated that the prevalence of anemia is higher in rural place than the urban schools of Belgaum district. The present study also showed the parents' education, parents' occupation, socio-economic status, family size; dietary intake will directly influence the anemia among the community.

Hence, improvement of society's economic status and poverty mitigation is one of a critical tactic to minimize the anemia prevalence.

Conflict of Interest: Nil

Source of Funding: Self

Ethical Clearance: Ethical Clearance was obtained from ethical committee of Himalayan University, Itanagar, Arunachal Pradesh.

References

1. De Benoist B, World Health Organization, Centers for Disease Control and Prevention (U.S.).

- Worldwide prevalence of anaemia 1993-2005 of: WHO Global Database of anaemia [Internet]. Geneva: World Health Organization; 2008 [cited 2019 Nov 20]. Available from: http://whqlibdoc.who.int/publications/2008/9789241596657_eng.pdf
2. Pan America Health Organization, WHO, Anemia among adolescent and young adult women in Latin America and the Caribbean: A cause for concern, Website: <http://www.paho.org>
3. Biradar, S. S., Biradar, S. P., Alalagi, A. C., Wantamutte, A. S., & Malur, P. R. (2012). Prevalence of anaemia among adolescent girls: a one year cross-sectional study. *Journal of Clinical and diagnostic Research*, 6(3), 372-7
4. Devi S, Deswal V, Verma R. PREVALENCE OF ANEMIA AMONG ADOLESCENT GIRLS: A SCHOOL BASED STUDY. 2015;5:4.
5. NNMB_Third_Repeat_Rural_Survey___Technicl_Report_26.pdf [Internet]. [cited 2019 Nov 20]. Available from: http://nnmbindia.org/1_NNMB_Third_Repeat_Rural_Survey___Technicl_Report_26.pdf
6. Kaur S, Deshmukh PR, Garg BS. Epidemiological Correlates of Nutritional Anemia in Adolescent Girls of Rural Wardha. 2006;31(4):4.
7. Prayag A, Ashtagi GS, Mallapur MD. A STUDY ON ASSESSMENT OF SEVERITY OF ANAEMIA AMONG URBAN AND RURAL CHILDREN OF BELAGAVI, KARNATAKA. 2016;7(8):4.
8. Siddharam. S.M., Venketesh, G.M., & Thejeshwari, H.L. (2011). A study of anemia among adolescent girls in rural area of Hassan district, Karnataka, South India. *Int J Biol Med Res*, 2-924
9. Pattnaik, S., Pattnaik, L., Kumar, A., & Sahu, T. (2012). Prevalence of Anemia among adolescent girls in a rural area of Odisha and its epidemiological correlates. *Indian Journal of Maternal and Child Health*, 15(1).
10. Chand MIA, Nandan M, Biswas AB. AN EPIDEMIOLOGICAL STUDY OF ANAEMIA AND ITS ASSOCIATED RISK FACTORS AMONG ADOLESCENT GIRLS IN RURAL AREA OF KATI HAR. *J Evid Based Med Healthc* [Internet]. 2019 Aug 5 [cited 2019 Nov 20];6(31):2117–20. Available from: https://jebmh.com/assets/data_pdf/Alam_Chand_-_FINAL.pdf

Relative Effect of Conventional and Specific Hockey Skill Training on Selected Motor Fitness, Physiological Variables and Playing Ability of Hockey Players in Tamil Nadu

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Abstract

The purpose of the study was to study conventional and specific hockey skill training on Motor fitness, physiological and playing ability of Hockey players. There were selective three motor fitness and three physiological components which were used as a criterion measures for this study. For analysis the data and to find out the relationship between selective motor fitness, physiological and playing ability Pearson product moment relationship was applied. Level of confidence was set at .05 levels. Firstly, selective motor fitness, Second, physiological components were evaluated. The result of the study clearly disclosed that specific hockey skill training has considerable relationship with the playing ability of Hockey players in SRM University, Tamil Nadu. On the basis of results and associated discussion it may be concluded that conventional training and playing ability had low correlation. There might be some reasons of the low correlation in the perspective of good scientific coaching. There was the possibility of the lack of coaching aspects, which shows clearly in the findings that the specific hockey skill training was less correlated with playing ability.

Keywords: *Conventional training, specific hockey skill training, playing ability.*

Introduction

Hockey is one of the favourite of all. Hockey is the game of skill; it is a well-known concept of ancient Indian hockey which elaborates the importance of conventional and specific of skills training. Hockey is a dynamic field game, played by male and female, requiring high level skills, excellent conditioning and well coordinated team efforts¹. Hockey is one of the most popular and attractive sports in the world. Hockey is a sport with many complex techniques and tactics that can be seen speed, power, endurance and movement frequently in it⁵.

Research in the field of Physical Education and Sports is highly demand of the today. Researches in this field brought so many fitness in and various skill training. We can say that the progress of the field directly linked with research. It is fact that at present situation research in Physical Education, and Sports is an important area of study to improve the sports performance. The past decades have seen the rise of an area of study called futurism or futuristic, which attempts to scientifically examine the future².

A physiological benefit available, through motor activity is positively associated with aspects of psychological well-being. In particular, significant relationships have been identified between self-perceived health and motor activity. The argument exists, therefore, that the promotion of sports participation and achieve leisure pursuits may at least be rewarded by better health perceptions. The poor performance of Indian sportsman and sports women in the international competitions is the result of lack of motor fitness. Therefore, it is felt that

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there is a dire need to improve the motor fitness level of Indian youth for raising the performance and standard in games and sport⁴.

Motor fitness, physiological variables have been considered as important prerequisite for sportsmen to secure the top level performance in the game. A good hockey player must have the following physical activity. He must have the motor fitness to perform the specific skills training that the game of hockey requires. These include speed endurance, muscular endurance, and aerobic endurance with precision accuracy and confidence. Perfection in vital capacity, respiratory rate, and respiratory volume is most important for all good players irrespective.

Coaching in the sports would be based on scientific and systematic information derived from research³. With regard to physical fitness there are several factors that a number of overlapping activities. The term physical fitness has been divided into two distinct categories: skill-related and physiological-related motor fitness.

Methodology of the study

Selection of Subjects: For the purpose of present study forty five field hockey players from SRM University, Department of Physical Education and Sports Science, Kattankulathur, Chennai, Tamil Nadu State, India were selected as subjects at random and their ages ranged from 18 to 25 years. These subjects were divided in three groups. Each group would be consists of 15 players.

Selection of Variable: Twelve weeks conventional training and specific hockey skill training acts as an independent variable and motor fitness, physiological acts as dependent variable for the present study.

Research Design: The selected subjects (N=45) were divided into three groups equally and randomly. Of which one group was undergoing conventional method of training to develop selected dependent variables whereas the other group underwent specific hockey skill training to develop the selected motor fitness, physiological variables and playing ability and the third group acted as control group.

Collection of Data: Before the administration of conventional and specific hockey skill training, the motor fitness, physiological test were administered on both the experimental and control groups to collect pretest data.

After the completion of 12 weeks of specific hockey skill training again the same tests were conducted to collect the post training data. Necessary instructions were given to the subjects before administration of the tests.

Experimental Design: For the study pretest & posttest randomized group design, which consists of no training group (n=15) and two experimental group (n=30) was used. Equal numbers of subjects were assigned randomly to the group. Two groups served as experimental group (conventional training and specific hockey skill training group) on treatment.

- Experimental Group I: subjects were considered as Conventional training on regular male field hockey players.
- Experimental Group II: Subjects were allowed to perform Specific hockey Skill training on regular male field hockey player.
- Control Group III: Subjects were not given special training other than the training on regular male field hockey players respectively.

For experimental group I & II the present study training given for three days per week (alternate days) for twelve weeks. Every training session lasted for 60 to 90 minutes. The training program was scheduled for the morning between 6.00 am to 8.00 am.

However, they were participating in their regular physical activities and game practice. The subject underwent their respective programme under strict supervision prior to and during every session. Subject underwent training for & 90 minutes including warm up and cool-down exercises which included jogging, stretching, striding and warm-ups. Measurement of motor fitness, physiological variables, and playing ability was taken for the three groups.

Hence the results concluded that specific hockey skill training influences the speed endurance, muscular endurance, aerobic endurance, vital capacity, respiratory rate, and respiratory volume, of the players. It was also proved that the better effect was seen in regular male field hockey players in group II.

Statistical Procedure: To find out the effect of static and conventional training and specific hockey skill Training on motor fitness, physiological and playing ability of the subjects the pretest and post test scores were analyzed by using descriptive statistical

and Analysis of Co-Variance (ANCOVA). To test significance of difference among means test was applied. The data analyzed with the help of (IBM) SPSS (20.0

version) software and the level of significance was set at 0.05 level of confidence.

Findings of the Study:

Table I: Analysis of covariance of means of conventional training and specific hockey skill training and no training groups on speed endurance

	Conventional Training	Specific Hockey Skill Training	No Training	Source of Variance	Sum of Squares	df	Means Squares	F-ratio
Pre-Test Means	6.08	6.23	6.05	BG	0.27	2	0.14	1.31
				WG	4.47	42	0.10	
Post-Test Means	5.76	5.85	5.32	BG	2.37	2	1.18	8.55*
				WG	5.83	42	0.13	
Adjusted Post-Test Means	5.76	5.85	5.32	BG	2.304	2	1.15	8.10*
				WG	5.830	41	0.14	

*Significant at 0.05 level of confidence.

The table-I indicated that the pretest means conventional training and specific hockey skill training and no training groups were 6.08, 6.23 and 6.05 respectively. The obtained F-ratio for the pre-test was 1.31 and the table F-ratio was 3.22. Hence the pre-test mean speed endurance F-ratio was insignificant at 0.05 level of confidence for the degree of freedom 2 and 42. The post-test means of the conventional training and specific hockey skill training and no training groups were 5.76, 5.85 and 5.32 respectively. The obtained F-ratio for the post-test was 8.55 and the table F-ratio

was 3.22. Hence the post- test mean speed endurance F-ratio was significant at 0.05 level of confidence for the degree of freedom 2 and 42. The adjusted post-test means of the conventional training and specific hockey skill training and no training groups were 5.76, 5.85 and 5.32 respectively. The obtained F-ratio for the adjusted post-test means was 8.10 and the table F-ratio was 3.23. Hence the adjusted post-test mean speed endurance F-ratio was significant at 0.05 level of confidence for the degree of freedom 2 and 41.

Table II: Analysis of covariance of means of conventional training and specific hockey skill training and no training groups on muscular endurance

	Conventional Training	Specific Hockey Skill Training	No Training	Source of Variance	Sum of Squares	df	Means Squares	F-ratio
Pre-Test Means	11.45	11.59	11.19	BG	1.23	2	0.62	1.35
				WG	19.28	42	0.45	
Post-Test Means	10.61	11.12	9.52	BG	20.20	2	10.10	18.73*
				WG	22.65	42	0.53	
Adjusted Post-Test Means	10.64	11.10	9.51	BG	19.99	2	9.99	18.33*
				WG	22.36	41	0.54	

*Significant at 0.05 level of confidence.

The table-II indicated that the pretest means conventional training and specific hockey skill training and no training groups were 11.45, 11.59 and 11.19 respectively. The obtained F-ratio for the pre-test was 1.35 and the table F-ratio was 3.22. Hence the pre-test mean muscular endurance F-ratio was insignificant at 0.05 level of confidence for the degree of freedom 2 and 42. The post-test means of the conventional training and specific hockey skill training and no training groups were 10.61, 11.12 and 9.52 respectively. The obtained F-ratio for the post-test was 18.73 and the table F-ratio

was 3.22. Hence the post- test mean muscular endurance F-ratio was significant at 0.05 level of confidence for the degree of freedom 2 and 42. The adjusted post-test means of the conventional training and specific hockey skill training and no training groups were 10.64, 11.10 and 9.51 respectively. The obtained F-ratio for the adjusted post-test means was 18.33 and the table F-ratio was 3.23. Hence the adjusted post-test mean muscular endurance F-ratio was significant at 0.05 level of confidence for the degree of freedom 2 and 41.

Table III: Analysis of covariance of means of conventional training and specific hockey skill training and no training groups on aerobic endurance

	Conventional Training	Specific Hockey Skill Training	No Training	Source of Variance	Sum of Squares	df	Means Squares	F-ratio
Pre-Test Means	42.40	44.33	42.40	BG	2	18.68	2	1.01
				WG	42	18.44	42	
Post-Test Means	51.53	52.46	47.93	BG	2	85.95	2	3.77*
				WG	42	22.77	42	
Adjusted Post-Test Means	50.35	53.05	48.52	BG	2	77.99	2	10.52*
				WG	41	7.41	41	

*Significant at 0.05 level of confidence.

The table-X indicated that the pretest means conventional training and specific hockey skill training and no training groups were 42.40, 44.33 and 42.40 respectively. The obtained F-ratio for the pre-test was 1.01 and the table F-ratio was 3.22. Hence the pre-test mean aerobic endurance F-ratio was insignificant at 0.05 level of confidence for the degree of freedom 2 and 42. The post-test means of the conventional training and specific hockey skill training and no training groups were 51.53, 52.46 and 47.93 respectively. The obtained F-ratio for the post-test was 3.77 and the table F-ratio was 3.22. Hence the post- test mean aerobic endurance F-ratio was significant at 0.05 level of confidence for the degree of freedom 2 and 42. The adjusted post-test means of the conventional training and specific hockey skill training and no training groups were 50.35, 53.05 and 48.52 respectively. The obtained F-ratio for the adjusted post-test means was 10.52 and the table F-ratio was 3.23. Hence the adjusted post-test mean aerobic endurance F-ratio was significant at 0.05 level of confidence for the degree of freedom 2 and 41.

Discussion on Findings

The prime intention of the researcher was to analyse the relative effect of conventional training and specific hockey skill training on selected motor fitness, physiological and playing ability of field hockey players. The theme behind this study was to observe the influences of conventional training, specific hockey skill training and no training as a alternate means to develop the selected physical, physiological and playing ability of field hockey players. To achieve this, two different training were designed as conventional training group, specific hockey skill training group and no training group. The results of the effect of two training packages on variables used in this study are analysed so as to reach the theme of the present study, and sources behind such similarities and variations observed on variables between the training groups, have been discussed here using scientific studies and logical in nature.

Conventional training is using another sport, activity or training techniques to help improve playing ability in

the primary sport activity. Specific hockey skill training is specifically designed to develop the playing ability related field hockey players.

Hence, compared the effects of three different training improvements in vertical jump performance and leg strength⁶. Speed endurance training facilitates aerobic endurance processes, whereas resistance training increases muscular endurance and vital capacity⁷. The speed endurance, muscular endurance and aerobic endurance and agility increased significantly after training⁸. Compared the changes in running economy, foot impact shock, run performance, and resting respiratory rate and respiratory volume elicited by increases in training volume via run training and conventional and specific hockey skill training⁹.

In a field hockey game players need a high level of energy and analytical skill to fulfill the requirements. Sports-specific physical training is paramount in field hockey¹⁰. There was no significant improvement in the shooting, passing and dribbling ability of the control group. The developed an effective testing battery for male field hockey by using anthropometric, physiological, and skill-related tests to distinguish between regional representative male field hockey players. These sprinting speed, agility, dribbling control, aerobic and muscular power, and shooting accuracy can distinguish between male field hockey players¹¹.

Conventional training effects never exceed those induced by the specific hockey skill training mode. For the general population, conventional training may be highly beneficial in terms of overall fitness. Similarly, conventional training may be an appropriate supplement during rehabilitation periods from physical injury and during periods of overtraining or psychological fatigue. Since, conventional training was one of the most advanced forms of sports training the combination with specific hockey skill training produces significant changes. Anyhow these two different training when in conjunctive nature, the effect might have been strengthened as a value added one.

Conclusion

The result of the present study reported that participation in the specific hockey skill training program; improve playing ability in experimental group. Hence significant difference was found between the regular male field hockey players of SRM University,

Chennai in relation to motor fitness, physiological and playing ability.

- The specific hockey skill training group had shown significant improvement in all the performance variables than the conventional training group.
- The specific hockey skill training with conventional training group had shown significant improvement in all the selected motor fitness, physiological and playing ability.
- The control group has shown significant no improvement in all the selected motor fitness physiological and playing ability variables.

Ethical Clearance: Nil

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Reference

1. Inder Kerketta, Dr. Ratnesh Singh. Comparison of cardiovascular endurance between male soccer and hockey players of G.G.V. Bilaspur. *International Journal of Physical Education, Sports and Health*, 2015; 2(2): 326-327.
2. Sendhil R. Hockey playing ability with relation to selected physical fitness physiological and skill variables. *International Journal of Physical Education, Sports and Health*, 2015; 1(4): 95-99.
3. Tarun Rawat, Dr. Vijay Francis Peter. Motor Fitness and Playing Ability of University Level Hockey Players of D.A.V.V., Indore. *International Journal of Research in Engineering and Social Sciences*, 2016; 06 (8): 36-38.
4. Vileep KS, Sampath Kumar C. Correlation between vital capacity and selected motor fitness variables among field hockey players. *International Journal of Physiology, Nutrition and Physical Education*, 2017; 2(1): 226-227.
5. Yaghoobi A, Goodarzi B. Sport injuries comparison of hall and lawn hockey of professional teams in Iran. *Academic Sports Scholar*, 2014; 3(10):1.
6. Fatouros IG, Jamurtas AZ, Leontsini D, Taxildaris k, Aggelousis N, Kostopoulos N, Buckenmeyer P. Evaluation of plyometric exercise training, weight training, and their combination on vertical jumping performance and leg strength. *Journal of strength and conditioning Research*, 2000; 1(14): 470-476.

7. Tanaka H, Swensen T. Impact of resistance training on endurance performance. A new form of cross-training?. *Sports Med*, 1998; 25(3):191-200.
8. Anindra KB, Banerjee AK. Effects of 6 weeks conditioning programme on some performance variables among tribal students. *Journal of Physical Education and Sports Science*, 1990;11(11): 37-39.
9. Pizza FX, Flynn MG. Run training vs cross training: influence of increased training on running economy, foot impact shock and run performance. *Int J Sports Med*, 1995;16(3):180-4.
10. McManus A, Stevenson M. Quantifying the physical demands in non-elite field hockey to develop training guidelines that minimise injury through adequate preparation. *Australian Conference of Science and Medicine in Sport*, 2007; 13.
11. Keogh JW, Weber CL, Dalton CT. Evaluation of anthropometric, physiological, and skill-related tests for talent identification in female field hockey. *Can J Appl Physiol*, 2003; 28(3):397-409.

Effect of Yoga on Body Composition in Person with Visual Disabilities

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Abstract

Aim: The aims of this study were to determine the effect of selected yoga asanas on body composition of visually challenged School Going Children.

Materials and Method: Total of 24 visually disabled male school going children (12 to 18 years) were participated as subjects in this study. It was divided into two equal groups as experimental group (n=12) and control group (n=12). The experimental group was regularly practiced 15 minutes warming up and selected yogic asana for 45 minutes per day, 05 days per week, for 6 weeks with proper technical assistance. The pre-test and post-test were taken of all the body composition parameters before and after six (6) weeks of yogic exercise training program. The body composition variables were Age, Height, Weight, Blood Pressure (B.P.), Pulse Rate, BMI, BMR, Body Fat and Visceral Fat%, which were measured by standard body composition analyzer. To test the significance of changes made from the pre and post-test on two groups (Experimental and Control) groups' paired sample -test was used.

Results: Significant reduction ($P < 0.005$) in the percentage of Body Fat, Basal Metabolic Rate (B.M.R), Pulse Rate and Blood Pressure (s) were noted in the experimental group after 06 weeks of yoga training. However, there were no significant differences in Visceral Fate, Body Mass Index (B.M.I), Blood Pressure (d) in the yoga and control group. These changes might be due to yoga training but for more significant results, yoga training required for visually disabled person longer duration time with proper assistance.

Keywords: *Yogic asana, Body Mass Index (BMI), Basal Metabolic Rate, Visceral Fat, Visual Disability.*

Introduction

The word of yoga is derived from the Sanskrit word "yuj", which means summation or union. Pantanjali described the word of yoga as an eight-limbed path consisting of Yamas, Niyamas, Asana, Pranayama, Pratyahara, Dharana, Dhyana, and Samadhi²⁰. The yoga is a scientific discipline of psycho-somatic-spirituality for achieving the union of Body, Mind, and Soul¹⁷. Yoga

is also known as the way of life in ancient India, which includes meditation, social, behavioral changes, and the practice of asana for enhancing the different levels of fitness and wellness²⁰. The major objective of this study was to find out the effect of some selected yogic asana on the body composition of visually challenged school-going children. Categorizations of visual disabilities based on its degree of severity which is notified in Gazette of India, 2001.

The proper function of the body of an individual depends upon the optimum function of the major muscle groups, level of physical fitness and flexibility, without the proper function of it the individual health may be under risk. It is necessary for a healthier lifestyle for

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children to promote proper growth, development and an active lifestyle in their aptitude. It is most important for an individual to continue being active throughout their lives. In the case of the visually disabled persons, they required extra energy due to disability for various day to day activities such as finding direction, locating the position and daily normal activity².

Visually disabled children were physically inactive^{19,12} less physically fit¹⁹, lower quality of life⁴ and poor in locomotors activity¹⁰ than their peer group without disability⁰⁵. Optimum levels of motor skills are essential for successful acquiring motor fitness and healthy lifestyle¹⁹. Previous studies reported that yoga plays an important role to maintain physical fitness, balance¹², normal function of GAIT¹⁹ and posture also prevent falls⁰⁴. Yoga asanas were seen as good benefits on fitness related to health in muscle strength⁰³, endurance^{05, 04}, flexibility and cardiovascular tolerance for school children. Its positive effects in children with visual impairment are also well documented, including autonomic stimulation²⁴, balance¹³, and proprioception¹⁸.

Despite all these benefits, children with visual disabilities are more restricted in their participation in physical activity, have a lower level of fitness and have a higher level of obesity than their peers without disabilities¹¹. The fear of injury is one of the reasons for visually challenged person's lack of participation in physical activity¹¹. Lack of physical activity leads to a different kind of bodily changes/differences as compared with the peer without disabilities¹⁵. To Till date, no studies were found to found out the effect of yoga on body composition on visually challenged persons in the Indian scenario. The main aim of this study is to find out the effect of selected Yoga asana on Body Composition of Visually Disabled School going Children.

Materials and Method

Twenty Four (n-24) Visually Disabled school going children 12 to 18 years of age male students of Ahmadi School for the Visually Challenged, Aligarh Muslim University., Aligarh, India were selected as subjects for this study. Twenty four (n-24) visually disabled persons were equally divided into two equal groups. The first group was treated as a control group (n-12) and the second group treated as the experimental group (n-12). Quasi Experimental design was used for this study.

In the Experimental group, selected assistive yogic exercises were performed five (n-05) times per week for six (n-06) weeks under the direction of trained yoga experts. This experimental session, Yoga exercises (60-minute duration) include stretching, pranayama, asana, and meditation. Some of Asana's exercises were as follows: Tadasana (standing on the right), Trikonasana (normal triangle), Vrikshasana (tree pose), uttanasana (standing and forward bend), Dundasana (sitting on the right) and Sidhasana (Guru Vidha). Meditation (relaxation) was carried out in the last ten minutes of each workout.

In Control group (n-12) subjects did not participate any training program during the course of study. Subjects were also advised not to change their lifestyle during the study. The pre-test and post-test were taken of all the body composition parameters before and after six (6) weeks of yoga training. The body composition variables were Age, Height, Weight, Blood Pressure (B.P.), Pulse Rate, BMI, Body Fat %, Subcutaneous Fat %, Visceral Fat%, which were measured by standard body composition analyzer.

The results are expressed as the mean ± standard deviation. Within-group comparisons were made using paired sample t-tests. Statistical examinations were carried out by using SPSS version 20.0 for Windows.

Results

The results of the study on effect of 06 weeks of yoga as programmed with selected variables of body composition of experimental group and control group .The experimental group was received the daily yoga training of one hour duration which consists of 15 minutes warming and stretching exercises and remaining 45 minutes yoga and relaxation.

Table 1. Descriptive statistics of the subjects.

	Measures	Mean ±SD	
		Pre	Post
Experimental Group	Weight (kg)	57.12±13.03	55.48±11.65
	Height (cm)	165.41±8.62	
	Age (year)	15.33±2.15	
Control Group		Pre	Post
	Weight (kg)	47.3±6.94	46.22±6.34
	Height (cm)	16.41±5.56	
	Age (year)	13.58±1.31	

Table 2. Two measure of Body Composition in two groups.

Paired Samples Test								
Groups	Variables	Mean & SD Mean		Paired Differences			t	P- Value
				Std. Deviation	Std. Error Mean			
Experimental	Body Fat %	Pre	20.65±4.95	0.31	2.87	0.83	0.37	0.72
		Post	19.75±4.44					
Control		Pre	16.45±5.96	0.67	0.65	0.19	3.56	0.00
		Post	15.78±5.98					
Experimental	Visceral Fat %	Pre	3.83±4.30	0.25	0.45	0.13	1.91	0.08
		Post	3.58±3.99					
Control		Pre	1.50±1.00	0.00	0.60	0.17	0.00	1.00
		Post	1.50±0.80					
Experimental	B.M.I kg/m ²	Pre	20.65±4.95	2.01	4.31	1.24	1.62	0.13
		Post	18.63±6.82					
Control		Pre	18.26±3.18	0.36	0.75	0.22	1.69	0.12
		Post	17.90±3.14					
Experimental	B.M.R kcal/day	Pre	1344±149.16	7.67	55.25	15.95	4.81	0.00
		Post	1420±139.25					
Control		Pre	1222±95.00	116.67	148.01	42.72	2.73	0.02
		Post	1338±175.26					

Significant reduction ($P < 0.05$) in the percentage of body fat, Basal Metabolic rate (B.M.R), Pulse Rate and Blood Pressure (s) were noted in the experimental group after 06 weeks of yoga training. However, there were no significant differences in visceral fate, Body Mass Index (B.M.I), in the experimental.

Table 03. Two measure of physiological variables in two groups.

Paired Samples Test								
Groups	Variables	Mean & SD Mean		Paired Differences			t	P- value
				Std. Deviation	Std. Error Mean			
Experimental	Pulse Rate	Pre	95.67±11.22	1.83	10.26	2.96	4.00	0.00
		Post	83.83±6.42					
Control		Pre	89.75±16.76	2.50	10.27	2.96	0.84	0.41
		Post	87.25±9.74					
Experimental	Blood Pressure (s)	Pre	121±13.71	5.92	8.41	2.43	2.44	0.03
		Post	115±7.89					
Control		Pre	125±11.98	3.83	7.88	2.75	1.68	0.20
		Post	121±10.40					
Experimental	Blood Pressure (d)	Pre	76.42±12.23	1.67	5.91	1.71	0.98	0.35
		Post	74.75±9.79					
Control		Pre	80.83±18.30	1.58	6.82	1.97	0.80	0.44
		Post	79.25±14.21					

Significant reduction ($P < 0.05$) in the percentage Pulse Rate and Blood Pressure (s) were noted in the experimental group after 06 weeks of yoga training. However, there were no significant differences in Blood Pressure (d) in the experimental and control group.

Discussion

Results of the study deal with the analysis of data collected from visually disabled school-going children. Results of the study revealed that insignificant differences existed between pre- and post-testing of children with disabilities in the experimental group's of Body Fat%. Body fat% was insignificantly decreased in the yoga group compared with the control group ($p > 0.05$). This result contra indicates with previous studies^{1,7,8,9} indicate that the significantly increase body density and weight it's maybe due to yogic training program reduce body fat^{1,7,9}. The results of the study show that there were insignificant differences exist between pre and post-test of disabled children in their, visceral fat and BMR of the experimental group and control group ($p > 0.05$). The results of the study found that reducing BMI as compared to that of the previous studies^{24,25}. Our findings clearly suggested that obesity in visually disabled persons can be reduced by assistive yoga therapy for a longer period of time. Results show that there were significant differences exist between pre and post-test of disabled children in their B.M.I (kg/m^2) of the experimental group and control group ($p < 0.05$). This proved that there was significant differences exist between the groups of pre and post-test of both experimental and control groups. The mean difference between pre and post shows that the effects of yogic exercises on BMI are positive and significant. The result of this study on Body Mass Index (BMI) has in line with the previous studies^{26,01}, who has conducted the study on yoga: managing overweight and found that the BMI decreased significantly. Exercise training significantly improved, body mass index, lean muscle mass, resting HR, fitness, and systolic blood pressure^{27,28}. The analysis of data shows that there were insignificant differences exist between pre and post-test of disabled children in their Blood Pressure (Systolic and Diastolic) of the experimental group and control group²⁷. Mean differences between pre and post-test shows that yoga exercises were positively affecting on body composition of visually disabled persons. But better and significant results of yoga exercises on the body composition of the visually disabled persons, it is suggested that yoga exercises should be a long duration and exercise with proper assistance. The result of this study on systolic blood pressure has in line with the study conducted by Shantakumari et al in 2012, has conducted a study on the effect of a yoga intervention on hypertensive diabetic patients and found that systolic and diastolic blood pressure decreased significantly²¹. The yoga asanas help the regularize and balance the

nervous system and maintain optimum health. Further, the function of the sympathetic and parasympathetic nervous system optimized through the regular practice of yogic asanas resulting in regulation of (B.P.) blood Pressure²¹. The asana belongs to the different body posture i.e. supine positions, forward bends, sitting, and inversions group regulate the Blood Pressure (B. P.). However, fundamental asanas of forward bends which can be helpful for regulate high Blood Pressure (B. P.)^{1,8}. The horizontal position of the body in these asanas regulates the heart function to slow down the stress to the heart to pump the blood against gravity^{20,21}. Our results support the findings which stated that the yoga practice reduces systolic and diastolic Blood Pressure (B. P.)²⁴. In addition, all participants were found to achieve good health after performing yoga. Our results support the findings which stated that the yoga practice reduces systolic and diastolic Blood Pressure (B. P.)²⁴. The analysis of data shows that there is significant differences exist between pre and post-test of disabled children in their Pulse Rate of the experimental group ($p < 0.05$). Whereas there is insignificant difference exists in their pulse rate of the control group ($p > 0.05$). Our result supported that pulse rate was significantly reduced in the pulse rate occurs in subjects practicing yoga ($P < 0.001$)^{22,06,15} and contraindicate with the results of the study¹⁴ reveal that there was no significant difference among the yogasana practices and physical training on systolic blood pressure, diastolic blood pressure and pulse rate.

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References

1. Bera TK, Rajapurkar MV, Ganguly SK. Effect of yogic training on body density in school going boys. NIS Sci J. 1990 Apr;13:23-35.

2. Bishop VE. Teaching Visually Impaired Children: Virginia E. Bishop; with a Foreword by Natalie C. Barraga; Drawings by Charles Denzler and Virginia Bishop; Computer Graphics and Charts by Liz Broussard. Charles C Thomas Publisher; 2004.
3. Chen TL, Mao HC, Lai CH, Li CY, Kuo CH. The effect of yoga exercise intervention on health related physical fitness in school-age asthmatic children. *Hu li za zhi the journal of nursing*. 2009 Apr;56(2):42-52.
4. Cho KH, Bok SK, Kim YJ, Hwang SL. Effect of lower limb strength on falls and balance of the elderly. *Annals of rehabilitation medicine*. 2012 Jun;36(3):386.
5. D'souza C, Avadhany S. Effects of yoga training and detraining on physical performance measures in prepubertal children--a randomized trial. *Indian J Physiol Pharmacol*. 2014;58(1):61-8.
6. Ebnezar J, Nagarathna R, Yogitha B, Nagendra HR. Effect of integrated yoga therapy on pain, morning stiffness and anxiety in osteoarthritis of the knee joint: A randomized control study. *International Journal of Yoga*. 2012 Jan;5(1):28.
7. Gharote ML. Effect of short term yogic programme on the physical fitness of school boys. *Avagaham*, 1 (1). 1976:9-15.
8. Gharote ML. Effect of every day and alternate day yoga training on the physical fitness of school children. *Ayurveda & Yoga*. 1987;7:9-15.
9. Gharote ML. Effect of yogic training on physical fitness. *yoga mimamsa*. 1973 Jan;15(4):31-5.
10. Granacher U, Gollhofer A, Hortobagyi T, Kressig RW, Muehlbauer T. The importance of trunk muscle strength for balance, functional performance, and fall prevention in seniors: a systematic review. *Sports medicine*. 2013 Jul 1;43(7):627-41.
11. Hartman E, Houwen S, Scherder E, Visscher C. On the relationship between motor performance and executive functioning in children with intellectual disabilities. *Journal of Intellectual Disability Research*. 2010 May;54(5):468-77.
12. Jadelis K, Miller ME, Ettinger Jr WH, Messier SP. Strength, balance, and the modifying effects of obesity and knee pain: results from the Observational Arthritis Study in Seniors (OASIS). *Journal of the American Geriatrics Society*. 2001 Jul;49(7):884-91.
13. Jeter PE, Nkodo AF, Moonaz SH, Dagnelie G. A systematic review of yoga for balance in a healthy population. *The journal of alternative and Complementary Medicine*. 2014 Apr 1;20(4):221-32.
14. Johnson P, Anjaneyulu M. Effects of Practicing Yogasanas and Physical Training on Selected Physiological Variables. *International Journal of Physical Education, Fitness and Sports*. 2014 Mar 30;3(1):94-9.
15. Bharshankar JR, Bharshankar RN, Deshpande VN, Kaore SB, Gosavi GB. Effect of yoga on cardiovascular system in subjects above 40 years. *Indian journal of physiology and pharmacology*. 2003 Apr;47(2):202-6.
16. Kerić M, Ujsasi D. Quantitative differences within motor abilities of pupils of higher grades in primary school. *TIMS. Acta*. 2014;8(1):23-30.
17. Madanmohan D. Effect of yogic practices on different systems of human body. Professor and Head, Department of Physiology and Programme Director, ACYTER, JIPMER, Puducherry-605.;6.
18. Mohanty S, Pradhan B, Nagathna R. The effect of yoga practice on proprioception in congenitally blind students. *British Journal of Visual Impairment*. 2014 May;32(2):124-35.
19. Nallegowda M, Singh U, Handa G, Khanna M, Wadhwa S, Yadav SL, Kumar G, Behari M. Role of sensory input and muscle strength in maintenance of balance, gait, and posture in Parkinson's disease: a pilot study. *American journal of physical medicine & rehabilitation*. 2004 Dec 1;83(12):898-908.
20. Satchidananda S. The yoga sutras of Patanjali. Buckingham, VA. 2004.
21. Shantakumari N, Sequeira S, Eldeeb R. Effect of a yoga intervention on hypertensive diabetic patients. *Journal of Advances in Internal Medicine*. 2012 Jul 23;1(2):60-3.
22. Shepal A V. Effect of yoga on bio-markers linked with development of diabetic complications in type 2 diabetes patients, *International Journal of Recent Scientific Research*. 2013; 4(4): 401
23. Sinaki M, Brey RH, Hughes CA, Larson DR, Kaufman KR. Balance disorder and increased risk of falls in osteoporosis and kyphosis: significance of kyphotic posture and muscle strength. *Osteoporosis international*. 2005 Aug 1;16(8):1004-10.
24. Telles S, Naveen VK, Balkrishna A, Kumar S. Short term health impact of a yoga and diet change

- program on obesity. *Medical Science Monitor*. 2009 Dec 21;16(1):CR35-40.
25. Telles S, Dash M, Naveen KV. Effect of yoga on musculoskeletal discomfort and motor functions in professional computer users. *Work*. 2009 Jan 1;33(3):297-306.
26. Tikhe AS, Pailoor S, Metri K, Ganpat TS, Ramarao NH. Yoga: Managing overweight in mid-life T2DM. *Journal of mid-life health*. 2015 Apr;6(2):81.
27. Wong PC, Chia M, Tsou IY, Wansaicheong GK, Tan B, Wang JC, Tan JC, Kim CG, Boh G, Lim D. Effects of a 12-week exercise training programme on aerobic fitness, body composition, blood lipids and C-reactive protein in adolescents with obesity.
28. Zorofi F, Hojjati Z, Elmiyeh A. Effect of yoga exercises on the body composition of fasting females. *Journal of Nutrition, Fasting and Health*. 2013 Dec 1;1(2):70-8.

Uncorrected Refractive Error as a Cause of Headache: A Cross Sectional Study

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Abstract

Purpose: Many patients suffering from unexplained headache go through a battery of investigations without much resolution. In a large number of these patients, searching for and correcting an underlying refractive error often provides permanent relief. We aimed to search for an association in the population visiting Ophthalmology OPD in our hospital.

Method: Four hundred patients with headache were investigated for refractive error under cycloplegia and any refractive error detected was classified into myopia, hypermetropia, astigmatism or compound refractive error. The prevalence of refractive error and the various sub types was calculated.

Conclusions: Refractive errors coexist with headache frequently. Patients with persistent headache need to be investigated thoroughly for refractive error as correction of the same can provide permanent and cost effective resolution of the headache.

Keywords: Headache, ocular, refractive error.

Introduction

Headache is defined as pain above the orbitomeatal line¹. Ocular headache is defined as headache having evidence of causation demonstrated by at least two of the following:

Headache has developed and/or significantly worsened in temporal relation to the onset or worsening of the refractive error(s); headache has significantly improved after correction of the refractive error(s); headache is aggravated by prolonged visual tasks at an angle or distance at which vision is impaired; headache significantly improves when the visual task

is discontinued². Various studies on ocular causes of headache have reported the role of refractive error and accommodative deficiency as a having a possible role⁴. Many cases having refractive error and associated headache consult the Neurologist first thus subjecting themselves to expensive and time consuming investigations that could be avoided if an Ophthalmologist had been consulted in the primary instance.⁵ Thomas et al observed that the proportion of headache patients visiting an Ophthalmologist were nearly similar to the proportion of patients visiting a general practitioner, being 21% and 27% respectively.⁶

In 1966, Gordon et al forwarded the claim that minor refractive contributed more towards headache and eye strain symptoms than major refractive errors.⁷

The aim of the present study was to analyze the prevalence of uncorrected refractive error in patients with headache complaints, presenting to a general ophthalmology Out Patient Department, in a community based hospital.

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Method

The study was approved by the Government Institute of Medical Sciences Greater Noida institutional review board and was fully compliant with the principles of the Helsinki Declaration.

The study had a descriptive cross sectional design. We enrolled 400 consecutive patients between 5 – 30 years of age, visiting the ophthalmology department and complaining of headache. Patients with pre existing conditions predisposing to headache like migraine, hypertension, pregnancy, presbyopia were excluded. All the patients had not been investigated for refractive error previously and none of them were currently on any medication for headache. All the patients underwent complete ophthalmological examination including assessment of visual acuity, ocular alignment, ocular motility, pupillary assessment, slit lamp biomicroscopy and dilated fundus examination. All patients under the age of 18 years underwent cycloplegic refraction with 2% Homatropine. Subjective refraction was carried out after 3 days in these patients. Refractive status was divided into emmetropia (-0.25D - +0.25D), hypermetropia ($\geq +0.50D$), myopia ($\geq -0.50D$), astigmatism ($\geq 0.50D$ cyl), compound error (spherical+ cylindrical error). All refractive examinations were performed by a single optometrist who did not know the headache history of the patient. All patients were reviewed after two weeks

from the start of wearing refractive correction to evaluate the amelioration of headache symptoms.

Results

During the course of our study we studied 400 patients who visited our OPD with the main complaint of headache. 278 (69.50%) of all patients were female and 122 (30.50%) were males. (Figure 1) This female preponderance was maintained through all the age groups except in the 6 – 10 year age group where there was a slight male predominance (55.6% male and 44.4% female). Figure 2. The mean age of the patients was 21.3 years (SD= 5.4) 226 (56.5%) patients reported the site of headache as frontal, whereas 95 (23.75%) and 79 (19.75%) had temporal and global headache respectively. The temporo-frontal localisation of the headache was statistically significant by Chi Square Test ($p=0.04$). In a large majority of patients, visual acuity in the worse eye at presentation was between 6/6 – 6/9 in 249 (62.25%). Of the remaining, 71 patients (17.75%) had visual acuity 6/12 – 6/18, 62 (15.5%) had 6/24 – 6/36 and 18 (4.5%) had visual acuity in the worse eye $\leq 6/60$. Of these a total of 159 patients (39.5%) had uncorrected visual acuity of 6/6 in both eyes at presentation. A total of 231 patients complained of nausea and vomiting associated with the headache. There was positive correlation between astigmatism and complaints of Nausea/vomiting (chi square: $p=0.03$).

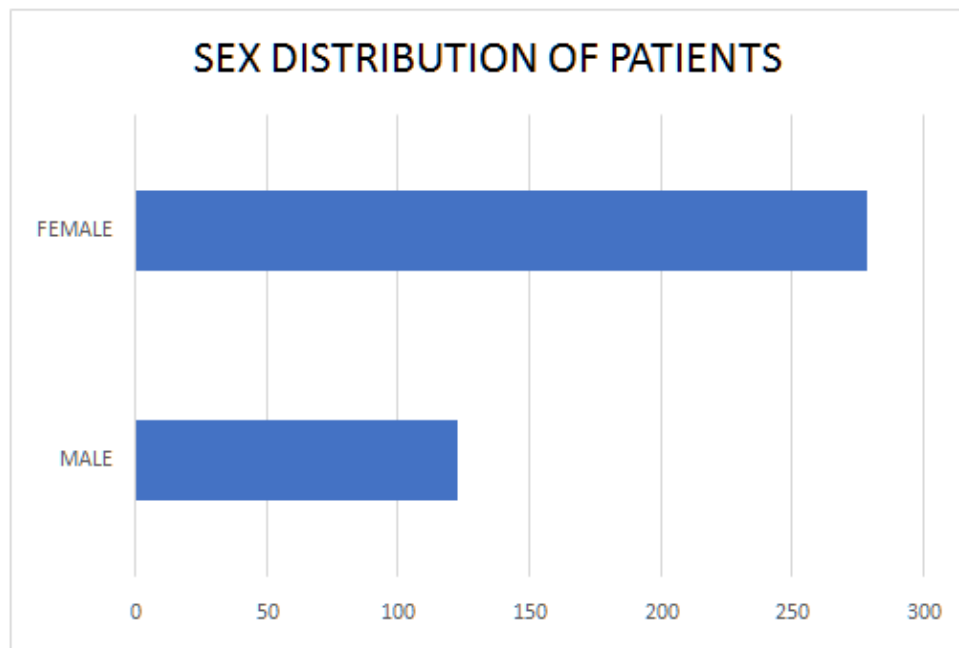


Figure 1

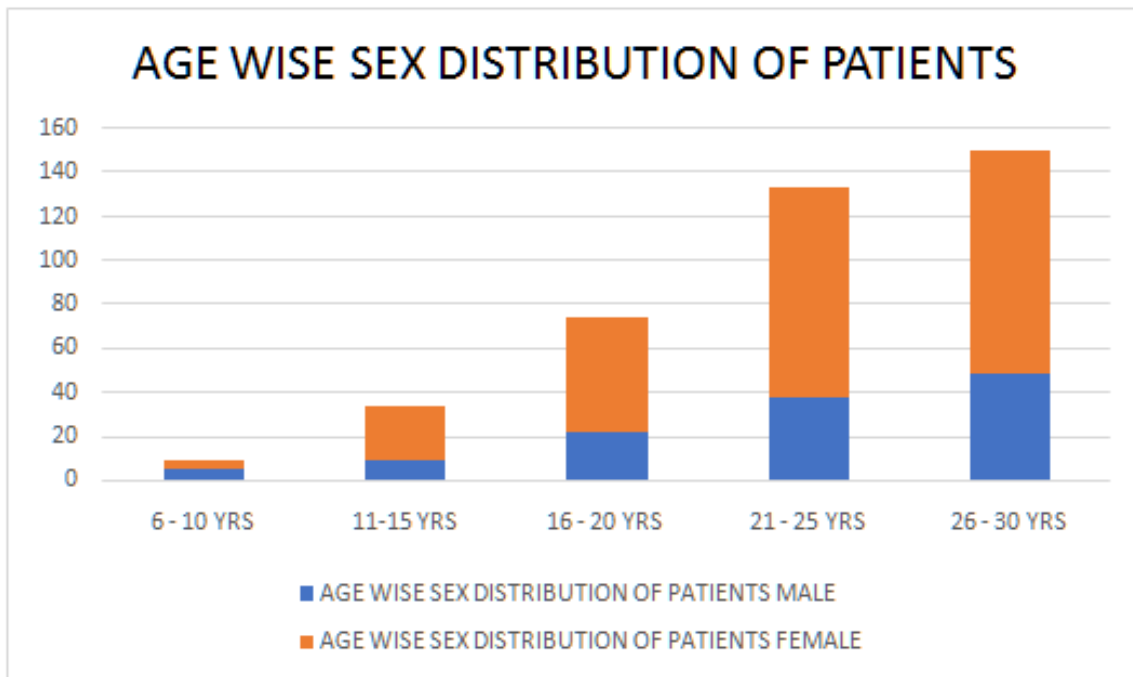


Figure 2

Of the 400 patients 380 (95%) were diagnosed as having an uncorrected refractive error. The remaining 20 (5%) patients did not have any refractive error. They were found to have convergence deficit on further examination and were advised convergence exercises.

The refractive error diagnosed of 89(23.42%) patients was myopia, of 117 (30.79%) patients was hypermetropia, of 149 (39.21%) patients was astigmatism and of 25 (6.58%) patients was compound ametropia. Figure 3.

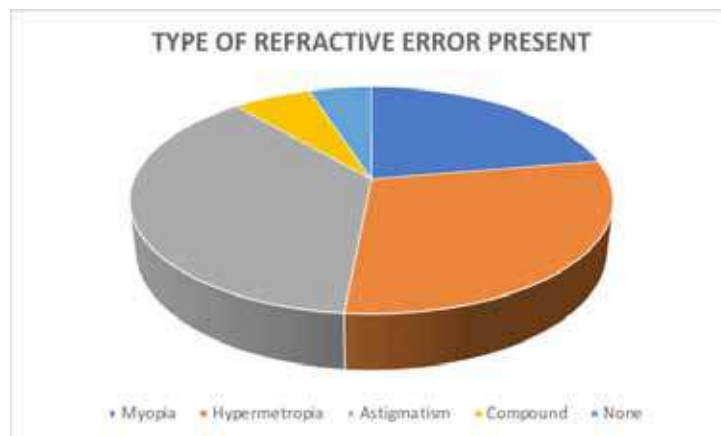


Figure 3

Of the 159 patients with B/L 6/6 presenting acuity and headache, 79.2% (126) were eventually diagnosed with astigmatism or hypermetropia (chi square=0.008;

Odds Ratio=1.862). The rest were accounted by myopia and convergence deficit (13 and 20 patients respectively). Figure 4

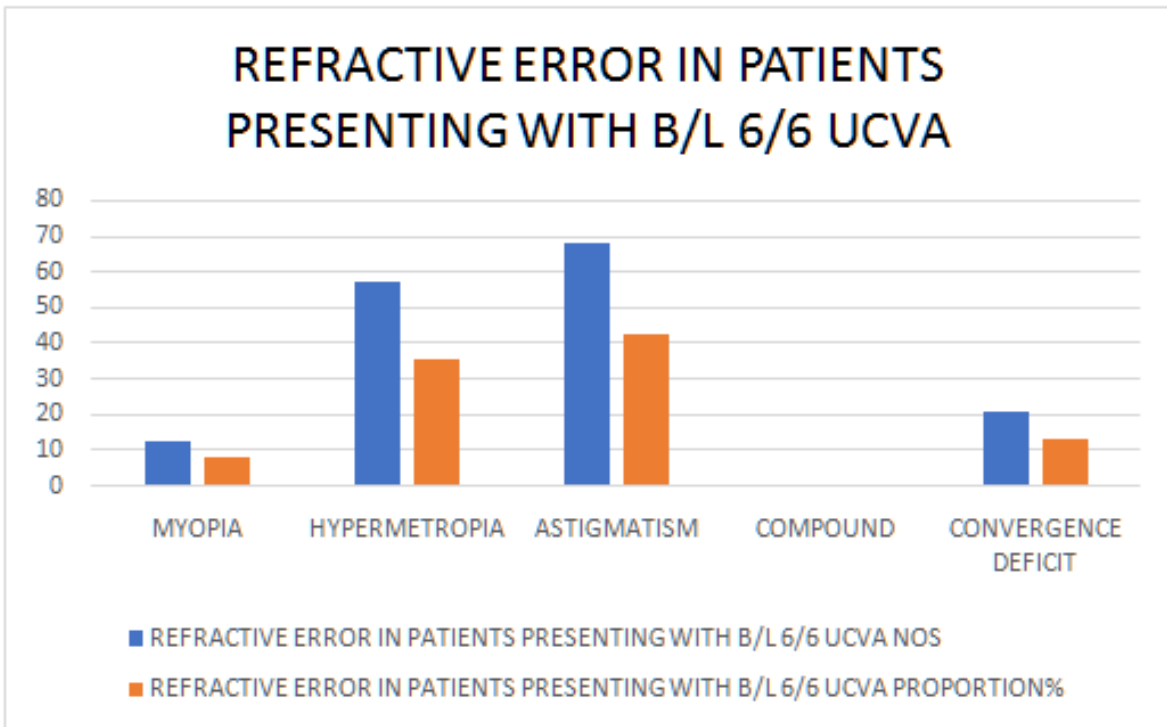


Figure 4

In all the various subgroups of ametropia, the most common localization of headache was frontal, followed by temporal headache. Figure 5.

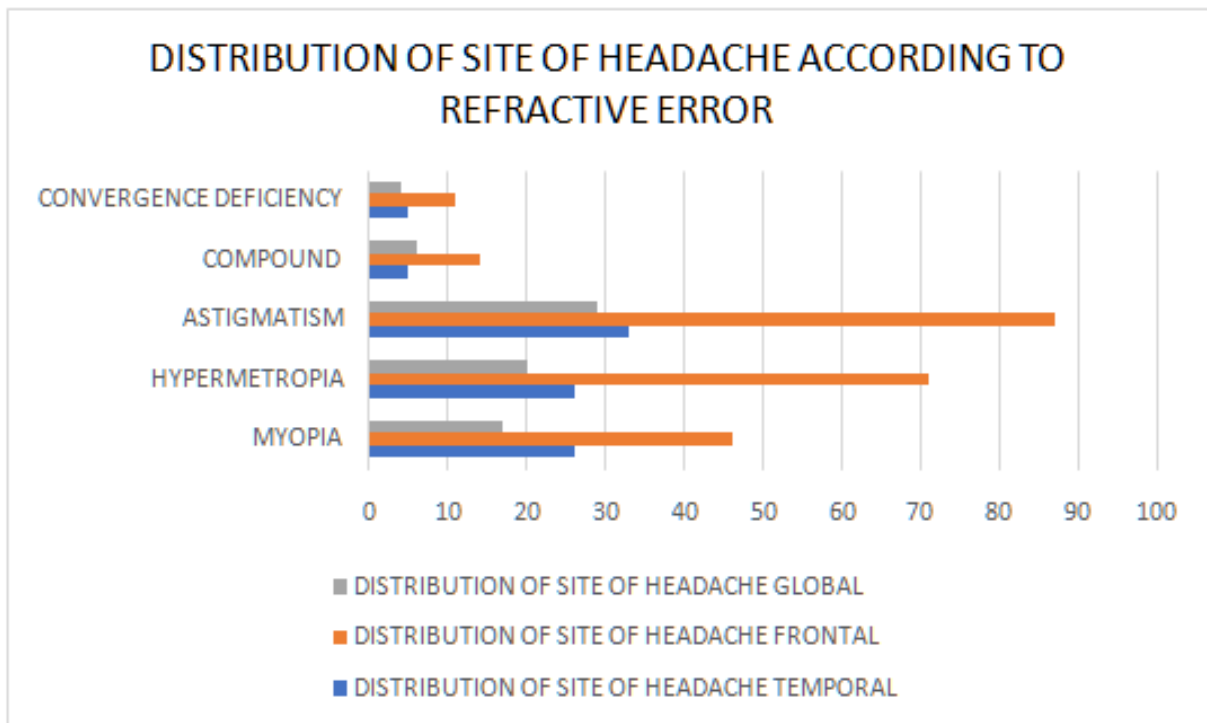


Figure 5

A total of 226 patients(59.5%) reported experiencing frontal headache whereas only 90(23.7%) and 79(20.8%) patients reported temporal and global headache respectively.

Two weeks following refractive correction 337(88.68%) of the 380 patients reported a complete resolution of headache. 43(11.32%) patients had incomplete resolution of headache and required

additional convergence exercises. Only the 20 patients who were diagnosed with convergence deficit alone and no refractive error, responded only to convergence exercises. Figure 6.

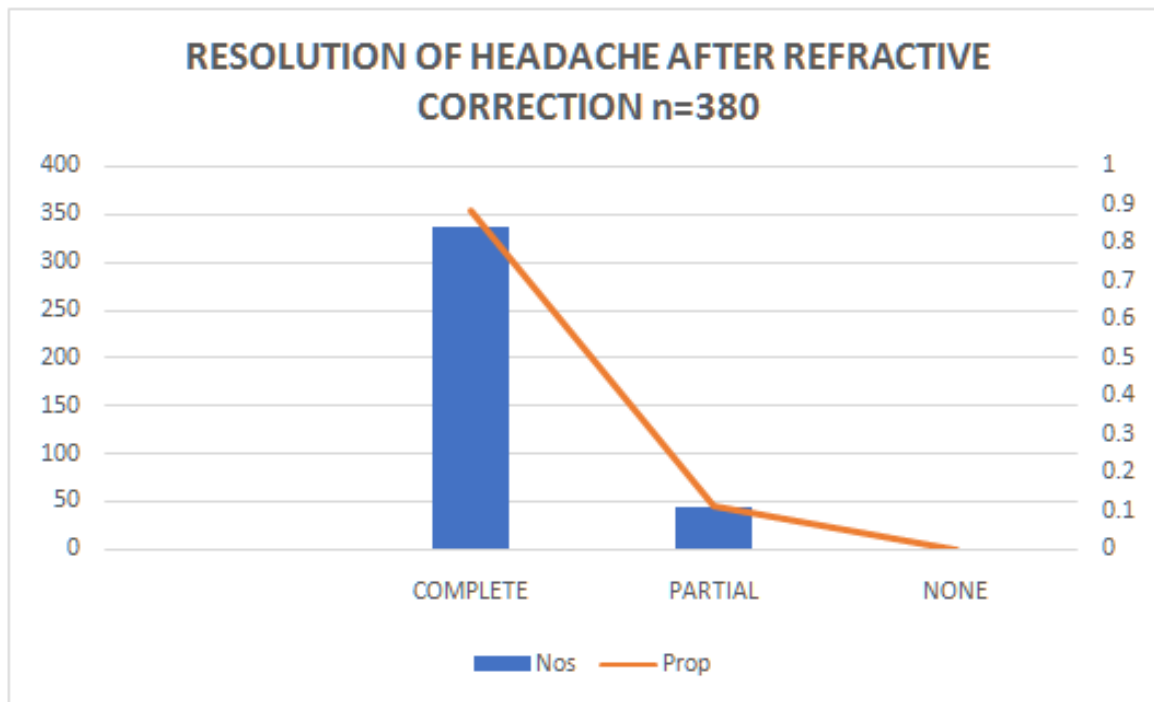


Figure 6

Discussion

In our study we describe 400 patients who had presented with the main complaints of headache. Other systemic examination was normal in all the patients. In a large majority uncorrected refractive error was diagnosed and two weeks after using refractive correction there was complete resolution of headache in most of them.

Headache is a complaint frequently encountered in the Ophthalmological practice. It is important to be able to recognise headache complaints caused due to refractive error from other causes.

Various studies on headache have reported the role of visual anomalies like refractive error and vergence deficiencies³. The uncorrected refractive errors are often believed to be associated with frontal or occipital headache⁸.

Cameron⁹ estimated a low prevalence of refractive error in 50 patients suffering from headache. Jain et

al¹⁰ reported only 1.48% prevalence of refractive error in headache patients. Noticeable in these studies is the inclusion of all patients of headache without excluding patients with other known pathologies predisposing to headache.

In our study we observed a prevalence as high as 95% of uncorrected refractive error in patients of headache. This exceeds the prevalence observed in the study by Marasini et al¹¹, of 45%; and by Fasih et al¹² who reported a prevalence of 16.36%.

Our study observed a preponderance of female patients presenting with headache. 278(69.5%) of our patients were females. Compared to male patients the proportion of female patients was 2.28 times more. This finding was in concurrence with a study by Hendricks et al¹³ who reported headache more frequently in girls than boys; as did Fasih et al¹² who observed a female prevalence of 59.4%. We observed that the largest number of patients lay in the 26–30 year age bracket,

showing a prevalence of 37.5%, closely followed by 21 – 25 years age group at 33.25%. These observations were corroborated by Marasini et al¹¹ who also reported a higher prevalence in the pre presbyopia age group.

There are some researchers who claim that there is no difference in occurrence of headache in persons with and without refractive error¹⁴. Others like Korczyn et al¹⁵ and Hedges¹⁶ hold the view that refractive errors are not an important contributory cause of headache. These authors attribute the relief of headache following refractive correction to a placebo like effect.

Contrary to these, in our study we observed that 380(95%) patients who presented with headache were diagnosed with an uncorrected refractive error and of these 337(88.6%) reported complete relief of headache symptoms within two weeks of using refractive correction. These findings are similar to observations made by Marasini et al¹¹. Gil Gouveia et al¹⁴ also observed that 73% of subjects had improvement in symptoms after optical correction which included 38% who reported complete relief from headache.

Additionally, our results suggest that low degrees of refractive error have more predilection towards causing headache, as demonstrated by the observation that 249(62.25%) patients had presenting visual acuity between 6/6 – 6/9 in the worse eye. In fact, 159 patients had presenting visual acuity of 6/6 in both eyes. These findings are comparable to a study in Nepal¹¹ in which 88% of patients had a presenting visual acuity ranging from 6/6 – 6/9. This may be explainable by the hypothesis that lower degrees of ametropia induce greater effort from the eye in an attempt to reduce the blur. Hypermetropia can cause sustained effort of accommodation and thereby induce headache due to painful ciliary muscle contracture^{13,17}. Myopia may cause headache by increasing the squinting of eyelid and forehead in an effort to achieve pin hole effect¹³. The mechanism causing headache in astigmatism is not fully understood, but in all likelihood, is related to visual blur¹⁸. One hypothesis claims that even minor degrees of astigmatism cause changes to visual perception that alter the hyperexcitability in visual cortex of headache sufferers¹⁹. Astigmatic blur may exacerbate the perception of striped patterns that are hypothesised to be important visual triggers in various kinds of headaches²⁰.

We have observed in our study that prevalence of astigmatism is the highest (43.68%) in headache sufferers, followed by hypermetropia, myopia and compound

refractive error in that order (32.11%, 20.53%, 3.68% respectively). These findings are in agreement with those of Marasini et al¹¹ and of Patwardhan and Sharma²¹ who found similar trends in their studies.

Our study has some limitations which should be considered while interpreting its results. Firstly, our patients were recruited from the population visiting a hospital outpatient department and thus may not be truly representative of the general population as a whole. Secondly, we did not have a control group so we cannot determine whether the prevalence of uncorrected refractive error in patients with headache is different from that in patients without headache. Prospective, case control studies may be required to establish the correlation more strongly. The strength of our study was in its very selective patient enrolment. We have excluded all the other common causes of headache prior to enrolling our patients.

Conclusion

In conclusion, uncorrected refractive error is a possible cause of headache. Therefore, all patients presenting with headache should undergo complete ophthalmological examination to rule out that pathology. Patients with no visual complaints should also be evaluated as many patients having headache correlated to refractive error apparently had no visual anomalies at presentation. Accurate identification and correction of refractive error provide a definitive cure to these patients, while at the same time sparing them the expense and anguish of undergoing a lengthy battery of investigations.

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Ethical Clearance: Taken from Government Institute of Medical Sciences Institutional Ethics Committee.

References

- Olsen J, Bes A, Kunket R et al. The International Classification of Headache Disorders. 2nd edition. Headache Classification Subcommittee of the International Headache Society: Blackwell Publishing. Cephalalgia 2004;24:150
- 11.3.2 Headache attributed to refractive error

- ICHD-3. The International Classification of Headache Disorders 3rd edition
3. American Optometric Association. Care of the patient with accommodative and vergence dysfunction. Optometric clinical practice guideline; 2010
 4. American Optometric Association. Care of the patient with accommodative and vergence dysfunction. Optometric clinical practice guideline; 2010
 5. Olsen J, Burst R, Ashina M, Tfelt – Hansen P. Origin of pain in migraine: evidence for peripheral sensitization. *Lancet Neurol.* 2009; 8: 679 – 90
 6. Thomas E, Boardman HF, Ogden H, Millson DS, Croft PR. Advice and care for headaches: who seeks it, who gives it? *Cephalalgia.* 2004;24:740-752.
 7. Gordon DM. Some headaches in an ophthalmologist's office. *Headache.* 1966;6:141-146.
 8. Bellows JG. Headache and the eye. *Headache.* 1968;7:165 – 170
 9. Cameron ME. Headaches in relation to the eyes. *Med J Aust.* 1976;1:292 – 294
 10. Jain AP, Chauhan B, Bhat AD. Sociodemographic and clinical profile of headache – a rural hospital – based study. *Indian Acad Clin Med.* 2007;8:26 – 28
 11. Marasini S, Khadka J, Sthapit PRK, Sharma R, Nepal BP. Ocular morbidity on headache ruled out of systemic causes – A prevalence study carried out at a community based hospital in Nepal. *Journal of Optometry.* 2012Apr –Jun;5(2):68 – 74
 12. Fasih U, Shaikh A, Shaikh N. Aetiology of headache in clinical ophthalmic practice at a tertiary care hospital of Karachi. *Journal of the Pakistan Medical Association.* 2017 Feb; 67(2):166-170.
 13. Hendricks TJW, De Brabander J, Horst FVD, Hendrikse F, Knottnerus AJ. Relationship between habitual refractive errors and headache complaints in school children. *Optometry and Vision Sciences.* 2007Feb;84(2):137 – 143.
 14. Gil – Gouveia R, Martins IP. Headaches associated with refractive errors: myth or reality? *Headache.* 2002;42:256 – 262
 15. Korczyn AD, Carel RS, Peres I. Correlation of headache complaints with some physiological parameters in a healthy population. *Headache.* 1980;20:196 – 198.
 16. Hedges TR. An ophthalmologist's view of headache. *Headache.* 1979;19:151–155.
 17. Ip JM, Robaei D, Rochtchina E, Mitchell P. Prevalence of eye disorders in young children with eyestrain complaints. *American Journal of Ophthalmology.* 2006;142:495–497.
 18. Akinci A, Güven A, Degerliyurt A, Kibar E, Muthu M, Citirik M. The correlation between headache and refractive errors. *Journal of American Association for Pediatric Ophthalmology and Strabismus.* 2008;12(3):290–293.
 19. Breslau N, Andreski P. Migraine, personality and psychiatric comorbidity. *Headache.* 1995;35:382 – 386.
 20. Wilkins A, Nimmo-Smith I, Tait A, et al. A neurological basis for visual discomfort. *Brain.* 1984;107:989 – 1017
 21. Patwardhan SD, Sharma P, Saxena R, Khanduja SK. Preferred clinical practice in convergence insufficiency in India: a survey. *Indian Journal of Ophthalmology.* 2008;56:303 – 306

Tuberculosis Knowledge: A Survey among Students of a Medical College from Coastal Karnataka, India

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Abstract

Background: Tuberculosis (TB) is one of the most common diseases, and globally, it ranks second, first being AIDS. It has been said that one-third of the global population is already infected with *M. tuberculosis*. By 2020, an estimated 200 million of these people would contract TB. A very crucial step for containment of TB is to make sure that there is understanding of its risk factors, mode of transmission, and diagnosis.

Aims and Objectives: This study aimed to assess the knowledge and understanding of MBBS students at coastal Karnataka, India Medical College, about Tuberculosis.

Methodology: An online survey was conducted addressing areas of general factors, risk and transmission factors, diagnosis factors, treatment, and prevention factors. A total of 31 statements were given in the online survey.

Results: The respondents showed overall good knowledge about Tuberculosis. The females had a better understanding than males, and the interns scored better on the study than the other MBBS students.

Conclusion: This study has shown that the students have high essential awareness about TB. However, section by section analysis shows that knowledge about a few topics needs to be strengthened.

Keywords: Tuberculosis, Survey, Medical students, Knowledge.

Introduction

Tuberculosis (TB) is one of the most immemorial diseases in humankind's history. Globally, it is amongst the top 10 diseases, only second to AIDS. In 1882, Robert Koch discovered the bacilli that causes Tuberculosis, *Mycobacterium tuberculosis*.¹ The causative agent of Tuberculosis is known as the *Mycobacterium tuberculosis* complex.¹ The *M. tuberculosis* complex

consists of *M. tuberculosis*, *M. bovis*, *M. microti*, *M. africanum*. Of these, the leading causative agent of tuberculosis is *M. tuberculosis*. In other animal species, *M. bovis* is a significant cause of Tuberculosis.¹ Humans are infected by *M. bovis* by consuming milk, milk products, or meat of such animals.² Tuberculosis, a contagious disease, is transmitted from one person to another through air. Persons who are infected with active lung tuberculosis have a higher chance of spreading the disease when they speak, cough, sneeze, and spit.³ Hence, those in close contact with these infected people are at a greater risk of acquiring the infection. Symptoms of pulmonary tuberculosis include a chronic cough with/without bloody sputum, fever, sweats at night, weight loss.⁴ It is said that one-third of the global population is already infected with *M. tuberculosis*. By 2020, an

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estimated 200 million of these people would contract TB, and around 35 million deaths would be caused among them unless the infection is curtailed.⁵ Around 10.4 million new TB cases were present worldwide, in 2016, as per the world health organization report. Of these cases, 6.2 million were men, 3.2 million were women, and 1 million were children. 64% of the new cases were from seven countries, viz. India, Indonesia, China, Philippines, Pakistan, Nigeria, and South Africa.⁶ Out of these, the highest number of TB cases in the world are accounted for by India.⁷ Many newer method of diagnosis and treatment of TB have been established over the years, but unfortunately, people still suffer from this disease. Most anti-tuberculosis drugs have been used for years, and due to this, the resistance to these drugs is widespread. Multidrug-resistant tuberculosis (MDR-TB) is caused by bacteria that do not respond to at least one of the two most potent and effective anti-tuberculosis drugs, Isoniazid, and Rifampicin.⁸ Apart from MDR-TB, another form is Extensively drug-resistant tuberculosis (XDR-TB), which is also resistant to two groups of second-line anti-tuberculosis drugs. XDR-TB makes it even more challenging to treat patients with tuberculosis.⁸ Directly observed treatment short course (DOTS) is a strategy that ensures not only a clinical approach to patients but also patient adherence to treatment, adequate drug supply, management of public health systems.¹ Since the dawn of DOTS, awareness, diagnosis, and treatment of TB have greatly improved.⁹

A very crucial step for containment of TB is to make sure that the understanding of its risk factors, mode of transmission, and diagnosis.¹⁰ Various studies have been undertaken in the form of surveys in different demographic regions, different colleges, and universities. The objective of the present study was to assess the knowledge and understanding of MBBS students at Kasturba Medical College, Mangalore, Karnataka about Tuberculosis.

Materials and Method

A cross-sectional study was done in the form of an online survey. The online survey consisted of an informed consent form, and only those participants that voluntarily agreed to participate in the study were included. The survey was conducted among MBBS students of second last year, last year and interns. The questionnaire had four parts viz. General factors, Risk and Transmission factors, Diagnosis factors, Treatment, and prevention factors.

Results

312 students participated voluntarily in this study. Females accounted for 54.5%, and males were 45.2%. The ages ranged from 21 years to 25 years. The questions and the percentage of responses are given in Table 1 and 2.

Table 1: General factors, risk and transmission factors

Statement	Agree	Disagree	I Don't Know
<i>Mycobacterium tuberculosis</i> causes tuberculosis (TB)	98.7%		
<i>Mycobacterium</i> could be dormant for many years and get reactivated	98.1%		
TB is confined only to the respiratory tract		98.7%	
Multidrug-resistant TB (MDR-TB) is caused by organisms that do not respond to Isoniazid & Rifampicin	94.6%		
Extensively drug-resistant TB (XDR-TB) is another form of MDR-TB that does not respond to any two groups of second-line anti-tubercular drugs	75.6%	11.2%	13.1%
TB is caused by a virus		98.7%	
Close contact with a person having pulmonary TB is harmless		98.4%	
Crowded places are excellent environments for the transmission of TB	98.7%		
You can acquire TB by drinking raw milk from an infected animal	88.8%		
Keeping a pulmonary TB patient at home carries the risk of infecting others	95.5%		
There is a close relationship between HIV and TB	50.6%		47.4%
The most common mode of transmission of pulmonary TB is through inhalation of aerosols	98.7%		

Table 2: Diagnosis, Treatment and Prevention factors.

Statement	Agree	Disagree	Idon't Know
Every patient with pulmonary TB coughs out bloody sputum		95.8%	
Fever, cough, weight loss, chills are some of the symptoms of TB	98.7%		
Albert's staining is the best staining method for <i>Mycobacterium</i>	20.5%	68.3%	11.2%
Mantoux test is a tuberculin test used to check for active infection	74.4%	24.7%	
The prevalence of TB infection can be detected by the Mantoux test	36.5%	11.2%	52.2%
Lowenstein-Jenson medium is most commonly used to culture <i>Mycobacterium</i>	85.9%		11.2%
MGIT stands for <i>Mycobacterium</i> growth indicator tube. It is a system used to cultivate <i>Mycobacterium</i>	33%		63.8%
The GeneXpert MTB/RIF is a rapid test to identify the DNA and resistance to Rifampicin	84%		14.7%
The Mantoux test is used to detect the exposure to TB	41%		52.2%
TB is a treatable disease	99.7%		
Anti-tubercular drugs can be classified into the first line and second line drugs	99%		
Precautions like wearing a mask, washing hands & proper ventilation are helpful while taking care of a pulmonary TB patient	100%		
First line drugs consist of Isoniazid, Rifampicin, Pyrazinamide, Ethambutol, Streptomycin	94.9%		
Directly Observed Treatment Short Course (DOTS) is a TB control strategy recommended by the WHO	94.6%		
Short course chemotherapy is divided into an intensive phase (spreads throughout 2-3 months) & a continuation phase (extends up to 4-5 months following the intensive phase).	98.1%		
BCG vaccine is used to prevent childhood tuberculous meningitis and miliary disease	88.1%		7.4%
MDR-TB treatment program was implemented in India to provide diagnosis facilities & standardized treatment.	56.1%	19.6%	24.4%
One of the main aims of the DOTS programme is to improve the patient's compliance	98.7%		
For prevention, in India, the WHO recommends Danish 1331 strain of BCG	41.3%		57.7%

The responses were scored as correct and incorrect. This was done for easy comparison between the gender wise responses and responses amongst different batches of MBBS students. SPSS version 20 was used for statistical analysis, and the tests applied were the Chi-Square test and students T-test. Total number of questions was 31. The mean score scored by females was 25.786, and males were 25.172. Females had a slightly higher rating than males (51% and 49% respectively). This is depicted in figure 1. Comparison of the scores was also made between the MBBS interns and the second last and final year MBBS students' responses. As expected, the interns scored better than the other students. The mean score of the interns was 26.9394, and that of the other MBBS students was 25.3441. This is depicted in figure 2. These scores were statistically significant (P<0.05).

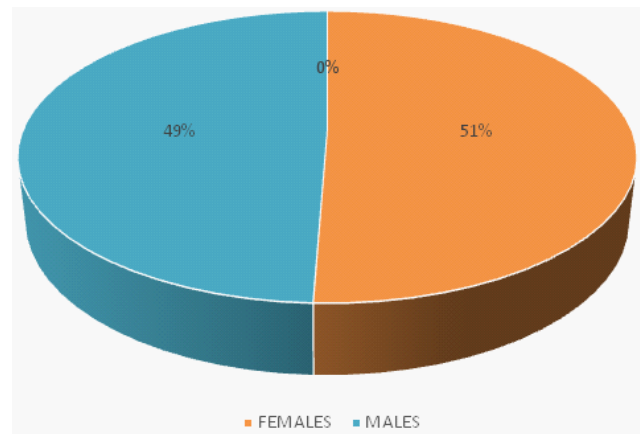


Figure 1: Comparison of knowledge between Females and Males

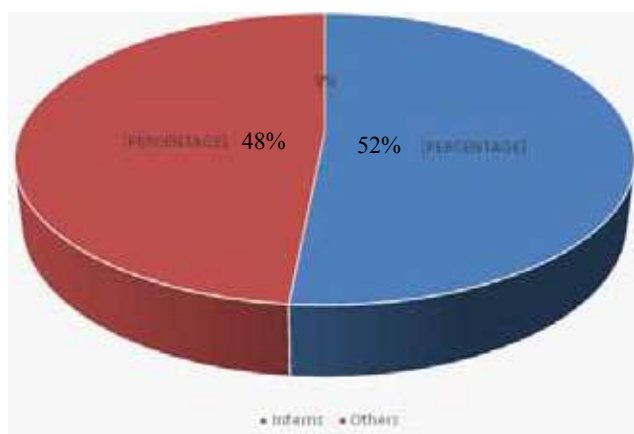


Figure 2: Comparison of knowledge between Interns and Other MBBS students

Discussion

Tuberculosis is one of the most well-known infectious diseases worldwide. India accounts for about one-fifth of the global TB incidence.¹¹ It becomes very crucial when a doctor has to apply his theoretical knowledge practically and treat patients that presumably have tuberculosis. Undergraduate medical students and interns are also at this threshold, and hence, it is necessary to assess their understanding of this disease and its related aspects. This study revealed an overall good knowledge and understanding of Tuberculosis amongst the students. However, for specific questions, ambiguities were seen. In the first section, that was, General factors, uncertainty was seen in the question which addressed Extensively drug-resistant tuberculosis. In the next section, Risk and Transmission factors, about 47.4% of the respondents lacked knowledge about the close association between TB and HIV. In the diagnosis section, there were mixed responses about the staining method, and about 20.5% said Albert's staining method was the best staining method for *Mycobacterium* whereas 11.2% did not know about the staining method. A lot of ambiguity was seen in questions related to the Mantoux test. Only 33% of the respondents knew about the MGIT (*Mycobacterium* growth indicator tube). Overall, a lot of mixed responses came from the Diagnosis section. This similar pattern was also seen in another study conducted in a medical college in Chennai wherein 80% of the students had correct general knowledge about the disease, but gap about knowledge in the diagnosis section was huge.¹² Another study done in China showed that older medical students had more knowledge about the diagnosis of tuberculosis than the newer students.¹³ In the Treatment and Prevention section, 56.1% of the

respondents agreed that the programme implemented in India to provide diagnosis facilities, and standardized treatment was known as the MDR-TB programme. However, the answer to this question was the DOTS programme.

Conclusion

This study has shown an overall good knowledge, necessary awareness, and understanding of Tuberculosis amongst the MBBS students. However, section by section analysis showed that knowledge in a few areas need to be strengthened. These areas involve knowledge about the Mantoux test, Extensively drug-resistant tuberculosis and the BCG vaccine. Females showed a slightly better response than the males, and as expected, the interns had a better understanding than the other students. More emphasis has to be given on the Diagnosis part of the existing curriculum since health education is one of the essential defenses in the era of the ever-increasing drug-resistant infection.

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References

1. Sandhu G. Tuberculosis: Current Situation, Challenges, and Overview of its Control Programs in India. *J Glob Infect Dis.* 2011; 3:143-50.
2. Prasad H, Singhal A, Mishra A, Shah N, Katoch V, Thakral S, et al. Bovine tuberculosis in India: Potential basis for zoonosis. *Tuberculosis.* 2005; 85:421-8.
3. Ali Mohammad Alelyani, Abdullah Mohammed Zain Aldeen, Rahaf Ghazi Altwairqi, Shatha Sameer Alim, Jaber Mohammed Alelyani. Knowledge, Attitude and Practice against Tuberculosis Infection among Medical Students Medical School at Taif University, Taif city, Kingdom of Saudi Arabia. *Int J Med Res Prof.* 2017; 3:139-43. DOI:10.21276/ijmrp.2017.3.4.028

4. World Health Organisation. Tuberculosis. Fact sheets, 2018. Available at: <https://www.who.int/news-room/fact-sheets/detail/tuberculosis>
5. Raviglione MC. The TB epidemic from 1992 to 2002. *Tuberculosis*. 2002; 83:4-14.
6. World Health Organization. Tuberculosis. Global Tuberculosis Report, 2017. Available at: https://www.who.int/tb/publications/global_report/gtbr2017_main_text.pdf
7. Central TB division, DGHS, Ministry of Health and Family Welfare, Government of India. Official RNTCP website. New Delhi, India: TB INDIA2010- RNTCP status report. Available at: www.tbcindia.org
8. World Health Organization. Multidrug-resistant tuberculosis (MDR-TB), 2017 update. Available at: https://www.who.int/tb/challenges/mdr/MDR-RR_TB_factsheet_2017.pdf
9. Mehta D, Bassi R, Singh M, Mehta C. To study the knowledge about tuberculosis management and national tuberculosis program among medical students and aspiring doctors in a high tubercular endemic country. *Ann Trop Med Public Health* 2012;5:206-8
10. A.A. Al-Jabri, A.S.S. Dorvlo, S. Al-Rahbi, J.Al-Abri, S.Al-Adawi. Knowledge of Tuberculosis among medical professionals and university students in Oman. *Eastern Mediterranean Health Journal*. 2006;12:509-21
11. Chennaveerappa P. K, Rajashekar H. K, Jayashree Nagaral, Halesha B. R, Raghavendra Prasad K. U, Vinaykumar M. V, et al. "A Study on Awareness of Tuberculosis and RNTCP among Undergraduate Medical students and Interns." *Journal of Evolution of Medical and Dental Sciences* 2014; Vol. 3, July 21; Page: 8115-21, DOI: 10.14260/jemds/2014/3021
12. Revathi R, Dharanisri R. Knowledge about tuberculosis among undergraduate medical students in a private college in Chennai. *Int J Community Med Public Health* 2018; 5:644-6.
13. Yangjiang Ou, Zhenzhou Lou, Jinsong Mou, Hui Ming, Xiang Wang, Shipeng Yan, et al. Knowledge and determinants regarding tuberculosis among medical students in Hunan, China: a cross-sectional study. *BMC Public Health* 2018;18:730:1-7

Reviving the Lost Extremity: A Case Report

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Abstract

The hand in the human body plays a major role in daily life, communication, social contact and basic functions such as grasping. Finger and partial finger amputations are the most frequently found forms of hand loss and trauma which lead to an impact on the psychological health, functional abilities and aesthetics of an individual. A prosthesis with good fitting, comfort and aesthetics can make the patient feel capable and whole again. This article describes a technique for fabrication of a custom made glove type finger prosthesis using silicone elastomers along with a ring for providing more retention to the prosthesis. Shade matching has been achieved by using intrinsic acrylic paints. This case report paper describes a technique to prosthetic rehabilitation of an amputated finger by fabrication of custom finger prosthesis by using silicone elastomer, which is aesthetically acceptable, comfortable to use and is cost effective with a simple approach.

Keywords: *Silicone elastomer, finger prosthesis, color matching, retention.*

Introduction

It is rightly said “Grief is in two parts, the first is loss, and the second is the remaking of life.” The loss of a limb or a digit has an immense impact on one’s mind, it can manifest as anxiety, depression or post-traumatic stress disorder on an individual.^[1] Replacement of the missing finger by fabrication of an artificial finger is a very challenging process and technique sensitive procedure in the terms of artistic abilities and skill expertise. Prosthesis made for patients should be comfortable to wear, durable, light weight, aesthetically pleasing and easy to put on and remove.

Case Report: A 60 year old male patient reported to the Department of Prosthodontics Crown and Bridge, Maharishi Markendeshwar College of Dental Sciences

and Research, Mullana, Ambala, for the fabrication of Complete Denture. On general examination, it was noticed that the patient had lost part of his left index finger (distal phalange) about 5 years back, due a traumatic injury. On physical examination a solitary healed scar was seen on palmar surface of the amputated finger. The surrounding surface and area of the finger appeared to be normal with no signs of pain, infection or any inflammation. Informed consent was made with a detailed explanation of the procedure. [Figure 1].



Figure 1: Amputated left index finger

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Technique:

1. Patient was requested to keep his hand in normal resting position and not stretched. Lubrication with a

uniform thin layer of petroleum jelly is done, which prevents the adhering of the hydrocolloid to the skin on the site of the impression surface. A cardboard box was selected larger in size than the patient's hand. One side of the cardboard box was cut open to place and remove the hand.^[2] A thin uniform mix of hydrocolloid (*Zhermack*) was poured inside the box creating the base of the impression on which

the patient was instructed to place the palmar aspect of the hand over of the impression material, simultaneously the dorsal surface of the whole hand was covered.^[3] In the end, a layer of dental plaster (*Kalabhai Kaldent*) was poured over the impression material for imparting strength to the impression made as well as to prevent its tearing on removal of the patients hand. [Figure 2].



Figure 2: Alginate Impression and Impression surface

2. The impression made was poured with dental stone (*Kalabhai Kalstone*) with vigorous tapping ensuring the complete flow of the dental stone. A positive replica of the site was obtained and finished.^[2] [Figure 3].



Figure 3: Dental stone model

3. In this case, the wax pattern was fabricated by Donor Finger which involved making a hydrocolloid impression of the donor index finger. The donor finger should be of the same side of the patient's amputated finger and same sex. The donor was selected by matching the appearance and size of the fingers using the model obtained. The impression made was poured with heated liquid modelling wax (*MAARC*).^[4] The wax pattern is carefully sculpted hollow from the inside followed by finishing and carving to give it a natural appearance. [Figure 4]
4. The custom made glove type wax pattern prosthesis is tried on the patient's amputated index finger. Proper fit and length is established with verification of the correct orientation. [Figure 4].



Figure 4: Trial of wax pattern on amputated finger

5. The wax pattern was invested. After complete set, de-waxing is carried out. A mould is obtained.^[5]
6. Silicone (RTV Silicone, MP Sai Enterprises, Mumbai) was used along with acrylic paints (KURTZY Acrylic color paintv12 shades) as intrinsic shades. The colors Red, Blue, Yellow, Black, were used to create the natural skin tone of the patients hand, mixing was carried out on a glass slab. Color matching was done in natural light.^[6] After desired shade was achieved and the silicone material was packed into the mould, bench pressed and was left overnight for processing.^[Figure 5]



Figure 5: Shade Matching

7. A prefabricated artificial nail was used (Electromania Acrylonitrile Butadone Styrene Style Plane Nail

Tips Pack of 24).

8. The final prosthesis was retrieved, excess was trimmed and finished. The artificial nail was trimmed and glued according to esthetics, followed by insertion of the final prosthesis on the patient's amputated left index finger. A ring was placed over the silicone finger prosthesis, which provided more retention to it. The prosthesis was delivered to the patient, was completely satisfied and contented with the outcome.^[4]
9. To maintain its hygiene, the prosthesis should be washed with antibacterial soap from inside and outside air dried and then worn.^[7] Exposure to high temperatures should be avoided. Smoking may discolour and stain the prosthesis. The prosthesis is not to be worn overnight as it will lead to irritation of the underlying skin.^[Figure 6]



Figure 6: Silicone Finger Prosthesis

Discussion

It has been reported that the most common found amputations are partial hand amputations, presenting with loss of one or more fingers. They are commonly resulted from occupational hazard, automobile accidents.^[3] Other causes of amputations can be congenital, diabetes, gangrene and infections resulting from lack of basic public health. Partial finger amputations lead to functional deficiencies, aesthetic problems resulting in poor self-esteem, and psychological instability and economic damage to the individual. Many materials such as Acrylic, Polyurethane, polyvinylchloride have been used to produce finger prosthesis.^[7] The restoration of the lost limb, finger depends upon the amount of the tissue involved and bone involvement, the level and the angle of amputation along with the number of fingers involved and the choice and acceptance of the person for the restoration of the finger. There are numerous replacement techniques accessible to restore the finger.^[8] A well fitted and color matched prosthesis gets rid of the constant reminder of disability to a person.^{[9][10]}

Conclusion

Rehabilitating the finger or its partial finger segment with an artificial prosthesis can be rewarding and satisfying with a pleasant outcome for a maxillofacial prosthodontist. The artificial prosthesis given can greatly enhance the psychological health, self-esteem of the patient. The process requires great skill, technique sensitivity and artistic skills along with the understanding of the patients need.

Ethical Clearance: Not Applicable

Source of Funding: Self

Conflict of Interest: Nil

References

1. Kamble VB, et al. Silicone finger prostheses for single finger partial amputations: Two case reports, Indian Journal of Dentistry (2012)
2. Dogra, et al. Fabrication of a silicone finger prosthesis, The Journal of Indian Prosthodontic Society, September 2008, Vol 8, Issue 3, page number-166-68
3. Mehta S, Leela B, Karanjkar A, Halani AJ. Prosthetic rehabilitation of a partially amputated finger using a customized ring-wire substructure. J Indian Prosthodont Soc 2018;18:82-85.
4. Deepesh Saxena et al. Rehabilitation of Digital Defect With Silicone Finger Prosthesis: A Case Report Journal of Clinical and Diagnostic Research. 2014 Aug, Vol-8(8): ZD25-ZD27
5. Shanmuganathan N et al. Aesthetic Finger Prosthesis, J Indian Prosthodont Soc (Oct-Dec 2011);11(4):232-237
6. Mallikarjuna Ragher et al. Finger Prosthesis Made Easy: A Case Report Sch. Acad. J. Biosci., 2014; 2(11):841-844
7. Anand, Shafi FM, Pradeep N (2015) A Cost Effective Method to Fabricate an Interim Finger Prosthesis. Dentistry 5: 323.
8. Satyanarayana N et al, Beauty At Fingers Tips: An Anaplastic Finger Prosthesis case report Indian Journal of Dental Sciences, December 2013, Issue:5, Vol.:5
9. Wilson RL, Carter-Wilson MS. Rehabilitation after amputations in the hand. Orthop Clin N Am. 1983; 14: 851-72.
10. Kanter CJ, The use of RTV silicones in maxillofacial prosthetics. J. Prosthet Dent. 1970; 24 (6):646-53.

Research Trends in Dermatologist Level Automatic Classification of Various Skin Lesions using Deep Learning

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Abstract

In today's modern world, diseases are increasing day by day. Amid the different types of diseases, cancer has turned out to be a deadliest disease in human beings. According to the latest medical statistics, Cancer is accountable for high mortality rate. Skin cancer is usually identified beginning with preliminary screening by clinicians and followed possibly by dermoscopic investigation, a biopsy and histopathological inspection. Differentiating and predicting different types of skin lesions on inspection of images is one of the most challenging and difficult task because of the minute variations in the appearance of skin lesions. The images of different lesions seem to be identical and it is very difficult to manually differentiate them. Hence, deep convolutional neural networks are now emerging as a solution to address this problem. The main objective of this work is to review the indexed papers that addresses the issues of automatic classification of skin lesions. This paper summarizes about the different types of datasets available, the type of deep learning models used for training and the parameters used for performance measurements.

Keywords: Skin lesion classification, Deep Learning, Data Augmentation, Artifacts, Transfer Learning.

Introduction

Cancer is one of the common disease accountable for 0.3 million deaths per year. Almost every instance of cancers have been found in Indian population. Out of all cancers in India, skin cancer constitutes about 1 to 2 percent of all diagnosed cancers.

Tropical countries like India receive higher levels of UV radiation and this raises the risk of skin cancer. Different types of skin cancer are found in India. The three most common types are Basal Cell Carcinoma, Squamous Cell Carcinoma and Melanoma. These three types of skin cancers are classified on the basis of three different types of skin cells found in the epidermis - Squamous Cells, Basal Cells and Melanocytes. Various categories in pigmented lesions include Actinic Keratoses (AK) and intraepithelial carcinoma/Bowen's disease (akiec), basal cell carcinoma (bcc), benign keratosis-like lesions (solar lentiginos/seborrheickeratosis and lichen-planus like keratoses, bkl), dermatofibroma (df), melanoma (mel), melanocytic nevi (nv) and vascular lesions (angiomas, angiokeratomas, pyogenic granulomas and hemorrhage, vasc).

Differentiating and predicting different types of skin lesions on inspection of images is one of the most challenging and difficult task because of the minute variations in the appearance of skin lesions. The images of different lesions seem to be identical and it is very difficult to manually differentiate them. Hence, deep convolutional neural networks are now emerging as a solution to address this problem. It has been found that some literatures are evolving to solve this issue from 2015 onwards.

This paper is mainly focused on organizing a systematic review of the literatures of skin cancer classification using deep learning.

Skin Cancer Lesion Characteristics: Bkl includes lichenoid keratosis and seborrheic keratosis. Lichenoid keratosis will usually be a little swollen macule or slim pigmented plaque. Seborrheic keratosis will be in the forms of fissures, comedo-like openings, and milia-like cysts and it is almost similar to nevi. The figure 1(a) is the histopathology bkl picture of a 80 year old male on scalp, figure 1(b) is the histopathology bkl image of a 40 year old male on upper extremity and figure 1(c) is

the histopathology bkl image of a 70 year old female on back.

Df are benign skin growths and the color varies from pink, gray, red or brown and may change color over the years. It will be firm and hard and can be found anywhere on the body. The figure 1(d) is the histopathology df image of a 75 year old male on back, figure 1(e) is the histopathology df image of a 55 year old female on upper extremity and figure 1(f) is the consensus image of a 50 year old male on lower extremity.

Melanomas are malignant and its presence shows various shades of black, brown or tan. The figure 1(g) is the histopathology mel image of a 40 year old female on chest, figure 1(h) is the histopathology mel image of a 70 year old male on face and figure 1(i) is the histopathology mel image of a 85 year old female on lower extremity.

Vascular lesions include lesions of angiokeratomas and angiomas. Angiokeratomas are the type of vascular lesions that are shiny, soft, dark red nature of size 2–10 mm papules that may end up in blue to black color and a surface scale. Cherry angioma will seem like firm red, blue or purple papule of size varying from 0.1–1 cm in diameter. The figure 1(j) is the consensus vasc image of a 85 year old female on back, figure 1(k) is the consensus vasc image of a 5 year old male on back and figure 1(l) is the histopathology vasc image of a 70 year old female on abdomen.

A melanocytic nevus can either be malignant or benign containing nevus cells. It appears as small brown, tan, or pink spots. The figure 1(k) is the follow-up nv image of a 45 year old male on abdomen, figure 1(l) is the follow-up nv image of a 60 year old male on lower extremity and figure 1(m) is the histopathology nv image of a 40 year old male on back.

BCCs look like sores that are open, patches that are red with pink growths, bumps that will be glittery, growths that are slightly elevated with a central indentation. AK are usually small in size (0.5-2.0 cm) and look like patches of rough, scaly skin which vary in colors of pink, red, brown, or the same colour as normal skin. Bowen’s disease patches appear as more red and scaly when compared to AK and size varies from 0.5-2.0 cm in size. The figure 1(n) is the histopathology image of a 70 year old male on upper extremity, figure 1(o) is the histopathology image of a 40 year old male on abdomen and figure 1(p) is the histopathology image of a 65 year old male on neck.

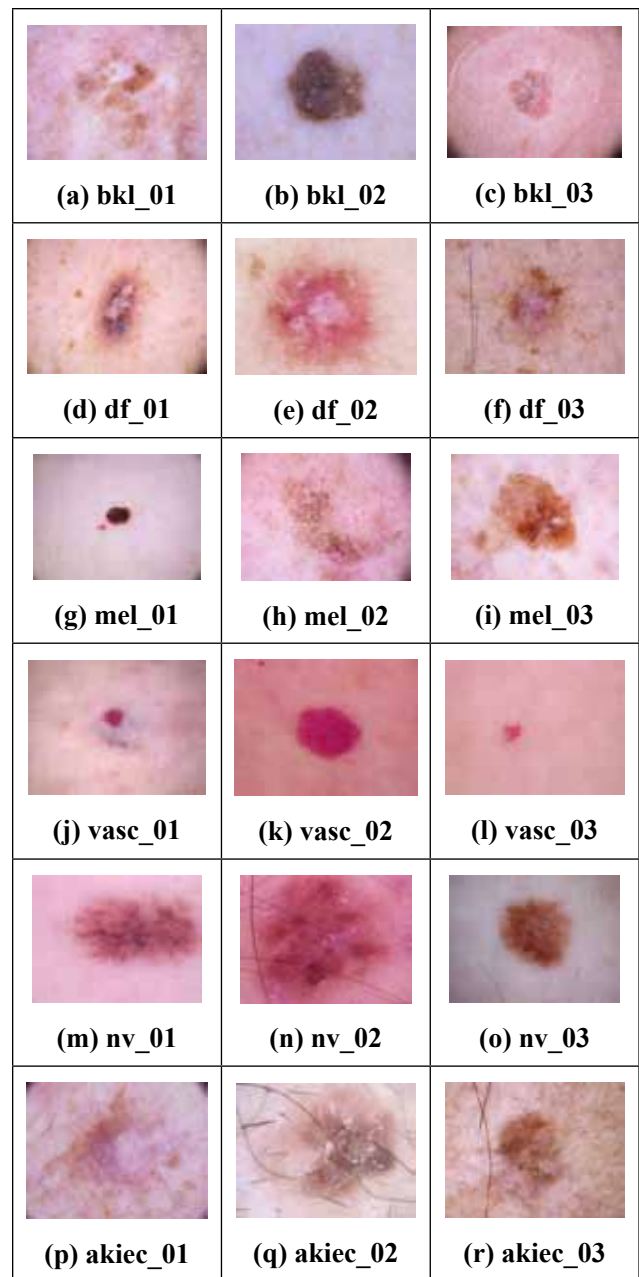


Figure 1 Sample Skin Cancer Lesions

The characteristics are analyzed from the medicinal information available from dermoscopia. In order to find the lesion as benign or malignant, the lesion class has to be identified. From the figure 1, it can be seen that most of lesion colors are similar and it is difficult to classify on visual investigation. Thus only a well-experienced clinician can correctly classify the lesions. To err is the human and hence the problem of classification of skin lesions is becoming a research trend in deep learning.

Some of the sample images taken from MNIST dataset are shown in figure 1. Three images from each seven classes of lesions are shown in the figure.

Materials and Method

Datasets: Training of deep convolutional neural network for accurate classification of lesions needs large datasets. Many datasets are publicly available. The datasets that has been used in the standard publications are discussed here.

The PH database consists dermatoscopic images of 200 melanocytic lesions that includes lesions of common nevi, atypical nevi, and melanomas. The information includes medical annotation of manual segmentation, the clinical diagnosis, and the identification of several dermoscopic structures, performed by expert dermatologists, in a set of 200 dermoscopic images.¹

The Atlas Dermofit Image Library is a collection of 1,300 skin lesion images and their segmentation masks divided among 10 classes. The diagnoses were provided by knowledgeable dermatologists and dermatopathologists, generating a gold standard ground truth. Although this dataset isn't publicly offered, it can be purchased.

HAM10000 ("Human Against Machine with 10000 training images") dataset consists of 10015 dermatoscopic images of 7 classes which includes lesions of bcc, bkl, df, mel, nv and vas. The images are acquired from different population through examination by clinicians, pathology, while the ground truth for the rest of the cases was either follow-up, expert consensus, or confirmation by in-vivo confocal microscopy. HAM10000 dataset has been deposited at the Harvard database. It is publicly available. Most of the recent researches are found to use this dataset.²

The International Skin Imaging Collaboration (ISIC) archive contains the largest publicly available collection of quality controlled dermatoscopic images of skin lesions. Presently ISIC 2019 challenge contains 25,331 images available for training across 8 different categories. Future researches may use ISIC 2019 dataset.³

Data Preparation: Training a machine learning model needs tuning its parameters such that it can map a particular input (say, an image) to some output (a label). The optimization goal is to chase that sweet spot where the model's loss is low, which happens when the parameters are tuned in the right way.. Naturally, if there are a lot of parameters, the model should be shown a proportional amount of examples, to get good

performance. The main problem with the skin cancer datasets is the class imbalance and availability of only few thousands of images. In order to have a good training accuracy, the dataset should be large and classes should be balanced. So the solution to this problem is data augmentation. The different types of augmentation techniques are flipping, rotating, scaling, color changing, illumination etc.

Most of the literatures used augmentation techniques such as rotation, flipping and shifting. Augmentation techniques such as color changing and illumination are not preferred for skin cancer classification because the lesions are characterized by its color. Changing color or illumination may results in loss of information. The data augmentation performed on MNIST image is shown in figure 2.

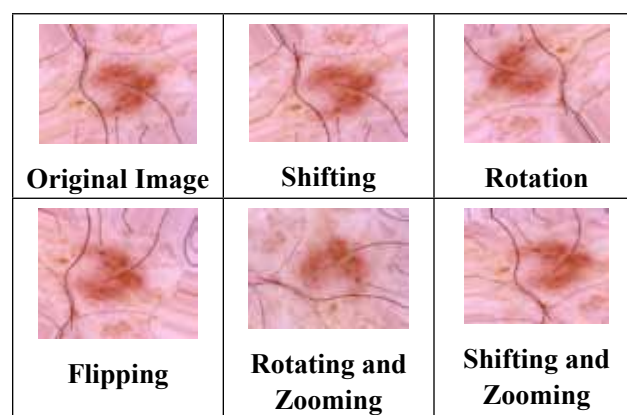


Figure 2 Data Augmentation

Some of the literature preprocessed the dataset by removing unwanted artifacts in the image such as the hairs and performed lesion segmentation¹¹ while some literature did not do preprocessing and lesion segmentation.

Deep learning in classification of lesions: Esteva et al⁴ trained the convolutional neural network with a dataset of size 1,29,450 images consisting of 2032 different diseases. They employed transfer learning and trained using Google's Inception v3 model. They analyzed using three way classification and nine way classification of lesions. Three way classification involves classifying of lesions as benign, malignant and neoplastic lesions and obtained an accuracy of 72.1%. Nine way classification obtained a accuracy of 55.4%. The lower accuracy may be due to the fact that their dataset consists of images acquired under varying lighting and capturing conditions (more like practical case) whereas most of the other dataset consists of

images obtained under standard lighting and capturing conditions. The larger dataset is the combination of ISIC Dermoscopic Archive, the Edinburgh Dermofit Library and data from the Stanford Hospital. The main advantage of this work is that they created disease taxonomy of inference classes and training classes.

Chaturvedi et al⁵ trained the convolutional neural network with HAM10000 dataset of size 10,015 images consisting of 7 different classes. They employed transfer learning and trained using MobileNet model. The classification obtained an accuracy of 83.1%. This model has been employed as a web application for public use. The main merit of this model is lighter architecture and faster performance.

Fisher et al⁶ investigated the classification of 10 different types of skin lesions from Edinburgh Dermofit Library. Two families of architectures such as semi-learned hierarchical classifiers and deep net classifier were explored. The limitation of this work is that images in the dataset were acquired under standard lighting and capturing conditions.

Hosny KM et al⁷ in their work investigated the classification of skin lesions using AlexNet model. They analyzed the results with three data sets ISIC dataset, MED-NODE dataset and The DermQuest dataset. They performed training with each dataset separately and done two kinds of experiments, one with augmentation and the other without augmentation. The average accuracy with the DermIS- DermQuest, MED-NODE dataset and ISIC dataset are 96.86%, 97.70% and 95.91% respectively.

Haenssle et al⁸ used GoogLeNet Inception v3 model for skin lesion classification with transfer learning for classification of dermatoscopic images of melanoma versus benign nevi. The AUC ROC achieved for this task was .86. The limitation of this work is data is not clearly provided about the training data and the

important merit is that it included comparison result with 52 dermatologist and it has been proved that additional clinical information improves the accuracy of the model.

Han et al⁹ used Resnet 152 model for skin lesion classification of 12 different skin diseases. They trained for 19398 images obtained from Asan dataset, MED-NODE dataset, and atlas site images. The important merit is that it included comparison result with 16 dermatologist and it has been proved that additional clinical information improves the accuracy of the model.

Sourav Kumar Patnaik et al used three pre trained models such as Inception V3, Inception Resnet V2, Mobile Net. The results from the three models were combined and the disease was predicted with the maximum voting from the three models.¹⁰

Halil Murat Ünver et al employed Yolov3, a deep learning for object detection. This work combined Yolo model and grabcut algorithm and performed lesion segmentation after the removal of the artifacts.¹¹

Performance Metrics: The different types of performance metrics found in the literature are accuracy, precision, recall and F1-Score. The equations of the evaluation metrics are shown in the equations 1,2,3 and 4 respectively.

$$Accuracy = \frac{TP+TN}{TP+TN+FP+FN} \tag{1}$$

$$Precision = \frac{TP}{TP+FP} \tag{2}$$

$$Recall = \frac{TP}{TP+FN} \tag{3}$$

$$F1 - Score = \frac{2*(Precision*Recall)}{Precision+Recall} \tag{4}$$

Where TP, TN, FP and FN denotes true positive, true negative, false positive and false negative respectively.

Table 1: Comparison of different existing models for skin cancer classification

Literature	Dataset	No of classes	Total images	Data augmentation	Model	Type of learning	Results Accuracy
4	ISIC Dermoscopic Archive, the Edinburgh DermofitLibraryand data from the Stanford Hospital	3	1,29,450	Rotation and flipping	Google’s Inception v3	Transfer learning	72.1%
		9					55.4%
5	HAM10000	7	10015	Rotation, flipping, shifting and zooming	MobileNet	Transfer learning	83.1%
6	Edinburgh Dermofit Library	10	1300	-	Resnet50	Transfer learning	78.7%

Literature	Dataset	No of classes	Total images	Data augmentation	Model	Type of learning	Results Accuracy
7	DermIS-DermQuest	2	206	Rotation	AlexNet	Transfer learning	96.86
	MED-NODE	2	170				97.70
	ISIC	3	2000				95.91
10	Not mentioned	6	-	-	InceptionV3	Transfer learning	68.15%
					Inception Resnet V2		79.07%
					MobileNet		46.72%
11	PH and the ISBI 2017	4	2950	-	YoloV3	-	94.40% 96% (detection)

Conclusion and Future Work

With increase in diseases due to change in the environmental factors and food habits, it is need of the day to diagnose the disease as early as possible. Earlier diagnosis of the diseases will help in curation of the diseases. Early, accurate and automatic diagnoses need a highly advanced deep learning model to be developed. From the literature review of the various works related to skin cancer classification, many works are evolving to accurately predict the type of skin lesions. Most of the works preferred transfer learning rather than scratch learning. Already pretrained networks were used to fit in for the medical data. Comparison of the different works is not possible as the datasets and number of lesions classified varies between the literatures. Thus it can be concluded that developing a highly accurate deep learning model to classify the different types of skin lesions is still a challenging task. More research works need to emerge to address this issue and to make a standard model for preliminary skin disease diagnosis.

Ethical Clearance: Nil (Not Required)

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Conflict of Interest: Nil

References

- Mendonça T., Ferreira P. M., Marques J. S., Marcal A. R. S. & Rozeira J. PH₂ - A dermoscopic image database for research and benchmarking, 2013 35th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC), Osaka, 2013, pp. 5437–5440. 2013.
- Tschandl, P. et al. The HAM10000 dataset, a large collection of multi-sourcedermatoscopic images of common pigmented skin lesions. *Sci. Data* 5:180161 doi: 10.1038/sdata.2018.161.2018.
- Noel Codella, Veronica Rotemberg et al. Skin Lesion Analysis Toward Melanoma Detection 2018: A Challenge Hosted by the International Skin Imaging Collaboration (ISIC), 2018; <https://arxiv.org/abs/1902.03368>
- Esteva, Andre & Kuprel, Brett & Novoa, Roberto & Ko, Justin & Swetter, Susan & Blau, Helen & Thrun, Sebastian. Dermatologist-level classification of skin cancer with deep neural networks. 2017. *Nature*. 542. 10.1038/nature21056.
- Chaturvedi, Saket & Gupta, Kajol & Prasad, Prakash. Skin Lesion Analyser: An Efficient Seven-Way Multi-Class Skin Cancer Classification Using MobileNet. 2019.
- Fisher, Robert B. et al. Classification of Ten Skin Lesion Classes: Hierarchical KNN versus Deep Net. 2019
- Hosny KM, Kassem MA, FoadMM . Classification of skin lesions using transfer learning and augmentation with Alex-net. *PLoS One*. 2019;14(5):e0217293. doi:10.1371/journal.pone.0217293
- H A Haenssle, C Fink, R Schneiderbauer, F Toberer, T Buhl, A Blum, A Kalloo, A Ben HadjHassen, L Thomas, AEnk, L Uhlmann. Reader study level-I and level-II Groups, Man against machine: diagnostic performance of a deep learning convolutional neural network for dermoscopic melanoma recognition in comparison to 58 dermatologists, *Annals of Oncology*, Volume 29, Issue 8, August 2018, Pages 1836–1842, <https://doi.org/10.1093/annonc/mdy166>

9. Han SS, Kim MS, Lim W, Park GH, Park I, Chang SE. Classification of the clinical images for benign and malignant cutaneous tumors using a deep learning algorithm. *J Invest Dermatol.* 2018 Jul;138(7):1529–1538. doi: 10.1016/j.jid.2018.01.028.
10. Patnaik S. K, Sidhu M. S, Gehlot Y, Sharma B, Muthu P. Automated Skin Disease Identification using Deep Learning Algorithm. *Biomed Pharmacol J* 2018;11(3).
11. Ünver, Halil & Ayan, Enes. Skin Lesion Segmentation in Dermoscopic Images with Combination of YOLO and GrabCut Algorithm. *Diagnostics.* 2019. 9. 72. 10.3390/diagnostics9030072.

Epidemiology of Osteoporosis: A Case-Control Study among the Pre and Post Menopausal women of Allahabad District

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Abstract

Osteoporosis is a bone disorder which is a prevalent global public health problem associated with compelling morbidity, mortality and socioeconomic burden. This disorder can be prevented and treated if diagnosed early and accurately. This study was conducted among the pre and post-menopausal women of Allahabad District aged between 35-65 years to observe the strength of association between the risk factors and the prevalence of osteoporosis. A total number of 316 respondents were screened through P-DEXA scan in a hospital based free BMD check-up camps and a WHO guideline for the diagnosis of osteoporosis was used to assess the prevalence of osteoporosis in the selected respondents. Diagnosed patients of osteoporosis were identified as cases (N=84) while controls (N=84) of the study were free from less bone mineral density. A pre-tested questionnaire was used to collect information regarding behavioral, Anthropometric, Clinical and genetic risk factors of the osteoporosis. The finding shows that 27.22 percent women were normal while 46.2 percent had osteopenia and 26.58 percent had osteoporosis. The study shows the strong association of different risk factors like lack of physical activity (OR= 3.003), high consumption of tea/coffee (OR=1.437), less exposure to sun light (OR=2.608), obesity (OR=1.3125), large body frame (OR=1.313), poor hand grip strength (OR=1.819), prior history of fracture (OR=2.426) and maternal history of fracture (OR=7.604) with the prevalence of osteoporosis. This study recommended a healthy life style pattern in the daily life as osteoporosis is highly preventable disease and most of the associated risk factors are modifiable.

Keywords: Osteoporosis, Osteopenia, Prevalence, Epidemiology, Bone mineral density.

Introduction

Osteoporosis is a bone disorder which is a prevalent global public health problem associated with compelling morbidity, mortality and socioeconomic burden. The prevalence of osteoporosis intensifies with age for all sites and according to World Health Organization

(WHO) definition of osteoporosis up to 70% of women above the age 80 years have osteoporosis. Worldwide, women over 45 years of age, more than 200 million have osteoporosis and this is responsible for over 1.5 million fractures annually.^[1] Osteoporosis is a bone disorder that can be prevented and treated if diagnosed early and accurately. Unfortunately, it is mostly undiagnosed until a fracture occurs. So the number of people encouraged to be screened for this disease should be increased. Measurement of Bone Mineral Density is a major tool for the diagnosis of Osteoporosis. Osteoporosis is also prevented by obtaining peak bone mass during skeletal growth, preserving bone mass during adulthood, and reducing loss of bone density with advancing age. Thus, people should be encouraged to adopt healthy life style behaviors for ideal skeletal health by increasing the level

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of weight bearing exercise, optimal intake of dietary calcium and vitamin D, proper nutrition and maintaining ideal body mass index, cessation of smoking, regular sun exposure for vitamin D and moderate intake of alcohol, caffeine and sodium.^[2]

Objectives: To observe the strength of association between the risk factors and the prevalence of osteoporosis among the pre and post-menopausal women of Allahabad District

Materials and Method

This study was a community based cross-sectional study conducted among the pre and post-menopausal women of Allahabad District aged between 35-65 years. This study was carried out in one specialized hospital named *Yashlok Hospital*, which provides advanced health services to the community and organized free BMD check-up camps regularly through P-DEXA machine for the general population of Allahabad district. All relatively healthy women aged between 30-60 years who came to the referral hospital outpatient department during the free BMD check-up camps were randomly

and purposively approached to participate in the study. A total number of 316 respondents were screened through P-DEXA scan and a WHO guideline for the diagnosis of osteoporosis was used to assess the prevalence of osteoporosis and osteopenia in the selected respondents.^[3] Diagnosed patients of osteoporosis were identified as cases (N=84) while controls (N=84) of the study were all participants that were identified as free from less bone mineral density after undergoing the P-DEXA scan. A pre-tested questionnaire was used to collect information from the selected respondents regarding behavioral risk factors of the osteoporosis like duration of sun exposure, intake of number of tea cups, type of physical activity, Anthropometric risk factors like BMI and Body Frame and Clinical and genetic risk factors like Hand grip strength, prior history of fracture and maternal history of fracture. The statistical representation of the data was done with the help of statistical techniques like chi-square test, level of significance at 5%, odds ratio and relative risk for analysis of the possible association and strength of association of behavioral factors with the prevalence of osteoporosis.

Results

Table 1: Estimation of Prevalence of Osteoporosis among the Pre and Post-Menopausal Women of Allahabad District

S. No.	Bone Mineral Density	No. of Respondents	Percentage
1.	T-Score (>-1) Normal	86	27.22
2.	T-Score (-1to-2.5) Osteopenia	146	46.20
3.	T-Score (=-2.5) Osteoporosis	84	26.58
Total		316	100

The finding after the screening of bone mineral density of selected women by using P-DEXA scan machine shows that among the women who were

selected as respondents in this study, 27.22 percent women were normal while 46.2 percent had osteopenia and 26.58 percent had osteoporosis.

Table 2: Estimation of Risk: According to the Behavioral Risk Factors of the Osteoporosis

S. No.	Physical Activity	Case		Control		Estimation of Risk			
		n	%	n	%	Odds Ratio	95% CI	Relative Risk	95% CI
1.	Walking	28	33.3	25	29.8	0.333	0.141 to 0.789	0.685	0.509 to 0.923
2.	Yoga	19	22.6	48	57.1	0.118	0.05 to 0.277	0.368	0.244 to 0.555
3.	No Exercise	37	44.1	11	13.1	3.003*	1.268 to 7.115	1.459*	1.084 to 1.965
*Significant									
S. No.	Number of Tea Cups	Case		Control		Estimation of Risk			
		n	%	n	%	Odds Ratio	95% CI	Relative Risk	95% CI
1.	2-4 Cup	28	33.3	30	35.7	1.111*	0.512 to 2.414	1.058*	0.7 to 1.598
2.	More Than 6 Cup	35	41.7	29	34.5	1.437*	0.671 to 3.075	1.198*	0.814 to 1.763
3.	No Intake	21	25	25	29.8	0.9	0.414 to 1.955	0.946	0.626 to 1.429
*Significant									
S. No.	Duration of Sun Exposure	Case		Control		Estimation of Risk			
		n	%	n	%	Odds Ratio	95% CI	Relative Risk	95% CI
1.	15 Minute	56	66.7	34	40.5	2.608*	1.127 to 6.035	1.607*	1.003 to 2.575
2.	Half an Hour	16	19	31	36.9	0.817	0.319 to 2.095	0.879	0.485 to 1.595
3.	One Hour	12	14.3	19	22.6	0.384	0.166 to 0.887	0.622	0.388 to 0.997
*Significant									

Table 2 shows the results regarding estimation of odds and relative risk in concern with the physical activity of the selected women shows that the respondents with no physical exercise had a strong association with the occurrence of osteoporosis (**OR=3.003**) and they had **1.459** times more risk to develop this disease in comparison with other group of respondents who performed some physical exercise like walking (**OR=0.333**) and yoga (**OR=0.118**) regularly while the data regarding caffeine intake in the form of number of tea cups among the respondents revealed that women with more than 6 cups daily consumption of tea had a

strong association with the occurrence of osteoporosis (**OR=1.437**) and they had **1.198** times more risk to develop this disease in comparison with other group of respondents who had 2-4 cups consumption (**OR=1.111**) and no consumption (**OR=0.9**) of tea in their daily life. Less sun exposure with sun light for the absorption of Vitamin D in the skin also shows the strong association with the occurrence of osteoporosis (**OR=2.608**) and these women had **1.607** times more risk to develop this disease in comparison with women with half an hour daily sun exposure (**OR=0.817**) and one hour exposure to sunlight daily (**OR=0.384**).

Table 3: Estimation of Risk: According to Anthropometric Measurements among Case and Control

S. No.	BMI	Case		Control		Odds Ratio	95% CI	Relative Risk	95% CI
		n	%	n	%				
1.	Overweight	15	17.9	18	21.4	1.313*	0.69 to 2.497	1.333*	0.988 to 1.8
2.	Obese	23	27.4	24	28.6	0.807	0.385 to 1.692	0.902	0.627 to 1.296
3.	Underweight	8	9.5	10	11.9	0.674	0.238 to 1.91	0.819	0.468 to 1.433
4.	Healthy	38	45.2	32	38.1	0.702	0.306 to 1.611	0.837	0.544 to 1.289
*Significant									
S. No.	Body Frame (r- Value)	Case		Control		Estimation of Risk			
		n	%	n	%	Odds Ratio	95% CI	Relative Risk	95% CI
1.	Large (<10.1)	38	45.2	42	50	1.313*	0.69 to 2.497	1.143*	0.834 to 1.566
2.	Small (>11.0)	8	9.5	10	11.9	0.674	0.238 to 1.91	0.819	0.468 to 1.433
3.	Medium (10.1-11.0)	38	45.2	32	38.1	0.762	0.4 to 1.45	0.88	0.639 to 1.199
*Significant									

The results regarding estimation of odds and relative risk in relation with the Body Mass Index of the selected respondents shows that the overweight respondents had a strong association with the occurrence of osteoporosis (**OR=1.3125**) and they had **1.333** times more risk to develop this disease in comparison with other group of respondents like obese respondents (**OR=0.807**) underweight respondents (**OR=0.674**) and

healthy respondents (**OR=0.702**) While Body Frame of the respondents shows that the respondents with large body frame had a strong association with the occurrence of osteoporosis (**OR=1.313**) and they had **1.143** times more risk to develop this disease in comparison with other group of respondents who had medium body frame (**OR=0.762**) and small body frame (**OR=0.674**).

Table 4: Estimation of Risk: According to Clinical Assessment and Genetics among Case and Control

S. No.	Hand Grip Strength	Case		Control		Estimation of Risk			
		n	%	N	%	Odds Ratio	95% CI	Relative Risk	95% CI
1.	Poor (>20 Kg)	39	46.4	27	32.1	1.819*	0.899 to 3.679	1.34*	0.945 to 1.887
2.	Average (26-29 Kg)	18	21.4	23	27.4	0.986	0.44 to 2.187	0.992	0.635 to 1.549
3.	Good (34-38 Kg)	27	32.2	34	40.5	0.549	0.272 to 1.112	0.749	0.5301 to 1.059
*Significant									
S. No.	History of Prior Fracture	Case		Control		Estimation of Risk			
		n	%	N	%	Odds Ratio	95% CI	Relative Risk	95% CI
1.	Yes	17	20.2	32	38.1	2.425*	1.216 to 4.839	1.623*	1.071 to 2.459
2.	No	67	79.8	52	61.9	0.412	0.207 to 0.823	0.617	0.407 to 0.934
*Significant									
S. No.	Maternal History of Fracture	Case		Control		Estimation of Risk			
		n	%	n	%	Odds Ratio	95% CI	Relative Risk	95% CI
1.	Yes	31	36.9	6	7.1	7.603*	2.967 to 19.489	2.071*	1.61 to 2.663
2.	No	53	63.1	78	92.9	0.132	0.051 to 0.337	0.483	0.376 to 0.621
*Significant									

The results regarding Hand Grip Strength of the respondents revealed that with poor hand grip strength had a strong association with the occurrence of osteoporosis (**OR=1.819**) and they had 1.335 times more risk to develop this disease in comparison with other group of respondents who had average hand grip strength (**OR=0.986**) and good strength of hand grip (**OR=0.549**). While presence of history of previous fracture among the respondents had a strong association

with the occurrence of osteoporosis (**OR=2.426**) and they had 1.623 times more risk to develop this disease in comparison with women with no history of previous fractures (**OR=0.412**). Presence of maternal history of fracture among the respondents had a strong association with the occurrence of osteoporosis (**OR=7.604**) and these women had **2.071** times more risk to develop this disease in comparison with women with no history of maternal fractures (**OR=0.132**).

Discussion

The results of the study show that among the selected respondents, 46.2 percent had osteopenia and 26.58 percent had osteoporosis. In comparison, a study reported that the prevalence of osteopenia and osteoporosis in the lumbar spine of the urban Indian pre and post-menopausal women aged between 40-75 years was 48.4 percent and 25.8 percent respectively.^[4] Our estimations of prevalence of osteoporosis (26.58 percent) were similar when compared with other studies like in Hyderabad (29 percent) among the low income group women aged between 30-60 years^[5], followed by in Jammu (20.25 percent) among the urban women aged between 25-65 years^[6]. However, among the women from low income group aged between 30-60 years, bone mineral density at all skeletal sites was much lower than value reported from developing countries, with a high prevalence of osteopenia (52 percent) and osteoporosis (29 percent).^[7]

In the estimation of the risk of developing osteoporosis in relation with the behavioral factors among the respondents shows that lack of physical activity, less exposure to the sun light and extra consumption of caffeine in the form of number of tea cups show the strong association with the occurrence of disease. This strong association between no physical exercise and prevalence of osteoporosis has shown in some studies^[8] in which it was observed that physical activity and fitness reduced the risk of osteoporosis, related fractures and fall related injuries. The epidemiological studies revealed that sports activity, therapeutic and weight bearing exercise, household chores and fewer hours of daily sitting are significantly associated with the reduced risk of osteoporosis.^[9] In some other studies it was observed that high caffeine intake from the tea or coffee is significantly associated with osteoporotic fracture and according to some studies it is a known risk factor for osteoporosis.^[10]

Osteoporosis is a severe bone condition which is heavily influenced by the vitamin D level in the body. Studies documented that sunlight exposure can increase the bone mineral density of vitamin D deficient bone and lead to the prevention of non-vertebral fractures.^[11] It was suggested that 10-15 minutes sun exposure of hand, arm and face, 2-3 times per week is sufficient for the synthesis of required amount of vitamin D in the body.^[12]

Among the anthropometric risk factors of the osteoporosis, body mass Index and Body Frame

shows the positive association with the prevalence of osteoporosis in which obese and women with large body frame had more chances for developing this disease. The co-relation between the body mass index and prevalence of osteoporosis and related fractures are well documented in the various epidemiological studies. Recent studies show that overweight, obesity and larger body frames were also significantly linked with the future osteoporotic fractures but independent of bone mineral density.^[13]

Assessment of clinical and genetic risk factors of the osteoporosis, it was observed that poor hand grip strength, prior history of fracture and maternal history of fracture had a strong association with occurrence of the disease. Hand Grip Strength is generally is an indicator of normal muscle strength but it is a potentially useful objective parameter to predict fracture as it is associated with the fragility and propensity to fall. A cross sectional study^[14] confirms the association of poor hand grip strength is a predictor of future fracture risk and that its effect is independent of BMD and other clinical risk factors. History of previous fracture is a well-documented risk factor for future fracture risk but its relation with BMD and prevalence of osteoporosis is still not well established.^[15] But some studies reported that non-traumatic fractures in women are significantly associated with the osteoporosis at the femoral neck and the site of previous fractures impacts on future osteoporotic fractures independent of BMD.^[16]

Maternal history of fracture especially hip fracture is a well-documented genetic risk factor for the osteoporotic fractures that is independent of BMD among the women.^[17] Furthermore, the effect of family history is not a general but site specific predisposition to fractures. But the data on effect of family history on the prevalence of low bone mineral density is still not a well-documented risk factor for osteoporosis

Conclusion

The study concluded that most of the women after 40 years of age were suffering from low bone mineral density while advanced age women after the age of 50 were osteoporotic and may experienced osteoporotic fractures and associated mortality and morbidity. The data regarding associated risk factors of the osteoporosis revealed that behavioral risk factors like lack of physical activity, extra consumption tea and coffee and less exposure with the sun light, anthropometric risk factors

like High Body Mass Index and Large Body Frame, Clinical risk factors like poor hand grip strength and prior history of fracture and genetic risk factor like maternal history of fracture had a strong association with the occurrence and prevalence of osteoporosis.

Recommendations: This study recommended a healthy life style pattern in the daily life as osteoporosis is highly preventable disease and most of the associated risk factors are modifiable. So regular exercise and healthy diet pattern is the major tool to maintain a healthy body weight and hand grip strength which will contribute in the maintenance of healthy bone mineral density and reduced risk of fractures and related consequences. Regular exposure with the sun for getting recommended amount of vitamin D will help in the absorption of more calcium in the body and improvement of bone mineral density.

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References

1. Khatoon N. Management of osteoporosis among post-menopausal women in a selected hospital of Delhi, The Nursing Journal of India. 2013; 104(3):112-6.
2. National Institutes of Health Consensus Development Conference Statement: Adjuvant Therapy for Breast Cancer. Journal of the National Cancer Institute. 2001; 93(13):979-989.
3. WHO (1994). Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Report of a WHO Study Group, World Health Organization Technical Report Series 843: 1-129.
4. Kadam N, Chiplonkar S, Khadilkar A, Divate U, Khadilkar V. Low bone mass in urban Indian women above 40 years of age: prevalence and risk factors. Gynecology Endocrinology. 2010; 26(12):909-17.
5. Shatrugna V, Kulkarni B, Kumar PA, Rani KU, Balakrishna N. Bone status of Indian women from a low-income group and its relationship to the nutritional status. Osteoporosis International. 2005; 16: 1827-183.
6. Sharma S, Tandon VR, Mahajan A, Kour A, Kumar D. Preliminary screening of osteoporosis and osteopenia in urban women from Jammu using calcaneal QUS. Indian Journal of Medical Science. 2006; 60(5):183-9.
7. Facts and Statistics, International Osteoporotic Foundation, (2015)
8. Bonaiuti D, Shea B, Iovine R. Exercise for preventing and treating osteoporosis in postmenopausal women. Cochrane Database Systemic Review: 2002; CD000333.
9. Feskanich D, Willett WC, and Colditz GA. Walking and Leisure-Time Activity and Risk of Hip Fracture in Postmenopausal Women, The Journal of the American Medical Association. 2002; 288(18):2300-2306.
10. Rapuri PB, Gallagher JC, Kinyamu HK and Ryschon RL. Caffeine intake increases the rate of bone loss in elderly women and interacts with vitamin D receptor genotypes. American Journal of Clinical Nutrition. 2001; 74(5):694-700.
11. Sato Y, Iwamoto J, Kanoko T, Satoh K. Amelioration of osteoporosis and hypovitaminosis D by sunlight exposure in hospitalized, elderly women with Alzheimer's disease: a randomized controlled trial. Journal of Bone and Mineral Research. 2005; 20:1327.
12. National Osteoporosis Foundation. Physician's guide to prevention and treatment of osteoporosis. Washington, DC: National Osteoporosis Foundation; 2005.
13. Tanaka S, Kuroda T, Saito M, Shiraki M. Overweight/obesity and underweight are both risk factors for osteoporotic fractures at different sites in Japanese postmenopausal women. Osteoporosis International. 2013; 24(1):69-76.
14. Cheung CL, Tan CBK, Bow CH, Soong CSS, Loong CHN., Chee Kung AW. Low handgrip strength is a predictor of osteoporotic fractures: cross-sectional and prospective evidence from the Hong Kong Osteoporosis Study, AGE. 2012; 34 (5):1239-1248.
15. KanisJA, Johnell O, De Laet C, Johansson H, Oden A, Delmas P, Eisman J, Fujiwara S, Garnero P, Kroger H, McCloskey EV, Mellstrom D, Melton

- LJ, Pols H, Reeve J, Silman A, Tenenhouse A. A meta-analysis of previous fracture and subsequent fracture risk. *Bone*, 2004; 35(2):375-82.
16. Morin SN, Lix LM, Leslie WD. The importance of previous fracture site on osteoporosis diagnosis and incident fractures in women. *Journal of Bone and Mineral Research*. 2014; 29(7):1675-80.
17. Kanis JA, Johansson H, Oden A, Johnell, O, De Laet C, Eisman JA, McCloskey EV, Mellstrom D, Melton L, Pols HA, Reeve J, Silman AJ, Tenenhouse A. A family history of fracture and fracture risk: a meta-analysis. *Bone*. 2004; 35(5):1029-37.

Work Life Balance of Hotel Employees: An Empirical Study

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Abstract

Introduction: Work life balance (WLB) is a very critical issue for people wellbeing and satisfaction, due to the work environment and nature of work hotel employees experience a lower level of WLB that result in to various issues like stress, lack of satisfaction etc, the main objective of the paper is to measure the levels of WLB.

Methodology: The study is based on the information collected from 521 hotel employees through a questionnaire. The information was analyzed with the help of statistical tests like factor analysis, ANOVA, Tukey HSD and student's T test to interpret.

Results: It was found that hotel employee do not experience satisfactory WLB. Significant differences were found in WLB of employees of different departments. Gender, marital status and age were found to have significant association with levels of WLB.

Research limitations/implications: Study provide a quantitative measure of WLB of hotel employees and assess empirically levels of association of factors like department, age, marital status & gender.

Originality/value: Study provides an empirical approach to measure levels of WLB of hotel employees in context of department and demographic factors.

Keywords: WLB, luxury hotel, employee, and department.

Introduction

Hotel industry is a people oriented industry, dependent on skills and performance of employees to deliver quality services to guests and achieve its objectives. Work in hotel is known for its characteristics like irregular and stretched working hours, heavy workloads, rigid work schedules, handling difficult customers and job insecurity.^{1,2,3,4,5}

Such work characteristics have direct impact on WLB of an individual leading to variable issues. WLB is equal engagement and satisfaction in work and family

roles⁶ and there is a direct relation between WLB and satisfaction and between employee satisfaction and performance at work^{7,8}. WLB helps in better employee retention and recruitment of better staff^{9,10} a positive WLB is considered as a successful business strategy¹¹.

In Indian context as we analyze feedback of employees on various job portals and job review sites, we observe that major issues reported by employees is lack of WLB or too long work duration, a well established and accepted fact by hoteliers. The primary objective of this paper is to measure the WLB experienced by employees and assess results to ascertain that employee from different department have same levels of WLB and to analyze the levels of WLB in context of factors like gender, age and marital status.

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Theoretical background: WLB is a state of equilibrium where employee is able to meet

requirements arising from his workplace and family domains^{12,13} achieving WLB require equal distribution of personal resources like energy, time and commitment¹⁴ but trend of individuals spending more time on work and lesser time on other aspects of lives¹⁵ lead to issues of WLB. It can be stated that WLB prevails if there is proper functioning at work and at home with a minimum of role conflict¹⁶ In context of Indian hotel industry, as per Federation of Hotel & Restaurant Association of India one of the main reason and concern about the high attrition rate in hotel industry of competent staff and seeking offshore assignments is the lack of WLB, as per estimates the attrition rate in hotel industry is around 45%, indicate WLB as a critical factor in controlling the attrition rate in Indian hotels.

Work in hotels requires to achieve hard deadlines, unexpected interactions with guests, shift working & issues of coordination resulting in to difficulties in achieving a suitable WLB, employee has to work on festivals and unable to celebrate with family, they need to put more efforts and devote more time during festivals and busiest shift times in hotels are weekends and public holidays when majority of people enjoy their leisure time with family and friends¹⁷ this affects their personal lives as they cannot provide enough quality time to their family and personal life leading to further degradation of WLB and decrease in moral¹⁸ complicating the matter further¹⁹ hotels also lack family supportive work environments necessary for the benefit of employees and organization^{20,21,22} and is more prominent in Indian context.

WLB issue is not a minor issue but affects performance of employee²³ considering the fact that hotels are 24 hour industry & employees are pushed to work round the clock²⁴ requires innumerable hours at work & sacrifice their family & personal life²⁵. Gender of employee has been investigated as a predictor of WLB^{26,27} studies found that men & woman face almost similar issues related to WLB & gender of employee is not a significant factor^{26,28,29-34,35} as it was stated levels of women's involvement at work did not differ from men, both experience negative consequences only relationship is found to be stronger in case of women. In case of India, women may experience more issues of WLB as they are assumed to be more responsible because of childbearing engagements, cooking & managing home whereas males are considered as bread winners this lead to different challenges for women & men in managing work life matters.

Need of WLB increases with changes in marital status & family structures as individual desire to achieve a balance between career progression & focus towards family & get attracted towards organizations that offer flexibility to manage both. Studies have found that individual's with different marital status & family structure has differential levels of WLB. Single have lesser issues of WLB in comparison to married counterparts. At same time married individual may experience a better WLB if spouse is supportive increasing the ability of individual to decrease impact of work life imbalance⁴³ & balancing work life is also related to happier marriages³¹. Studies have shown that WLB practices help to improve financial results of company as it improve productivity, enhance retention & decrease the levels of absenteeism⁴⁴. Primary aim of study is to ascertain the levels of WLB of employees in hotels & to find any definitive association of demographic factors of the employee & the department of work with the WLB experienced by them.

Hypotheses for the study:

H1: Hotel employees have WLB.

H2: Employee from different departments experience different levels of WLB.

H3: The levels of WLB is different for both male & female employees.

H4: The WLB of employees from different age group is different.

H5: The WLB of married & single employees is not different.

Material and Method

The study was based on the information collected from 521 employees of the luxury hotels of Delhi, the capital of India. The data was collected with the help of a questionnaire developed after an explorative research where in the available literature on the issue was reviewed, review of employee feedback on job portals was conducted, interviews of Indian hoteliers in articles were analyzed, followed by in depth interviews with academician, HR managers & employees. The explorative research helped to identify four dimension of WLB namely quality time, involvement, satisfaction & health & to formulate statements. A research instrument was developed in the form of a self-administered questionnaire that has statements pertaining to WLB &

after a pilot study the information was collected from the sample. A combination of random & convenience sampling were used. Only criteria followed to identify the participant for study was employee should be employed in hotel for minimum of one year in any of the operational department of the hotel to an extent of supervisory level. The managers were excluded. Participants were requested to record agreement or disagreement on a five point Likert scale. The participants were required to provide their responses on the basis of their own experience & opinions. Each dimension was assigned equal weight & total score was level of WLB. Total score for WLB was 400 & score of 300 was considered to be threshold value to consider the levels as satisfactory, as it signify respondent's agreement to majority of statements. In the instrument some of the statements were negatively quoted, for analysis the scores for such statements were reversed.

More than 700 questionnaires were delivered & 578 were received, only 521 were found to be complete & fit for further analysis for the study. Data was fed in to SPSS software & analyzed through statistical tests like KMO, factor analysis, student t test, ANNOVA & Tukey HSD to draw any inferences.

Findings and Discussions

Values for KMO were found to be 0.845 & Bartlett's test of sphericity was significant (p value less than 0.05), ensuring sample adequacy for factor analysis & statistically significant correlations among the variables.

A total of 29 statements were analyzed through factor analysis, principle component analysis was employed & the data was rotated through varimax rotation to extract only 4 factors for the study. As per the result of principal component analysis, it was noted that four factors accounted for 71.27 percent variation in overall sample. The result of one sample t test, Table-1 test value of 300 as a threshold was considered for acceptance, with p value less than 0.05 & t value -12.684, the hypothesis H1: Hotel employees has WLB, was rejected. Results of ANOVA test, indicate (p<0.05) there exist significant differences in the levels of WLB among employees of different departments of hotels, accepting hypothesis H2 employee from different departments experience different levels of WLB. Result of Tukey HSD (p<0.05) indicated that WLB of employee from front office is highest followed by

employees from f & b service & housekeeping, lowest levels of WLB found for employee of food production department. ANOVA result (p<0.05), reflect WLB levels for women employee were significantly different from men, accepting hypothesis H3 levels of WLB is different for both male & female employees. Results of ANOVA, (p<0.05), proves WLB levels are different for the employees from different age groups, accepting the hypothesis H4 WLB of employees from different age group is different. As per the result of Tukey HSD, the highest levels of WLB was recorded for employee between 25-30 years & then there is a gradual decline in the levels of WLB till the age group of 35-40, & then WLB levels again increase from the age group of 40-45 & 45-50 years. As per results of ANOVA, (p<0.05), WLB was found significantly different for employee with different marital status, accepting hypothesis H5: The WLB of married & single employee is not similar.

Conclusion

The study found that there is a lack of satisfactory WLB for hotel employee, employees working in different departments of hotels have significantly different levels of WLB, the highest level of work life was recorded for employees working in front office, followed by employees from housekeeping & food & beverage service, the lowest level of WLB was found for employee working in food production. Levels of WLB were found to be significantly different for male & female, female employees have higher levels of WLB as compared to males, this was in contrast to assumptions & other studies. WLB levels for employees in age group 25-30 years & 45-50 years were found to be highest, whereas employees in the age group of 30-45 years were found to have lower levels of WLB. Study also concludes that WLB for married employees were found to be less than single.

Implications of the Study: The study provides an empirical approach towards measurement of WLB of hotel employees; the study has assessed the levels of WLB & analyzed it with factors like department of work, gender, age & marital status. Further study can be done to find the reasons behind the differences noted in the levels of WLB among different employee classifications. The study can help individual aspiring a career in the hotel industry & to hotels to introspect & devise interventions that can improve the levels of WLB of employees.

Table 1: One-Sample Student T Test to assess the levels of WLB

	Test Value = 300					
	T	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
WLB (WLB) Score	-12.954	520	.000	-27.84366	-29.9678	-21.8902

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References

- Hsieh, M. H., Pan, S. L., & Setiono, R. Product, corporate & country image dimensions & purchase behavior: A multicountry analysis. *Journal of the Academy of Marketing Science*. 2004; 32(3): 251–270.
- Xiao, Qu, & O’Neill, John W. Work-family balance as a potential strategic advantage: A hotel general manager perspective, *Journal of Hospitality & Tourism Research*. 2010;34(4): 415-439.
- Karatepe, O.M., & Bekteshi, L. Antecedents & outcomes of work–family facilitation & family work facilitation among frontline hotel employees. *International Journal of Hospitality Management*. 2008; 27(1): 517–528.
- Deery, M.A., & Shaw, R.N. An Investigation of the Relationship between Employee Turnover & Organisational Culture. *Journal of Hospitality & Tourism Research*. 1999; 23(4): 387-400
- Rowley, G. & Purcell, K. As cooks go, she went: Is labour churn inevitable? *International Journal of Hospitality Management*. 2001; 20(2) 163-185.
- Greenhaus, H.J., Collins, M.K. & Shaw, D.J. The relation between work-family balance & quality of life. *Journal of Vocational Behaviour*. 2003; 63(1): 510-531.
- Adams, G.A., King, L.A., & King, D.W. Relationships of job & family involvement, family social support, & work-family conflict with job & life Satisfaction. *Journal of Applied Psychology*. 1996; 81(4): 411-420.
- Dixon, M. A., & Warner, S. Employee satisfaction in sport: Development of a multidimensional model in coaching. *Journal of Sport Management*. 2010; 24(2):139-168.
- Evans, A. & Vernon, K. WLB in Hong Kong: Case Studies. *Community Business*, June 2007.
- Pocock, B. Work care regimes: institutions, culture & behavior: the Australian case. *Gender, Work & Organization*. 2005; 12(1): 32-49.
- Graham, C.W., Sorell, G. T., & Montgomery, M. J. Role related identity structure in adult women. *Identity: An International Journal of Theory & Research*. 2004; 4(3): 251-271.
- Greenhaus, J.H, & Powell, G. N. When work & family are allies: A theory of work family enrichment. *Academy of Management Review*. 2006; 31(1): 72-92.
- Beham, B. & Drobnic, S. Satisfaction with work-family balance among German office workers. *Journal of Managerial Psychology*. 2010; 25(6): 669-89.
- Kirchmeyer C. Perceptions of non-work-to-work spillover: Challenging the common view of conflict-ridden domain relationships. *Basic & Applied Social Psychology*. 1992; 13(1): 231–249.
- Lockwood, N. R. Work/life balance: challenges & solutions. *Society for Human Resource Management: Research Quarterly*. 2003; 2(1): 1-12.
- Sturges, J. & Guest, D. Working to live or living to work? Work/life balance early in the career. *Human Resource Management Journal*. 2004;14(1): 5-20.
- Magnini, Vincent P. Underst & ing & reducing work-family conflict in the hospitality industry, *Journal of Human Resources in Hospitality & Tourism*. 2009; 8(1): 119-136.
- Yildiz Z. The development of tourism sector & its effect on employment. *Visionary E-Journal*. 2011; 3(5): 54-71.
- Almeida, H., Campello, M. & Weisbach, M.S. The Cash Flow Sensitivity of Cash. *Journal of Finance*.

- 2004;59(1):1777-1804.
20. Cullen, J. & McLaughlin, A. What drives the persistence of presenteeism as a managerial value in hotels? Observations noted during an Irish work-life balance research project. *International Journal of Hospitality Management*. 2006;25(3): 510-516.
 21. Deery, M. Talent management, work-life balance & retention strategies. *International Journal of Contemporary Hospitality Management*. 2008;20(7): 792-806.
 22. Farrell, K. Work-home balance: A management perspective. *Hospitality & Society*. 2012;2(3): 273-291.
 23. Ozdevecioglu, M., & Doruk, C. N. The effects of work family conflict & family work conflict on employee's job & life satisfaction in organizations. *Erciyes UniversitesiIktisadiveIdari Bilimler Fakultesi Dergisi*. 2015; 0(33): 69-99.
 24. Kauppenen, T. The 24 hour society & industrial relations strategy' paper presented at the 6th European Congress of International Industrial Relations Association (IIRA) Oslo. 2001.
 25. Bartholomew, P. S., & Garey, J. G. An analysis of determinants of career success for elite female executive chefs. *Hospitality Research Journal*. 1996; 20(2): 125-135.
 26. Aryee, S., Srinivas, E.S., & Tan, H.H. Rhythms of life: Antecedents & outcomes of work-family balance in employed parents. *Journal of Applied Psychology*. 2005; 90(1):132-146.
 27. Minnotte, K. L. Perceived discrimination & work to life conflict among workers in the United States. *The Sociological Quarterly*. 2012; 53(2): 188-210.
 28. Biggs, A., & Brough, P. Investigating the moderating influences of gender upon role salience & work-family conflict. *Equal Opportunities International*. 2005; 24(2): 30-41.
 29. Eagle, B. W., Miles, E. W., & Icenogle, M. L. Inter role conflicts & the permeability of work & family domains: are there gender differences? *Journal of Vocational Behavior*. 1997; 50(2): 168-184.
 30. Emslie, C., Hunt, K., & Macintyre, S. Gender, work-home conflict, & morbidity amongst white-collar bank employees in the United Kingdom. *International Journal of Behavioral Medicine*. 2004; 11(3): 127-134.
 31. Milkie, M.A., & Peltola, P. Playing all the roles: gender & the work-family balancing act. *Journal of Marriage & Family*. 1999; 61(2): 476-490.
 32. Stevens, D. P., Kiger, G., & Riley, P. J. His, hers, or ours? Work-to-family spillover, crossover, & family cohesion. *The social science journal*. 2006; 43(1): 425-436.
 33. Swanson, V., Power, K. G., & Simpson, R. J. Occupational stress & family life: a comparison of male & female doctors. *Journal of Occupational & Organizational Psychology*. 1998; 71(10): 237-260.
 34. Triplett, R., Mullings, J. L., & Scarborough, K. E. Examining the effect of work home conflict on work related stress among correctional officers. *Journal of Criminal Justice*. 1999; 0(27): 371-385.
 35. Winslow, S. Work-family conflict, gender, & parenthood. *Journal of Family Issues*. 2005; 26(1): 727-755.

Perceptions of Nurses Regarding Barriers to Implement Maternal and Newborn Care at Rural Community Health Centers of Madhya Pradesh, India: A Phenomenology Study

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Abstract

Introduction: Nurses are vital to providing high-quality rural maternity care throughout the continuum of adolescence, pregnancy, birth and postpartum period. Objectives: The objective of this study is to examine the barriers perceived by nurses in maternal and newborn care at community health centers in rural areas of India. Material and Method: A qualitative study was conducted to identify barriers at two selected community health centers of Madhya Pradesh. Participants were interviewed and data were analyzed using Atlas.ti software. Results: Major themes that surfaced during data analysis were related to manpower, facilities, nurses, culture and rural area. Conclusion: It is very crucial to address these reported barriers in order to provide better & evidence based maternal and newborn care in rural areas.

Keywords: Nurses perception, Rural health care, Barrier, Maternal care, Neonatal care.

Introduction

WHO fact sheet on maternal mortality (2017) projected that approximately 810 women die every day across the world due to pregnancy related complications¹. A wide gap in maternal mortality ratio (MMR) has continued to persist between developed, developing and least-developed countries. About 94% of maternal deaths have been reported in the low and middle-income countries¹. In 2017, Nigeria and India had the highest estimated numbers of maternal deaths, accounting for approximately one third (35%) of estimated global maternal deaths². MMR in India has declined in the last ten years from 254 (2004–2006) to 130 (2014–2016)³. As per NITI Ayog Data (2014-16) MMR in India is 130 per 100000 live births and needs to be improved to 100 by 2020^{4,5}. Current maternal mortality ratio in Madhya Pradesh is 173 which is significantly high in comparison

to the national database and thus is a matter of grave concern⁶.

The global health observatory data about infant mortality rate (IMR) in India is alarming. In 2017, 4.1 million infant deaths occurred within the first year of life^{5,7}. Inequality in IMR persists among the States/ Union Territories of India. It ranges from 9 in Manipur to 50 in Madhya Pradesh for 2015⁸.

Majority of the maternal deaths occur due to severe bleeding, infections in post-natal period, high blood pressure during pregnancy and complications during delivery and unsafe abortion¹. A skilled pair of hands to help mothers and newborns around the time of birth, along with clean water, adequate nutrition, basic medicines and vaccines, can make the difference between life and death⁹.

Women who reside in rural and remote communities should receive high-quality care near to her home. It should be collaborative & women and family centered^{8,10}. Given the non-availability of doctors in remote areas of India nurse's role and contribution is imperative. Nurses are essential for the provision of high-quality rural maternity care throughout pregnancy, birth and the post-

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partum period^{8,10}. Under the national health mission (NHM) initiative of the government of India, there is a strong felt need for providing newer roles to nurses in far-flung areas where doctors are not available¹¹.

Nursing care providers in remote areas of the country face many barriers while providing maternal & neonatal care. Therefore, the objective of this study is to assess the perceptions of nurses regarding the barriers to maternal and newborn health-care –in rural community health centers (CHC) of Madhya Pradesh.

Material and Method

Study area: The study was conducted in the state of Madhya Pradesh. A rural district with 77 % of rural population was selected from Bhopal division. Out of total CHCs of the study district two CHCs one maximum and one minimum performing CHC were selected. Maximum and minimum performing CHC selection was based on Health Management Information System (HMIS) indicators such as the percentage of institutional deliveries to total ANC registration in the year 2018-2019.

Participant's Selection Criteria: Three categories of nurses based on their experience in maternal and newborn care were selected. Category 1- Experience more than 10 years, category 2- Experience between 5 to 10 years, category 3- Experience less than 5 years. Two pilot interviews were conducted.

Research Study Method: In-depth interviews of nurses were conducted between May and August 2019. The duration of each interview ranged from twenty to sixty minutes. All interviews were conducted at the CHCs and in Hindi language. Each interview was audio recorded by the researchers.

Ethical Considerations: Administrative approvals from government authorities were obtained. Investigator obtained written informed consent from each participant prior to start of each interview. The data collected from participants was kept confidential.

Trustworthiness: It was ensured by following the Guba's (1985) four criteria credibility, Transferability, dependability and conformability^{11,12}. Robust triangulation method were applied to enhance the confirmability of data and constructs emerged from current study.

Analysis: Total of six interviews (3 nurses from

minimum performing and 3 from maximum performing) were analyzed by Atlas.ti qualitative data analysis software.

Results

Table 1: Demographic distribution of participant's profile (N=6)

Age (Years)	Qualification	Year of Experience
37	G.N.M.	13
25	G.N.M.	03
26	P.C B.SC Nursing	05
47	G.N.M.	20
30	G.N.M.	05
28	G.N.M.	04

Participant's age varied between 25 to 47 years. Their experience also varied between 3 to 13 years.

Barriers observed by Nurses:

1. Manpower Linked:

Shortage of Nurses: The majority of the participants have voiced their concern that there is an extreme shortage of nurses as per workload.

"Number of nurse's post must be enhanced"

If one nurse goes on leave another nurse has to do double shift or when patient load increases nurses are asked to return from home after their scheduled duty hours to assist.

"There are lots of vacant posts of nurses. Many nurses retired but vacant post is not filled."

Shortage of specialist doctor: Doctors who are working at community health center are MBBS qualified and they are not expert in labour cases and newborn care.

"We don't have Obstetrics and Gynecology specialist, if we would have, we could do LSCS (Lower Section Caesarean Section) here only"

Shortage of supporting staff:

"we have problem of laundry, Dai (Birth Attendants), security guards"

2. Facility Linked:

Infrastructure: Lack of diagnostic facilities creates difficulty in the decision-making process in obstetric emergency cases.

“There is lack of investigation services on twenty-four hours basis”.

Participants expressed the opinion that management of postpartum hemorrhage (PPH) cases in absence of any arrangement for blood transfusion is risky.

“There is lack of blood transfusion facilities. We provide basic care. As we do not have blood bank, that’s why no major surgeries are performed here”.

Lack of medicine inventory management:

A participant informed that medicine supply and consumption are not balanced.

“We get sufficient medicine. Some medicine like dopamine & hydrocortisone are not prescribed to patients, hence these medicines expire. There should be rational use of medicine.”

Inadequate basic facilities: Nursing is a noble profession however these professionals are struggling for basic amenities like toilet etc.

“We do not have exclusive duty rooms while on night duty, we take rest in a meeting room. Earlier we use to sleep on floor while night duty”

Security and safety threats: Almost all participants expressed their concern regarding safety and security threats while on the job.

“I don’t feel safe, when I am on duty as there is no security guard, no other gents. We fight for our self as compare to security guards”.

3. Nurses Linked:

Unclear task shift to nurses: One of the key themes which emerged from narration was that task assignment to individual nurses is frequently ambiguous making for difficulty in effective discharge of duty.

“Many times, doctors do not support us if we commit any mistake. We feel fear when we work alone like dealing with PPH cases and eclampsia cases”.

Nurses are targeted by everyone related to the health system.

“I bear because he is a patient if he lodges a complaint to government, ultimately government will blame me.”

Direct patient care is the prime responsibility of nurses however due to administrative reasons nurses are engaged in clerical work like data entry and maintenance of register.

“Sometimes I feel bad as we have to maintain many registers”

“We do pending work at our home finish my register and other pending documentation at home. In hospital clinical work is our top most priority.”

No promotion opportunity: Senior participants reported the lack of any scope for career progress.

“I will be working as staff nurse only from joining to retirement. We should have opportunity to get promotion. I wish to upgrade from class three to class two rank.”

Contractual Job: Another challenge faced by some nurses is the absence of job and hence financial security as they are hired on contractual basis.

“I am on contractual basis. Salary is not sufficient. Many times, I wish I should also get a permanent job”

No provision of financial incentive for higher education: Nurses did not get any financial incentive after acquiring higher education.

“After completion of course our skills improve but financial raise should be there it will sustain our motivation.”

Ineffective patient-provider communication: Effective communication is the key to fruitful maternity health care. However the participants highlighted the difficulties they face while trying to interact with patients which ranged from simple lack of understanding to even outright verbal arguments.

“I explain multiple time same thing to patients and they expect again same repetition.

“Sometime family member approach us and tell there is patient in labour go and see her, when we ask bring patient here, they start fighting with us”.

4. Culture Linked: Male gender preference: The participants revealed that the rural community is still heavily biased towards the male gender of the child and thus while conducting deliveries nurses have to act accordingly.

“If women deliver a son family feels okay if women deliver second son than it superb and satisfactory for them. If a daughter born then everyone seems to be sad. Then we support and encourage mother”.

The participants in this study also reported that many myths regarding breastfeeding are prevalent in the rural society and they try hard to dispel them while at the same time motivating the new mothers to opt for early feeding.

“Relatives say that yellow color milk is bad and it should be discarded but we encourage that it should be fed to baby.”

Post-natal care practices: Similarly, the participants also shed light on the myths regarding post-natal maternal and neonatal care that they have to fight against. One common practice followed in Bhopal is the burning of cow dung to generate smoke which is then aired to the genitalia of women who recently delivered. New mothers are not allowed to consume ordinary food while neonates are fed honey and pre-lacteal feed.

“There are many factors such as myths of patients like eating harira just after delivery

“They often give honey to new born, apply oil on umbilical cord, prelactal feedings etc. (participant number three)

Rural area linked: Many participants voiced their issues that arise as a result of serving in rural areas for which they either have to commute daily or as an alternative have to reside away from their spouse/family.

“I am sacrificing a lot here; I live alone with my younger daughter in campus & manage it with many difficulties. My nights are sleepless.”

On the other hand nurses who are young and unmarried experienced a different kind of problem while adapting to rural lifestyle. They spoke of loss of freedom of attire and the sarcastic comments from male family members that they have to bear while working in hospital. Often their youth was equated with inexperience by their patients and thus adding to their issues in patient interaction.

“My dressing style is different; mostly I wear western dresses so people take it in other way that why I pretend as a strong woman. When I insert intravenous cannula, male patients pass sarcastic comments such as

sister be gentle, I feel bad as I could sense what actually they mean.”

“I am unmarried that’s why many women hesitate to tell me their history. I am short heighted and young so many patient and family members are doubtful in my abilities to handle labour cases.”

Limited internet connectivity: Limited network connectivity was a major barrier perceived by the participants.

“This is a small place & I cannot do many online works. I can’t apply online for other job even I could not process renewal of my Registration certificate as there is no cybercafé here.”

Discussion

Analysis of participant’s interviews verified that spectrum of barriers ranges from shortage of nurses coupled with high patient volume and low supporting staff. Similar constraints have been previously reported by other studies¹³⁻¹⁵. It has thus been suggested that sufficient staffing of nurses in rural health centers should be enacted to compensate for nursing shortage and to enhance the efficiency of public health care services in rural areas¹⁵.

Results of the current study demonstrates that extensive documentation work required for keeping detailed records of the maternal and newborn health care dispensed by the CHCs was a burden on already overworked nurses. Factors that compound this problem such as time, the attitude of the midwives and the relatively few numbers of midwives working in each shift have also been reported by Dike et al. in 2015 from their study conducted in Nigeria¹⁶. Fear of blame was evident from the respondent interviews. Nurses are not only blamed by doctors but also by patient and family members in adverse situations. These findings were supported by published literature.^{13,15}. An article published in 2014 lists other prominent fears reported by nurses such as the death of a baby at the time of delivery, missing something that causes harm, obstetric emergencies, maternal death, being watched, being the cause of a negative birth experience, dealing with the unknown and losing passion and confidence around normal birth¹⁷. Research findings of this study illustrates that nurses are deprived of basic facilities such as a decent duty room, toilet, and even seating space. Similar results have been found in other studies as well¹⁸.

Unavailability of basic facilities is not conducive to delivery of effective health care.

In the current study nurses were not provided any accommodation facility within the campus of the community health centers to which they were attached which was a major cause of disquiet among the respondents. Working in rural areas away from their native place seems to adversely affect the family life of nurses and this finding is supported by an article published by Sumankuuro et al. in 2018¹⁵. Priscilla Poga (2019) also highlighted in her study that accommodation plays a vital role in staff retention^{16,18}. Security and safety threats were widely reported by nurses in our study. The study by Poga also showed that nurses are generally more concerned with the 'internal factor' of safety than with other external factors. It reveals that safety at the workplace is highly prized by rural nurses because without it, they cannot achieve their aims¹⁸.

Manpower linked barrier such as shortage of specialist doctors and supporting staff also emerged as a major theme in this study. Similar constraints have been reported in different studies^{14,15}. Further, this study has identified several cultural linked barriers such as male gender preference, myths about breast feeding and intra-natal and post -natal maternal care rituals. Results of a similar nature have been published by other studies as well^{14,15}. Rural area linked barriers such as Illiterate community, limited telephone network and internet connectivity has been revealed by this study. Young nurses in our study, especially those hailing from different ethnic and language backgrounds faced diverse challenges in integration and acceptance as has documented previously¹⁹.

Limitation of study: This study has been conducted focusing on the nursing staff of the selected community health centers of rural Madhya Pradesh and the challenges faced by nurses working in the limited geographic area might not accurately represent the scenario faced by nurses elsewhere. Such individual expression bias and lack of generalizability is inherent to the qualitative research methodology and thus persists in our study as well. However, the contextually rich data obtained through in-depth interview compensates for any loss in reproducibility.

Conclusion

To improve maternal and neonatal health care in the rural sector it is of utmost importance to resolve the

barriers identified by this study. Manpower shortage should be addressed on a priority basis & measures to improve the diagnostic resources available in rural health care setting need to be considered. Task delegation of nurses should be unambiguously defined. Career progress schemes are vital to motivate and retain nurses working in rural areas. Basic amenities for nurses such as provision of duty room and nurses work stations must be provided. Effective communication is vital for both patient and nurse's satisfaction and thus nursing staff should be educated regarding the same. Finally, the felt need to generate awareness among the rural community about the significance of following evidence-based maternal and newborn healthcare should be acknowledged by policymakers and appropriate efforts should be initiated.

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Source of Funding: Self funded.

Ethical Clearance: Administrative approval taken from concern officials. Written consent were obtained from each participant.

References

1. Maternal mortality Available at <https://www.who.int/news-room/fact-sheets/detail/maternal-mortality>.
2. Trends in maternal mortality 2000 to 2017: estimates by WHO, UNICEF, UNFPA, World Bank Group and the United Nations Population Division. Geneva: World Health Organization; 2019. Licence: CC BY-NC-SA.0 IGO. Available at <http://documents.worldbank.org/curated/en/793971568908763231/pdf/Trends-in-maternal-mortality-2000-to-2017-Estimates-by-WHO-UNICEF-UNFPA-World-Bank-Group-and-the-United-Nations-Population-Division.pdf>.
3. Sarma UC, Kakoty SD. Maternal mortality: An equity issue. Indian journal of public health. 2017 Oct 1;61(4):231. Available from: https://doi.org/10.4103/ijph.IJPH_323_17.
4. Data from Niti Ayog Govt of India. Maternal Mortality Ratio (MMR) (per 100000 live births). Available at: <https://niti.gov.in/niti/hi/content/maternal-mortality-ratio-mmr-100000-live-births>.
5. National Health Policy. Ministry of Health and Family Welfare. Government of India; 2017. p. 4, 11. Available from: <https://mohfw.gov.in/documents/policy>.

6. SRS Bulletin Sample Registration System, Office Of The Registrar General, India Available at http://censusindia.gov.in/vital_statistics/SRS_Bulletins/SRS_Bulletin-Rate-2017-_May_2019.pdf.
7. Infant mortality: Situation and trends Available at https://www.who.int/gho/child_health/mortality/neonatal_infant_text/en/.
8. State/UT-wise Infant Mortality Rate (IMR), 2015. Available at <https://data.gov.in/resources/stateut-wise-infant-mortality-rate-imr-2015>. accessed on 30.12.2019.
9. Surviving birth: Every 11 seconds, a pregnant woman or newborn dies somewhere around the world Available at <https://www.unicef.org/press-releases/surviving-birth-every-11-seconds-pregnant-woman-or-newborn-dies-somewhere-around>.
10. Miller KJ, Couchie C, Ehman W, Graves L, Grzybowski S, Medves J, et al. Rural maternity care. *J Obstet Gynaecol Can.* 2012;34(10):984-991. doi: [https://doi.org/10.1016/S1701-2163\(16\)35414-7](https://doi.org/10.1016/S1701-2163(16)35414-7).
11. Crisp N. Nursing—the wave of the future. *BMJ.* 2018;361. doi: <https://doi.org/10.1136/bmj.k2355>.
12. Shenton AK. Strategies for ensuring trustworthiness in qualitative research projects. *Education for Information.* 2004;22(2):63-75. doi: <https://doi.org/10.3233/EFI-2004-22201>.
13. Liu L, Oza S, Hogan D, Chu Y, Perin J, Zhu J, et al. Global, regional, and national causes of under-5 mortality in 2000–15: an updated systematic analysis with implications for the Sustainable Development Goals. *Lancet.* 2016;388(10063):3027–3035. doi: [https://doi.org/10.1016/S0140-6736\(16\)31593-8](https://doi.org/10.1016/S0140-6736(16)31593-8).
14. Saxena, M., Srivastava, A., Dwivedi, P., & Bhattacharyya, S. (2018). Is quality of care during childbirth consistent from admission to discharge? A qualitative study of delivery care in Uttar Pradesh, India. *PLoS ONE.* 13(9):1–20. doi: <https://doi.org/10.1371/journal.pone.0204607>.
15. Sumankuuro J, Crockett J, Wang S. Perceived barriers to maternal and newborn health services delivery: a qualitative study of health workers and community members in low and middle-income settings. *BMJ Open* 2018;8:e021223. doi: <https://doi.org/10.1136/bmjopen-2017-021223>.
16. Dike FM, Onasoga OA, Njoku E. Documentation in labour among midwives in Madonna university teaching hospital elele, rivers state, Nigeria. *Int J Reprod Contracept Obstet Gynecol* 2015;4(5):1404-1409. doi: <http://dx.doi.org/10.18203/2320-1770.ijrcog20150719>.
17. Dahlen HG, Caplice S. What do midwives fear? *Women Birth.* 2014;27(4):266-270. doi: <https://doi.org/10.1016/j.wombi.2014.06.008>.
18. Poga P. Exploring the sustaining factors that motivate nurses to work in the rural areas of Papua New Guinea. Available at <https://pdfs.semanticscholar.org/e15d/9ea5ca6f7fc6f84197f807bd313fc71cad20.pdf>.
19. Morgan MC, Dyer J, Abril A, Christmas A, Mahapatra T, Das A, Walker DM. Barriers and facilitators to the provision of optimal obstetric and neonatal emergency care and to the implementation of simulation-enhanced mentorship in primary care facilities in Bihar, India: a qualitative study. *BMC Pregnancy Childbirth.* 2018;18(1):1-4. doi: <https://doi.org/10.1186/s12884-018-2059-8>.

Morphological Study of Neurons in the Trigeminal Ganglion

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Abstract

The pseudounipolarneurons in the trigeminal ganglia carry sensation from the face to the brainstem. These neurons vary in its sizes that carry specific sensations. In this study trigeminal ganglion neurons are classified based on its diameters in to three types namely large, medium, small sized with the help of histomorphometry. The small sized neurons of trigeminal ganglion modulate pain sensation in migraine. To classify the trigeminal ganglion neurons in to large, medium and small sized and to study the diameter of the neurons in the trigeminal ganglion. Neurons in the trigeminal ganglion which is also sensory ganglion homologues to dorsal root ganglion were classified based on its diameter in to small (approx. > 22). Most nociceptors are responding to touch and pressure, thermal and chemical stimuli. Large neurons thatis mainly nociceptive.

Keywords: Pseudounipolar neurons, trigeminal ganglion, histomorphometry.

Introduction

Trigeminal ganglion is a ganglion on the sensory root of the fifth cranial nerve situated in a cleft within the dura matter on the surface of the pars petrosa of the temporal bone, and giving off the ophthalmic and maxillary and part of the mandibular nerve called also Gasserian or semilunar ganglion.¹ It comprises pseudounipolar neurons from three divisions of the trigeminal nerve. The pseudounipolar neurons can be classified in to different types based on its diameter in to type 1 cells that are large and contain scattered clumps of nissil substance connected to myelinated nerve fibres.² The remaining cells are classified as type II cells which are small sized

and contain coarser clumps of nissil substance connected mainly to unmyelinated nerve fibres. The small sized neurons of trigeminal ganglion modulate pain sensation in migraine.³ The aim of the present study to classify the trigeminal ganglion neurons in to large, medium and small sized and to study the diameter of the neurons in the trigeminal ganglion.

Materials and Method

Male albino wistar rats (n=6) of weight ranging from 200g was the histomorphometry in the present study. The rats were obtained from experimental animal; facility of saveetha medical college. The animal was kept in cages with not more than the three animals in one cage.⁴ They were maintained at 12hrs:12hrs light/dark cycles with water and food available ad libitum.

Tissue Collection: Fixation was done using 500ml of 4% formaldehyde in 0.1M phosphate buffered saline, through transcardiac perfusion then dissect the rat brain trigeminal ganglion was identified and removed. Tissues were sectioned (20µm) using cryostat and stained with Cresyl violet.⁵

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Morphometric Analysis of Trigeminal Neurons:

The Cresyl violet stained sections were visualized using progRes image capture from senoptik progRes capture pro 2.7 (Germany) in 20x objective in an e-600 nikon compound light microscope.⁷ The diameters of the neurons from energy fifth section were measured using progRes image analysis software. The measured diameters were then divided into three types small sized, medium sized and large sized using spss software.⁸

Results

Table 1. Frequency distribution of maximum diameter of right side

Total Number of Neurons Measured – 1462

S.No.	Range	Frequency	Percent (%)
1.	10-20 µm	302	21.9
2.	21-30 µm	721	47.2
3.	31-40 µm	384	25.3
4.	41-50 µm	52	3.4
5.	51-60 µm	3	0.2

Table 2. Frequency distribution of maximum diameter of left side

Total Number of Neurons Measured – 1548

S.No.	Range	Frequency	Percent (%)
1.	10-20 µm	328	21.2
2.	21-30 µm	772	49.3
3.	31-40 µm	373	24.1
4.	41-50 µm	67	4.2
5.	51-60 µm	7	0.5
6.	61-76.58µm	1	0.1

Table 3. Results of statistical analysis using SPSS

Statistical Measures	Right Trigeminal Ganglia Neurons (µm)	Left Trigeminal Ganglia Neurons (µm)
Mean	26.19	26.30
Median	25.4	25.38
Standard deviation	7.45	7.50
Std error of mean	0.17	0.17
Range	48.75	66.32
Minimum	10.55	10.26
Maximum	59.31	76.59
Percentiles	33.33	22.18
	66.66	29.1

Statistical Analysis: The means of diameter of right and left side trigeminal ganglion were compared using

student test which was found to be significant P>0.05. The statistical data were explained in the tables below;

The diameters of the neurons measured were analysed statistically using SPSS software and the values were divided into three groups.

Table 4. Classification of neurons

Types of Neurons	Right Trigeminal Ganglia Neurons (µm)	Left Trigeminal Ganglia Neurons (µm)
Small Neurons	<22.10	<22.20
Medium Sized Neurons	22.11-29.0	22.21-28.80
Large Neurons	>29.01	>28.81

Discussion

Dorsal root ganglia neurons had been classified in three main types (A, B, C) on the basis of their size.^{9,10} Type A neurons are large neurons (40 – 75 in diameter) Type B neurons correspond to medium neurons (20 – 40 in diameter) whereas Type C neurons are the smallest cells with a diameter of less than 20.^{11,12} In the present study, Neurons in the trigeminal ganglion which is also sensory ganglion homologues to dorsal root ganglion were classified based on its diameter in to small (approx. >22) Each type of neurons is concerned with different sensation, for e.g. small and medium sized neurons are mainly concerned with pain and temperature which are called nociceptors.^{13,14} Most nociceptors are respond to touch and pressure, thermal and chemical stimuli.¹⁵ Large neurons that are mainly nociceptive.¹⁶

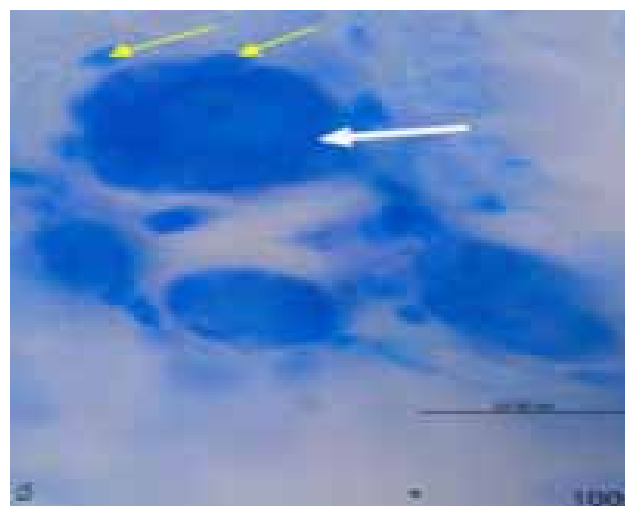


Figure 1: ACV stained picture showing large neurons (White arrow), Small Neurons (Red arrow) and satellite glial cells (Black arrow)

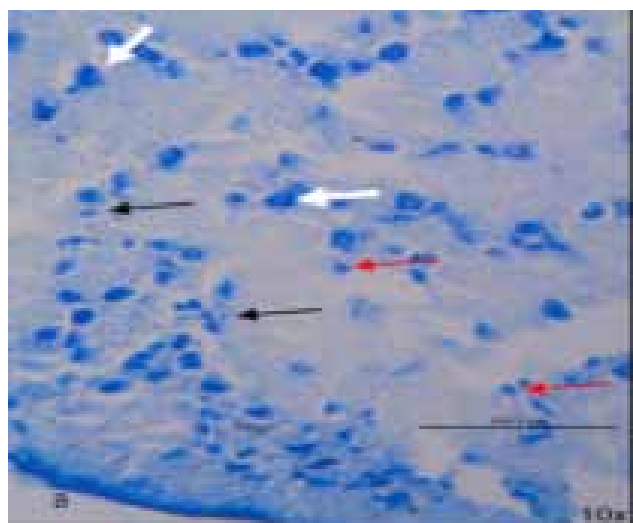


Figure 2: BCV stained picture Higher power showing large neurons (White arrow), and satellite glial cells (Yellow arrow)

Conflict of Interest: No Conflict of Interest

Source of Funding: Self

Ethical Clearance: Obtained from Institutional Animal Ethical Committee

References

1. Basbaum AI, Woolf CJ: Pain. Recognition and Alleviation of Pain in Laboratory Animals *Curr Biol* 1999; 9: 429-443.
2. Bensimon, G., Lacomblez, I., Meininger, V. and ALS/Riluzole study group: A controlled trial of riluzole in amyotrophic lateral sclerosis. *N. Engl. J. Med.* 1994; 330: 585-591.
3. Carlton SM, Hargett GL. Colocalization of metabotropic glutamate receptors in rat dorsal root ganglion cells. *J Comp Neurol* 2007; 501:780-789.
4. Danbolt NC: Glutamate uptake. *Prog Neurobiol* 2001; 65:100-105.
5. Doble A, The pharmacology and mechanism of action of riluzole. *Neurology.* 1996; 47: 233-241.
6. Hebert T, Drapeau P, Pradier L, Dunn RJ, Block of the rat brain IIA sodium channel α subunit by the neuroprotective drug riluzole. *Mol Pharmacol.* 1994; 45:1055-1060.
7. Iversen HK, Olesen J, Tfelt-Hansen P, Intravenous nitroglycerin as an experimental headache model. Basic characteristics. *Pain*, 1989; 38:17-24.
8. Mizoule, J., Meldrum, B., Mazadier, M, Croucher, M., Ollat, C., Uzan, A., Legrand 2-amino-6-trifluoromethoxy benzothiazole, a possible antagonist of excitatory amino acid neurotransmission I. *Neuropharmacology*, 1985; 24:767-773.
9. Messlinger K. Migraine: where and how does the pain originate? *Exp Brain Res.* 2009; 196:179-193.
10. Martin D., Thompson M. A. and Nadler J. V. The neuroprotective agent riluzole inhibits release of glutamate and aspartate from slices of hippocampal area CA1. *Eur. J. Pharmacol.* 1993;250: 473-476.
11. Moskowitz MA. The visceral organ brain: implication for the pathophysiology of vascular head pain. *Neurology*, 1991; 41:182-186.
12. Malick A, Burstein R. Cells of origin of the trigeminohypothalamic tract in the rat. *J Comp Neurol*, 1998;400:125-144.
13. Olesen J, Iversen HK, Thomsen LL. Nitric oxide is a key molecule in migraine and other vascular headaches. *Trends Pharmacol Sci*,1993;15:149-153.
14. Pardutz AI, Krizbai I, Multon S, Vecsei L, Schoenen J. Systemic nitroglycerin increases Nnos levels in rat trigeminal nucleus caudalis. *Neuroreport.* 2000; 11(14):3071-3075.
15. Prene, G.H. M., Gwan, G.K., Postema, F., Zuiderveen, F. and Korf, J.: Cerebral cation shifts in hypoxic-ischemic brain damage are prevented by the sodium channel blocker tetrodotoxin. *Exp. Neurol.* 1988; 99:118-132.
16. P.K. Sankaran., Histomorphometric study of neurons in the trigeminal ganglion in male wistar albino rats, 2012;4(6): 28-31.

Determinants Influencing Towards the Consumption of Green Products among the Consumers: A Structural Equation Approach

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Abstract

Rationale of the Study: The extensive writing on consumer of green newly focus by the marketers and markets. Even though consciousness environmental in Indian consumers is examined through the literature, their buying behavior towards products green is not so far implicit. Therefore, the present study is contemplate on make out the determinants influencing the consumption of green products in Chennai city.

Research Design: The research makes use of survey method technique to test a hypothetically grounded position of hypotheses. A simple convenience sampling method used and collected the data from 709 users of organic food products. To test the hypothesis of the study, the Structural Equation Modelling utilized.

Findings: The determinants, namely environmental protection, environmental responsibility, Experience of personal, Social Appeal aspect, and Environmental kindness, significantly influence the buying decision of green products in the study area.

Implications of the Study: The study results are useful to the marketing professionals of green products. It also helps the organizations to frame the strategies of marketing aspect and also helpful to the organizations to identify the consumer's perception and satisfaction of using green products.

Keywords: Consumer, Consumer Behaviour, Green Products, Research on Marketing.

Introduction

The attentiveness of annihilation of natural supplies out come from the behavior of human has lifted the subject of ecological fortification and the perception environment in behavior of consumer. It has enhanced the stipulate for green category merchandises in the market universal. A green category items defined the product manufactured using at no cost toxic components and environmentally-gracious process, and which specialized as distinguishd organization¹. Greening manufactured goods takes consign over its complete life-cycle from product intend and procurement of raw material to the process of production, storeroom, carrying, practice, and post-practice activities. While familiarity of users marketplace and capriciouss inspiring buying behavior

of green enlarge to have momentous implications. The cross-countries, studies connected to behavior of green, have observe the developing ecological consciousness in the mind of consumers. The study reveal prioritize of Indian consumers in different category products and services from environmentally gracious organizations and are becoming hard to please in their behavior of purchase in expressions of predilection for products of green, quality of product, their spirited values and their responsibility in the stores of product².

Decisions of Green product buying: The consumers of green are portrayed the environmental significances of their utilization prototypes and propose to change their buying intensions and the behavior of consumption for decreasing the environmental aspect.

The green consumers purchase decision originate to be the middle subject in the current condition of study on behavior of consumers related to green.

The decision of buying supporting the organizations of the green, preferences of eating green commodities and probable to expend additional for green products. Mostly two important factors pressure the buying decisions of green consumers. The genuine behavior outcome of consumers' habitual habits, product information, and the environmental factors namely the campaign of promotional.

Supporting Environmental Protection: Shore up environmental fortification is important causes for users to perform environmentally gracious in buying decision³. The users distinguish the responsibility of merchandises of green in increasing the excellence level of the atmosphere, and consumers demonstrate prop up for ecological safety by buying and owning products of green. The consumers capable to transmit the correctness of superior level prices of products category of green benefits suggested by them and build up a positive perception in the intelligences of consumers.

H1: Consumers are significantly influencing towards the buying behavior of green products for the prime reason for support of environmental protection

Environmental Responsibility: The environmental liability drive related to users commitment level towards the protection challenges and individual focuses to enhance the quality of atmosphere. Realizing the unhelpful impact of atmosphere on human and consumers know responsibilities for environmental protection. The users inspired by natural think about the excellence of the world and inhabitants create to be above all engaged in environmental protection . Consumers ecological apprehension, compassion, and conviction in the subsistence of environmental predicaments at the personality level to execute environmentally gracious.

H2: The consumers preferring towards the buying behavior of green products for the reason of environmental responsibility

Experience of Green Product: Consumers' understanding of green products an extra powerful variable to persuade green products buying decisions. The users inquisitiveness to increase knowledge about the environmental characteristics of green products. The users struggle to study about green products on

individual and increase comprehension related to ingredients of green products⁴. Additionally, the users shre the information and knowledge of green products with companions⁵. The product assessment facilitates them to recognize the environmental advantages of green products and outcomes in successfully mounting predisposition towards green products⁶.

H3: Consumers prefer the usage of green category products because of their personal experience of green products consumption

Social Appeal: Consumers increase and understand the meaning of products when the users interrelate with others and collect related in sequence⁷. Consumers fraction of a society or social group, obtain and contribute to information, and identify what others believe for a meticulous product⁸ and assess the products pedestald on the observations and opinion of others⁹. Besides, consumers usually attracted with the product that enhances a intelligence of self and the approach want to be distinguished by others. Thus, the widespread application create influential in developing the preference of prodcuts. Never the less, users be set to buy products that go behind the perceptions of culture as well as build their social-identitie¹⁰.

H4: The consumers Buying decision of green products because of excellent Social Appeal

The society of environmental gracious, users extensively distinguish the reputational and contemporary technique of lifestyle to perform environmentally friendly¹¹. It has emblematic meaning of principles, thinking, nature-orientation, and eco-objectives. It guides to decisive functional outcomes for users, i.e., pro-social standing of being reliable, expensive companion, and status (prestige).

H5: The Consumers Buying Decision of Green Products because of Environmental friendliness

Methodology

The study is concentrate on make out the determinants influencing the consumption of green products among the consumers in Chennai city. The study used both primary and secondary level data. The study used both primary level and secondary level data. The secondary level data collected through articles, magazines, and research papers. The primary information collected from the consumers of green products in Chennai city. Overall,

709 responses are finalized and used for the analysis. The study used a convenience sampling method. The data is collected from the users of organic product consumers in Chennai city. To evaluate the association between the determinants of green products and purchase decisions, the construct was developed¹². The constructs of the study, such as environmental protection, environmental responsibility, personal understanding, Social type Appeal, and Environmental easiness buying decisions of green products. The study used Structural Equation Model to measure the relationship connecting the determinants of green products and buying decision.

Results and Discussion

Demographic Profile of green products consumers in the study region and the results reveal that the majority of 52.6 of the consumers are male category. Age group-wise, 26.9% of the consumers are in the age group of 31-35 years. The study demonstrates that the majority of the consumers married. Regarding the educational

qualification of consumers, the majority 35.3% of the consumers under-graduates, and the monthly earnings concern majority 41.5% of the consumer’s monthly income between Rs.50,001 – Rs.1,00,000. The study also exhibited that around 52.3% of the consumers are salaried class.

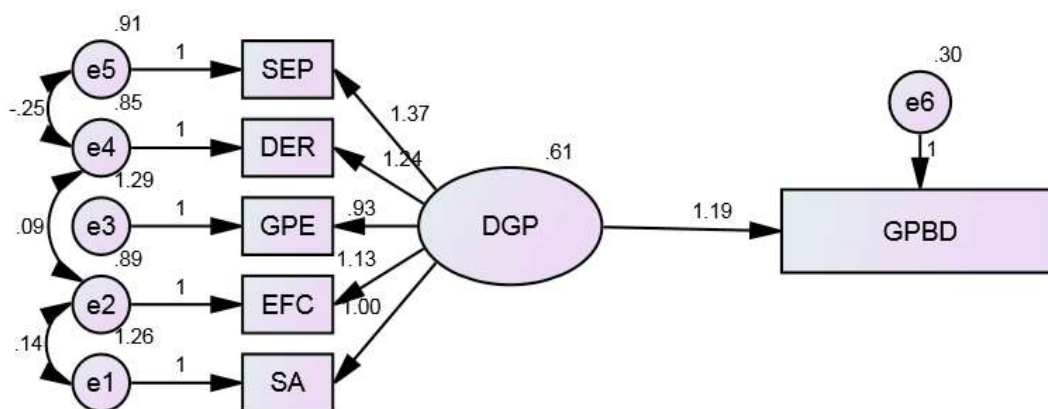
Structural Equation Modelling: SEM is a advanced statistical method that is utilized to scrutinize structural relationships. It the mixture of factor study and multiple model regression analysis, and it is utilized to scrutinize the structural relationship between measured segment of variables and latent type constructs. The hypothesized model of the study is whether the determinants of green products, namely support of environmental protection, environmental responsibility, personal experience, Social Appeal, and Environmental friendliness significantly influence towards the buying decision of green products in the study area. The SEM Model results are given below:

Parameter	CMIN/DF	P	GFI	AGFI	CFI	RMSEA
Results	1.628	0.135	0.995	0.984	0.998	0.030

The analysis indicates the CMIN/DF value is <3, GFI, AGFI, CFI values are >0.9, and the RMSEA value <0.05. Based on the results is that the proposed model is fit. The study inferred that the determinants of green products, namely support of environmental protection,

environmental responsibility, personal experience, Social Appeal, and Environmental friendliness, significantly influence towards the buying decision of green products among the consumers in the study area.

Determinants Influencing towards the Green Products Buying Decision among the Consumers



To test the proposed hypotheses of the study, i.e., Consumers are significantly influencing the buying behavior of green products for the prime reason for support of environmental protection. The output of the AMOS results indicates that the p-value for the buying behavior of green products for the prime reason for support of environmental protection is <0.01 . The results of the study maintain the hypothesis and confirm that environment protection significantly influencing consumers to use green products in the study area.

To examine the hypothesis, i.e., consumers preferring towards the buying behavior of green products for the reason of drive for environmental responsibility. The results mentioned that the p-value of these factors is <0.01 . The results of the study supported the hypothesis and inferred that environmental responsibility is also the prime reason for using green products in the study region.

As for the third hypothesis of the study is, Consumers prefer the usage of green category products because of their personal experience of green product consumption. The results indicate that the p-value is <0.01 . Therefore the could be inferred that the consumers are using the green products of their personal experiences. The study also supports that the consumers prefer to utilizing green products because of the environmental friendliness of the organization (p value= <0.05). The consumers inspired that the aspect of the environmental friendliness of the promoters. Supplementary, the connection linking social appeal of green product buying assessments is create statistically considerable of hypothesis (p= <0.05). it point outs individuals be part of environmentally welcoming culture and to put up up and prolong environmentally gracious customarys of income are additional credible to buy green products.

Conclusion

The enhancing environmental mindfulness of consumers inspired managers postion of green products to solicit details apprehensioning the environmentally welcoming buying behavior of consumers. The continuous advancement in the domain of green category research, current studies have concentrated on eating pattern, therefore the buying behavior of products green can be scrutinized. In the wake of these directions, the present study has endeavored to build up an considerate of consumers' observation of green products decreasing the effect of their eating patterns. The study results

specify that consumers in India have a high level of environmental consciousness, it is displayed in their green category product buying decisions. The consumers apprehensioned with environmental guard issues understand their responsibilities towards the protection, consider in the existence of environmental difficultys and their clarification at individual levels, comprehensively search for product-connected ecological information, and create environmentally gracious purchase decisions. The study inferred that the receipt of green products depends upon the commodities' environmental uniqueness needed by users. The research also registers that there is a meaningful association of supporting environmental shield and push for accountability of environmental with green category product buying conclusion substantiate that the choice to acquire a green product necessitates a free mindful assessment of environmental, personal, and social importance associated with products of green. It more indicates that consumers see for the accomplishment of their functional, emotional, and experiential requirements, which impact their buying decisions. It emulates an friendly existence in their using blueprints and the significance of green products to users. Subsequently, marketing experts for products green need speak how users attention about protection environmental and abilities environment are discussed by buy, using, and disposing of green products. Overall, the determinants, namely support of environmental protection, environmental responsibility, personal experience factor, Social Appeal aspect, and Environmental friendliness, significantly influence the buying decision of green group creations in the study area.

Conflict of Interest:- No potential conflict of interest was reported by the authors.

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Ethical Clearance: The research was approved by authors Institutions.

References

1. Gurău C, Ranchhod A. International green marketing: A comparative study of British and Romanian firms. *Int Mark Rev.* 2005;22(5):547-61.
2. Singh K, Saeed M, Bertsch A. Ethical Response Behavior: A Study of Indian Consumers. *Journal of Strategic Innovation and Sustainability.* 2012 Mar 1;7(3):16-34.

3. Gadenne D, Sharma B, Kerr D, Smith T. The influence of consumers' environmental beliefs and attitudes on energy saving behaviours. *Energy policy*. 2011 Dec 1;39(12):7684-94.
4. Laroche M, Bergeron J, Barbaro-Forleo G. Targeting consumers who are willing to pay more for environmentally friendly products. *Journal of consumer marketing*. 2001 Sep 19;18(6):503-20.
5. Khare A. Consumers' susceptibility to interpersonal influence as a determining factor of ecologically conscious behaviour. *Marketing Intelligence & Planning*. 2014 Jan 28.
6. Cegarra-Navarro JG, Martinez AM. Managing environmental knowledge through learning processes in Spanish hospitality companies. *The Spanish Journal of Psychology*. 2010 Nov; 13(2):827-40.
7. Oliver JD, Lee SH. Hybrid car purchase intentions: a cross-cultural analysis. *Journal of consumer marketing*. 2010 Mar 23.
8. Dholakia UM, Bagozzi RP, Pearo LK. A social influence model of consumer participation in network-and small-group-based virtual communities. *International journal of research in marketing*. 2004 Sep 1;21(3):241-63.
9. Escalas JE, Bettman JR. Self-construal, reference groups, and brand meaning. *Journal of consumer research*. 2005 Dec 1;32(3):378-89.
10. Ozaki R, Sevastyanova K. Going hybrid: An analysis of consumer purchase motivations. *Energy policy*. 2011 May 1;39(5):2217-27.
11. Grier SA, Deshpandé R. Social dimensions of consumer distinctiveness: The influence of social status on group identity and advertising persuasion. *Journal of Marketing Research*. 2001 May;38(2):216-24.
12. Kumar P, Ghodeswar BM. Factors affecting consumers' green product purchase decisions. *Mark Intell Plan*. 2015;33(3):330-47.

Effect of Methanolic Leaf Extract of *Ficus Religiosa* on Neuronal Degeneration: A Pilot Study in Male Albino Wistar Rats

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Abstract

The present study aims to evaluate the effect of *Ficus religiosa* (FR) leaf extract on aluminium chloride (AlCl₃) induced neurotoxicity in rats. Adult male albino Wistar rats were randomly arranged into 4 groups with 6 rats in each group. Group 1 was the control group, group 2 rats orally received 100mg/kg body weight of AlCl₃ for 25 days, group 3 and 4 comprise treated animals (*Ficus religiosa* leaf extract of 200mg/kg body weight and 300mg/kg body weight (per oral), respectively for 15 days) after the initial AlCl₃ administration for 25 days. On the last experimental day after FR treatment, behavioural changes were studied in all animals by passive avoidance test. Later the animals were sacrificed and the brain was removed & processed for histological study. Neuronal assay in the hippocampus of the brain tissue was conducted by staining with cresyl violet. In both behavioural test and neuronal assay, significant difference ($p < 0.001$) was seen when control and induced group AlCl₃ were compared. Similarly, when AlCl₃ administered rats were compared with FR extract treated rats, significant improvement ($p < 0.001$) was observed directing towards neuroprotective potential of FR leaf extract in aluminium-induced neurotoxicity.

Keywords: Hippocampus, *Ficus religiosa*, neurodegeneration, behaviour.

Introduction

There are many factors for neurodegeneration and aluminium (Al) is one among them, which enters our body knowingly or unknowingly¹. Aluminium accumulates in the hippocampus as well as frontal cortex of cerebrum. It can cause neurotoxicity, which increases the risk of neurological diseases like dementia and Alzheimer's disease (AD)^{2,3}. Al generates free radicals and is considered an attributing factor for the neurodegenerative disorders with alteration in behaviour and cognitive dysfunction^{4,5}. It is also reported that Al

causes loss of memory by producing inflammation in the brain⁶. AlCl₃, when administered in male Wistar rats for 30 days, increased the rate of lipid and protein damage in the brain⁷. Al has been found in the neurofibrillary tangle and senile plaques in brain of AD patients⁸. It is also believed that Al causes apoptotic loss of neurons, which is an indicator of neuronal degeneration in AD⁹.

Though there are several drugs available, which can control the neurodegenerative diseases, on many occasions these diseases are not properly treated. Adverse effects from the long term use of recognized drugs is also a concern. *Ficus religiosa* is a large tree, which consists of heart shaped, long tipped leaves. It is commonly known as 'peepal tree' in India¹⁰ and this has shown religious, mythological and medicinal importance¹¹. FR has phytoflavonoids and was used along with the antiepileptic drugs relieving the psychiatric and cognitive symptoms¹². Aim of our pilot study is to elucidate the effect of FR leaf extract on AlCl₃ induced neurodegenerative changes in the albino

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Wistar rats through behavioural and histomorphological parameters.

Materials and Method

Extract Preparation: The FR leaves were washed with water, dried over the shadow for one month, and made into a coarse powder form by using the grinder. About 70 grams of dried FR leaves coarse powder with methanol was placed in a Soxhlet apparatus, which was then heated to reflux. Methanol was used as a solvent in ratio of 1:1 along with distilled water. The heater of Soxhlet apparatus was set at 50°C and extraction procedure was performed for three days¹³, approximately 50 cycles. The silicon metallic balls were added on daily basis to identify the increased temperature. The extract was heated with Bunsen burner to evaporate methanol from the extract. The total dry extract was amounting to a yield of approximately 7%. This extract was kept in refrigerator (about 4°C) until further use.

Animals: The present study was carried on in-house bred male albino Wistar rats (12-16 weeks), weighing 200-250gms (at the commencement of the study) and they were given *ad libitum* food and water. The animals were accommodated in paddy husk bedded polypropylene cages, under controlled temperature, light and dark cycle (12:12 hours). Institutional animal ethics committee has given clearance for this investigation. The animals were maintained and used in accordance with the guidelines of government of India for the usage of laboratory animals¹⁴.

Animal Grouping: The rats were randomly distributed in 4 groups, with 6 rats in each group. The grouping details are as below:

Group 1: Control group

Group 2: Rats orally received 100mg/kg body weight of AICl₃ for 25 days

Group 3: Rats orally received 100mg/kg body weight of AICl₃ for 25 days. This was followed by 200mg/kg body weight of FR leaf extract orally for 15 days

Group 4: Rats orally received 100mg/kg body weight of AICl₃ for 25 days, which was followed by 300mg/kg FR leaf extract orally for 15 days

Induction of neuronal degeneration: The group 2, group 3 and group 4 rats were given AICl₃ solution

orally (100 mg/kg body weight) for 25 days to induce neuronal degeneration. The AICl₃ powder was mixed with distilled water and administered orally using oral gavage tube.

FR leaf extract treatment: The group 3 and 4 rats were treated orally with the FR leaf extract of 200mg and 300mg/kg body weight dosage respectively for 15 days. These group animals initially received oral AICl₃ for induction of neuronal degeneration.

Behavioural Study: Passive avoidance test: This behavioural test evaluates memory retention capability¹⁵. The apparatus had a large bright and a small dark area with floor having grid, which was attached to a shock source. On the 1st day of test, the rats were allowed to explore both the chambers for 5 minutes, which was followed by 3 test trials of 5 minutes each. The time spent in each compartment in each trial was noted. In the 4th trial, as soon as the rat moved into dark area, a foot shock was given and rats were replaced back in home cage. After 24 hours, rats were placed again in the test apparatus and their latency to enter the dark chamber was noted. Control group rats avoided moving into the dark chamber, as they remembered the shock stimulus given on previous day. Decreased latency of the rats to enter the dark chamber suggested reduced memory power in AICl₃ administered rats. The time spent in light chamber for each rat was noted in seconds and finally the mean value was calculated. This was done for all the groups individually and the data were expressed as mean ±SE. The analysis was done by using SPSS software (version 25). One-way ANOVA test was used to perform the comparison statistically. The 'p' value less than 0.001 was considered as statistically significant.

Histological Study: Perfusion and brain removal: Next day after the treatment with FR leaf extract, the animals were deeply anesthetized with sodium pentobarbital (40mg/kg body weight, given intraperitoneally). The heart was exposed by opening the chest cavity, followed by perfusion with 100-150ml of 0.9% normal saline through the left ventricle at a rate of 1ml per minute. This was followed by perfusion with 10% formalin at the same rate of flow. The brain was removed by dissecting cranial cavity in all the animals and kept in 10% formalin for 48 hours for further histological study.

Each brain was sectioned in coronal plane into two pieces and was kept in separate 10% formalin containers.

The posterior section was used in this study for the hippocampal neuronal assay. Standard histological tissue processing procedures were followed using different grades of alcohol and xylol. Paraffin blocks of the brain tissue were prepared and sections of 6-7 μ m thickness were taken using rotary microtome.

Staining: Cresyl violet is a reliable stain to study the morphological changes in the neurons as it highlights the structural features of it. This stain helps to count the number of neurons. In 100ml of distilled water, 100mg of Cresyl violet was dissolved and then 10% acetic acid is added to the same solution to reach a pH of 3.5 to 3.8.

Scoring: Six sections from each animal's brain was mounted serially on air-dried gelatinized slides. The slides were scrutinized with Nikon trinocular microscope (H600L) at 20X magnification. The imaging software NIS Elements Br version 4.30 was used to quantify the neurons. The number of viable neurons were counted in the CA3 region of both sides of hippocampus¹⁶. The cell count was expressed as the number of cells per unit length of the cell field (cells/250 μ m length) in hippocampus. The data is expressed as mean \pm SE. The analysis was done using SPSS software (version 25). One-way ANOVA test was used for statistical comparison. The 'p' value less than 0.001 was considered statistically significant.

Results

Among all cornuaamonis (CA) regions of hippocampus, CA3 region showed maximum neuronal degeneration in group 2 rats which were induced with AICI3 ($p < 0.001$). Fig. 1A shows the normal neurons at the CA3 region of the hippocampus in control (group 1) rats. The degenerated neurons were identified in 50X50 μ area by the disrupted cell membrane, pyknotic and peripheral nuclei or absent nuclei within the neuron (Fig. 1B). However, rats treated with FR leaf extract (group 3 & 4) showed significantly improved ($p < 0.001$) number (Fig. 3) as well as quality of neurons (Figs. 2A and 2B). The quality of neurons was better than that of the AICI3 induced group and they were with centrally placed nucleus and intact cell membrane. However, the difference was non-significant ($p > 0.05$) between group 3 and 4 with respect to the morphology of neurons in CA3 region of hippocampus (Fig. 3).

Similarly, the AICI3 administered rats showed significantly decreased latency to enter the dark compartment (Figure 4, $p < 0.001$) in AICI3 administered rats (group 2) when they were compared with that of control group rats (group 1). The latency again was enhanced significantly (Figure 4, $p < 0.001$) in FR extracted treated group of rats (group 3 and 4). However, there was no statistically significance difference in latency was observed between the animals of group 3 and 4 ($p > 0.05$).

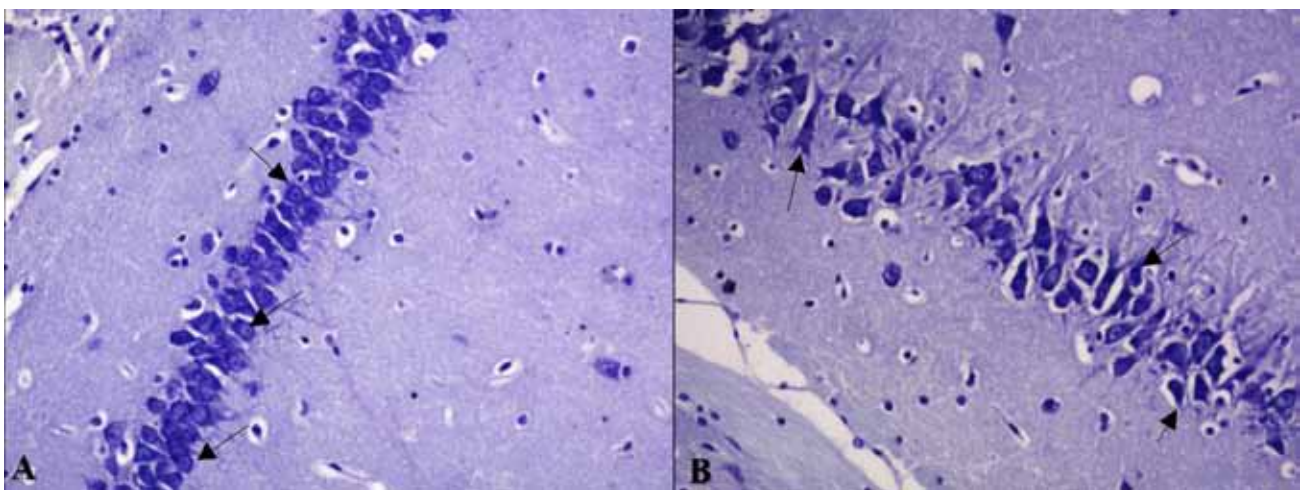


Fig. 1: Micrograph of CA3 region of hippocampus in control and AICI3 administered rats. Stain-cresyl violet, Magnification-20X; A - Group 1(control group) showing normal neurons (arrows); B - Group 2 (100mg/kg body weight of AICI3 for 25 days) showing degenerated neurons (arrows)

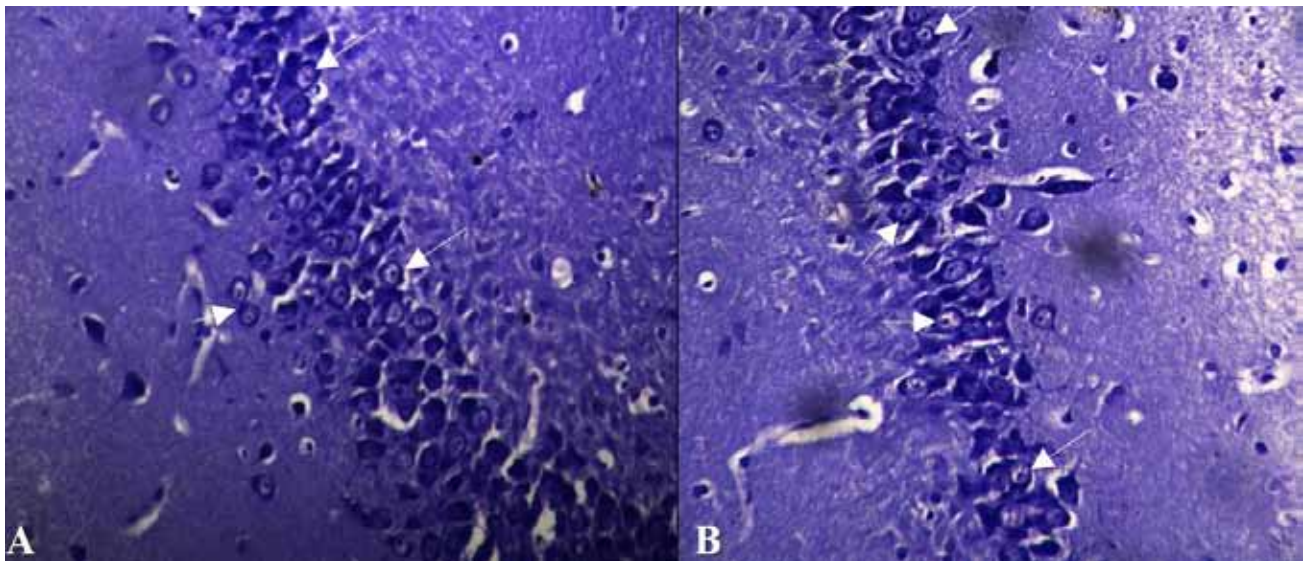


Fig. 2: Micrograph of CA3 region of hippocampus in FR leaf extract treated rats. Stain- cresyl violet, Magnification- 20X; A- Group 3 (200mg/kg body weight of FR leaf extract for 15 days) showing normal neurons (arrows); B- Group 4 (300mg/kg body weight of FR leaf extract for 15 days) showing normal neurons (arrows).

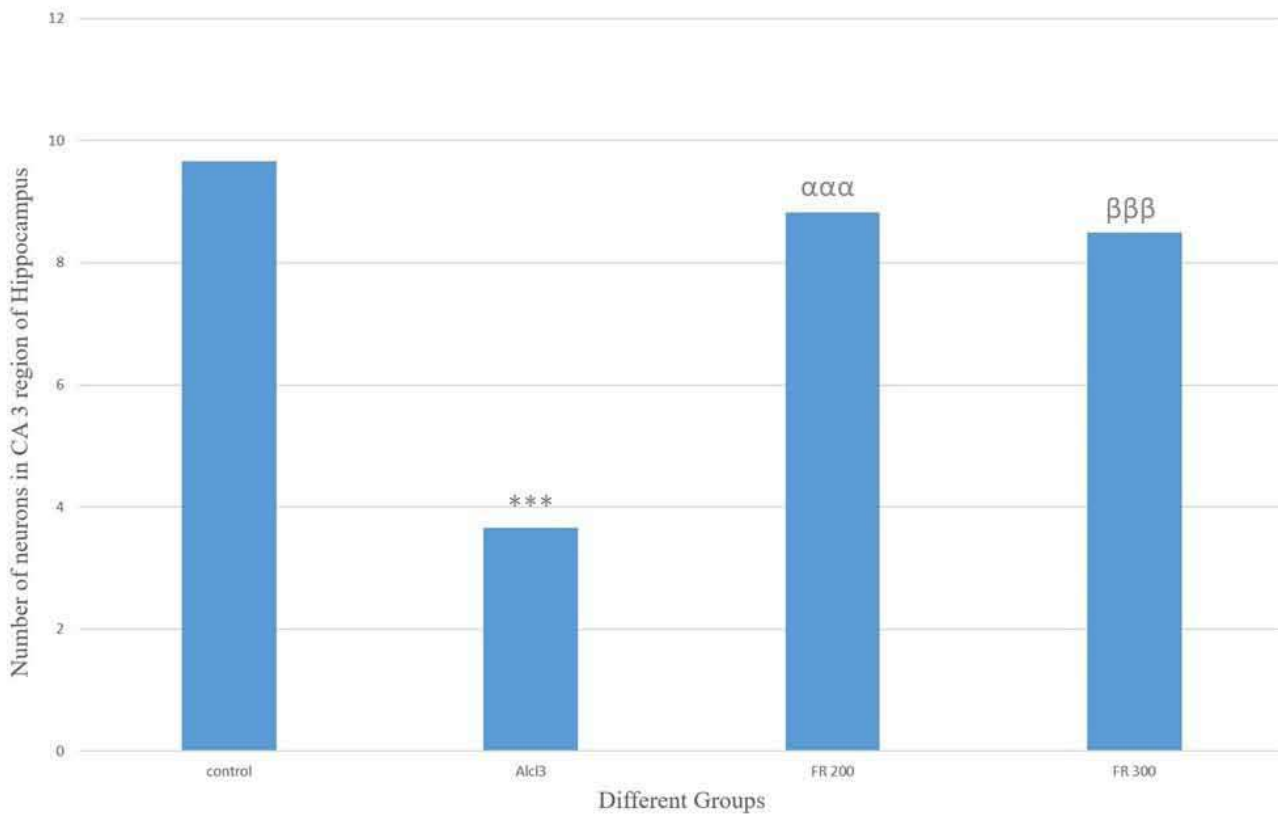


Fig. 3: Comparison of neuronal count at CA3 region of hippocampus in different groups

Control vs Alcl3 ***= p<0.001; Alcl3 vs. FR 200 ααα=p<0.001, Alcl3 vs FR 300βββ=p<0.001

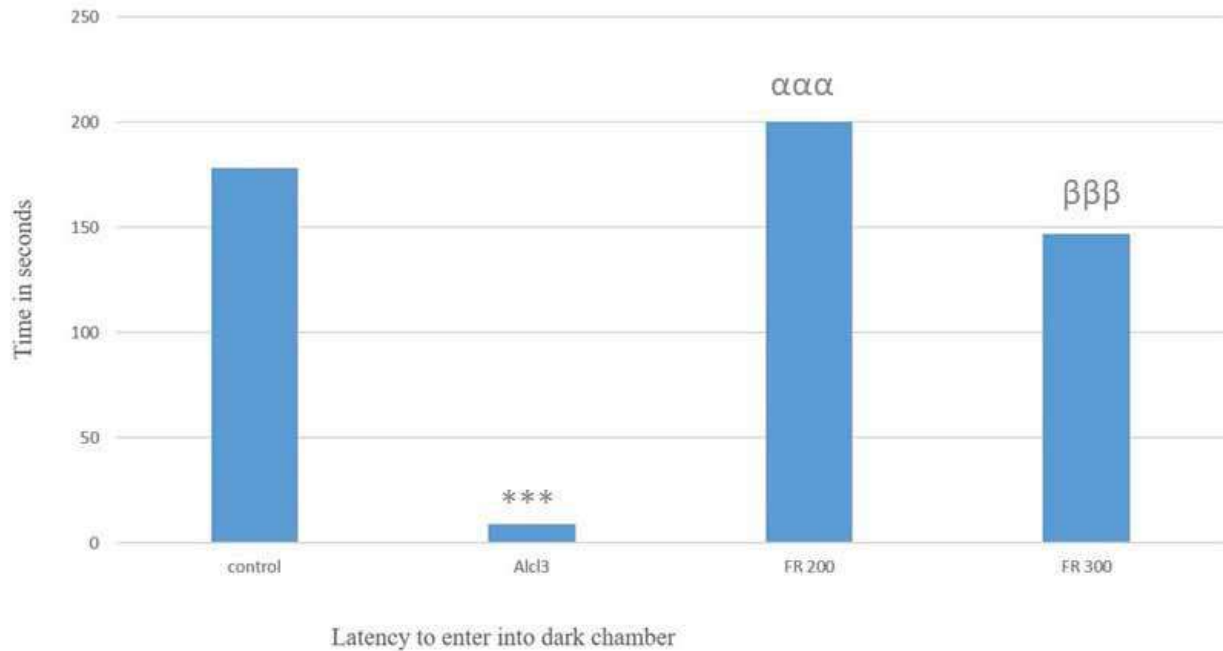


Fig. 4: Comparison of passive avoidance test result in different groups

Control vs AlCl3 *** = $p < 0.001$; AlCl3 vs. FR 200 ααα = $p < 0.001$, AlCl3 vs FR 300 βββ = $p < 0.001$

Discussion

Aluminium enters the body through drinking water, food, utensils, body deodorants and medicines¹. Roskams and Connor opine that Al crosses blood brain barrier through certain receptors¹⁷. Al accumulation leads to deteriorated antioxidant defence mechanism and increased amyloid deposition in the brain¹⁸. Al toxicity also causes necrosis and apoptosis, both types of neuronal cell death¹⁹. Al neurotoxicity causes memory loss, both short term as well as long term, and reduces locomotor activity²⁰. The present study displayed significantly decreased number of normal neurons in CA3 region of hippo campus in AlCl3 induced rats. The group 2 animals demonstrated chromatolysis of the neurons at the CA3 region. There was swelling of the perikaryon and eccentricity of the nucleus. These morphological features were suggestive of degeneration of neurons due to AlCl3. In the hippocampus CA3 region plays key role for memory consolidation, as suggested by Morris Maze study on mice²¹. The group 2 rats exhibited decreased latency period to enter the dark chamber, which was indicative of rats having dementia. Both these observations from the behaviour and microscopic study

of the neurons indicated that Al has induced neuronal degeneration.

Aiyegoro and Okoh²² warranted a thorough research for the competency of FR against neuro-inflammatory and neuropsychiatric disorders, as well as oxidative stress related disorders. AD can also be managed to some extent by the traditional usage of FR as suggested by Vinutha et al.²³. The present study hypothesizes that FR leaf extract may exert neuro-modulatory effect, leading to alleviation of AlCl3 induced inflammation-driven neurodegeneration. Bhangale et al.²⁴ have shown the promising effect of FR leaves on Huntington’s rat model. Petroleum ether extract of FR leaves disclosed beneficial effect in Parkinson’s induced rats²⁵.

Conclusion

The present study has witnessed increased latency of the Al administered rats to enter the dark compartment after FR treatment (groups 3 and 4), demonstrating their improved memory. This improvement in behavioural change was co-relating with the significantly improved normal neurons in the CA3 region of hippocampus in

FR leaf extract treated rats. Both these physiological and micro-anatomical observations were indicative of neuroprotective property of FR leaf extract. Therefore, this study believes that FR leaf extract is effective in oral doses and it may alleviate the symptoms of AD. This can be further endorsed with a larger sample size and more study parameters. This inference adds to the existing therapeutic benefits of FR and offers a substantial evidence for its future medicinal application.

Conflict of Interest: None

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Ethical Clearance: The ethics committee of our institution approved this research.

References

- Han D, Sen CK, Roy S, Kobayashi MS, Tritschler HJ, Packer L. Protection against glutamate-induced cytotoxicity in C6 glial cells by thiol antioxidants. *American Journal of Physiology* 1997; 273(5): R1771–R1778.
- Flaten TP, Aluminium as a risk factor in Alzheimer's disease, with emphasis on drinking water, *Brain Res. Bull.* 2001;55:187–196.
- Wang Z, Wei X, Yang J, Suo J, Chen J, Liu X, Zhao X. Chronic exposure to aluminum and risk of Alzheimer's disease: a meta-analysis, *Neurosci. Lett.* 2016;610:200–206. doi:10.1016/j.neulet.2015.11.014.
- Nampoothiri M, John J, Kumar N, Mudgal J, Nampurath GK, Chamallamudi MR. Modulatory role of simvastatin against aluminium chloride-induced behavioural and biochemical changes in rats. *Behav Neurol.* 2015; 2015:210169.
- Abu-Taweel GM, Ajarem JS, Ahmad M. Neurobehavioral toxic effects of perinatal oral exposure to aluminum on the developmental motor reflexes, learning, memory & brain neurotransmitters of mice offspring. *Pharmacol Biochem Behav.* 2012; 101:49-56.
- Campbell A, Becaria A, Lahiri DK, Sharman K, Bondy SC. Chronic exposure to aluminium in drinking water increases inflammatory parameters selectively in the brain. *J Neurosci Res.* 2004;75: 65–572.
- Jyoti A, Sethi P, Sharma D. *Bacopa monniera* prevents from aluminium neurotoxicity in the cerebral cortex of rat brain. *Journal of Ethnopharmacology*, 2007; 111: 56-62.
- McLachlan DR, Bergeron C, Smith JE, Boomer D, Rifat SL. Risk for neuropathologically confirmed Alzheimer's disease and residual aluminum in municipal drinking water employing weighted residential histories. *Neurology*, 1996; 46:401–405.
- Gulya K, Rakonczay Z, Kasa P. Cholinotoxic effects of aluminium in rat brain. *J Neurochem*, 1990;54:1020–1026.
- Singh S, Jain SK, Alok S, Chanchal D, Rashi S. A review on ficus religiosa - an important medicinal plant. *International Journal of Life Sciences and Review (IJLSR)*, 2016; 2(1):1-11.
- Prasad PV, Subhaktha PK, Narayana A and Rao MM, Medico-historical study of "aśvattha" (sacred fig tree), *Bull. Indian Inst. Hist. Med. Hyderabad*, 2006; 36:1-20.
- Singh P, Singh D, Goel RK. *Ficus religiosa* L. figs--a potential herbal adjuvant to phenytoin for improved management of epilepsy and associated behavioral comorbidities. *Epilepsy Behav.* 2014;41:171-8.
- Parameswari SA, Chetty CM, Chandrasekhar KB. Hepatoprotective activity of *Ficus religiosa* leaves against isoniazid+rifampicin and paracetamol induced hepatotoxicity. *Pharmacognosy Res.* 2013 Oct;5(4):271-6.
- Anon. Government of India notifies the rules for breeding of and conducting animal experiments. *Indian J Pharmacol* 1999; 31, 92–95
- Bures J, Buresova Olga, Huston JP. Techniques and basic experiments for the study of brain and behaviour. Elsevier Science Publishers, Amsterdam, New York. p 155, 1983.
- Shafri MAM, Jais AMM, Jaffri MDJ, Kim MK, Ithnin H, Mohamed F. Cresyl violet staining to assess neuroprotective and neuroregenerative effects of haruan traditional extract against neurodegenerative damage of ketamine. *International Journal of Pharmacy and Pharmaceutical Sciences.* 2012;4(4):163-168.
- Roskams AJ, Connor JR. Aluminium access to the brain: a role for transferrin and its receptors. *Proc Natl Acad Sci USA.* 1990; 87: 9024–9027.
- Oğuz EO, Enli Y, Şahin B, Gönen C, Turgut G. Aluminium sulphate exposure increases oxidative

- stress and suppresses brain development in Ross broiler chicks. *Med Sci Monit.* 2012; 18(3):BR103–BR108.
19. Brenner S. Aluminum neurotoxicity is reduced by dantrolene and dimethyl sulfoxide in cultured rat hippocampal neurons. *Biol. Trace Elem. Res.* 2002; 86: 85-89.
 20. Tair K, Omar Kharoubi, Oussama AnouarFair, NouriaHellal, Imene Benyettou, Abdelkader Aoues. Aluminium-induced acute neurotoxicity in rats: Treatment with aqueous extract of *Arthrophytum*. *Journal of Acute Disease.* 2016;5(6): 470–482.
 21. Florian C, Roullet P. Hippocampal CA3-region is crucial for acquisition and memory consolidation in Morris water maze task in mice. *Behaviural brain research.*2004;154(2):365-374.
 22. Aiyegoro OA and Okoh AI. Use of bioactive plant products in combination with standard antibiotics implications in antimicrobial chemotherapy. *Journal of medicinal plant research,* January 2010; 3(13):1147-1152.
 23. Vinutha B, Prashanth D, Salma K, Sreeja SL, Pratiti D, Padmaja R et al. Screening activity of selected Indian medicinal plant for acetylcholinesterase inhibitory activity, *J. Ethnopharmacol.* 2007; 109: 359–363.
 24. Bhangale JO, Acharya N, Acharya SR. Neuroprotective effect of petroleum ether extract of *Ficus religiosa* (L.) leaves in 3-nitropropionic acid induced Huntington disease. *Int. J. Pharm Tech Res.* 2015; 8 (10):57-69.
 25. Bhangale JO, Acharya SR. Anti-parkinson activity of petroleum ether extract of *ficus religiosa* leaves. *Advances in Pharmacological Sciences.* 2016; 9436106:1-9.

Abdominal Muscular Strength Endurance: Normative Reference Values for Children 11 to 15 Years of Age

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Abstract

Introduction: One minutesitups is one of the most popular standardized test which is used to measure the muscular strength endurance of the abdominal muscles.

Objective: To develop the norms for 1 minute Situptest for Indian youth aged 11-15 years.

Methodology: For the purpose of the study a sample of 5000 male (13.14 ± 1.316 years) and 4000 female (13.31 ± 1.163 years) school going students were selected for the study. One minutesitups was used for measuring abdominal muscular endurance. Various statistical method were opted for analysing the relationship between the variables, normalization and visualization of data and the development of norms.

Results and Discussions: The results of the study indicated significant differences (p value < 0.05) in male category across all the age groups. Whereas, in female category there were only 3 significant differences (out of 10) found between age 14 – 15, 14 – 13 and 14 – 11. It shows that the muscular strength endurance for male students changed significantly across these 5 years as compared to female students, which were found to be more consistent. Urban students (Male and Female) were also found to be significantly higher in muscular strength endurance than rural students.

Applications: Norms are necessary to test, compare, analyze and evaluate one's strengths and weaknesses. The norms will guide and direct the Indian youth about their muscular endurance status. It will also help coaches and trainers to design a training plan accordingly.

Conclusion: Urban students are better than rural students in one minutesitups. Due to the physiological differences, the muscular strength endurance for male students was greater in all terms than the female students. Norms were developed for the Indian youth aged 11 – 15 years.

Keywords: Norms, 1 minute Situp, Gender, Rural and Urban.

Introduction

Over the past 20 years, the invigoration of research regarding physical activity and physical education has

generated a greater understanding of its importance, and how they should be promoted^[1]. "Physical literacy" has subsequently emerged as a concept that captures both the desire to participate in physical activity, as well as learning from it. The concept was initially proposed by Whitehead (2001), in response to concerns as to the direction of physical education and the alarming levels of physical inactivity across the life course (Hallal et al., 2012)^[2,3,4]. Physical fitness is a good summative measure of the body's ability to perform physical activity and exercise, and it also provides an important summative indicator of health^[5,6,7].

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In addition to the health implications, physical fitness is an important determinant of success for many popular youth sports and athletic events^[8]. Positive trajectories of HRF in children and adolescents require an understanding of behavioral attributes and causative mechanisms that promote these outcomes^[9].

One minutesitups is one of the most popular standardized test which is used to measure the muscular strength endurance of the abdominal muscles. In this study we aimed to examine and develop sit ups norms for children aged 11 to 15 years. During the sit-ups test, subjects repeatedly bend and extend the torso at the hip for a specific period of time hence, endurance of abdominal and hip muscles is largely related^[10]. The simplicity of the sit-ups test that is not requiring special devices for it makes this test extremely practical. Since many modifications are made to sit-up exercises in an attempt to maximize the activation of abdominal muscles considered to contribute to trunk stability and minimize the compressive forces on the lumbar spine^[11,12].

The normative standards for measuring muscular endurance will increase the utility of the test and improve the efficiency in the interpretation of the test score in several ways. It may also help in prescribing curriculum for maintenance and improvement of Muscular strength endurance. It will help the coaches and trainers to design a training schedule and to select students for higher performance. Norms will help in classification of the students according to their performance level and remedial training could be undertaken to bring students to a predetermined level.

There are two objectives of the study, first to develop the norms for 1 minute Situp test for Indian youth aged 11 – 15 years and second to compare the muscular strength endurance of Rural and Urban children.

Methodology

Selection of the participants: A total of 9000 (male 5000 and 4000 female) healthy school going students from different schools of Pune district were enrolled for the study. The age of all the participants ranged from 11 to 15 years (Male 13.14 ± 1.316 years; Female 13.31 ± 1.163 years). The participants had no history of any major disease and also had no injury prior to the test. Stratified random sampling technique was used to select the participants from 20 different schools (10 Urban schools and 10 Rural schools). Informed consent was obtained from the parents and permissions were taken by the schools for conducting the test.

Selection of the variables: For the purpose of the study, the performance in 1 minutesitups was selected as a dependent variable along with age, gender, BMI, and Waist Hip Ratio as independent variables.

Data Collection: The test was conducted on different days in twenty different schools. The directions about the process of test administration were explicitly determined and conveyed to each student prior to the test. On the day of data collection for each school, all the participants were assembled for a briefing of the testing procedure and a unique identification number were marked on their uniforms to simplify and facilitate procedures. All the participants were instructed to do 5 minutes of jogging before the test. Participants were also instructed to take light meal 2-3 hours before the test and refrain themselves from any energetic physical activity for that period. The 1 minute situptest is a standardized test to measure muscular endurance with high test retest reliability (0.98), moderately high inter apparatus reliability (0.71), high inter tester reliability (0.76) and validity (0.67) ^[13].

Statistical Technique: Descriptive statistics such as mean, Standard deviation, skewness, kurtosis, CV etc were used to summarize the nature of data. Histogram with mean and standard Deviation as a part of descriptive statistics were used for data visualization. Kruskal Wallis H test was used for comparing the situps performance of five different age group and Mann Whitney U test was used for comparing the situps performance of rural and urban students. It was also used to compare the situps performance of male and female students. Percentile and Stanine scale was used to develop norms. All the statistical analysis were done in SPSS version 24. The level of significance was set at 0.05.

Results and Discussion

After collecting 5000 male and 4000 female participants data for 1 minutesitups performance, data cleaning was done. A total of 661 data entries were found to be bad data, typing errors, wrong entries, outliers and extreme scores, which were removed from the final data set. This final data set used for the development of the norms consisted of 4848 male and 3491 female participants. Before removing the outliers and extreme scores a two-step approach for transforming continuous variables to normal method has been used. In step one, all the data for the selected variables were transformed into fractional rank for getting the uniformly distributed probabilities. The second step consisted of applying the

inverse-normal transformation to the results of the first step to form a variable consisting of normally distributed z-scores^[14,15]. The descriptive statistics such as mean, standard deviation, skewness and kurtosis with their standard error are shown in the below table. It can be seen from the standard deviation value in table 1 that, the 1 minutesitups test data points are spread out over a wider range of values. Even it can be seen from the table that female participants have higher variability (CV) in the 1 minutesitupsas compared to male participants. After the transformation of data and removing the outliers and extreme scores, the data set for the beep test became normal as the skewness and kurtosis values were less than twice their standard error.

Table 1: Gender wise descriptive statistics for 1 minutesitups performance

Descriptive Statistics	Gender	
	Male (n = 4848)	Female (n = 3491)
Mean	22.2096	15.6009
Std. Deviation	10.35956	8.50159
Coefficient of Variation (CV)	.46644	.54494
Skewness	.014	.034
Std. Error of Skewness	.037	.041
Kurtosis	-.079	-.132
Std. Error of Kurtosis	.073	.083



Figure 1: Mean and Standard deviation for visualizing the gender wise comparison of 1 minute sit ups performance across all the age groups

The results of Kruskal Wallis H test shows a significant (p value = .000) difference while comparing the situps performance of five different age group (Genderwise). As Kruskal Wallis H test won't show which groups were different, Mann Whitney U test was performed. Bonferoni corrections (level of significance divided by number of comparison) was used to reduce the type 1 error. It was found that in male category there were significant differences among all the age groups. Whereas, in female category there were only 3 significant differences (out of 10) found between age 14 –15, 14

– 13 and 14 – 11. It shows that the muscular strength endurance for male students changed significantly across these 5 years as compared to female students, which were found to be more consistent.

Also, significant differences (p value = .000) were found between male and female students in across all age categories. The result shows that even from 11 to 15 years male abdominal muscular strength is more than of female, this is due to the sex-specific and age-specific differences^[16]. Gantiraga et al. (2006) has determined

that strength in boys before puberty is more than girls, although the difference is less and it keeps on increasing after puberty^[17]. Kriemler et al. (2008) has found that in children aged 6-13 years, boys had greater muscle strength and were more physically active than girls^[18].

In this study the age range of all the participants were from 11 to 15 years. Although, the onset of puberty varies from person to person. Puberty usually occurs in boys between the ages of 12 and 16, while in girls it generally occurs early, between the ages of 10 and 14^[19].

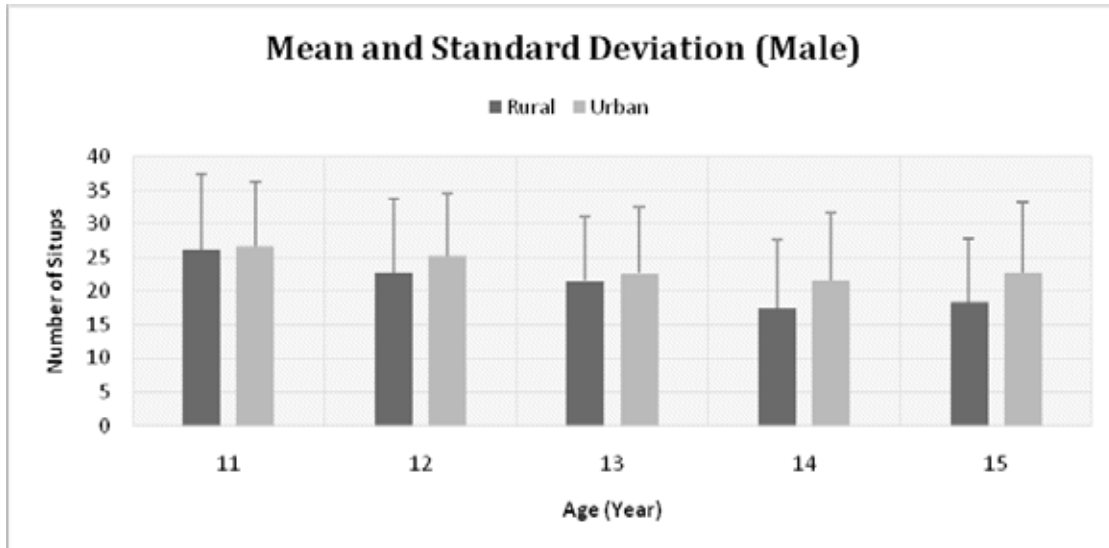


Figure 2: Mean and Standard deviation for visualizing the 1 minute sit ups performance of rural and urban male students across all the age groups

A comparative analysis has been carried out to investigate the differences in the abdominal muscular endurance of rural and urban students. It can be clearly seen from figure 1 and 2 that urban children have more abdominal strength endurance than rural children. Mann Whitney U Test was performed to check whether these differences are real. It was found that except 2 male

age categories (11 & 13 years), in all other categories abdominal muscular strength endurance of urban students were found to be significantly higher than rural students. In female, significant differences were found in all the age categories, where urban students score higher than rural students.

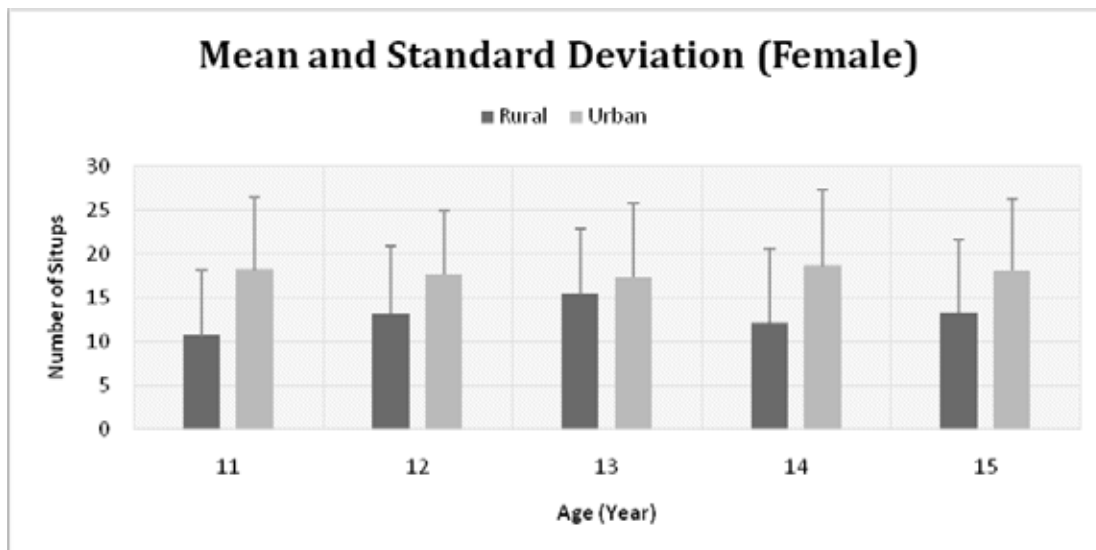


Figure 3: Mean and Standard deviation for visualizing the 1 minute sit ups performance of rural and urban male students across all the age groups

Studies have shown that in some physical parameters urban children are found to be better as compared to the rural children, especially in developed countries. These differences are due to the technological advancements, emerging trend of fit and healthy lifestyle and also

awareness about importance of fitness, nutrition and health in schools. Most of the Schools in urban areas have better transportation, sports facilities, advance equipments and playgrounds^[20,21,22,23].

Table 2: Percentile values for Male and Female participants

Percentiles	Male		Female	
	Transformed Score	Raw Score	Transformed Score	Raw Score
4 th	3.93	5	2.3850	3
22 nd	14.4351	13	8.9491	8
76 th	29.5260	30	22.0521	22
96 th	40.4175	40	30.2119	30

For normalization, we have transformed the entrie data set by using two-step approach as mentioned above. Standard nine (Stanine) scale was used to develop the

norms. Only four Percentile values were taken such as 4th Percentile, 22nd Percentile, 76th Percentile and 96th Percentile.

Table 3: Sit-up norms for youth aged 11-15 years

Gender	Age	Very Poor	Poor	Average	Good	Very Good
Male	11-15	< 5	5 – 13	14 – 30	31 – 40	> 40
Female	11-15	< 3	3 – 8	9 – 22	23 – 30	> 30

The developed norms shown in table 3 can be used for analyzing and evaluating abdominal muscular strength endurance (one minutesitup performance) of male and female students aged 11-15 years. It can be used to design training programmes by coaches or trainers for improving performance. These norms can also be used to compare the situps performance with other countries.

Conclusion

The purpose of the study was to develop the one minutesitupsnorms for youth aged 11 – 15 years and to compare the muscular strength endurance of urban and rural students. Urban students were better than rural students in one minutesitups. Due to the physiological differences, the muscular strength endurance for male students was greater in all terms than the female students. Standardized norms are necessary to test, compare, analyze and evaluate one’s strengths and weaknesses. The developed norms will guide and direct the Indian youth about their muscular strength endurance status. It will also help coaches and trainers to design a training plan accordingly. More research needs to be carried out in the development of norms, as the population in

India is very diverse in nature. In this study, we have only focused on the age range of 11-15 years. There is a scope to develop norms for other age range with similar characteristics of the population.

Conflict of Interest: None

Source of Funding: Self

Ethical Clearance: Necessary permissions and approval for conducting the research were taken from Research and Physical Education department of Pune University.

References

1. Allan V, Turnnidge J, Côté J. Evaluating Approaches to Physical Literacy Through the Lens of Positive Youth Development. *Quest.* 2017;69(4):515-530.
2. Whitehead M. The Concept of Physical Literacy. *European Journal of Physical Education.* 2001;6(2):127-138.
3. Whitehead M. *Physical literacy.* London: Routledge; 2011.

4. Hallal P, Andersen L, Bull F, Guthold R, Haskell W, Ekelund U. Global physical activity levels: surveillance progress, pitfalls, and prospects. *The Lancet*. 2012;380(9838):247-257.
5. Ortega F, Ruiz J, Castillo M, Sjörström M. Physical fitness in childhood and adolescence: a powerful marker of health. *International Journal of Obesity*. 2007;32(1):1-11.
6. Pate R, Daniels S. Institute of Medicine Report on Fitness Measures and Health Outcomes in Youth. *JAMA Pediatrics*. 2013;167(3):221.
7. Ortega F, Ruiz J, Castillo M, Sjörström M. Physical fitness in childhood and adolescence: a powerful marker of health. *International Journal of Obesity*. 2007;32(1):1-11.
8. Armstrong N, Tomkinson G, Ekelund U. Aerobic fitness and its relationship to sport, exercise training and habitual physical activity during youth. *British Journal of Sports Medicine*. 2011;45(11):849-858.
9. Kohl HW, Hobbs KE. Development of physical activity behaviors among children and adolescents. *Pediatrics*. 1998;101:549-54.
10. Takanori Noguchi, Shinichi Demura. Effect of Differences in the Exercise Frequency of Young People on Abdominal Strength and Muscle Thickness. *American Journal of Sports Science and Medicine*. 2014; 2(6):218-221
11. Jackson AW, Morrow Jr JR, Brill PA, Kohl III HW, Gordon NF, Blair SN. Relations of sit-up and sit-and-reach tests to low back pain in adults. *Journal of Orthopaedic & Sports Physical Therapy*. 1998;27(1):22-6.
12. Parfrey KC, Docherty D, Workman RC, Behm DG. The effects of different sit-and curl-up positions on activation of abdominal and hip flexor musculature. *Applied Physiology, Nutrition, and Metabolism*. 2008;33(5):888-95.
13. Diener M, Golding L, Diener D. Validity and reliability of a one minute half sit-up test of abdominal strength and endurance. *Journal of Sports medicine, training and Rehabilitation*. 1995;6(2):105 – 119.
14. Templeton G. A Two-Step Approach for Transforming Continuous Variables to Normal: Implications and Recommendations for IS Research. *Communications of the Association for Information Systems*. 2011;28(1):41 - 58.
15. Bagchi A, Nimkar N, Yeravdekar R. Development of Norms for Cardiovascular Endurance Test for Youth Aged 18–25 Years. *Indian Journal of Public Health Research & Development*. 2019;10(7):1486-1491.
16. Tomkinson G, Carver K, Atkinson F, Daniell N, Lewis L, Fitzgerald J et al. European normative values for physical fitness in children and adolescents aged 9–17 years: results from 2 779 165 Eurofit performances representing 30 countries. *British Journal of Sports Medicine*. 2017;52(22):1445-1456.
17. Gantiraga E, Katartzi E, Komsis G, Papadopoulos C. Strength and vertical jumping performance characteristics in school-aged boys and girls. *Biology of Sport*. 2006;23(4):367.
18. Kriemler S, Zahner L, Puder JJ, Braun-Fahrlander C, Schindler C, Farpour-Lambert NJ, Kränzlin M, Rizzoli R. Weight-bearing bones are more sensitive to physical exercise in boys than in girls during pre-and early puberty: a cross-sectional study. *Osteoporosis international*. 2008 Dec 1;19(12):1749.
19. Stöppler M, Shiel W. Puberty Definition, Stages, Duration, Signs for Boys & Girls [Internet]. *MedicineNet*. 2020 [cited 15 January 2020]. Available from: <https://www.medicinenet.com/puberty/article.htm>
20. Sylejmani, B., Myrtaj, N., Maliqi, A., Gontarev, S., Georgiev, G., & Kalac, R. (2019). Physical fitness in children and adolescents in rural and urban areas. *Journal of Human Sport and Exercise*, in press. doi:<https://doi.org/10.14198/jhse.2019.144.15>
21. Hian, T. C.; Mahmud, Z. F. & Choong, T. Y. Physical fitness level between urban and rural students-case study. *Procedia-Social and Behavioral Sciences*, 90:847-52, 2013.
22. Eiben, O. G.; Barabás, A. & Németh, Á. Comparison of growth, maturation, and physical fitness of Hungarian urban and rural boys and girls. *J. Hum. Ecol*, 17(2):93-100, 2005.
23. Loucaides, C. A.; Chedzoy, S. M. & Bennett, N. Differences in physical activity levels between urban and rural school children in Cyprus. *Health education research*, 19(2):138-47, 2004.

Functional and Aesthetic Rehabilitation of Missing Tooth by Using Immediate Implant Placement: A Case Series

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Abstract

Replacing a single or multiple tooth pose various clinical challenges to the clinician during prosthetic rehabilitation. This clinical challenge is more complicated with fixed dental prosthesis when there is an insufficient space for the pontic. Replacing the tooth in these quantifiable situation is best suited by implant supported prosthesis. In the presented case series, we present three such cases where missing teeth were restored with implant supported prosthesis immediately post extraction to satisfy patients aesthetic as well as functional needs.

Keywords: Immediate Implant, Post extraction, Tooth replacement, Esthetic zone.

Introduction

In this current era of advancement with newer techniques to restore single or multiple teeth gives ease of restoring missing teeth with optimum to ideal results. However, occasionally clinicians face clinical challenges depending on the kind of treatment cater to the patient. Fixed denture prosthesis provide adequate function but compromise esthetics due to small pontics. In some cases, maintenance of hygiene is also difficult due to ridge lap design of pontics and there is need to prepare adjacent abutment teeth. Similarly in a removable denture prosthesis esthetics and hygiene is acceptable but functionally it is inferior to a fixed prosthesis.^[1] Due to these existing shortcomings related to fixed and removable prosthesis, the dental rehabilitation is growing with implant supported fixed prosthesis since last few decades. Longitudinal studies have shown dental implants to have a success rate of above 90%.

Some prospective studies stated that implant survival rate varied from 84.9% to 100%.^[2] Conventional implant placement guidelines advocate a period of 3 months post extraction for soft and hard tissue healing followed by another 3 months and 6 months for loading the implant in mandible and maxilla respectively.^[3] This accounts to almost a year for single tooth replacement which is unacceptable functionally, esthetically and psychologically from the patients perspective view. Thus, a new protocol of immediate implant placement post extraction was introduced; wherein the time period of treatment was reduced to 3-4 months required for osseointegration. In some cases, depending on the pre-load or the torque achieved immediate provisionalization has produced good results. Plethora of research analysis have documented excellent results in terms of esthetics and optimal preservation of hard and soft tissues by immediate implant placement.^[4,5,6]

Case Report: In this case article, we narrate a series of three cases of tooth replacement by immediate implant placement post extraction.

Case 1: Single tooth replacement with immediate implant in the anterior esthetic zone.

A 53yr old female presented with a history of trauma with respect to maxillary left central incisor about 5yrs back. Post failure of an attempt for an endodontic

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treatment patient was advised to undergo extraction due to poor prognosis pertaining to that tooth. On examination there was Grade II mobility, spontaneous bleeding, deep periodontal pocket and suppuration. Radiographically, the tooth showed a periapical lesion with a radiopaque restoration in the pulp chamber. Some amount of external root resorption had also occurred (Fig 1).

After an atraumatic extraction of the tooth, the socket was thoroughly debrided, granulation tissue was removed and rinsed with sterile saline. A 4.3 × 15-mm Nobel Replace Select implant (Nobel Biocare, Sweden) was placed and temporization with Bisacryle composite material was done. Bio-Oss collagen graft (Bio-Oss® Collagen) was deposited between the surface of the implant and the wall of the socket.^[7,8] Shade selection was done. Stage 2 surgery was performed 7 months later and at re-entry, the graft was found to be properly integrated with the host bone. The implant was immobile, one of the criteria for success according to the parameters established by Albrektsson et al.^[9] For the final esthetic result cement retained porcelain fused metal crown was cemented over an esthetic abutment. Post cementation radiograph revealed properly seated crown over the integrated implant. (Fig. 2)

Case 2: Single tooth replacement with immediate implant in the posterior region.

A 25yr old male patient presented with fractured tooth resulting in insufficient remaining root length with respect to maxillary right second premolar. Clinical examination revealed non-vital tooth fractured at the gingival margin (Fig 3). Radiographic examination revealed endodontically treated tooth where obturation was short of root apex. Endodontic retreatment had a questionable prognosis and hence the tooth was indicated for extraction.

After atraumatic extraction of the tooth, the socket was examined. All the walls of socket was found to be intact. The socket was thoroughly curetted and debrided for any granulation tissue and rinsed with normal saline. A 4.3 x 11.5mm Nobel Replace Select implant (Nobel Biocare, Sweden) was placed taking anchorage on the palatal wall, about 3mm beyond apex and at the crest of the ridge. Cover screw was placed and the jumping distance on the buccal side was covered with synthetic hydroxyapatite bone graft (SyboGraf™ Plus). The flaps were completely approximated by interrupted sutures.

The second phase surgery was done 6 months later the earlier surgical procedure. The second-phase healing abutment was placed then the flaps were sutured. After 2 weeks on removal of healing abutment a well formed gingival cuff surrounding implant could be seen. The implant was restored with a cement retained porcelain fused crown (Fig 4). Clinical examination with radiographs demonstrated successful restoration of the prosthesis.

Case 3: Teeth replacement with single immediate implant in esthetic zone.

A 26yr old female patient presented with endodontic failure and root fracture with respect to maxillary right canine (Fig 5). Patient gave history of loosening of endodontic post with the crown followed by fracture of crown. Radiographic examination showed fractured tooth, obturated canal at the apex with prepared post space and congenitally absent adjacent lateral incisor. As the prognosis of endodontic retreatment was poor it was decided to extract the tooth.

Replacement of maxillary canine with implants immediately post extraction is a challenging proposition due to its long roots and thin facial bone. Careful atraumatic extraction was carried out with the help of periosteal elevator. The extracted tooth socket was examined for any facial bone fracture, debrided and measured to determine the length of implant. A 4.3 x 13mm Nobel Replace Select implant (Nobel Biocare, Sweden) was placed taking anchorage on the palatal wall and at the crest of the ridge (Fig 6).

Second phase surgery was done 6 months later implant placement. Esthetic abutment was placed. A porcelain fused metal crown with respect to canine and a splinted cantilevered crown with respect to lateral incisor was cemented. 7 month post-operative radiograph presented a successful osseointegrated implant prosthesis.

Discussion

The placement of immediate implants has become a routine clinical procedure. The idea of immediate implantation and provisionalization for replacing a tooth in the premaxilla are associated with some clear benefits: As it combines tooth extraction, implant surgery, and restorative treatment, the time gain can be optimized.^[10] The success rate is comparable to data published for single-tooth implants placed according to the standard

protocol in healed sites.^[11] The main benefits of placing immediate implants are the decrease in time of therapy, decrease in surgical periods and conservation of the bone and gingival tissues. Larger amount of bone resorption happens during the first 6 months subsequent to tooth extraction, if an implant is placed or a socket augmentation procedure performed. The timely maintenance of the gingival form significantly facilitates the peri-implant gingival tissue esthetics by preserving support for the interdental papillae.^[12] With respect to the distance between the socket wall and the implant, it was stated that if the jumping distance is above 2mm, grafting is suggested. Minorspaces could heal naturally. From the reviewed studies, it looks that ISQ values are slightly lesser in immediately placed implants compared to implants placed in pristine bone. However, these changes tend to vanish overtime. ISQ values seem to rise gradually during healing over the first few months in immediate implants.^[13] Immediate implants placed with a submerged or a non-submerged method display comparable success and survival rates with comparable behaviour of peri-implant hard and soft tissues, with a mean of 1mm of vertical recession of the papillae and the midfacial gingival margin when matched with the soft tissue levels before tooth extraction. Substantial decrease of keratinized tissue was witnessed when using the submerged method^[14]. It should be emphasized that the cause of the infection must be the diseased tooth, be it periodontally or endodontically involved, or the result of fracture and that during surgical treatment the cause of the infection, ie, the tooth, is removed. Another important part of the surgical treatment is the complete, thorough debridement and rinsing of the alveolus. If proper preoperative and postoperative care is provided, immediate implants can be placed successfully into chronically infected sites.^[15]



Fig 1: Periapical lesion with a radiopaque restoration



Fig 2: Cement retained porcelain fused metal crown



Fig 3: Non-vital tooth fractured at the gingival margin



Fig 4: Cement retained porcelain fused crown with respect to maxillary right second Premolar



Fig 5: Endodontic failure and root fracture with respect to maxillary right Canine



Fig 6: 4.3 x 13mm Nobel Replace Select implant (Nobel Biocare, Sweden) was placed

Conclusion

Early implantation helps in preservation of the alveolar anatomy and maintain the bony crest. The immediate restoration of dental implants engaged into the fresh extraction sockets has proved to be safe and probable procedure. The success rate, radiographic and clinical outcomes are similar to those found following the regular procedure. Short time survival rates and clinical results of immediate and delayed loaded implants are equivalent and similar to those of implants engaged in healed alveolar ridges. Thus, immediate implant placement has become a significant part of implant therapy which provides timely esthetic implant restorations.

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References

- Schiroli G. Immediate tooth extraction, placement of a Tapered Screw-Vent® implant, and provisionalization in the esthetic zone: a case report. *Implant dentistry*. 2003 Jun 1;12(2):123-31.
- Prashanti E, Sajjan S, Reddy JM. Failures in implants. *Indian J. Dent. Res.* 2011; 22(3):446.
- Khzam N, Arora H, Kim P, Fisher A, Mattheos N, Ivanovski S. Systematic review of soft tissue alterations and esthetic outcomes following immediate implant placement and restoration of single implants in the anterior maxilla. *Journal of periodontology*. 2015 Dec;86(12):1321-30.
- Álvarez-Camino JC, Valmaseda-Castellón E, Gay-Escoda C. Immediate implants placed in fresh sockets associated to periapical infectious processes. A systematic review. *Medicina oral, patología oral y cirugía bucal*. 2013 Sep;18(5):e780.
- Slagter KW, den Hartog L, Bakker NA, Vissink A, Meijer HJ, Raghoobar GM. Immediate placement of dental implants in the esthetic zone: a systematic review and pooled analysis. *Journal of periodontology*. 2014 Jul;85(7):e241-50.
- Sujeet Singh, Hemant Gupta, Deepak kumar. Immediate Implant Placement Along With Bone Graft And Delayed Implant Placement In A Grafted Socket: A Comparative Study, *International journal of implant and clinical research*. 2015;6(2),40-47.
- Novaes AB Jr, Novaes AB. IMZ implants placed into extraction sockets in association with membrane therapy (Gengiflex) and porous hydroxyapatite: A case report. *Int J Oral Maxillofac Implants* 1992; 7:536-540.
- Chen ST, Wilson TG, Hammerle CHF. Immediate or early placement of implants following tooth extraction: review of biologic basis, clinical procedures, and outcomes. *Int J Oral Maxillofac Implants* 2004;19:12-25
- Albrektsson T, Zarb GA, Worthington P, Eriksson RA. The long-term efficacy of currently used dental implants: A review and proposed criteria of success. *Int J Oral Maxillofac Implants* 1986;1:11-25
- Schiroli G. Immediate tooth extraction, placement of a Tapered Screw-Vent® implant, and provisionalization in the esthetic zone: a case report. *Implant dentistry*. 2003 Jun 1;12(2):123-31.
- De Rouck T, Collys K, Cosyn J. Single-tooth replacement in the anterior maxilla by means of immediate implantation and provisionalization: a review. *International Journal of Oral & Maxillofacial Implants*. 2008 Oct 1;23(5).
- Monish Bhola, Anthony L. Neely, Shilpa Kolhatkar, Immediate implant placement: clinical decisions, advantages and disadvantages; *Journal of Prosthodontics* 2008;17:576-581
- Martínez JO, Pascual TP, Bueno SM, Alfaro FH, Padró EF. Immediate implants following tooth

- extraction. A systematic review. *Med Oral Patol Oral Cir Bucal*. 2012 Mar 1;17 (2):e251-61.
14. Cordaro L, Torsello F, Rocuzzo M. Clinical outcome of submerged vs. non-submerged implants placed in fresh extraction sockets. *Clin Oral Implants Res*. 2009 Dec;20(12):1307-13. 15. Novaes Jr AB, Novaes AB. Immediate implants placed into infected sites: a clinical report. *International Journal of Oral & Maxillofacial Implants*. 1995 Sep 1;10(5).

Assessment of Physical Activity and Sedentary behaviour among Overweight Adolescents in Selected Urban Schools of Puducherry

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Abstract

Introduction: Physical inactivity is increasing among children and adolescents and may be contributing to the increasing prevalence of overweight and obesity. Only 30% of adolescents perform sufficient physical activity. Sedentary behaviours, especially watching TV, sitting at the computer and playing video games/mobile phones, are increasing among children. Aim: To assess the level of physical activity and sedentary behaviour among overweight adolescents and to examine the association between physical activity, sedentary behaviour and screen time with BMI.

Materials and Method: Participants were 140 overweight adolescents aged 11-14 years from 2 Urban schools of Puducherry. They were assessed for their physical activity and sedentary behaviour by using Modified Physical Activity Questionnaire -Older children and Adolescent Sedentary Activity questionnaire. The analysis was carried out using SPSS Statistics Version 25. Linear Regression coefficient was used to examine the association between physical activity, sedentary behaviour and screen time with BMI.

Results: More than half of the overweight adolescents (58%) engaged in low levels of physical activity with females being more physically inactive than males. Likewise the mean time spent in sedentary behaviour was more than 12 hours/day with a SD of 3.83. The mean time spent in screen time was 8 hours/day with a SD of 2.56. Use of smart phones contributed largely to the screen time that was significant at $p < 0.001$. Linear Regression analysis implies that screen time was positively associated with BMI at $P < 0.05$.

Conclusion: Overall, the current study has indicated a low prevalence of physical activity and high sedentary behaviour among overweight adolescents.

Keywords: *Physical activity, sedentary behaviour, adolescent, overweight, obesity.*

Introduction

World Health Organization defines physical activity as any bodily movement produced by skeletal muscles that requires energy expenditure including activities undertaken while working, playing, carrying out household chores, travelling, and engaging in recreational pursuits.¹ Physical inactivity is increasing among children and adolescents and may be contributing to the increasing prevalence of overweight and obesity. Modern environments and technological advancements have changed the way we live. Globally, 81% of adolescents aged 11-17 years had insufficient physical

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activity in 2010². In India, prevalence of insufficient physical activity among adolescents aged 11- 17 years was 71.6% and 69.6% among girls and boys respectively³. Overweight children and adolescents are more likely to become obese and to develop noncommunicable diseases (NCDs) during adulthood⁴. Physical activity in young people has become a major issue in public health as evidence emerges on the important role of physical activity in many health conditions, including overweight and obesity, type 2 diabetes, cardiovascular disease risk, skeletal health, and mental health. In particular, the issue of obesity in youth, and the link between this condition and type 2 diabetes, as well as the increases in diabetes⁵ is topical and currently demanding much attention in physical activity research.⁶

Reduction in physical inactivity would reduce between 6% to 10% of the major NCD's and increase life expectancy⁴. Adequate levels of physical activity throughout an individual's life ensure an optimal state of health. Only 30% of adolescents and 10% of adults perform sufficient physical activity to facilitate proper physical, psychological/mental and emotional development. International data published in the recent Lancet Physical Activity Series reports that 80% of 13–15 year olds do not meet the current physical activity recommendations of 60 minutes of moderate to vigorous physical activity per day, and also highlights the need for more physical activity.⁷ Sedentary behaviours, especially watching TV, sitting at the computer and playing video games/mobile phones are increasing among children in developed and developing countries. This trend is a major public health problem because sedentary lifestyle in childhood has been found to increase the risk of chronic diseases in adulthood.⁸

The aim of this study was to assess the level of physical activity and sedentary behaviour among overweight adolescents and to examine the associations between physical activity, sedentary behaviour and screen time with BMI.

Materials and Method

Descriptive Research design was used for the study. Participants were 140 overweight adolescents aged 11-14 years from 2 Urban schools of Puducherry. They were assessed for their physical activity and sedentary behaviour using the following tools.

Part I: Consisted of the socio-demographic data of children which included age, type of family, standard

of education, educational status of parents, mode of transport to school, BMI etc.,

Part II: Modified Physical Activity Questionnaire-Older Children (PAQ-C) was used for the study. The PAQ-C is a self-administered, 7-day recall instrument. It was developed to assess general levels of physical activity throughout the week for students from 11 to 14 years of age. The tool consisted of 10 items. The activity score is between 1 and 5 for each item excluding item number 10. The mean of the 9 items, results in the final PAQ-C activity summary score.⁹ A score of 1 to 2 indicates low physical activity, 3 moderate physical activity and a score of 5 indicates high physical activity.

Part III: Adolescent Sedentary Activity Questionnaire (ASAQ) was used for the study which assessed the time spent in a comprehensive range of sedentary activity outside of school hours. Students were asked to think about a normal week, during school term, and to report how long they usually spent in 11 different sedentary behaviours before and after school on each day of the week and on each day of the weekend. The time spent in sedentary behaviours were summed across weekdays and weekends to obtain the total time spent in doing sedentary behaviours per day.¹⁰ A score of >4 hours/day indicated high sedentary behaviour.

The overweight children who fulfilled the inclusion criteria were selected and informed consent was obtained from the mothers and assent from the adolescents. The adolescents were administered the physical activity questionnaire and were asked to find out the level of physical activity for the last 7 days. Similarly the adolescents were administered the ASAQ and were asked to write down how much time they spent in sedentary behaviour outside school hours both during the weekdays and weekends. The analysis was carried out using SPSS Statistics Version 25.

Results

Socio-Demographic Variables: Out of 140 overweight children 30% were in the age group of 11 years, 35% were in the age group of 13 years. 56.6% were females and 40.6% were males. 26.4% were in 8th standard and majority 34.3% were in 9th standard. 77.1% were from nuclear families and majority 37.9% were from upper middle class. Almost 80.7% were non vegetarians. Most of the students 40.7% came to school by two wheeler and 57.9% slept for 8 hours. The mean BMI of overweight children was 23.271 with a SD of 1.399.

Table 1: Distribution of level of Physical activity among overweight adolescents N=140

Level of Physical Activity	Frequency	Percentage	Male N(%)	Female N(%)	Mean	Standard Deviation
Low (1-2)	82	58.6	32(55%)	50(61%)	2	0.76
Moderate (3)	48	34.3	21(36%)	27(32%)		
High (4-5)	10	7.1	5(9%)	5(6%)		

Concerning physical activity most of the children 82 (58.6%) engaged in low levels of physical activity with more females being physically inactive than males. (61%versus 55% respectively). 34.3% engaged in moderate level of physical activity. Only 10(7.1%) engaged in high levels of physical activity. The mean physical activity was 2 with a standard deviation of 0.76 (Table 1).

Moreover nearly 50% of the children did not engage in physical activity either during recess or lunch break. Only 30% engaged in physical activity right after school 5 times a week, however most of the children 92% were active during Physical Education Classes.

Table 2: Distribution of time spent in sedentary behaviour and screen time among overweight adolescents N=140

Variable	Frequency	Percentage	Mean (SD) hours/day
Sedentary behaviour			
Low<4hours/day	3	2.1	12(3.83)
High>4hours/day	137	97.9	
Screen time			
< 2 hours/day	5	3.5	8(2.56)
>2hours/day	135	94.4	

Table 2 implies that 137(97.9%) of the overweight children had a sedentary behaviour of >4 hours/day and only 2% had less sedentary behaviour. The mean time spent in sedentary behaviour was 12 hours/day with a SD of 3.83.

94% of the overweight children spent more than 2 hours/day in screen time which included watching television, using smart phones for games, playing video games and the most common was using smart phones for games at p<0.001 level.

Table 3: Regression coefficients for Physical activity, sedentary behaviour, screen time and BMI

Variable	BMI
Physical activity	0.992
Sedentary behaviour(Non TV leisure time)	0.079
Screen time (watching TV, playing video games, using mobile phone for games)	0.041*

*p<0.05

The association between physical activity and sedentary behaviour examined by linear regression with BMI implies that physical activity and non TV leisure time were not associated with BMI while screen time that included watching TV, using mobile phones were positively associated with BMI. (p<0.05).

Discussion

The study findings revealed that out of 140 children nearly 60% of the children engaged in low physical activity with females being more physically inactive than males. This implies that children are becoming more sedentary in nature mainly due to media and smart

phones. The findings corroborate with a similar study findings where nearly 44.3% of the adolescents had low physical activity levels, with more females 55% being physically inactive than males.¹¹ These findings were also in accordance with studies conducted in Mangaluru, Puducherry and Punjab.¹²⁻¹⁵ The reasons probably might be that females are not allowed to play outside their homes.

50% children did not engage in physical activity either during recess or after lunch. This possibly could be that they wanted to finish their homework or were lazy or not motivated by their teachers. The findings are consistent with a similar study where only 38% of the children played hard at the time of recess and 43% out of 100 sat down normally at lunch.¹⁶

The study findings also revealed that only 30% of the children engaged in some form of physical activity right after school. The reason might be that nowadays right after school children are engaged with some other classes or watch television and while away their time in sedentary behaviours. The findings are supported by a similar study where the findings indicates that the late evening segment was significantly less active and showed the highest proportion of sedentary time.¹⁷

The present study also demonstrates that 98% of the children were highly sedentary > 4hours/day out of the 8 hours free time that they had out of school hours. The findings are similar to a study where 54.1% were highly sedentary.¹⁸ The mean time spent in screen time which included watching television, using computers/laptops for fun and playing with smart phones was 8 hours/day, with the most common being the use of smart phones $p < 0.001$, followed by watching television and use of computers. This probably might be that nowadays smart phones are seen in the hands of every child which has led to its addiction¹⁹.

Conclusion

Overall, the current study has indicated a low prevalence of physical activity and high sedentary behaviour among overweight adolescents. This implies that children should be motivated to engage in physical activity for at least 60 minutes a day and prime focus should be on reduction of screen time as it is primarily associated with obesity. Daily device-free social interactions and outdoor play should be encouraged. In addition, parents/teachers should be supported to devise and enforce appropriate screen time regulations and to model healthy screen-based behaviours.

Conflict of Interest: Nil

Source of Funding: Nil

Ethical Clearance: The ethical clearance was obtained from the Institutional Human Ethics Committee of Kasturba Gandhi Nursing College.

References

1. WHO. Physical Activity, 2017. Available at <https://www.who.int/dietphysicalactivity/pa/en/>. Accessed on 24 June 2019. A. P. Hills, L. B. Andersen, N. M. Byrne.
2. Physical activity and obesity in children. *British Journal of Sports Medicine*. 2011; 45(11): 866–870.
3. WHO. Key facts: Physical activity, 2018. Available at: <https://www.who.int/news-room/fact-sheets/detail/physical-activity>. Accessed on 24 June 2019.
4. WHO. Prevalence of insufficient physical activity, 2019. Available at: https://www.who.int/gho/ncd/risk_factors/physical_activity_text/en/. Accessed on 24 June 2019
5. I. Lee, E. J. Shiroma, F. Lobelo. Effect of physical inactivity on major non-communicable diseases worldwide an analysis of burden of disease and life expectancy. *The Lancet*. 2012; 380(9838) :219–229.
6. Massó-González EL, Johansson S, Wallander M-A, García-Rodríguez LA: Trends in the prevalence and incidence of diabetes in the UK: 1996-2005. *Journal of Epidemiology & Community Health*. 2009, 63: 332-6.
7. Stensel DJ, Gorely T, Biddle SJH: Youth health outcomes. Youth physical activity and sedentary behavior: Challenges and solutions. Edited by: Smith AL, Biddle SJH. 2008, Champaign, IL: Human Kinetics, 31-57.
8. Hallal PC, Andersen LB, Bull FC, Guthold R, Haskell W, Ekelund U. Group FTLPASWGlobal physical activity levels surveillance progress, pitfalls, and prospects. *Lancet*. 2012; 380: 247-257.
9. Eero A. Haapala, Anna-Maija Poikkeus, Katriina Kukkonen-Harjula, Tuomo Tompuri Niina Lintu, Juuso Väistöet.al. Associations of Physical Activity and Sedentary Behavior with Academic Skills – A Follow-Up Study among Primary School Children. *PLOS*. 2014

10. Kowalski, Crocker, M.Doner. The Physical Activity Questionnaire for Older Children (PAQ-C)2004,College of Kinesiology, Canada.
11. Hardy, L. L., Booth, M. L., & Okely, A. D.The reliability of the Adolescent Sedentary Activity Questionnaire (ASAQ). *Prev. Med.* 2007; 45(1): 71-74.
12. Mavis Asare, Samuel A Danquah. The relationship between physical activity, sedentary behaviour and mental health in Ghanaian adolescents. *Child & Adolescent Psychiatry and Mental Health.* 2015; 9-11.
13. Kundapur R, Baisil S. Assessment of difference in physical activities in urban and rural adolescents of Mangalore. *Indian J Community Health.* 2017;29(1):75-80.
14. Guthold R, Cowan MJ, Autenrieth CS, Kann L, Riley LM. Physical activity and sedentary behavior among school children: a 34-country comparison. *J Pediatr.* 2010;157(1):43-9.
15. Divyasree P, Kumar GD, Subitha L, Ramesh RS. Level, motivation and barriers to participate in physical activity among late adolescents in Puducherry. *Int J Adolesc Med Health.* 2018;05:1-8.
16. Esht V, Midha D, Chatterjee S, Sharma S. A preliminary report on physical activity patterns among children aged 8–14 years to predict risk of cardiovascular diseases in Malwa region of Punjab. *Indian Heart J.* 2018;70(6):777-82.
17. Rashmi Ronghe, Neha Gotmare, Shraddha Kawishwar. Physical activity level of school children of age 10-13 years. *International Journal of Biomedical and Advance Research.* 2016; 7(6): 281-285.
18. De Baere's, Lefeure J, Martelaer K, Philippaerts R, Seghers J: Temporal patterns of physical activity and sedentary behaviour in 10-14 years children on weekdays. *BMC Public Health.* 2015; 15(791).
19. Ngaire A Coombs, Emmanuel Stamatakis. Associations between objectively assessed and questionnaire based sedentary behaviour with BMI defined obesity among general population children and adolescents living in England. *BMJ Open,* 2015;5(6).

Effect of Activation of Deep Neck Muscles as an Adjunct to Vestibular Rehabilitation in Vertigo

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Abstract

Aim: The study was conducted to find effect of activation of deep neck muscles as an adjunct to vestibular rehabilitation in vertigo.

Materials and Method: A total 20 subjects (9 males and 11 females) between 18-30 years diagnosed with Vertigo were selected for study considering inclusion criteria. Subjects were grouped into Experimental group (Group A), Control Group (Group B). Group A received exercises for deep neck muscle activation along with vestibular rehabilitation and group B received Vestibular rehabilitation. Each session was conducted for 30 minutes duration, 3 days per week for 4 weeks. Outcome assessment used was Dizziness Handicap Inventory (DHI), Motion Sensitivity Quotient (MSQ) which was assessed pre, post exercise session. Statistical analysis was done using unpaired t test.

Result: Within group comparison-Pre-intervention, Post-intervention Mean \pm SD of Dizziness Handicap Inventory (DHI) of group A was 37 ± 6.48 and 23.6 ± 8.09 respectively. In DHI there was statistically extremely significant difference with $p < 0.0003$ and $t = 5.57$. Group B pre and post intervention mean \pm SD of DHI was 38.6 ± 3.27 and 23.6 ± 5 respectively which was statistically not significant with $p = 0.0786$ and $t = 1.98$. Pre and Post Mean \pm SD of MSQ of Group A was 30.82 ± 5.75 and 9.72 ± 4.83 respectively. Post treatment extremely significant improvement was noted according to the p value < 0.0001 , t value 16.95 and Group B was 30.62 ± 7.36 and 25.28 ± 7.19 respectively which was statistically not significant with $p = 0.075$ and $t = 2.013$.

Between group comparison-Post intervention mean \pm SD DHI was 23.6 ± 8.09 and 35.2 ± 5 respectively which was statistically extremely significant with $p = 0.0012$ and $t = 3.85$ with decrease in disequilibrium, dizziness and limitations in daily activities. MSQ post intervention mean \pm SD was 9.72 ± 4.83 and 25.28 ± 7 which was statistically extremely significant with $p < 0.0001$ and $t = 5.67$ with decrease in balance, functional mobility impairments.

Conclusion: Activation of deep neck muscles as an adjunct to vestibular rehabilitation in vertigo had significant effect in improving postural stability with balance, functional mobility, reduced impact of symptoms on daily activities. So, this study accepts alternate Hypothesis.

Keywords: Dizziness Handicap Inventory, Motion Sensitivity Quotient, balance, chronic dizziness, Vestibular Rehabilitation.

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Introduction

Vestibular dysfunction is characterized by vertigo, imbalances causing disturbances and postural instability.^[1] Dizziness is one of the common terminology describing several symptoms like Vertigo, light headedness, disorientation, etc., Commonly occurring in older individuals approximately 30%,

women are affected by 36% more than men 22%.^[2] Rotatory movement either of the self or surroundings is called Vertigo.^[2]

Dizziness may occur due to various diseases or disorders, causes of which can be Otological- middle ear disease, unilateral peripheral vestibular dysfunction, benign paroxysmal positional vertigo (BPPV), bilateral vestibular failure, Meniere's syndrome; Neurological- cerebellum, cranio-cervical junction, cortex issues, 7th cranial nerve damage.

Active neuronal changes in brainstem, cerebellum in response to sensory conflicts due to vestibular system pathology alters vestibular functions.^[3] Vertigo refers to illusion of self-motion on standing/sitting i.e. sense of spinning/falling due to alteration in the signals ascending vestibular nerves to vestibular nuclei.^[4] Integration of signals from vestibular system, visual system, neck proprioceptors, trunk aid in maintaining balance, equilibrium.^[5] Dysfunction of cervical spine, neck injuries, whiplash, cervical degeneration is main cause of dizziness.^[5]

In upper cervical region, neck pain, reduced proprioception of cervical region leads to dizziness which can be initiated due to end range movements of cervical spine. Pain, reduced cervical joint ROM, uncontrolled movements leads to deep cervical muscle insufficiency which indeed results in altered structure of deep neck muscles.^[6]

Cervical spine disorders not being highlighted in locomotor system dysfunction, deep neck flexors play an important role. Disequilibrium, vertigo, dizziness occurs due to alteration in locomotor system dysfunction.^[7]

Altered performance of cervical spine muscles results in impaired balance between posterior neck aspect and deep cervical flexors (DCF) with improper posture, alignment of the cervical spine leading to dysfunction and neck pain.^[8] To reduce dizziness and improve proprioception specifically for reducing neck pain, DCF activation regimes- gaze stability exercises, head and trunk control exercises and co-ordination of hand and eye exercises are being focused. Studies suggest that exercises for activation of deep cervical muscles improve altered neuromuscular control of the cervical flexors, reduces provocation of dizziness symptoms.^[8]

The main aspect of vestibular rehabilitation is graded exercise program including body, head/eye movements

reducing vestibular dysfunction thereby, eliminating fear, gaining confidence.^[9] The goals of vestibular rehabilitation mainly include education of patient about symptoms, balance training, Limiting motion provoking symptoms, Improve general conditioning, reduce disability etc.^[10] In cervical spondylosis, cervical zygapophyseal joints are under mechanical stress causing poor balance, dizziness linked with spinal degeneration.^[11]

Chronic dizziness is accompanied by anxiety, hyperventilation, neck pain caused by attaining a steady posture to avoid provocation of symptoms.^[12]

BPPV is described as episodes of vertigo on altered head position. Posterior canal BPPV occurs in 90% of cases whereas lateral BPPV 8% of the cases.^[13] Diagnosis of posterior canal BPPV is done with history of vertigo on changing head positions, nystagmus on performing Dix Hallpike test which determines semi-circular canal dysfunction and considered a gold standard test. Diagnosis of lateral BPPV is done with history of vertigo with changes in head position, presence of horizontal nystagmus on performing supine roll test.^[11,13]

Poor balance, postural issues due to provoked head movements are disabling for Vertigopatients having adverse effect on quality of life and health. It is necessary to improve stability of surrounding neck structures to improve strength of the muscles which would aid in attaining reduction of symptoms triggered on performing head movements, postural stability and achieve balance.

Materials and Methodology

Study type-Experimental study, Study Design-Comparative study (pre-treatment and post-treatment), study duration-3 months, Place of study- Physiotherapy OPD, KIMS Hospital, Karad, Sample size-20, Sampling Method-Simple random sampling.

Inclusion Criteria: Subjects diagnosed with dizziness or vertigo secondary cervical pathologies like stenosis, facet osteoarthritis, disc herniation, spondylosis, BPPV, Gender- Male, Female.

Age group 18 -30 years.

Exclusion Criteria: Subjects with a non-vestibular cause of dizziness, progressive central disorders, Diabetes Mellitus, Hypertension.

Outcome Measures: Ethical Clearance was obtained from Institutional Ethical Committee KIMSDU (0368/2018-2019). Demographic data was collected. Procedure was explained to included subjects, written consent was taken from patients willing to participate and were enrolled into control and experimental group (10 subjects each) by simple random sampling. Pre-assessment was done using DHI (test retest reliability $r = 0.97$, good internal consistency reliability $r = 0.89$)^[14] and MSQ^[14] [ICC]=0.99 and test sessions (ICC=0.98 and 0.99) following which the control group received Vestibular rehabilitation and Experimental group received exercises for activation of deep neck muscles with Vestibular rehabilitation. Post test subjects from both the groups were assessed for DHI and MSQ. Results were analyzed on the basis of differences between pre-assessment and post assessment.

Subjects in the Experimental group (group A) received Vestibular Rehabilitation along with exercises for activation of deep neck muscles for 4 weeks (3 days per week 30 minutes per session).

1. Gaze Stability Exercises.^[14]
2. BPPV treatment Techniques^[14]
 - (a) Canalith maneuver
 - (b) Liberatory Maneuver
 - (c) Brandt Daroff Exercises^[14]
3. Balance exercises and progressions ^[14,15]
 - (a) Begin with standing, feet shoulder width apart and arms across the chest. Progression-Bring feet together, close eyes and stand on cushion/foam.
 - (b) Begin with ankle sways: Medial, lateral, anterior, posterior. Progress to Circle sways with eyes closed.
 - (c) Walk with heel touching toe on firm surface. Repeat the exercise on carpet
 - (d) Walk 5 steps and turn 180 degrees left and right. Progress with closed eyes making smaller turns.
 - (e) Walk and move the head side to side, up-down. Count backward from 100 by threes.

Exercises for activation of deep neck muscles^[16]:

Isometric Exercises:

- (a) Flexion-Patient places both hands on forehead while pressing forehead on palms without moving head.
- (b) Side bending-Patient places one hand over the side of head attempting side bend, without any motion.
- (c) Axial Extension-Patient presses back of head against the hands placed at back on top of head.
- (d) Rotation-Patient presses one hand against superior region, lateral to the eye looking over shoulder without attempting movement.

Isometric resistance activities-a)Patient stands with inflatable ball between forehead and wall. Having chin tucked in, forward head posture is avoided. Position was maintained by superimposing arm positions. Progressed by adding weights to arm motions.

DCF-In supineposition having patient rest on wedge shaped bolster underthorax and head reducing effects of gravity. The patient was asked to practice chin tucking, head curl up. Progressed by decreasing angle of board/wedge and adding manual resistance.

Manual resistance-cervical muscle-Patient position was supine. Placing one hand on the patients head to oppose motion.

Functional exercises-Patient specific functional activities-pushing, lifting, reaching activities. Contracting DCF patient was asked to gently nod head so flexion occurs between head/neck. Progression of movement up to middle of neck.

Slowly return to neutral position. Patient was asked to move one vertebra at a time. Patient was asked to activate deep cervical core muscles indifferent positions for dynamic activities. Standing, back lying, Sitting, Stomach lying, Side lying, Quadruped, Squatting, Walking.

Subjects in Control Group (Group B) received Vestibular Rehabilitation for 4 weeks (3 days per week 30 minutes per session).

Results

1. Within Group Comparison

Dizziness Handicap Inventory

Group A:

Table No. 1

Dizziness Handicap Inventory			
PreTest		Post Test	
Mean	SD	Mean	SD
37	6.48	23.6	8.09

Interpretation-Pre and Post Mean and SD values which was 37±6.48 and 23.6±8.09 respectively. Post treatment extremely significant improvement was noted according to the P value-0.0003.

Group B:

Table No. 2

Dizziness Handicap Inventory			
Pre Test		Post Test	
Mean	SD	Mean	SD
38.6	3.27	35.2	5

Interpretation-Pre and Post Mean values which was 38.6±3.27 and 35.2±5 respectively. Post treatment improvement was not quite significant according to the p value -0.0786.

Motion Sensitivity Quotient:

Group A:

Table No. 3

Motion sensitivity Quotient			
Pre- Test		Post Test	
Mean	SD	Mean	SD
30.82	5.75	9.72	4.83

Interpretation-Pre and Post Mean and SD values which was 30.82±5.75 and 9.72±4.83 respectively. Post treatment extremely significant improvement was noted according to the p value-<0.0001.

Group B:

Table No. 4

Motion Sensitivity Quotient			
Pre Test		Post Test	
Mean	SD	Mean	SD
30.62	7.36	25.28	7.19

Interpretation-Pre and Post Mean values which was 30.62±7.36 and 25.28±7.19 respectively. Post treatment improvement was not considered significant according to the p values - 0.075.

2. Between Group Comparison

Dizziness Handicap Inventory

Table No. 5

Dizziness Handicap Inventory				
Group A	Group B	p value	t value	Inference
23.6±8.09	35.2±5	0.0012	3.852	ES

Interpretation-Post Mean and SD values which was 23.6±8.09 and 35.2±5 respectively in the study. Post treatment improvement was considered extremely significant according to the p values- 0.0012.

Motion Sensitivity Quotient

Table No. 6

Motion Sensitivity Quotient				
Group A	Group B	p Value	t Value	Inference
9.72±4.83	25.28±7.19	<0.0001	5.67	ES

Interpretation-Post Mean and SD values which was 9.72±4.83 and 25.28±7.19 respectively. Post treatment improvement was considered extremely significant according top value<0.0001.

Conclusion

Activation of deep neck muscles as an adjunct to vestibular rehabilitation in vertigo had significant effect improving postural stability, balance, functional mobility and reduced impact of symptoms on daily activities. So, this study accepts alternate Hypothesis.

Discussion

Among subjects,altered vestibular function, balance issues, postural instability; subjects in experimental group showed significant improvement with mean± SD

DHI for 1) Group A-23.6±8.09, 2) Group B-35.2±5 and MSQ were 1) Group A-9.72±4.83, 2) Group B-25.28±7.19.

A study conducted on Dizziness in older adults [17] suggests that more often women are affected by vestibular symptoms than men, accordingly our study includes 11 females, 9 males. Our study includes subjects within age group of 18-30 years with Mean± SD of 25.5±3.50, as in, a study conducted on presentation of dizziness in general practice community sample of working age group [12] suggested that dizziness occurring in younger population is more often linked to BPPV, labyrinthitis, anxiety disorders, etc.

Group B subjects received exercises for Vestibular Rehabilitation which included Gaze stability exercises, BPPV treatment techniques, Balance, progression exercises. Group A subjects received- Isometrics of neck, Isometric resistance activities, DCF, functional exercises, further progression exercises along with Vestibular Rehabilitation.

A study conducted on “Vestibular rehabilitation therapy: Review of indications, mechanisms and key exercises” [3] suggests that gaze stability exercises, exercises of eye, head movements, exercises done while standing on a narrow base or cushion with eyes closed improve postural stability, reduce vertigo symptoms, improve activities of daily living and aid in alleviating provocation of vertigo. In our study, subjects in control group who received Vestibular rehabilitation showed improvement in gaze stability, postural control, balance activities according to pre and post mean values of DHI - 38.6±3.27 and 35.2±5.0 and MSQ- 30.62±7.36 and 25.28±7.19 respectively.

Another study on “Clinical effects of DCF muscle activation in patients with chronic neck pain” [18] suggested that neck pain, functional status, neck-shoulder postures in chronic neck pain patients were improved by (DCF) exercises than simple general strengthening exercises. Similarly, in our study activation of deep neck muscles with vestibular rehabilitation proved effective as strengthening of deep neck muscles improved stability which aided for proper alignment of cervical spine along with improved proprioception thus reducing pain, dysfunction and dizziness levels.

A study on trigger points and head/neck posture in migraine individuals suggests, Correct alignment of the vertebra of the cervical spine is related to muscle contraction. [19] Accordingly, in the current study

activating the deep neck muscles along with vestibular rehabilitation aided the individuals to attain stability of deep neck muscles thereby maintaining correct head/neck posture alignment.

Attaining good cervical spine posture reduces tension, overloading on posterior cervical structures. [20] The endolymph moves effectively in each of semicircular canals with response to head movement. Therefore, gaining good stability for deep seated cervical spine muscles with activation reduces intensity of dizziness, imbalance, postural instability.

Thus, the results show that Experimental group had significant improvement in outcome variables reducing symptoms of Vertigo, improved postural stability, reduced dizziness, improved balance and activities of daily living. And confirmed using statistical analysis by ‘Paired t- test’ for within group comparison and ‘Unpaired t-test’ for between group comparisons.

This suggests that activation of deep neck muscles along with Vestibular Rehabilitation is effective in improving the postural control, balance, reducing cervical spine dysfunction, pain and limiting provocation of symptoms in vertigo. It can be due to specificity of exercise program that helped in achieving stability of neck muscles which aided the individuals attaining proper head/neck posture delaying spinal degeneration thereby nullifying symptoms.

Conclusion

The current study suggests that exercises for activation of deep neck muscles along with Vestibular rehabilitation were effective in reducing provocation of symptoms of vertigo, its impact on daily activities, disequilibrium, and balance issues.

Conflicts of Interest: Nil

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Ethical Clearance: Study approved by Institutional Ethics Committee of Krishna Institute of Medical Sciences Deemed to be University.

References

1. Ahmed H Alghadir, Zaheen A Iqbal, Susan L Whitney. An update on vestibular physical therapy. *Journal of the Chinese Medical Association.* 2013;76 :1-8.

2. Burak Kundakci, Anjum Sultana, Alan J Taylor, Mansour Abdullah Alshehri. The effectiveness of exercise-based vestibular rehabilitation in adult patients with chronic dizziness: A systematic review [version 1; referees: 2 approved] F1000 research 2018,7;276.
3. Byung In Hang, Hyun Seok Song, Ji Soo Kim. Vestibular rehabilitation therapy: Review of indications, mechanisms and key exercises. *J Clin Neurol.* 2011;7: 184-196.
4. Helen Cohen. Vestibular Rehabilitation Improves Daily Life Function. *The American Journal of Occupational Therapy.* 1994;48:10.
5. Susan A. Reid, Darren A. Rivett, Michael G. Katekar, Robin Calliste. Comparison of Mulligan Sustained Natural Apophyseal Glides and Maitland Mobilizations for Treatment of Cervicogenic Dizziness: A Randomized Controlled Trial. *Phys Ther.* 2014;94:466-476.
6. Marloes Thoomes-De Graaf, Maarten Schmitt. The Effect of Training the Deep Cervical Flexors on Neck Pain, Neck Mobility and Dizziness in a Patient with Chronic Nonspecific Neck Pain After Prolonged Bed rest. A case Report. *Journal of Orthopaedic and sports Physiotherapy.* 201;42:10.
7. Yifeng Shen, Qiauyin zhou, Xinyuezhu Zuyun Qiu, Yan Jia, Zixiang Liu et al. Vertigo caused by longus colli tendonitis. A case report and Literature review. *Medicine.* 2018;97:45(e13130).
8. Marwa Shafiek Mustafa Saleh, Nagwa Ibrahim Rehab, Moussa Abdel Fattah Sharaf. Effect of deep cervical flexors training on neck proprioception, pain, muscle strength and dizziness in patients with cervical spondylosis. A randomized control trials. *Physical therapy and rehabilitation.* 2018;5:4.
9. Lucy Yardley, Sandra Beech, Luke zander, Tyrrel evans, John Weinman. A randomized controlled trial of exercise therapy for dizziness and vertigo in primary care. *British Journal of General Practice.* 1998; 48, 1136-1140.
10. Michael Smith-Wheelock, Neil Shephard, Steven Telian. Physical Therapy Program for Vestibular Rehabilitation. *The American Journal of otology.* 1991;12:3.
11. Susan A Reid, Darren A Rivett, Michael G Katekar, Robin Callister. Efficacy of manual therapy treatments for people with cervicogenic dizziness and pain: protocol of a randomised controlled trial. *BMC Musculoskeletal disorders.* 2012;13:201.
12. Lucy Yardley, Natalie aowen, Irwin Nazareth, Linda Luxon. Prevalence and presentation of dizziness in a general practice community sample of working age people. *British journal of general practice.* 1998;48:1131-1135.
13. Anh T. Nguyen-Huynh. Evidence -Based practice: Management of Vertigo. *Otolaryngol Clin North Am.* 2012;45(5):925-940.
14. Susan O Sullivan, Thomas J Schimtz, George Fulk. Physical Rehabilitation. Edition -6. Chapter 21, Page no.-971-985.
15. Palak M Khichadiya, Kanase Suraj B. Effect of Specific Transverse Abdominal Muscle Strengthening and Conventional Therapy for Trunk Control in Paraplegic Subjects. *Indian journal of physiotherapy and occupational therapy,* 2017; volume 11 (2), 184-189.
16. Carolyn Kisner, Lynn Allen Colby. Therapeutic exercise, foundation and techniques, editin-6. Chapter 16. Page no. 522-523.
17. Lee R, Elder A: Dizziness in older adults. *Medicine.* 2013;41(1):16-19.
18. Jin Young Kim, Kwang il Kwag. Clinical effects of deep cervical flexor muscle activation in patients with chronic neck pain. *J. Phys. Ther. Sci.* 2016;28: 269–273.
19. Ferracini GN, Chaves TC, Dach F, Bevilaqua-Grossi D, Fernandez-de-las-Penas. C., Relationship between active trapezius trigger point and head and neck posture in patients with migraine. *Am J Phys Med Rehabil,* 2016;95:831-839.
20. Boyoung Im, Young Kim, Yijung Chung, Sujin Hwang. Effect of scapular stabilization exercise on neck posture and muscle activation in individuals with neck pain and forward head posture. *J Phys Ther Sci* 2016;28:951-55.

Life Beyond the Diagnosis of Breast Cancer: A Qualitative Study on the Lived Experiences of Breast Cancer Survivors

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Abstract

Background: The advances in biomedical technology that lead to an increase in early diagnosis and treatment have helped to increase the number of health breast cancer survivors in Indian as well as worldwide. Researches carried out on survivorship have focused mainly on the psychological impact and health outcome of the disease. The goal of this study was to focus on exploring the lived experiences of breast cancer survivors from diagnosis of the disease till the survivor life.

Objective: To explore the lived experiences of women who are breast cancer survivors.

Design, Setting and Participants: A purposive sampling strategy was used to recruit participants from a medical college hospital. A total of 18 women breast cancer survivors were interviewed.

Findings: The study concluded with four major themes that described lived experiences of women. These were factors from the diagnosis and treatment of breast cancer impacting survivorship, support system and relationships, and issues in survivor life. All the participants noted that it was so stressful journey that they went through after diagnosis till the completion of various treatment modalities. Each one found their own way to cope with the stress. Support from family was shared as the key which gave them strength and courage through the different stages of treatment. However, they found it difficult to explain what survivorship meant.

Conclusion: This study using in-depth interview techniques, shed light on the lived experiences of breast cancer survivors who have completed the treatment. All of them had fear and frustration during their diagnosis and treatment. They felt depressed due to body changes still the support they received from their partners and family helped them to come out of that feelings. However, they noted that they still live with the fear of recurrence of cancer.

Keywords: *Lived experiences, breast cancer, survivor, qualitative.*

Introduction

Breast cancer is now the most common cancer in most cities in India, and 2nd most common in the rural areas. In India, we are witnessing more and more numbers of

patients being diagnosed with breast cancer to be in the younger age groups¹. Breast cancer has ranked number one cancer among Indian females with age adjusted rate as high as 25.8 per 100,000 women and mortality 12.7 per 100,000 women. The age adjusted incidence rate of carcinoma of the breast was found as high as 41 per 100,000 women for Delhi, followed by Chennai (37.9), Bangalore (34.4) and Thiruvananthapuram District (33.7).²

At the same time, the number of breast cancer survivors is increasing due primarily to advances in

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biomedical technology leading to an increase in early diagnosis and treatment. Mortality rates also have been decreasing since 1990, and there are over 2.9 million women in the United States who have survived breast cancer.³ The cancer registry data at the urban city level show that India will face a rapidly increasing number of breast cancer survivors in future. However, this survivor population has until now received very little attention.⁴ Health professionals have low awareness of recognizing the long-term and late effects of cancer and its treatment and supportive care services specifically for cancer survivors are lacking in the country.⁵ Under such circumstances, breast cancer survivors are often marginalized in the health-care system and have many unmet medical and psychosocial needs, requiring special attention.

There is not much research done on the various experiences Indian women are undergoing after the diagnosis and treatment of Breast Cancer. The term survivor is defined as life without cancer after treatment.⁶ Thus, the purpose of this phenomenological study was to understand the lived experiences of breast cancer 'survivors'. The central research question was 'What is the experience to be a breast cancer survivor?'

Sub questions were as follows:

1. How did they cope with the diagnosis of cancer?
2. How did the cancer diagnosis affected their personal life?
3. How do breast cancer survivors perceive life after diagnosis and treatment?

Method

Ethics Approval: The central ethics committee of KSHEMA has approved the study. Each participant was informed about rights to withdraw from the study anytime they want and principles of protection of human subjects, and each approved their participation with a written informed consent.

Selection and recruitment of participants: All the women were recruited from K S Hegde Medical Academy. Women those who have come for follow up after two year were considered for sampling. A purposive sampling strategy was used by researcher to recruit the participants (N = 18). The desire was to have a sample that represented a variety of perspectives but shared some common experiences. The aim of the purposive strategy was to recruit participants that represented a

range of perspectives within the follow up cases.

A diversity of experiences was based on age at diagnosis, stage at diagnosis and financial background. The goal was to get a broad cross section of perspectives within this framework. At eighteen participants, we had reached a level of saturation with the population of breast cancer survivors from our potential sample frame. There was no further new information that contributed to our analysis of the breast cancer survivor experience. The inclusion criteria were women: (i) 18-70 years of age (ii) English-speaking; (iii) a diagnosis of breast cancer; and (iv) completion of treatment, surgery, chemotherapy and/or radiation.

Data Collection: The data collection method was by a one-to-one semi-structured, in-depth interview with all participants in the counseling room of the Oncology OPD. Topic guides were developed based on the cancer literature and the researchers' experiences working with cancer patients. During the interview the participant's statements provoked further questions and clarifications.

Analysis: The research was focused to develop a set of logical and consistent understandings based on the perspectives of women with breast cancer. Data were analyzed following phenomenological coding guidelines. Analysis of data began after all tapes were reviewed by the researchers several times to get familiar with data and expressions of participants in regard to their breast cancer experience. Initially a line-by-line analysis of the data was conducted and the identified statements were highlighted. Next the overlapping statements were eliminated. From the final list of statements, the researchers created meanings without disrupting the original meaning of the participants. Codes were assigned to all meaningful units, which were then organized into categories of similar codes. Finally the themes were developed by considering all categories of codes to include the commonalities that cover several categories which gave a clear understanding of the experiences of breast cancer survivors.

Reliability and validity of the study: The following measures were taken by the researchers to ensure the reliability and validity of the instrument and study: (i) the first author who interviewed all participants transcribed tapes verbatim and completed the first phase of analysis (ii) the second and third authors reviewed the codes and themes to ensure the validity of the themes and subthemes with the reality (iii) finally all the authors met to explore differences and final refinement of codes.

Rigor: To ensure rigor we initially established methodological coherence by ensuring the validity across the study that each part matches the research objective and also is consistent with its methodological assumptions. Secondly, we adopted the rule of purposive sampling by ensuring that 18 participants selected were able to provide a rich and in-depth understanding of survivorship experience. To enhance the reliability of the study, we used a single researcher and the same interview schedule to increase the consistency of data collection.

Findings: Eighteen breast cancer survivors participated in interviews that lasted from 60 to 90 min. The age of participants ranged from 32 to 69 years. Of the eighteen women, five were diagnosed at stage I, eight at stage II and five women had stage III cancer. Nine women had been cancer free between 6 and 12 months, while eight reported between 1 and 2 years cancer free. Analysis of the interviews identified three major themes that were important to the lived experiences of the women. These were (i) diagnosis and treatment of breast cancer impact on survivorship (ii) support system impact on survivorship (iii) and issues in survivor life.

Factors from the diagnosis and treatment management impacting survivorship: According to some of them though very little, the awareness they had about breast cancer helped them to identify early and they feel happy about it. However most of them agreed that they didn't have much knowledge about breast cancer and hence they ignored the appearance of lump as a common symptom of any infection and expected to disappear in due course. Only when it grown to severe extend where it was very much palpable they seek for medical checkup, by then it crossed first stage.

Survivor 3 explained that one day accidentally she felt 'a small lump on the left lateral side of her breast, which was of the size of a small peanut' and she could sense the danger that something is wrong with her breast. She was happy that she had enough awareness about breast cancer from the media and society and she rushed for the treatment. Although she was happy that she could diagnose her cancer in the initial stage she worries about the larger portion of society who is ignorant about the same and landing up in the late stages for the diagnosis and treatment.

Stage at diagnosis was another factor that impacted the survivorship. Survivors explained about the reaction

at the point of diagnosis as 'shocked' or as 'end of life' feeling. Survivor 2 who was diagnosed stage 2 expressed as 'I thought it is going to be end of my life as the recurrence may be at any time and any form'. Though she was a health worker, she ignored the initial symptoms and postponed her screening test at the earlier stage which she is regretting very badly. Those survivors who had an early stage diagnosis were happy that their recurrence chances are less. Whereas those who had late diagnosis were more upset and fearful as they were having a fast recurrence.

The changes in their physical appearances were the major problem they had faced. None of them seemed to be bothered about the disfigurement by mastectomy; however all of them had a difficult time to cope with their emaciated body and the evident hair loss during chemotherapy. The financial burden was expressed by two of them who didn't have any insurance coverage. During treatment they had to literally sell of many things to fetch money for the treatment. Who had health insurance were thankful for that so that they could maintain a good quality of life during treatment which was difficult if they didn't have an insurance coverage.

According to them the journey after cancer diagnosis and treatment was a 'terrific one with full of anxieties and uncertainties' which was even complicated by other associated problems of family, work and financial issues.

Support system impact on survivorship: All of them had expressed that the support they had received during and after the treatment of cancer was the key factor for their successful completion of cancer journey. Survivor 12 said 'I was so surprised to see the overwhelming care and concern that was showered up on me by my relatives and was feeling so blessed to know my importance for all of them'.

Participants also expressed that even the friends and colleagues have turned up to be so caring and protecting in all the phases of the treatment. Emotionally, physically and financially all of them had offered themselves to these participants. Survivor 7 expressed her concern for her parents by saying 'I was feeling that I had gone back to my childhood, seeing the way my parents caring for me as if I was in my preschool period, and it was hurting me that instead of caring for them in their retirement life, they had to care for me'. All of them agreed that the support they had received from their closed ones have gave them strength and motivation to complete the journey successfully.

Issues in survivorship: Each participant had their own way of explaining their survivor life. They agree that it was a tough journey, though were not sure what lies in future. Most of them still had a fear of recurrence at any time but said that they are ready to face anything that comes in their life. Most of them were happy that they could come back to their normal life.

Survivor 9 said ‘Now I feel I am more confident on myself and I know what I have to do in my future. I have a plan for each day and a list of things to complete before it (cancer) hits me back again..The days in my hand I feel are counted and will be grateful to God for every blessing he showered up on me’

Discussion

This study envisaged to explore the lived experiences of a cancer survivor and various factors that are affecting the survival life of breast cancer survivors. In the analysis various factors emerged to be having an influence on the survival life and the issues that they experience during their survivorship.

Individuals who had undergone their breast cancer treatment and living a cancer free life are often called as cancer survivors. However most of the survivors are not happy to be called as cancer survivor as it brings all the painful memories to their mind. Some of them expressed that they are still not sure that they are really cancer free. Though the active medical treatment is stopped and they need not go for regular check- ups to hospital, they feel they still have some ailments for which much attention is not given.

Some of them said that the care they were receiving from family and friends have suddenly dropped caring and they found it difficult to adjust as their recovery is not complete. From this study the major problem breast cancer survivors faces is the fear of recurrence. They live their day and night thinking when it will come back. One of them even expressed her wish to surrender to death if recurrence occurs. Along with the fear of recurrence they also had concerns about body disfigurement, resuming their family and work responsibilities, sexual life post mastectomy which was supported by other studies.⁷

Social support was one of the key factors which helped them to cope with the stress effectively.⁸ Support from family members, friends and co-workers motivated them and gave them encouragement to fight with cancer. Similar studies also showed the effectiveness of social

support in breast cancer women.⁴ Most of the participants also had the same experiences. Other important factors which came out in the present study were the influencing factors such as stage at diagnosis, age of women during diagnosis etc which had a greater impact on the survivorship. Young women were more depressed and worried about their future and commitments and those who diagnosed cancer at the later stages were having more fear of recurrence and death. This also was supported by similar studies. Consistent with other study findings the hair loss decreased their self esteem and self confidence to a larger extent⁹; in fact the mastectomy did not affect much. Financial burden came from the treatment cost had affected the quality of life of women who were not insured, however others thankful for the services they had received from the insurance.

Conclusion

This study tried to shed some light in to the undiscovered experiences of women went through the traumatic life experiences after breast cancer diagnosis and treatment. It also tried to explore the experiences of survivorship and what it actually meant for them to live in a society with all fears of recurrence. These experiences what they have shared should be a guiding light for health care professionals to plan policies and protocols to support women to undergo the journey of breast cancer survivorship effectively. The three areas identified during the in-depth interviews can be explored further by researchers so that those areas can be focused in the management of women with breast cancer.

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Conflicts of Interest: None declared.

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References

1. Breast Cancer in India, statistical report. Breastcancerindia.net. 2019. [Online]. Available at: <http://www.breastcancerindia.net/statistics/trends.html>. [Accessed 2 Jul. 2019].
2. National centre for disease informatics and research, Three-Year Report of Population Based

- Cancer Registries 2012-2014, National cancer registry programme Indian council of medical research, March 2016. Published NCDIR-NCRP (ICMR), Bengaluru. Ncdirindia.org. (2019). [Online]. Available at: http://www.ncdirindia.org/nrcrp/ALL_NCRP_REPORTS/PBCR_REPORT_2012_2014/ALL_CONTENT/PDF_Printed_Version/Preliminary_Pages_Printed.pdf. [Accessed 2 Jul. 2019].
3. American Cancer Society. Cancer Treatment & Survivorship Facts & Figures 2019-2021. Atlanta: American Cancer Society; 2019.[online] Cancer.org. (2019). Available at: <https://www.cancer.org/research/cancer-facts-statistics/survivor-facts-figures.html>. [Accessed 2 Jul. 2019].
 4. Ali I, Wani WA, Saleem K. Cancer Scenario in India with Future Perspectives. Cancer therapy. 2011 Jan 1;8. [online]. Available at https://scholar.google.co.in/scholar?hl=en & as_sdt=0%2C5 & q=Cancer+Scenario+in+India+with+Future+Perspectives.+Cancer+Therapy & btnG. [Accessed 2 Jul. 2019].
 5. Naughton MJ, Weaver KE. Physical and mental health among cancer survivors considerations for long-term care and quality of life. North Carolina medical journal. 2014 Jul 1;75(4):283-6. [online]. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4503227>. [Accessed 2 Jul. 2019].
 6. Williams F, Jeanetta SC. Lived experiences of breast cancer survivors after diagnosis, treatment and beyond: qualitative study. Health expectations. 2016 Jun;19(3):631-42. [Googlescholar.]. [Accessed 2 Jul.2019].
 7. Northouse LL. Psychological impact of the diagnosis of breast cancer on the patient and her family. Journal of the American Medical Women's Association (1972). 1992;47(5): 161-4. [Google scholar.]. [Accessed 2 Jul.2019].
 8. Salonen P, Tarkka MT, Kellokumpu-Lehtinen PL, et al. Effect of social support on changes in quality of life in early breast cancer patients: A longitudinal study. Scand J Caring Sci. 2013;27:396–405. [PubMed] . [Accessed 2 Jul.2019].
 9. Dumrongpanapakorn P, Liamputtong P. Social support and coping means: The lived experiences of Northeastern Thai women with breast cancer. Health Promot Int. 2017;32(5):768–77. [PubMed]. [Accessed 2 Jul.2019].
 10. Chou AF, Stewart SL, Wild RC, Bloom JR. Social support and survival in young women with breast carcinoma. Psycho-Oncology.2012Feb;21(2):125-33. doi:10.1002/pon.1863. [Googlescholar.]. [Accessed 2 Jul.2019].

Virtual Prominence of Prognosticator Variable in Discriminating Cost Gears. A Pragmatic Analysis in Select Pharma Companies

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Abstract

The purpose of this paper is to identify the cost variables that are relatively important in discriminating Pharmaceutical Companies. The manufacturing costs are a major part of company's total expenses in pharmaceutical industry⁽¹⁾. In this study, a thorough investigation on the cost components and income categories of pharmaceutical companies are analyzed and their relationships were found to understand, to know the difference among various types of pharmaceutical companies. The analysis on the data set between 2009 and 2018 reveals that, costs play a dominant role and they are different for all the five companies that are listed. The study also reveals that there is a considerable amount of discrimination in the cost of manufacturing and operating expenses which discriminate the pharmaceutical companies in their approach towards the market. The Structural Equation Modelling has explained that the variables chosen has a good impact as predicted and it implies that the performance of the company is growing among the years chosen for the study.

Keywords: COGS, Pharmaceutical Manufacturing Companies, Discriminate, Structural Equation Modeling.

Introduction

India is the largest provider of generic drugs globally. Indian Pharmaceutical sector, discovers, develops, produces, and supplies over 50 per cent of global demand for various vaccines, 40 per cent of generic demand in the US and 25 per cent of all medicine in UK to be administered to patients to cure them, vaccinate them and alleviate a symptom. Presently over 80 per cent of the anti-retroviral drugs used globally to combat AIDS are supplied by Indian Pharmaceutical

firms. Every business eventually boils down to a rupee sign, and Pharma Companies are no exception to it. All the manufactured products must be sold for a profit to ensure the company survive and grow with an assurance of competitive advantage in the domestic and global market.

Statement of Problem: In Pharmaceutical sector, the cost of bringing a new drug to the market place has been steadily increasing (2). But at the same time the market grew 5.5 per cent in 2017 to 7.1 per cent. Medicine sales in India increased 8.1 per cent year-on-year in November 2017. Much expenses are incurred in the pre-clinical trials. Further it takes about 7 to 10 years of gestation period to bring in adequate revenue to cover up the developmental costs. This place, pharma companies on a mission mode in discovering a successful drug that clears the approval mechanism, and brings in sufficient revenue on commercialization, and helps firms achieve the desired profits. All this could be possible

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only if the sector is conscious of its inherent cost. Hence this study has been undertaken.

Objectives of the Study:

The following are the main objectives of the study:

1. To Infer the Relative Importance of variables that discriminates pharma companies with lower operating profit and higher operating profit.
2. To Investigate the nature of relationship that exists between various cost components and its profitability

Research Design and Methodology

This study is descriptive in nature which quantifies the behavior of cost components and traces it to the firm performance measured in terms of profitability. The data used in this work were extracted from secondary sources like, the annual reports of the respective pharma companies, web resources from Bombay Stock Exchange, National Stock Exchange, besides, databases like PROWESS, ACE and HOOVERS were also rallied upon. Top Five Pharmaceutical companies, which are extremely performing well were selected based on the annual revenues for 2018. These companies engage themselves in manufacturing of branded generic and prescription drugs, development of wide range of formulation's and therapies. The data, pertains for a period of 2008-09 to 2017-18. Inferential statistics were used to investigate the different dimensions on the selected Pharma companies which include Discriminant Analysis, Multiple Regression, and Path coefficient analysis. The results are presented accordingly in the subsequent pages.

Literature Review: Basu, Et. al. (2008) International Society for Pharmaceutical Engineering, "In the pharmaceutical industry, costs attributed to manufacturing are a major part of a company's total expenses⁽¹⁾. The analysis shows that, between 1994 and 2005, manufacturing costs (as a percentage of total sales) are different for the three groups of companies listed above. Okunbor (2013) "The issue of cost behaviour and cost estimation is vital and fundamental in tactical decision-making, planning and control⁽²⁾. Novák, et. al (2014) "Cost management is one of the most important issues of corporate performance and corporate financial management. This study compares four models that predict cost behavior. From the results of transformed model we believe that asymmetric cost behavior is affected by asymmetric behavior of the production in

kg in proportion to the production time⁽³⁾. Novák et. al. (2014) "The paper is focused to the variability of costs, cost behaviour and discusses the issues of sticky costs. The main goal of this paper is to analyze the issue of the author's project targeted at the topic of cost behaviour and its projection to the costing systems and confront it with the current state of knowledge in the field⁽⁴⁾. "Oberholzer M (2004) "Cost behaviour classification and cost behaviour structures of manufacturing companies. The purpose of this paper is to determine the cost structures of companies that formed part of an empirical investigation⁽⁵⁾. Aleem, et. al. (2016) "After its induction in the 19th century, the pharmaceutical industry covered a long way and now it became one of the most successful and influential industries in the world, with both praise and controversy on its part. Like the other profit-driven organizations, the main aim of the pharmaceutical firms is to earn the maximum profit. The profitability also depends on the costing system. The current paper evaluates the costing systems, the level of satisfaction regarding the costing system, the major problems faced during the costing process and the best method of costing in the pharmaceutical sector⁽⁶⁾. Al-Hebry et. al. (2017) has aimed to show such theoretical cost approach in accounting thought. The article has divided the cost approach into two groups, the traditional approach that includes the volume based costing, French cost accounting approach and contemporary cost approaches which include four approaches activity-based costing (ABC), time-driven ABC, resources consumption accounting and lean accounting⁽⁷⁾. Oluwagbemiga et. al. (2014) "This study investigates the relationship that exists between cost management practices and firm's performance in the manufacturing organizations using data from 40 manufacturing companies listed on the Nigeria stock exchange during the period of 2003 to 2012⁽⁸⁾. Drury (2008) "whether a cost is fixed or variable with respect to a particular activity measure or costs driver is affected by the length of the time span under considerations, stressing that the longer the time span, the more likely the cost will be variable⁽⁹⁾. Lucey (2007) states that classification of cost into fixed and variable, according to their behaviour and characteristics is an essential preliminary to be able to make any form of cost prediction and classification⁽¹⁰⁾.

Relative Importance of Cost Variables Discriminating Pharma Companies: The relative importance of Cost Variables Discriminating Pharma Companies has been studied with the help of discriminant

analysis, path analysis and inter correlation matrix. The results are presented below

Discriminant Analysis: Discriminant analysis is a statistical technique which allows to study the differences from two or more groups with respect to several variables simultaneously and provide a means of classifying any object/individual into the group with which it is most closely associated and to infer the relative importance of each variable used to discriminate from different groups. A linear combination of predictor variables, weighted in such a way that it will best discriminate among groups with the least error is called a linear discriminant function and is given by:

$$D = L_1.X_1 + L_2.X_2 + \dots + L_K.X_K,$$

where Xi 's are predictor variables, Li's represents

the discriminant coefficients, and D is the value of the discriminant function of a particular individuals/element such that if this value is greater than a certain critical value $D^*=(D1 \text{ bar} + D2 \text{ BAR})/2$, the individual would be classified in group I (n1 = 5); otherwise the individual would be classified in Group II (n2 = 6).

In the present study there are two groups namely those Years with Lower Operating profit (Group I n1=5) and Years with Higher Operating profit (Group II n2=6).. Seven Predictor variables considered for the analysis includes the following: Raw material consumes-X1,,Power & fuel used-X2, Employees cost-X3, Other manufacturing expenses-X4, General & Administrative expenses-x5, Selling and Distribution expenses-X6 and Miscellaneous expenses-X7

Table 1: Tests of Equality of Group Means Univariate ANOVAs

Explanatory Variables	Wilk's Lambda	F (DF=1, 9)	Sig
Raw Material-X1	0.16	45.57*	0.00
Power & Fuel-X2	0.17	45.08*	0.00
Employee Cost-X3	0.24	27.74*	0.00
Other Manufacturing Exp-X4	0.39	14.24*	0.00
General Administrative Exp-X5	0.21	34.44*	0.00
Selling & Distribution Exp-X6	0.27	23.89*	0.00
Miscellaneous Exp-X7	0.42	12.24*	0.01

** Significant at 1 % level

The above table showed that the mean difference between two groups with respect to the variables namely X3, X4, X5 and X6 is significant.

Relative Importance of Predictor Variable:
The relative importance of each predictor variables in discriminating from the two groups is obtained and the results are presented below.

Table 2: Relative Importance of Variables in Discriminating Between the Groups

Explanatory Variables	Importance value of the variable (Ij)*	Relative Importance (Rj) %	Rank
Raw Material-X1	27.0034	37.8	1
Power & Fuel-X2	5.4217	7.6	5
Employee Cost-X3	19.9275	27.9	2
Other Manufacturing Exp-X4	9.7009	13.6	4
General Administrative Exp-X5	2.9969	4.2	6
Selling & Distribution Exp-X6	11.8108	16.5	3
Miscellaneous Exp-X7	0.5509	0.8	7
Total	77.4121	108.4	

*(mean difference between lower & higher operating profit) *Disc. coefficient

It is seen from the above table that three variables namely *Raw Material (X₁)*, *Employee Cost (X₃)*, and *Selling & Distribution Expenses (X₆)* are substantially important variable in discriminating between the two groups namely years with lower operating profit and respondents with higher operating profit among Companies..

Path Coefficient Analysis: The Path coefficient analysis segregates the total correlation of each independent variable with the dependent variable Y into direct response and indirect response via other independent variables. The direct effect of each of the explanatory variables on the dependent variable and the indirect effect of each explanatory variable on the dependent variable through other explanatory variables are furnished in the Table No. 4

Table 3: Direct & Indirect Effect of Explanatory Variables on Y-Operating Profit

	RM	PF	EC	OME	GA	SD	MISC	OPPROF
RM-X1	0.57	0.01	-0.62	0.37	0.10	0.19	-0.13	0.49
PF-X2	0.43	0.01	-0.61	0.36	0.11	0.21	-0.09	0.41
EC-X3	0.39	0.01	-0.90	0.52	0.16	0.39	-0.19	0.37
OME-X4	0.35	0.01	-0.78	0.60	0.13	0.33	-0.15	0.49
GA-X5	0.30	0.00	-0.78	0.42	0.19	0.32	-0.26	0.19
SD-X6	0.23	0.00	-0.75	0.42	0.13	0.47	-0.10	0.41
MISC-X7	0.18	0.00	-0.45	0.24	0.12	0.12	-0.39	-0.17

Significant at 5 % level.

It is seen from the above table that among the explanatory variables, the variable Raw Materials (X1) showed higher positive direct effect on the dependent variable Operating Profit (Y). The variable X1 also had higher positive indirect effect on Y through Other Manufacturing Cost (X4) and Selling & Distribution Expenses (X6). The variable Other Manufacturing Expenses (X4) showed higher positive direct effect on Operating Profit (Y) this variable X4 also had higher

positive indirect effect on Y through Raw Material (X1) and Selling & Distribution Expenses (X6) this variable X6 also had higher positive direct effect on Y. Selling & Distribution Expenses (X6) also had higher positive indirect effect on Y through X1 and X4. Hence the three variables Raw Material – X₁, Other Manufacturing Expenses – X₄ and Selling & Distribution Expenses – X₆ are substantially important contributing variable for the dependent variable Operating profit-Y.

Structural Equation Model Determining the Path on the Variables Identified of Select Pharma Companies

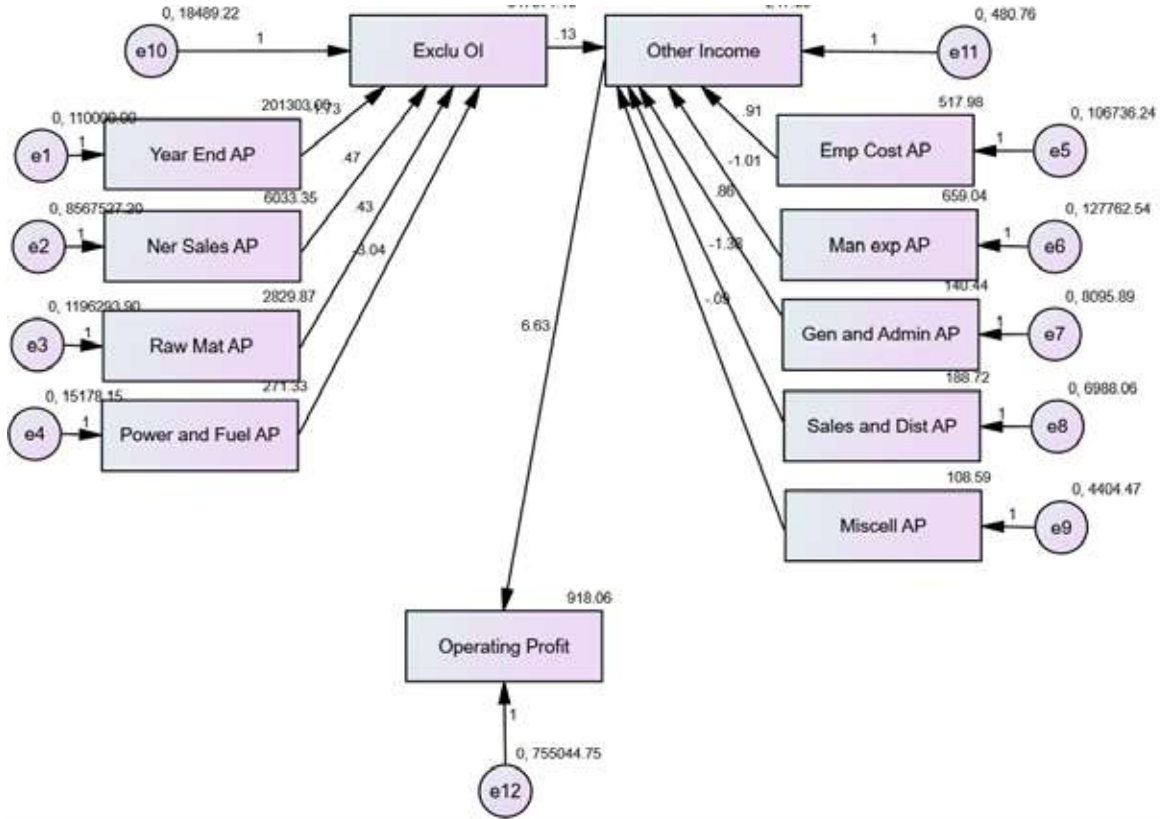


Fig 1. SEM Model for Aurobindo Pharma

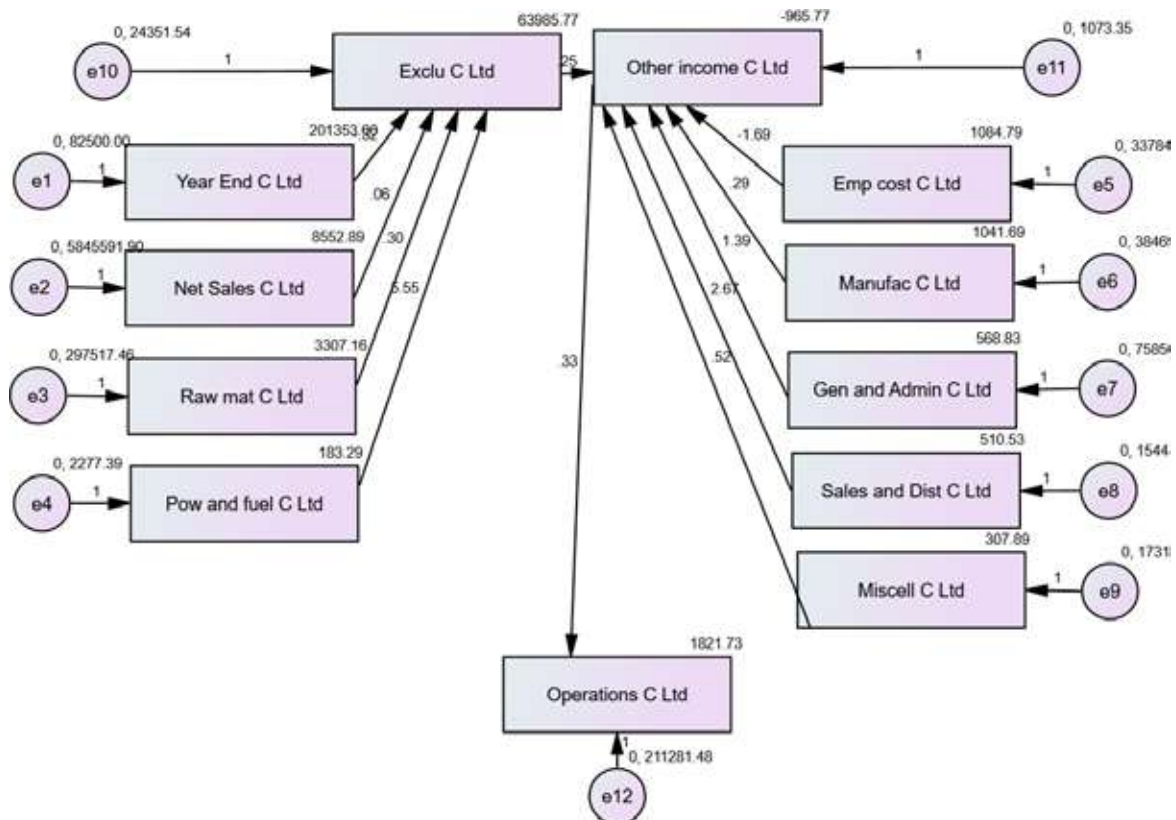


Fig 2. SEM Model for Cipla

The expenses of Aurobindo, Cipla, Dr. Reddy’s, Lupin Pharma Companies has an impact on the Company’s income generated and also has an interdependence among other expenses which reveals the cost behavior and the Firm’s performance level. The values indicate that the variables chosen has a good impact as predicted and it implies that the performance of the company is growing among the years chosen for the study.

Regression Analysis: Multiple regression analysis with Operating profit-Y with a set of independent variables namely X1, X2, X3, X4, X5, X6 and X7, the following regression model is fitted for performance.

$$Y_2 = b_0 + b_1X_1 + b_2 X_2 + b_3 X_3 + \dots$$

Where b1, b2, and b7 are partial regression coefficients; b0-constant and the results are presented in the following equation.

$$\text{Regression Fitted: } Y = -414.83 + 0.60 X_1 + 0.08 X_2 - 1.65 X_3 + 1.31 X_4 + 0.59 X_5 + 1.89 X_6 - 2.46 X_7$$

Table 4: Analysis of Variance for Regression

Source	SS	DF	MS	F
Regression	30334049	7	4333436	7.66**
Residual	26598452	47	565924.5	
R ²	.533			

** Significant at 1 % level

The Multiple regression model indicated that out of the explanatory variables under study six variables namely Raw Materials (X1), Other Manufacturing Expenses (X4), Selling & Distribution Expenses (X6) and Miscellaneous Expenditure (X7) are significantly contributing to Operating Profit - Y. The analysis of variance of multiple regression model for Y indicates the overall significance of the model fitted. The coefficient of determination R² value showed that these variables put together explained the variations of Operating profit-Y to the extent of 53.3 %.

Findings of the Study:

1. Raw Material (X₁), Employee Cost (X₃), and Selling & Distribution Expenses (X₆) are substantially important variable in discriminating between the two groups.
2. Path Coefficient reveals that the three variables Raw Material – X₁, Other Manufacturing Expenses

–X₄ and Selling & Distribution Expenses – X₆ are substantially important contributing variable for the dependent variable Operating profit-Y.

3. The Multiple regression model indicated that out of the explanatory variables under study six variables namely Raw Materials (X1), Other Manufacturing Expenses (X4), Selling & Distribution Expenses (X6) and Miscellaneous Expenditure (X7) are significantly contributing to Operating Profit - Y.
4. The expenses of the company have an impact on the income generated and also has an interdependence among other expenses. The values indicate that the variables chosen has a good impact as predicted and it implies that the performance of the company is growing among the years chosen for the study.

Therefore the present study confirms the earlier studies by Basu, Et. al. (2008)⁽¹⁾ Okunbor (2013)⁽²⁾. Novák, et. al (2014) in the theory that “Cost management is one of the most important issues of corporate performance, and the issue of cost behaviour and cost estimation is vital and fundamental in tactical decision-making, planning and control.

Recommendations for Management: It is recommended for the Management of these Pharma Companies to concentrate on Cost Components like Raw Materials, Selling & Distribution expenses, Other Manufacturing Expenses and Miscellaneous Expenditure, who are significantly contributing to Operating Profit. The Firms to organize adequate training programs on cost management and cost control by professional cost and management accountants.

Limitations of the Study: The author has assumed that the data reported by the companies in their financial statements are based on the same interpretation of various categories. The study is only a representation of companies under pharma sector, a significant number of companies have not been included in the study.

Conclusion

Given the proliferation of Indian Pharmaceutical sector, for various vaccines assumes greater significance in the Market place as they serve the health industry and contribute for the longevity of life of every human being. They are bound to supply the drugs at a price that is affordable to the downtrodden and at the same time balance their competitive advantage for the survival and growth of their enterprise.

Ethical Clearance: This study is an original study by the author's and all references were acknowledged in the references with due reverence.

Source of Funding: Self - Supported

Conflict of Interest: Nil

References

1. Basu, Prabir, Joglekar, Girish, Rai, Saket, Suresh, Pradeep, Vernon & John. Analysis of Manufacturing Costs in Pharmaceutical Companies. *J Pharm Inn.* 2008. 3. 30-40. 10.1007/s12247-008-9024-4.
2. Jonathan A. Okunbor, The Application of Cost Behaviour and Estimation in Organizational Decision Making Process, *J of Res in Natl Dev*, 2013, Vol 11, 1, pp217-227.
3. Suresh P, Basu PK. Improving pharmaceutical product development and manufacturing: impact on cost of drug development and cost of goods sold of pharmaceuticals, *Pharmaceutical Technology & education center*, Purdue University, February 2006.
4. Novák, P., Popesko, B. Cost Variability and Cost Behaviour in Manufacturing Enterprises, *Econ and Sociol*, 2014, Vol. 7, No 4, pp. 89-103. DOI: 10.14254/2071-789X.2014/7-4/6
5. Oberholzer & Jee Ziemerink. Cost behaviour classification and cost behaviour structures of manufacturing companies. *Accoun Res* 2004, Vol. 12 No. 1, 179–193
6. Aleem, M., Khan, M.H. and Hamad, W. A comparative study of the different costing techniques and their application in the pharmaceutical companies, *Audi Fin*, 2016, vol. XIV, no. 11(143)/2016, pp. 1253-1263, DOI: 10.20869/AUDITF/2016/143/1253
7. Adeeb Abdulwahab Al-Hebry & Ebrahim Mohammed Al-Matari, A Critical Study of Cost Approaches in the Accounting Thought: Conceptual Study, *Int Rev of Mgt and Marktg*, 2017, Vol. 2, 3, pp105-112.
8. Oluwagbemiga, O.E., Olugbenga, O.M., & Zaccheaus, S.A. Cost Management Practices and Firm's Performance of Manufacturing Organizations. *Int J of Eco and Fin*, 2014 6(6), 234.
9. Drury, C. *Management and Cost Accounting*, 2008, London, Book Power/ELST
10. Lucey, T. *Management Accounting*, 2007, Britain, Book Power.

Effect of Interdental Brushing as Modality of Plaque Reduction in Ongoing Fixed Orthodontic Patients: A Randomised Clinical Trial Study

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Abstract

Fixed Orthodontic treatment is used to enhance the form, function and aesthetics of an individual. The biggest drawback of a fixed appliance is the increase in plaque and bacteria around the appliance due to the inherent nature of the appliance and inability to clean all the surfaces thoroughly leading to plaque accumulation. This study was designed to evaluate the effect of interdental brushes in reducing plaque accumulation. A randomised split mouth study was done and the results showed a significant reduction of plaque accumulation in the experimental side. The results were statistically significant at $p < 0.001$.

Keywords: Plaque reduction, Interdental brushes, Fixed orthodontic treatment.

Introduction

Fixed Orthodontic treatment entails the use of fixed components on the tooth surfaces to enable the movement of teeth. Although Orthodontic treatment helps in improved facial appearance and confidence of the patients, it does bring with it, a significant risk of periodontal disease in patients who do not keep a meticulous oral hygiene. Several methods of keeping good oral hygiene and reduce plaque accumulation have been devised and the Orthodontist, General Dentist and Periodontist share a responsibility to keep it within acceptable limits. Along with meticulous brushing method the use of interdental brushes for removing plaque around fixed attachments have been advocated. This study aims to quantify the effect of interdental brushing in fixed orthodontic patients. The study is designed to a randomised clinical trial study.

Method and Methodology: 55 fixed Orthodontic patients were selected for the study after excluding patients who had significant periodontal degradation. The patients were evaluated by two examiners and were divided into two groups, the selection of the group was done by picking of lots and the maxillary left set of teeth were selected as controls.

The Plaque index was used to measure the quantity of plaque at the start of treatment (T1) and the end of three months (T2).

Results: The results show a significant difference in accumulation of plaque on the control side after the completion of the study T2. 6 patients discontinued the study as they did not follow a stringent protocol. Overall the difference of plaque formation was significant compared to the control side. The results were statistically significant at $p < 0.001$.

Table 1: Legend: Group 1 Table showing the PI (Plaque Index) of 25 patients undergoing Orthodontic treatment divided into experimental and control group.

Experimental	T1	T2	Control	T1	T2
1	0.5	0.9		0.5	1.3
2	0.2	0.7		0.2	1.4
3	0.3	0.8		0.3	1.3
4	0.5	0.7		0.4	1.5
5	0.4	0.8		0.5	1.4
6	0.3	0.9		0.5	1.5
7	0.4	0.8		0.4	1.6
8	0.5	0.7		0.5	1.4

Experimental	T1	T2	Control	T1	T2
9	0.3	0.8		0.5	1.4
10	0.4	0.9		0.4	1.3
11	0.3	0.8		0.4	1.5
12	0.3	0.7		0.5	1.4
13	0.2	0.5		0.4	1.5
14	0.4	0.5		0.5	1.6
15	0.3	0.4		0.3	1.4
16	0.5	0.8		0.4	1.5
17	0.3	0.7		0.3	1.4
18	0.4	0.7		0.3	1.5
19	0.4	0.8		0.2	1.6
20	0.5	0.7		0.4	1.4
21	0.3	0.8		0.5	1.6
22	0.4	0.7		0.4	1.4
23	0.5	0.8		0.5	1.5
24	0.4	0.7		0.5	1.4
25	0.5	0.8		0.5	1.6

Table 2: Legend : Group 2 Table showing the PI (Plaque Index) of 24 patients undergoing Orthodontic treatment divided into experimental and control group

Experimental	T1	T2	Control	T1	T2
1	0.5	0.7		0.4	1.3
2	0.2	0.5		0.2	1.2
3	0.3	0.6		0.3	1.4
4	0.5	0.8		0.4	1.5
5	0.4	0.7		0.4	1.6
6	0.3	0.6		0.4	1.4
7	0.4	0.8		0.5	1.6
9	0.5	0.5		0.5	1.5
10	0.3	0.6		0.4	1.5
11	0.4	0.7		0.4	1.6
12	0.3	0.8		0.4	1.5
13	0.3	0.7		0.4	1.4
14	0.2	0.5		0.3	1.5
15	0.4	0.7		0.4	1.5
16	0.3	0.5		0.5	1.4
17	0.5	0.8		0.4	1.5
18	0.3	0.7		0.5	1.4
19	0.4	0.7		0.5	1.5
20	0.4	0.6		0.5	1.4
22	0.5	0.7		0.5	1.5
23	0.3	0.6		0.5	1.4
24	0.4	0.6		0.5	1.5

Discussion

Maintenance of Oral hygiene is off paramount importance especially when a patient is undergoing fixed orthodontic treatment . Studies have proved that there is an increase in the bacterial count a few hours after fixing the orthodontic attachments¹. Several efforts have been made to improve patient compliance to meticulous oral hygiene, but the peculiarity of the appliance makes it very difficult to rely primarily on tooth brushing with tooth brushes as an effective mean of reduction of plaque accumulation during orthodontic treatment . Several adjunct measures like incorporating oral mouth rinses, interdental brushes and water flossing have been advocated^{1,2} . Studies showing the role of interdental brushes in the reduction of plaque index (PI) have been few and non conclusive³. The role of poor oral hygiene and development of periodontitis and later enamel decalcification in the form of “white spot lesions “ have also been widely published . Hence all method to improve oral hygiene in fixed orthodontic appliances must be taken^{4,5,6,7,8,9,10,11,12,13,14,15} .

The current study was focused on understanding the role of interdental brushing and reduction of PI in patients undergoing orthodontic treatment using interdental brushes . The study was designed as a randomised split mouth study . Both the patients and evaluators were blinded . The results were statistically significant p<0.001 .

Conclusion

The study of effect of interdental brushing using interdental brushes was designed as a randomised split mouth study, the results show a significant reduction in plaque index between the control and experimental side . The use of interdental brushes help in significantly lowering the plaque in fixed orthodontic patients .

Source of Funding: Self

Conflict of Interest: Nil

Ethical Clearance: Institutional ethical clearance (SBDCH).

References

1. Reichardt E, Geraci J, Sachse S, Rödel J, Pfister W, Löffler B, Wagner Y, Eigenthaler M, Wolf M. Qualitative and quantitative changes in the oral bacterial flora occur shortly after implementation

- of fixed orthodontic appliances. *American Journal of Orthodontics and Dentofacial Orthopedics*. 2019 Dec 1;156(6):735-44.
2. Eroglu AK, Baka ZM, Arslan U. Comparative evaluation of salivary microbial levels and periodontal status of patients wearing fixed and removable orthodontic retainers. *American Journal of Orthodontics and Dentofacial Orthopedics*. 2019 Aug 1;156(2):186-92.
 3. Bock NC, Von Bremen J, Kraft M, Ruf S. Plaque control effectiveness and handling of interdental brushes during multibracket treatment—a randomized clinical trial. *The European Journal of Orthodontics*. 2009 Dec 3;32(4):408-13.
 4. ZAGHRISSEON BU, ZACHRISSEON S. Caries incidence and oral hygiene during orthodontic treatment. *European Journal of Oral Sciences*. 1971 Aug;79(4):394-401.
 5. Hamp SE, Lundström F, Nyman S. Periodontal conditions in adolescents subjected to multiband orthodontic treatment with controlled oral hygiene. *The European Journal of Orthodontics*. 1982 May 1;4(2):77-86.
 6. Berlin-Broner Y, Levin L, Ashkenazi M. Awareness of orthodontists regarding oral hygiene performance during active orthodontic treatment. *European journal of paediatric dentistry: official journal of European Academy of Paediatric Dentistry*. 2012 Sep;13(3):187-91.
 7. LUNDSTRÖM FR, HAMP SE. Effect of oral hygiene education on children with and without subsequent orthodontic treatment. *European Journal of Oral Sciences*. 1980 Feb; 88(1):53-9.
 8. Hobson RS, Clark JD. How UK orthodontists advise patients on oral hygiene. *British journal of orthodontics*. 1998 Feb;25(1):64-6.
 9. KLOEHN JS, PFEIFER JS. The effect of orthodontic treatment on the periodontium. *The Angle Orthodontist*. 1974 Apr;44(2):127-34.
 10. Mitchell L. Decalcification during orthodontic treatment with fixed appliances—an overview. *British Journal of Orthodontics*. 1992 Aug 1;19(3):199-205.
 11. Årtun J, Brobakken BO. Prevalence of carious white spots after orthodontic treatment with multibonded appliances. *The European Journal of Orthodontics*. 1986 Nov 1;8(4):229-34.
 12. Chang HS, Walsh LJ, Freer TJ. Enamel demineralization during orthodontic treatment. Aetiology and prevention. *Australian Dental Journal*. 1997 Oct;42(5):322-7.
 13. Lees A, Rock WP. A comparison between written, verbal, and videotape oral hygiene instruction for patients with fixed appliances. *British Journal of Orthodontics*. 2000 Dec; 27(4):323-8.
 14. Trossello VK, Gianelly AA. Orthodontic treatment and periodontal status. *Journal of periodontology*. 1979 Dec 1;50(12):665-71.
 15. Glans R, Larsson E, Øgaard B. Longitudinal changes in gingival condition in crowded and noncrowded dentitions subjected to fixed orthodontic treatment. *American journal of orthodontics and dentofacial orthopedics*. 2003 Dec 1;124(6):679-82.

Epidemiological Profile of Trauma Victims Attending a Tertiary Care Hospital in Delhi and Application of Haddon Matrix to Identify Risk Factors of Road Traffic Accidents

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Abstract

Background: Injury is one of the leading causes of morbidity and mortality in both developed and developing nations, accounting for 12% of total global burden of disease worldwide and the fourth leading cause of death for all ages. The aim of this study was to improve the understanding of the mode of trauma, severity of injuries, and analyzing the injury patterns to determine the factors associated with their outcomes.

Objectives: To study the epidemiological profile of trauma victims attending the emergency department, to identify the risk factors of road traffic accidents (RTA) using Haddon Matrix and the factors associated with the outcomes of injury in these patients.

Methodology: Cross-sectional hospital based study was conducted amongst 248 patients with injuries aged 15 years and above coming to the Emergency department (ED) using a predesigned semi-structured interview schedule. 9 cell Haddon Matrix was also used for recording the host, agent and environmental factors existing in the pre-event, event and post event phase of the injury.

Results: The mean age of the study participants was found to be 38.06 years with a SD of 16.26. Road traffic accident emerged as the single most important mode of injury (50.8%), followed by fall (23.6%) and assault (13.2%). The mean Glasgow Coma score of the study participants was 13.25 ± 3.14 (mean \pm SD). Around 13% of the participants had sustained vascular injury during the accident. Important host factors identified in Haddon Matrix leading to RTA were over speeding, young age of participants, alcohol intake and fatigue of the driver.

Conclusion: Our study shows that RTA and falls are the predominant causes of trauma.

Keywords: *Epidemiological profile, trauma victims, Haddon Matrix.*

Introduction

Injury is one of the leading causes of morbidity and mortality in both developed and developing nations,

accounting for 12% of total global burden of disease worldwide and the fourth leading cause of death for all ages. Of the various modes of injury, RTA alone contributes to nearly one fourth of the total injury related deaths. For adult men aged 15-44 years road traffic accidents are the biggest cause of ill health and premature death worldwide. ⁽²⁾ According to WHO report on road safety, road traffic accidents would be the fifth leading cause of death worldwide by the year 2030. ⁽³⁾ Incidence of injury is greatest in young adults less than 45 years is associated with a far greater rate of years of life lost (YLL) per death as revealed by the study

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of Indian Council of Medical Research on 'causes of death by verbal autopsy'.⁽⁴⁾ Each year, several thousand people sustain injuries serious enough to produce long term disability.⁽⁵⁾

A majority of trauma deaths also occur in the pre hospital periods due to insufficient pre-hospital care where the first 60 min after trauma has been considered as the "golden hour" of trauma.⁽⁶⁾

The aim of this study was to improve the understanding of the mode of trauma, severity of injuries, and analyzing the injury patterns to determine the factors associated with their outcomes.

Our study also endeavoured to use a 9-cell Haddon's Matrix^(7,8) which is an extension of the well known epidemiological triangle to assess road traffic accidents during the three phases of its occurrence i.e. the pre event phase (i.e. before an injury occurs), the event phase (while an injury is occurring) and the post event phase (after an injury occurs) to identify personal, equipment-related, and environmental risk factors which served as a tool to analyze individual injury events and had a potential to suggest preventive interventions pertinent to each phase.

Objectives: To study the epidemiological profile of trauma victims attending the emergency department, to identify the risk factors of road traffic accidents (RTA) using Haddon Matrix and the factors associated with the outcomes of injury in these patients.

Material and Method

This Cross-sectional hospital based study was conducted at a tertiary care health facility in Delhi from May 2017 to June 2017.

Study Population/participants: Patients with injuries aged 15 years and above coming to the Emergency department (ED) of the Hospital.

Inclusion Criteria: Patients with injuries or their attendants (in case of unconscious patients) giving written consent to participate in the study

Exclusion Criteria:

- Patients with burn injuries, poisoning and with other medical or surgical emergencies
- Patients who have already succumbed to their injuries at the time of arrival

Sample size:1049 persons with injuries attended the emergency department during the months of May and June 2017; out of which 329 required admission in various departments of the hospital and 248 met the above mentioned inclusion criteria, so were included for the purpose of this study.

Data collection tool: A predesigned semi-structured interview schedule comprising of 4 sections was used for the study. First section comprised of socio-demographic details of the participants, second section had questions pertaining to the details of injury sustained in terms of date and time of occurrence of injury and the time of arrival to the ED, mode, type, site, intent and mechanism of injury and any other chronic illness suffered by the patient prior to the occurrence of the injury, the third section contained the details of care received by the patient at the hospital like recording of vital statistics, classification of severity of injury based on Glasgow Coma Score, Revised Trauma Score and presence of vascular injury, investigations done, and information about whether the patient was discharged from ED, required to be admitted or succumbed to his injuries. The fourth section of the schedule had the 9 cell Haddon Matrix in which the host, agent and environmental factors existing in pre-event, event and post event phase of the injury was recorded.

Method: Patients with injuries aged 15 years and above attending the emergency department and meeting the inclusion criteria were included as the study participants. After patient had been evaluated and stabilized (in case of patients with severe injuries) or attended to by the team in the ED, they were contacted by the investigator. They were explained about nature and significance of the study and assured about the confidentiality of the information given by them. Those consenting to participate were interviewed personally by the investigator using a semi-structured schedule. Since it was not possible for the researcher to be physically present in the ED round the clock, the patients who had been admitted were to be contacted in the various departments of the hospital. Those patients who were discharged from the ED before they could be contacted by the researcher, their injury related information was extracted from the record being maintained by the ED.

Data analysis: The data was analyzed using SPSS version 20.0. Simple descriptive tabulation was done for the socio-demographic variables and classification of injuries. Mean/median time delay between the

occurrence of injury and arrival to the hospital was computed. Qualitative analysis was done for Haddon matrix to identify the risk factors of RTA. T test and Chi square tests was used for continuous and categorical variables respectively to find out the factors associated with outcomes of injury. P-value <0.05 was considered as statistically significant result.

Results

A total of 248 participants were included in the study. The mean age of the study participants was found to be 38.06 years with a SD of 16.26. Majority of the participants were males (77%) and were married (60%). Nearly one third of the participants were unmarried. More than one- fourth of our participants were illiterate and a very small fraction had received professional education. The monthly family income of most participants ranged between Rs 5843 to Rs 36551.

Table 1: Details of injury sustained by the study participants (n=248)

S.No.	Variable	Number (%)
1.	Health Facility Visited prior to this hospital:	
	Yes	112 (53.2%)
	No	136 (44.8%)
2.	Able to reach this hospital in the Golden hour	
	Yes	77 (31.2%)
	No	171 (68.8%)
3.	Intent	
	Intentional	41 (15.8%)
	Unintentional	197 (78.2%)
4.	Type of Injury	
	Superficial	117 (45.6%)
	Deep	131 (54.4%)
5.	Mode of Injury	
	RTA	127 (50.8%)
	Fall	59 (23.6%)
	Assault	33 (13.2%)
	Electrocution	2 (0.8%)
	Industrial Accident	11 (4.4%)
	Sports Related	8 (3.2%)
Other	8 (2.8%)	
6.	Mechanism of Injury	
	Collision	70 (28.2%)
	Fall from height	48 (19.4%)
	Fall on level ground	44 (17.7%)
	Blunt Trauma	48 (19.4%)
	Sharp Trauma	18 (7.2%)
	Crush Injury	45 (18.1%)
others	4 (1.6%)	
7.	Site of Injury	
	Head & Neck	73 (29.4%)
	Limbs	175 (70.6%)
	Chest	51 (20.3%)
	Spinal	43 (17.2%)
	Abdomen	31 (12.4%)
	Facial	64 (25.4%)
Poly-trauma	65 (25.7%)	

S.No.	Variable	Number (%)
8.	Injury Setting	
	Home	70 (28.2%)
	Workplace	35 (14.1%)
	School	8 (3.2%)
	Road	130 (52.4%)
	Others	5 (2.1%)
9.	Chronic Illness	
	No	207 (83.5%)
	Yes	41 (16.5%)

Table 1 shows the details of the injury sustained by the study participants. Nearly half of the study participants had visited some other health facility prior to visiting this hospital. Only around one – third of the study participants were able to reach the hospital within the crucial golden hour after the injury. In majority of the study participants (78%) injury was unintentional. Almost 55% of participants had suffered

deep injuries. Road traffic accident emerged as the single most important mode of injury (50.8%), followed by fall (23.6%) and assault (13.2%). Most common mechanisms of injury identified were collision (28.2%) followed by fall from height and blunt trauma (19.4% each). Majority of the study participants suffered from limb injuries. Most of the injuries were sustained on the roads (52.4%) followed by home.

Table 2: Details of care received by the study participants at the hospital(n=248)

S.No.	Variable	Number (%)
1.	Vital Statistics at the time of arrival	
	Observed	140 (56.5%)
	Not observed	108 (43.5%)
2.	Vascular Injury	
	Yes	32 (12.9%)
	No	216 (87.1%)
3.	Investigations*	
	Xray	207 (83.5%)
	CT Scan	123 (49.6%)
	MRI	25 (10.1%)
	ABG	99 (39.9%)
	Blood Tests	221 (89.1%)
	USG	79 (31.9%)
	None	2 (0.8%)
	*numbers (%) do not add up-to 248 as some subjects underwent multiple investigations	
4.	Referral to other department of the hospital*	
	General Surgery	118 (47.4%)
	Neurosurgery	88 (35.3%)
	Orthopedics	163 (65.5%)
	ENT	45 (18.1%)
	Ophthalmology	41 (16.5%)
	Plastic Surgery	32 (12.9%)
	*numbers (%) do not add up-to 248 as some subjects were referred to more than one department	
5.	Operative procedure done within 48 hours of arrival	
	Done	126 (50.8%)
	Not Done	122 (49.2%)

The mean Glasgow Coma score of the study participants was 13.25 ± 3.14 (mean \pm SD). Details of care received by study participants at our hospital (Table 2) showed that vital statistics were observed for more than 56% of the victims. Around 13% of the participants had sustained vascular injury. Investigations most frequently done on the study participants were X ray (83.5%), CT scan (49.6%) and blood tests. Departments to which the study participants were mostly referred were Orthopedics (65.5%) followed by General Surgery (47.4%) and Neurosurgery (35.5%). Nearly 50% of the study participants required some form of operative procedure within 48 hours of arrival at this hospital.

In order to identify the factors associated with the outcomes of injury we studied the association between various socio-demographic variables, severity of injury (GCS) and site of injury, pre-morbid condition of patient and the outcomes. Statistically significant association was seen between age and outcome of injury with participants in the age group of 18 – 30 years showing better outcome in terms of not requiring any surgical intervention as compared to those above 30 yrs. (p value = 0.03). Participants with head and neck injury and those with GCS >13 showed greater likelihood of surgical intervention in our study as compared to participants with injuries of other parts and GCS <13 and this difference was also statistically significant (P= 0.01 and 0.04 respectively).

Qualitative analysis of the Haddon's matrix was done to identify the agent, host and environmental factors operating before, at the time and after the accident took place. Important pre-event factors which were identified were over-speeding, fatigue of driver & alcohol intake (Host factors), faulty brakes (Agent Factor) and low illumination (Environmental Factors). The factors playing a role at the time the event took place were young age, pre-morbid condition of the subject (Host factors), riding on two wheelers, type of vehicle (Agent Factor), and tree too close to the road, ditches (Environmental Factors). Similarly important post event factors identified were severity of injury and bleeding from the wound (Host factors), entrapment (Agent Factor), and slow emergency response and improper handling of the victim (Environmental Factors).

Discussion

Only around one – third of the study participants were able to reach the hospital within the crucial

golden hour after the injury. In majority of the study participants (78%) injury was unintentional. Almost 55% of participants had suffered deep injuries.

Road traffic accident emerged as the single most important mode of injury (50.8%), followed by fall (23.6%) and assault (13.2%). Most common mechanisms of injury identified were collision (28.2%) followed by fall from height and blunt trauma (19.4% each). Most of the injuries were sustained on the roads (52.4%) followed by home.

Similar findings were observed in a retrospective study done by Kundavaram et al at the department of Emergency Medicine at Christian Medical College, Vellore.⁽⁹⁾ Road traffic accident (RTA) (65%) was the most common mode of injury, followed by fall on level ground (13.5%), fall from height (6.3%), work place injuries (6.3%), and others in their study.

In our study majority of the study participants suffered from limb injuries. Head and neck injury was also reported in a substantial proportion of subjects. Study done by Kundavaram et al also showed that traumatic brain injury was seen in 17% of patients while 13.3% had polytrauma with two-wheeler accidents contributing to the majority.⁽⁹⁾

The mean Glasgow Coma score of the study participants was 13.25 ± 3.14 (mean \pm SD). Departments to which the study participants were mostly referred were Orthopedics (65.5%) followed by General Surgery (47.4%) and Neurosurgery (35.5%). Nearly 50% of the study participants required some form of operative procedure within 48 hours of arrival at this hospital. Study of Kundavaram et al also showed that the ED team alone managed 23.4% of patients while the remaining 76.6% required evaluation and treatment by the trauma, surgical teams.⁽⁹⁾

Conclusion & Recommendations

Trauma is a major problem in India with severe and wide-ranging consequences for individuals and society as a whole. Our study shows that RTA and falls are the predominant causes of trauma. The study provides baseline information about the types of injuries which commonly affects the community, has helped identify groups which are particularly vulnerable and also helped elicit the factors which influence the outcome of injuries. This knowledge would go a long way in designing comprehensive intervention strategies like awareness

campaigns and capacity building at all levels of health care to tackle injuries and reduce its impact on those affected.

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Conflict of Interest: None declared

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References

1. Peden M, McGee K, Sharma G. The injury chart book: A graphical overview of the global burden of injuries. Geneva, World Health Organization, 2002. p. 05.
2. World Health Organization. 2nd Global Status Report on Road Safety. 2011. Available from: <http://www.who.int/entity/violence./globalstatusreport/flyeren.pdf>. [Last accessed on 2015 Jan 03].
3. Shah B, Menon GR, Preface Workshop on development of a feasibility module for road injury surveillance, July 11 th -12 th 2006.
4. Injuries in south east asia region: Priorities for policy and action. New Delhi: WHO SEARO; 2002.
5. National Centre for Health Statistics: Health, United States, 1998. Hyattsville, MD, Public Health Services, 1998.
6. Carr BG, Caplan JM, Pryor JP, Branas CC. A meta-analysis of prehospital care times for trauma. *Prehosp Emerg Care* 2006;10:198-206.
7. Barss P, Smith GS, Baker SP, Mohan D. The epidemiologic basis for prevention. In: *Injury Prevention: an International Perspective*. Epidemiology, Surveillance, Policy. New York: Oxford University Press, 1998:12-19.
8. Barss P, Smith GS, Baker SP, Mohan D. Determinants of injuries. In: *Injury Prevention: an International Perspective*. Epidemiology, Surveillance, Policy. New York: Oxford University Press, 1998:75-102
9. Kundavaram Paul Prabhakar Abhilash, Nilanchal Chakraborty, Gautham Raja Pandian, Vineet Subodh Dhanawade, Thomas Kurien Bhanu, Krishna Priya. Profile of trauma patients in the emergency department of a tertiary care hospital in South India. *J Fam Med Primcare*. 2016. 5;3:558-63
10. Boyle MJ, Smith EC, Archer FL. Trauma incidents attended by emergency medical services in Victoria, Australia. *Prehosp Disaster Med* 2008;23:20-8.
11. Babatunde AS, Adedeji OA, Chima PK, Sulyman AK, Ukpong SU, Lukman OA, et al. Clinical spectrum of trauma at a university hospital in Nigeria. *Eur J Trauma* 2002;28:365-9.
12. Mishra B, Sinha Mishra ND, Sukhla S, Sinha A. Epidemiological study of road traffic accident cases from Western Nepal. *Indian J Community Med* 2010;35:115-21.
13. Rastogi D, Meena S, Sharma V, Singh GK. Epidemiology of patients admitted to a major trauma centre in northern India. *Chin J Traumatol* 2014;17:103-7.
14. Shameem AM, Shabbir KM, Agrawal D, Sharma BS. Outcome in head injured patients: Experience at a level 1 traumacentre. *Indian J Neurotrauma* 2009; 6:119-22.

Pattern of Utilization in Primary Health-Care Facility: A Case Study in Nagaon District

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Abstract

A sound health care system is the prime requisite for the effective health conditions of the people of a nation. But unfortunately the performance of India in this respect is quite disappointing. Evidences showed that studies on public health care delivery system are limited both in Indian as well as in the context of the North Eastern Region. This paper is an attempt to assess the pattern of utilization of primary health care. The study is based on primary data. The study found that there are problems associated with health care delivery system like lack of accessibility to the public health care facilities, shortage of medical equipment, shortage of medicines in government hospitals, lack of infrastructural facilities, low seat capacity and over crowdedness etc.

Keywords: *Health, Primary Health Centers, Rural health, Manpower, Health infrastructure.*

Introduction

The most widely acceptable definition of health is that given by WHO (1984), "Health is a state of complete physical, mental and social well-being, not simply the absence of disease". Healthier workers are likely to be able to work longer, be generally more productive than their relatively less healthy counterparts, and consequently be able to secure higher earnings than the latter. Although India has made considerable progress in health infrastructure under NRHM, the improvement has been quite uneven across regions with large-scale inter-state variations (Kumar, 2013¹; Hazarika, 2013²; Baruet *al.*, 2010³). In India a large proportion of people live below poverty line. So, expanding utilization of primary health care is a critical priority for the government of India. Efforts to that have addressed numerous issues and much progress can be reported. The health care

system in India, at present, has a three-tier structure to provide health care service to its people. The first tier knows as the primary tier has been developed to provide health care services to the vast majority of rural people. The primary tier comprises two types of health care institutions: Sub Centre (SC), Primary Health Centre (PHC). Various types of family welfare programme, immunization programme and family planning measures are executed by these entire primary health care service providers.

Utilization of health care is an important component of overall health system and has a direct impact on the burden of disease. Assam government took various steps to increase the accessibility of primary health service to improve health outcomes in the state. In Assam the crude birth rate, death rate and infant mortality rates shown a secular declining trend since 1981, but it has been found to be higher for the state than that of national average as a whole which. In the state the key infrastructure for delivery of primary health care are PHC's, CHE's and SC's.

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The main objective of the study is: To examine the pattern of utilization of primary health-care facility.

Significance of the study: A well-developed health infrastructure contributes positively to better health

status among the people which in turn contributes positively to economic development. In Assam the Crude Birth Rate, Crude Death Rate and Infant Mortality Rates has shown a secular declining trend since 1981, yet it has been found to be higher for the state than that of national average. In the state the key infrastructure for delivery of primary health care are PHCs and SCs. These services are very important for health outcomes. So it is essential to examine the utilization of primary health care services. So far as no significant study has been done on utilization of primary health care service, therefore the study has been attempted.

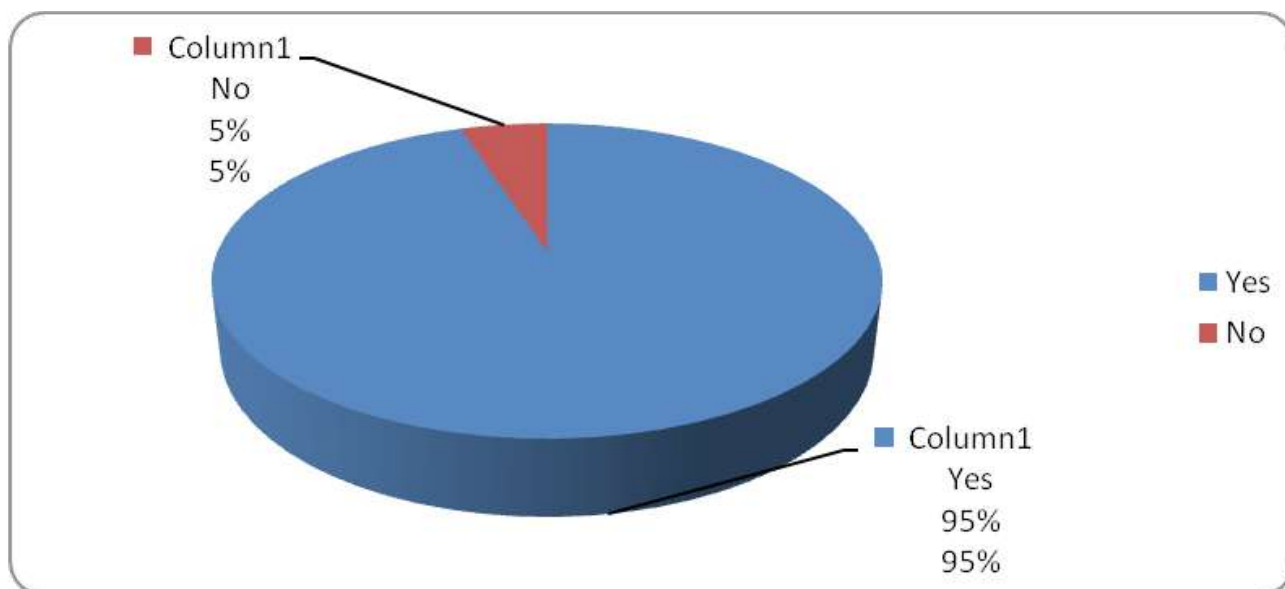
Materials and Method

This research work is based on the primary data collected through a sample survey. The geographical location for the present study has been selected as Nagaon district under judgment sampling method. Nagaon district has two sub divisions viz. Nagaon and Kaliabar comprising 13 development blocks namely Khagorijan, Pakhimoria, Dolonghat, Raha, Batadrba, Juria, Ruphihat, Bajigaon, PachimKaliabor, Kaliabor,

Lowkhowa, Barhampur and Kathiatoli. In the next step one block from each sub division i.e. Juria from Nagaon sub division and Kaliabor from Kaliabar sub division have been selected, as they have highest population in their respective sub division. From the two blocks Balikotia and Jakhalabandha revenue villages were randomly selected for the study. A total of 100 respondents are selected for this survey.

Findings and Discussion: This study tries to analyze utilization of primary health care. For access to government health service, they should be of good quality because of increasing competition from private sources. The reasons behind the low preference for government service are also analyzed in the study.

Knowledge about Primary Health Centre: The following figure (1) presents the level of knowledge of the people about the existence of primary health centres. It shows that major proportion of people knows about the primary care centres. On average, around 95 percent of the total sample population knows about the primary health centres in their area.

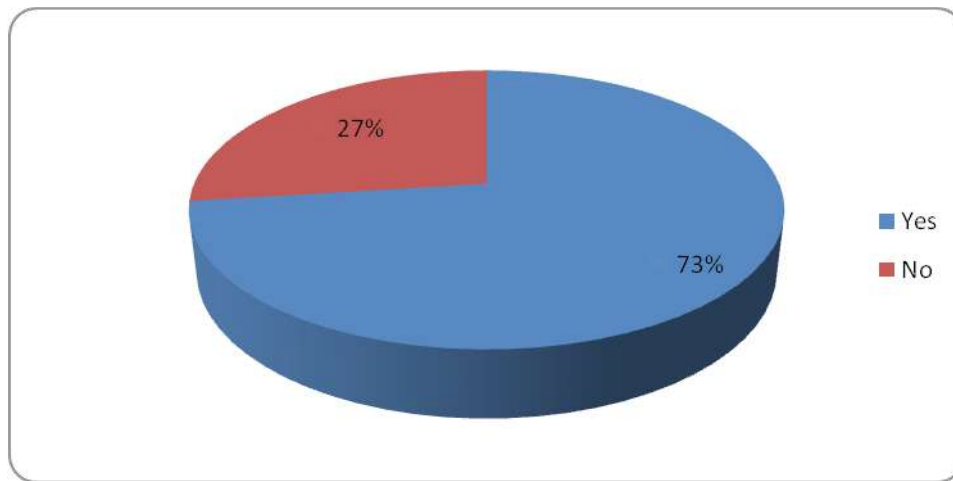


Source: Compiled from Field Survey

Fig. 1: Knowledge about PHC

Ever visit to Primary Health Centre to receive service: The following pie diagram (2) presents the proportion of people who have ever visited to primary health centres to receive services. It shows that around 73

percent of people have visited to primary health centres in their lifetime to receive services. The difference is very high in comparison to knowledge and use of service at primary health centre.



Source: Compiled from Field survey

Fig. 2: Sample Households who have visit to Health Centre

Selection of health institutions by morbid persons:

Selection of institution depends on type of disease and distance to the facility. The sample households reported that the complex cases which cannot get cured in rural health institutions are referred to a higher facility as most of the PHC and CHC are not in a position to deliver the specialized health care service.

Table 1: Distribution of morbid persons seeking treats in different types of health institutions

Type of Institutions	No. of Morbid Persons	Percentage
PHC	16	16%
District hospital	38	38%
Private hospital	20	20%
Private clinic	26	26%
Total	100	100

Source: Compiled from Field survey

It appears from the table (1) that 38 percent of morbid persons seek treatment from district hospital. Likewise 16 percent seek treatment in PHC. However, treatment sought from private hospital is relatively lower (20). 26 percent of morbid persons visit to private clinic for treatment. It has been observed that a relatively higher proportion of morbid person visit to district hospital.

Place of Delivery: Most of the maternal deaths are attributed to the lack of proper care at delivery. In Nagaon district it seems to have been working good and almost all the mothers during 5 years in the survey area reported that their delivery took place in various health institutions.

Table 2: Place of delivery

Place of Delivery	Percentage of Child
Home	7
PHC	19
CHC	23
District Hospital	45
Private hospital	6
Total	100

Source: Compiled from Field survey

Place of Child Vaccine: In the surveyed area it has been reported that most of the children getting vaccine in government institutions like SC, PHC, CHC and government hospital.

Table 3: Place of vaccination

Place of vaccine	Percentage of child
SC	60
PHC	9
CHC	3
District hospital	18
Private hospital	10

Source: Compiled from Field survey

Reason behind low preference for government services:

The major issue emerged in the survey are as follows:

- There are lack of basic facilities at PHC’s and Sub-Centre’s like building, water and electricity, no proper in-patient facility. Moreover at many places, there is no laboratory facility and basic medicines

are also not available. So most of the tests are to be done outside.

- Most of the doctors are more interested in their private practice rather in providing the services through government health services. So, they are speedy and not ready to hear all the problems of patients.
- Lack of cleanness and rush also reported as two major reasons for low preference of government health service.
- Another problem in the government health institutions is the problem of low seat capacity and over crowdedness.

Table 4: Response of the households on reasons behind low preference towards government services

Reason	No. of Households	Percentage
No proper inpatient facility	67	67
Shortage of doctor	55	55
Rush	63	63
Lack of cleanness	74	74
Time consuming	68	68
Many a time lack of medicine	70	70
Most of the test are to be done outside	75	75
Rough behavior of nurses	20	20
Speedy-not ready to hear all problems	40	40

Total sample households: 100

Source: Compiled from Field survey

From the response of the respondents it has been observed that 75 percent of households mentioned most of the test done outside as a major reason behind low preference for government services. Apart from this lack of medicine, lack of cleanness and time consuming are also mentioned as major issues regarding low preference towards government health institutions.

Conclusion

The study indicates that there are problems of accessibility, infrastructure, and rude behavior of the health personnel, shortage of medical equipments, and shortage of medicines, low bed capacity and shortage of manpower in the sample villages. Complaints related to the supply of medicines, lack of testing laboratory were major factors hindering utilization of health care service in primary health centre. Very few medicines are available there and rest have to be brought from outside and most of the test are to be done in outside. Though the households at large are aware of the availability of service at primary health care centre's but the motivation for utilization is very poor. It needs the effective and continuous strategy to develop the demand

and motivation towards the primary health services. The entire health system needs to be reformed to ensure efficient and effective delivery of good quality health services.

Ethical Clearance: It is a review article.

Source of Fund: Self.

Conflict of Interest: Nil

References

1. Kumar, J. R. Role of public Health Systems in the Present Health Scenario: Key Challenges. *Indian Journal of Public Health*. 2013; 57 (3): 133 – 137
2. Hazarika, I. Health Workforce in India: assessment of availability, production and distribution. *South-East Asia Journal of Public Health*. 2013; 2 (2): 106-112
3. Baru, R. Acharya, A. Acharya, S. Shiva Kumar, A. K. and Nagaraj, K. Inequities in Access to Health Services in India: Caste, Class and Region. *Economic and Political Weekly*. 2010; 45 (38): 49-58.

Measuring Adequacy and Optimization of Antenatal Quality of Care and Client Satisfaction During Pregnancy: A Cross Sectional Study of Two Aspirational Districts of Jammu & Kashmir

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Abstract

Ameliorating the mother-child health care has been a global and national priority as evidenced from persistent socio-economic and health policy interventions like National Health Mission. Despite the long standing public policy commitments and interventions to address lack of high-quality health care to scale down mother child mortality, the progress so far has been far from optimal especially during the pregnancy. This study elaborates how service quality structure-processes and the use of proficiencies typically associated with “service quality framework” can have direct application across the continuum of care architecture.

This Study by design is a cross-sectional, based on mixed methodology approach. Study showed that there are lacunae and evidences of inequity, inaccessibility and exclusion in MCH service quality and delivery, we need strategies and service infusion policy interventions aimed at delivering quality health services.

Keywords: *Antenatal care, Quality of care, client satisfaction, Aspirational districts.*

Introduction

Healthcare quality has tenaciously been neglected since early decades in India due to adoption of didactic model of care based on western philosophy, emphasizing less of the structural, social values and traditions of India which has ultimately led to an immense gap that needs to be covered in terms of service quality improvement standards. Despite the long standing public policy commitments and interventions to address lack of high-quality care to reduce maternal-child related deaths and complications, the progress so far has been far from optimal particularly, during the pregnancy and at the time of delivery. Regardless there has been substantial increase in coverage of service delivery, but without convergent improvement of quality of care¹. The suboptimal achievement of MDG goals related to mother-child health in the last decade and now recent concern to achieve goals related to National Health policy 2017 and SDG health goals has elucidated the ignored health quality agenda. Ameliorating the mother-child health has been a global and national priority as

evidenced from persistent socio-economic and health policy interventions like National Health Mission and recent Ayushman Bharat Mission.

Around an estimated 27 million women become pregnant and 17 million newborn babies are delivered each year in India and most of them do not receive appropriate care or care that is as per recommended standards. Access and availability to optimal quality care, during continuum of care is crucial for maternal outcomes and early-infant development. In India it is approximated that annually, the mortality of pregnant women is around 30000 during delivery and about seventy percent of newborn die (WHO 2017) due to poor in effective service delivery, quality processes and deficient health system².

In designing quality care interventions, service process optimization is a crucial element to the health outcomes and benefits related to service factors which matter most to maternal-child health³. During the early phase of pregnancy, the availability and accessibility of

care provided by the competent service providers have been found to be important factor for optimization of care⁴. Enhancing the efficiency and quality are decisive factors in service delivery optimization as it represents around 80% of the cost of healthcare, as compared to 20% for skilled services³. There are evidences of inequity, gaps in management practices and lack of access to high service care throughout continuum of care, especially during critical period of pregnancy⁵. The care during the pregnancy has seen lack of evidence-based intervention and best practices, which could otherwise strengthened the existing maternal-child healthcare system especially in fragile and intense regions like Kashmir valley⁶.

Antenatal Period and Dimensions of Care:

Antenatal care is defined as “the care provided by skilled health-care personnel to women during pregnancy and at the time of labour in order to ensure the quality positive health outcomes”. Care provided during the antenatal period establishes a grounding base across continuum of care, during and after pregnancy⁷, studies have demonstrated that impelling service interventions and managing complications during antenatal period will significantly decrease the maternal and neonatal mortality by 50-60%⁸. Researchers have argued about formulating composite and combining indicators for ANC, but have not been able to deliver within a logic framework for evaluating continuity and adequacy of quality care. In this study, antenatal care quality model assessment based on three dimensions of ANC process—access to antenatal care services; timeliness of services provided and appropriateness of care are used.

Structure of Quality-Care and Models of Measurement: There is no ubiquitously defined structure and definition of “quality care”, it is considered to be a “composite and multilayered” dimensional system existing between provider and client. As per Hulton (2000) maternal quality of care is defined as “the degree to which maternal health services for individuals and populations increases the likelihood of timely and appropriate treatment for the purpose of achieving desired outcomes that are both consistent with current professional knowledge and uphold basic reproductive rights”⁹.

Measurement of quality is a core element of standards of care. Defining measures of quality is challenging task due to multidimensional nature of care, many models have been used to devise a conceptual quality framework, standards and measurement of quality care.

These frameworks can channelize service providers and implementers to augment service quality and delivery. A number of quality care models have been accounted in the literature (Donabedian, 1980; Maxwell, 1992; Ovreteit, 1992; Institute of Medicine, 2001). Many method of assessment have been devised which review quality measurement initiatives and frameworks for monitoring progress in maternal-child healthcare¹⁰. This study applied the Donabedian’s model of quality care coupled with WHO quality care framework as shown in Figure:1.

Donabedian Quality of Care Framework and Customer Satisfaction as Quality Parameter:

This framework underlines client satisfaction as an outcome of care, an crucial parameter of farming quality health care system¹¹. Assessment of quality can be done through its parameters by measuring input, process, and output indicators. Measures of quality includes standards that “assess, measure and monitor” the care as per statements of quality. Many studies explored the gaps in delivery of services and consumer perception of high-quality care and these have shown that health service quality should be measured as perceived quality instead of objective quality due to intangible and inhomogeneous nature of service quality¹².

Objectives of Study: This study tries to allay the continuum of care literature gap and examines deficiencies at different levels of service implementation in delivering MCH services to clients against the backdrop of NITI Ayog mapped SDG framework of “Transformation of Aspirational Districts”. The objectives of study are:

1. To assess and measure structure-process outcome of service quality in J & K region,
2. To examine the implementation of National Health Mission Program in context to antenatal service architecture across continuum of care, and;
3. To suggest evidence-based data driven optimization of SDG aspirational health goals.

Materials and Method

Study design: The study is an ecological cross-sectional based on mixed methodology approach. The study consisted of three gauged data collection survey instruments as:

1. The facility-based checklist measuring the access,

availability and infrastructure related to service delivery.

2. The service provider schedule and observations capturing the structure-process, perceptions and application of standard service delivery.
3. Client interviews-schedules capturing and understanding the knowledge, attitude and perception of how the services were delivered to them.

Sampling Strategy: Study was done between January-October 2019 across two aspirational districts Baramulla and Kupwara of Jammu and Kashmir. The inclusion criteria of health facilities included were ANC services were provided and were at least one lady doctor and two auxiliary ANC staff were present. Table: 1 depicts the sampling strategy used in the study for two aspirational districts.

Measurement of Variables: Measurement of quality was assessed on three parameters of quality; structure, process and outcome. The structural parameters came from the facility assessment and provider interview; the process variables came from the observations and the exit interview of end users; the outcome parameter was client's measured satisfaction and service coverage-utilization indicators.

Structure and process indicators: These were framed through the WHO quality care framework for Service Availability and Readiness Assessment (SARA)¹³, OCED indicator framework¹⁴ and facility assessment SDG index framework given by NITI Ayog for aspirational districts. The structural variables were facility's inventory related to MCH service access and availability, physical infrastructure, quality assurance committees and were combined into a composite index score, using factor analysis. The process variables included socio-personal and competent aspects of the provider-client reciprocation with coverage utilization indicators (shown in figure 1). The Process variables were combined into a composite index, using factor analysis.

Outcome Variables: Client's satisfaction was assessed by a composite index using principal component analysis based on responses to 22 qualitative and quantitative statements-questions related to visit to facility.

Covariates-cofounding variables: Controlling of factors of service provider and clients such as years of experience, maternal age, order of ANC visit which could affect client's satisfaction was done.

Statistical Analysis: Categorical variables were tested for independence, mean differences and changes in continuous variables using ANOVA F test and T tests. Factor analysis was done for composite indexing of structural and process variables. GLM regression was used to assess the relationship between the outcome, structural and process attributes. Analyses was done using SPSS 25 and Atlas.

Findings: The services provided during the ANC period in both aspirational districts were below the recommended levels provided by the NITI Ayog's aspirational performance framework and WHO standards¹³, despite that access and availability of ANC services have increased across all levels of NRHM implementation in Jammu and Kashmir. Access and availability of different structural services provided at public facilities in two districts are summarized in Figure 2.

Status of Antenatal Services: In Baramulla district 32% pregnant women (PW) had four or more visits with appropriate ANC content as compared to 28.8% in Kupwara district, the level of services during ANC period varied widely; 91 % PW were checked for weight, only two-thirds had a urine sample checked and less than half were informed of signs of pregnancy complications in Baramulla, the situation was similar to worst in Kupwara. In both districts, most structural measures varied significantly between facility types. The higher-level facilities generally scored higher on structural measures than PHC facilities. The Figure:3 summarizes the status of service delivery to clients in two aspirational districts.

Client's Satisfaction: Waiting time for consultation was significant variable measure of client satisfaction given by all PW at all facility types and was significantly shorter at PHC's than higher facilities. In Baramulla district client satisfaction score did not significantly vary in facility types as compared to Kupwara were score was higher at DH and CHCs. In Baramulla, increased client's satisfaction was associated with a higher structure score. Among process attributes, receiving essential medicines and TT vaccination were crucial to satisfaction of clients.

Table 1: Showing sampling of Health facilities in two Aspirational Districts of Union Territory of Jammu and Kashmir

Aspirational Districts	Baramulla	Kupwara
	N (%) weighted	N (%) weighted
Public Health Facilities		
District Hospital	01 (2.5)	01 (2.6)
Sub District Hospital (SDH/CHC)	06 (15.3)	07 (18.5)
Primary Health Centre (PHC)	31 (79.7)	30 (78.9)
Specialized MCH hospital	01 (2.5)	-
Total Facilities	39 (100)	38 (100)
Service Provider		
Doctor	47	42
ANM/staff related to ANC	64	68
Total Service Providers	111	110
Client-Enduser Interview		
End-user Pregnant Women-Mother	158	138

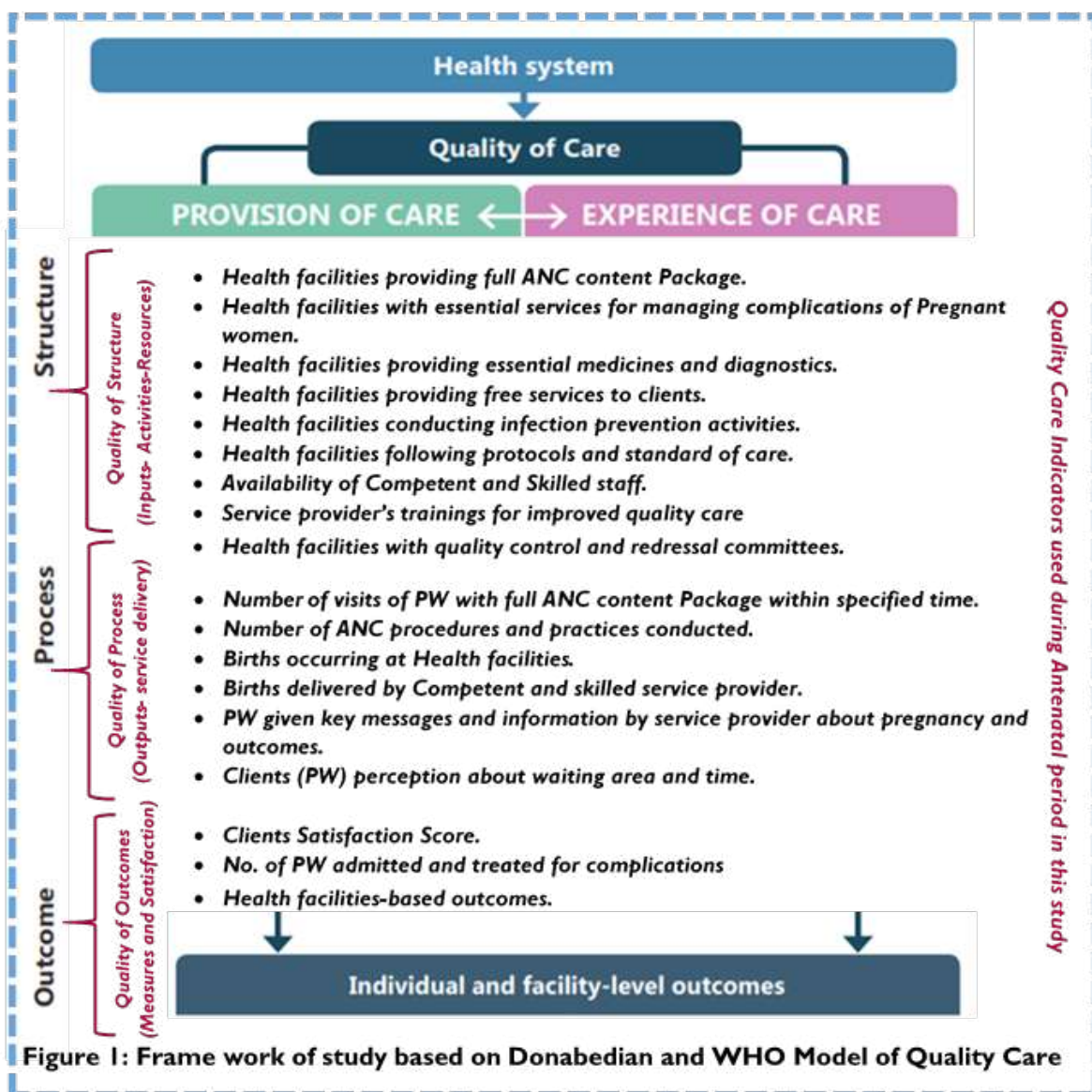


Figure 1: Frame work of study based on Donabedian and WHO Model of Quality Care

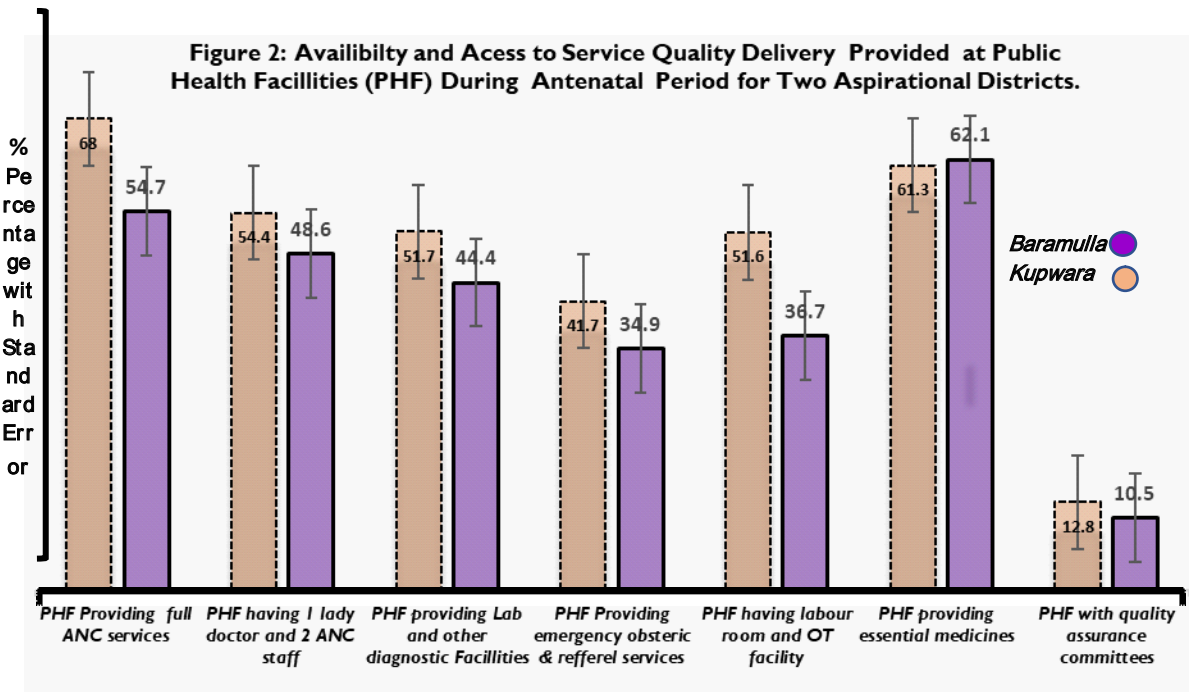


Figure 2: Availability and Access to Service Quality Delivery Provided at Public Health Facilities (PHF) During Antenatal Period for Two Aspirational Districts.

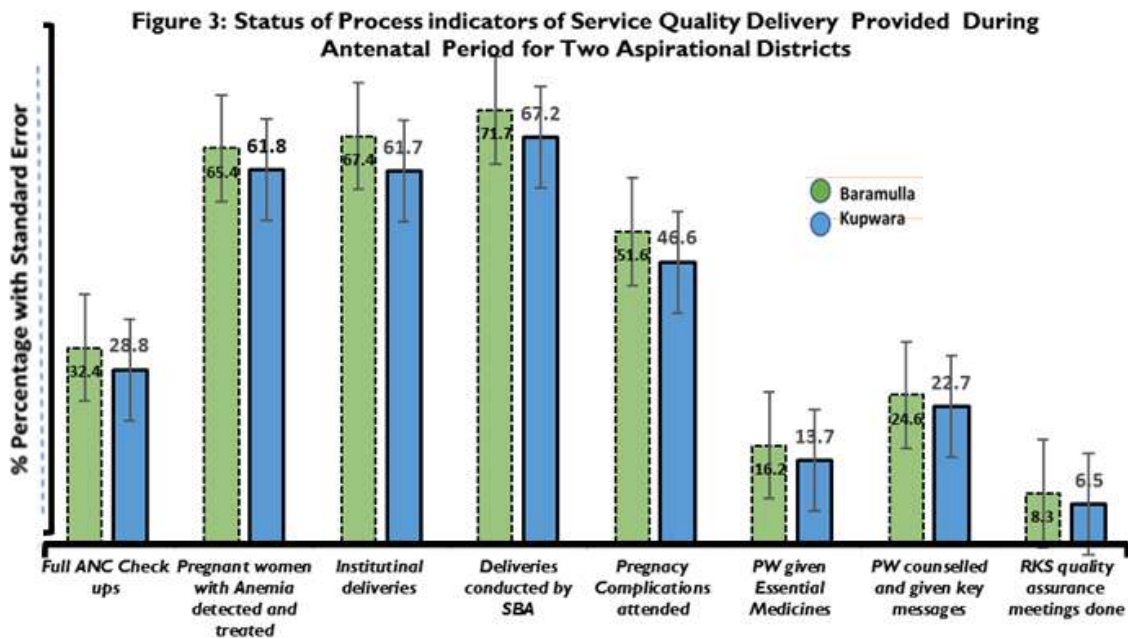


Figure 3: Status of Process indicators of Service Quality Delivery Provided During Antenatal Period for Two Aspirational Districts

Discussion

The study showed that gaps exist in access, availability and delivery of quality healthcare which affect the client's satisfaction. The recent NITI Ayog report 2018 on performance of aspirational districts had put Baramulla on 33rd rank and Kupwara on 37th out of

101 aspirational districts. The report showed marginal decrease in ANC service care and institutional deliveries to the previous base year which was consistent with our findings. Availability of staff was the major variable which contributed to services being provided because of demand for services at district and specialized hospitals

is much higher, resulting in more allocated resources. In Kupwara, both interaction about pregnancy outcomes and preparing for delivery scored higher at lower-level facilities than higher-level facilities showing that better structural attributes may not necessarily improve the quality of service delivery¹⁵. Long waiting time which is important contributing service factor^{16,17} showed negative association with client satisfaction and was consistent with literature findings¹⁸. Results showed that structure attributes were important for determining client satisfaction, which was inconclusive with other studies¹⁹. This study also showed positive relation though not always significant between client's satisfaction and process dimensions, and conclusions were consistent with other studies depicting that receiving essential medicines was an important factor for client's satisfaction^{18,20}. Our study suggests that twinning data from health facilities and providers about satisfaction of client can offer a comprehensive solution for the optimization of quality care.

Conclusion

There are evidences of inequity, inaccessibility and exclusion in MCH service quality and delivery across regions of Jammu & Kashmir. To address these deficiencies, we need strategies and service infusion policy interventions aimed at delivering quality healthcare. Providing optimal quality care should be essence of all strategies improving health outcomes especially in line with achieving SDGs. Implementing agencies, targeting improvement interventions in quality care should focus on decentralized structure, incorporating management service science, edification of institutional capacity and encouraging a culture of data-driven actions based on quality data sets. A paradigm shift is required in integrating newer innovations both technological and social to overcome the barriers in scalability and sustainability of chronically deficit mother-child ecosystem. A renewed course of action and resources stimulated by the 2030 SDG deadline are needed to augment this translational shift towards achieving sustainable universal access to quality care for maternal-child health.

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References

1. Rani M, Bonu S, Harvey S. Differentials in the quality of antenatal care in India. *International journal for quality in health care*. 2007;20(1):62-71.
2. Akram M. Looking beyond the Universal Health Coverage: Health Inequality, Medicalism and Dehealthism in India. *PHR Public Health Research*. 2013;2(6):221-228.
3. Althabe F, Bergel E, Cafferata ML, I. Strategies for improving the quality of health care in maternal and child health in low and middle income countries: an overview of systematic reviews. *Paediatric and perinatal epidemiology*. 2008;22:42-60.
4. Austin A, Langer A, Salam RA, Lassi ZS, Das JK, Bhutta ZA. Approaches to improve the quality of maternal and newborn health care: an overview of the evidence. *Reproductive health*. 2014;11(2):S1.
5. Kerber KJ, de Graft-Johnson JE, Bhutta ZA, Lawn JE. Continuum of care for maternal, newborn, and child health: from slogan to service delivery. *The Lancet*. 2007;370(9595):1358-1369.
6. Kadir A, Shenoda S, Goldhagen J. Effects of armed conflict on child health and development: A systematic review. *PLoS One*. 2019;14(1):e0210071.
7. Guliani H, Sepehri A, Serieux J. What impact does contact with the prenatal care system have on women's use of facility delivery? Evidence from low-income countries. *Social science & medicine*. 2012;74(12):1882-1890.
8. Murray CJL. Towards good practice for health statistics: lessons from the Millennium Development Goal health indicators. *Lancet*. Mar 2007;369(9564):862-873.
9. Hulton LA, Matthews Z, Stones RW. Applying a framework for assessing the quality of maternal health services in urban India. *Social science & medicine (1982)*. 2007;64(10):2083-2095.
10. Say L, Chou D, Gemmill A, et al. Global causes of maternal death: a WHO systematic analysis. *The Lancet Global Health*. 2014;2(6):e323-e333.
11. Donabedian A. Method for deriving criteria for assessing the quality of medical care. *Medical care review*. 1980;37(7):653.

12. Parasuraman A, Zeithaml VA, A conceptual model of service quality and its implications for future research. *Journal of marketing*. 1985;49(4):41-50.
13. WHO. Service availability and readiness assessment (SARA): an annual monitoring system for service delivery: World Health Organization; 2016.
14. Arah OA, Westert GP, Klazinga NS. A conceptual framework for the OECD Health Care Quality Indicators Project. *International Journal for Quality in Health Care*. 2006;18(suppl_1):5-13.
15. Brook RH, McGlynn EA, Shekelle PG. Defining and measuring quality of care: a perspective from US researchers. *International journal for quality in health care*. 2000;12(4):281-295.
16. Oche M, Adamu H. Determinants of patient waiting time in the general outpatient department of a tertiary health institution in Nigeria. *Annals of medical and health sciences research*. 2013;3(4):588-592.
17. Aldana JM, Piechulek H, Al-Sabir A. Client satisfaction and quality of health care in rural Bangladesh. *Bulletin of the World Health Organization*. 2001;79:512-517.
18. Tafese F, Woldie M, Megerssa B. Quality of family planning services in primary health centers of Southwest Ethiopia. *Ethiopian journal of health sciences*. 2013;23(3):245-254.
19. Hutchinson PL, Agha S. Measuring client satisfaction and the quality of family planning services: a comparative analysis of public and private health facilities in Tanzania and Ghana. *BMC health services research*. 2011;11(1):203.
20. Mitike G, Osman M. Satisfaction on outpatient services in hospitals of the Amhara Region. *Ethiopian medical journal*. 2002;40(4):387-396.

Administration of Magnesium Sulphate Prior to Vecuronium: Effects on the Speed of Onset and Duration of Neuromuscular Block

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Abstract

Background: We commonly encounter surgical patients who are on magnesium therapy in the operation theatre. It is important to know the interaction of magnesium on anaesthetic drugs including neuromuscular blocking agents. Our aim is to observe and compare the onset and duration of action of vecuronium following magnesium pre-treatment.

Material and Method: 50 patients were randomly divided into 2 groups. Group 1 (n = 25) received placebo (normal saline) and group 2 (n=25) received 40 mg/kg magnesium sulphate added to 100 ml of normal saline infused over a period of 15 minutes prior to induction. Following the induction of anaesthesia muscle relaxation was achieved by 0.1 mg/kg vecuronium and time for onset, duration of neuromuscular block and vecuronium dose requirement during surgery was assessed by monitoring the tactile response to Train of four stimulation.

Results: Onset of time for intubation was significantly reduced to 120.19±6.53 seconds in the magnesium group compared to 259.150±26.131 seconds in the control group (P< 0.001). It was observed that the average duration of neuromuscular blockage of vecuronium was almost doubled and statistically significant (P = 0.001) in the magnesium group (26.89±2.91) as compared to the control group (42.28±1.41). The total dose of vecuronium used or required was significantly less in the magnesium group when compared to the control group (p=0.008). Duration from last dose of vecuronium to reversal of anaesthesia was prolonged in the magnesium group (40.2±3.96) compared to the control group (29.8±6.03) which is statistically significant (p<0.001).

Conclusion: Magnesium sulphate administered before vecuronium significantly accelerates the onset of neuromuscular block necessary for intubation of trachea and significantly increase the time course of neuromuscular blockade. Intraoperative consumption of vecuronium was less in the magnesium group.

Keywords: Vecuronium, magnesium sulphate, neuromuscular block, TOF.

Introduction

Magnesium sulphate (MgSO₄) is a chemical salt,

by nature and has many uses in medical emergencies like eclampsia, acute asthma and complex cardiac arrhythmias. It is abundant in intracellular space and we commonly under-diagnose the magnesium-related symptoms^[1]. We frequently encounter patients on magnesium sulphate treatment for preeclampsia in obstetric anaesthesia. We usually recommend regional blocks for these obstetric conditions but because of associated coagulation irregularities we often end up

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in general anaesthesia. $MgSO_4$ has a unique action at neuromuscular junction (NMJ) as it augments the action of skeletal muscle relaxants^[1,2]. The presence of magnesium at neuromuscular junction naturally antagonises the calcium ion that binds to acetylcholine vesicles thus reducing the amount of acetylcholine released. At postsynaptic area the presence of excessive extra cellular magnesium reduces the strength of acetylcholine evoked responses^[3,4]. Magnesium sulphate as an adjuvant to general anaesthesia may modulate nociception through its interaction with NMDA receptors^[2].

Vecuronium is a commonly used relaxant in our hospital and we frequently encounter many patients who are on magnesium sulphate. At the NMJ magnesium concentration of 5 mmol/l and above produces significant neuromuscular blockade. Magnesium potentiates the action of vecuronium and prolongs the duration of all nondepolarising muscle relaxants^[5].

We investigated the interaction between magnesium sulphate and vecuronium from an anaesthesia perspective. We compared the effect of onset and duration of action of vecuronium with and without magnesium pre-treatment.

Materials and Method

Ethical committee approval from KMC medical college and informed consent from each of the patients participating in the study were obtained. Fifty patients undergoing various elective intra-abdominal and limb surgeries lasting for at least 2 hrs, belonging to ASA1 and 2 classes and in the age group 20-60 yrs were included in the study. Patients belonging to ASA class 3 and above, those with renal, liver, cardiac or neuromuscular dysfunction, possible difficult airway, atrioventricular block, asthma, chronic obstructive respiratory disease, and who were hypertensive and on calcium channel blocker, as well as pregnant female patients were not included in the study.

Patients were randomly divided in to 2 groups by block randomization. Group 1 (control group) received 100 ml normal saline over a period of 15 min prior to induction. Group 2 received 40 mg/kg magnesium sulphate added to 100 ml normal saline. This was infused over 15 minutes prior to induction. Parenteral solution was prepared by an independent anaesthetist who was not involved in the study. A peripheral nerve stimulator was used to evaluate the neuromuscular blockade and it was done by tactile assessment of

twitch response of adductor pollicis muscle to supra maximal stimuli (2 Hz) for 2 seconds. Monitoring of neuromuscular blockade was performed from the time of induction till neuromuscular recovery was completed by applying supramaximal stimuli initially every 12 seconds during induction and thereafter every 5 minutes till appearance of T1 and then every 1 minute till the end of study. Monitors used were ECG, non invasive BP, pulse oximeter and ETCO₂. The core body temperature was monitored and maintained between 36-37 degree centigrade using a forced air warmer.

All the patients received fentanyl 2 mcg/kg and midazolam 0.02mg/kg prior to induction of anaesthesia with thiopentone 5 mg/kg. A peripheral nerve stimulator was used to stimulate ulnar nerve. Tactile response of adductor pollicis muscle to TOF stimulation was monitored every 12 seconds. Following induction, patients were paralysed with a loading dose of vecuronium (0.1mg/kg). All patients were intubated with endotracheal tubes of appropriate sizes when no twitch response could be felt with TOF stimuli. Intubating conditions were graded as excellent, good or poor and noted in each case. All the patients were ventilated with oxygen and nitrous oxide in the ratio of 1:1 and appropriate concentration of isoflurane to keep Minimum alveolar concentration value at 1. Intermittent bolus dose of vecuronium 0.02mg/kg was given when 2nd response to TOF was noticed. Residual neuromuscular blockade was antagonised with neostigmine (0.05mg/kg) and glycopyrrolate (0.01 mg/kg) when 3rd response to TOF was present. Patients were extubated when all the 4 twitches were present without fade in response to TOF stimuli and also when patients met the subjective criteria for extubation (eye opening on calling, head lift for 5 sec, can protrude tongue, hand grip). Time duration from last dose of vecuronium to reversal, reversal to extubation, and last dose of vecuronium to extubation was noted and compared. Patellar jerk was elicited in the immediate postoperative period, and the response was noted in all patients.

The sample size was calculated using the formula:

$$n = 2 (Z\alpha + Z\beta) 2X \sigma^2 / d^2$$

where $Z\alpha = 1.96$ (95% confidence interval)

$$Z\beta = 0.84 \text{ (80\% power)}$$

$$\sigma = 0.39$$

$$d = 0.29$$

The observations and results were analysed using Students unpaired 't' test and P value less than 0.05 was considered statistically significant.

Results

There was no significant difference between the two groups with respect to age, sex, weight, and duration of surgery (Table 1).

Table 1. Age and weight of the patients studied and the duration of surgery.

	Group	N	Mean	SD	Z/P
Age	1	25	40.850	11.235	0.109 P = 0.914
	2	25	42.75	7.506	
Weight	1	25	61.200	8.675	0.1380 P = 0.89
	2	25	60.75	7.30	
Duration	1	25	2.869	0.407	1.890 P = 0.066
	2	25	3.161	0.558	

The two groups were comparable in terms of age, weight and duration of surgery.

Onset of time for intubation was significantly reduced (120.15 ± 6.53 seconds) in the magnesium group compared to the control group (259.150 ± 26.131 seconds) with the P value less than 0.001 (Table 2). Intubating conditions were comparable between the 2 groups.

Table 2. Onset time (loading dose to intubation)

Onset time	Group	N	Mean	Std Deviation	Z/P
	1	25	259.15	26.131	5.413 P < 0.001
	2	25	120.19	6.531	

Onset of time was significantly reduced to 120.19 ± 6.53 seconds in the magnesium group compared to 259.150 ± 26.131 seconds in the control group ($P < 0.001$).

Duration of neuromuscular blockage by vecuronium was almost doubled and statistically significant ($P = 0.001$) in the magnesium group (42.28 ± 1.41) when compared to the control group (26.89 ± 2.91) (Table 3). Total dose of vecuronium consumption was reduced significantly in the magnesium group ($P = 0.008$). The rate of vecuronium consumption (mg/kg/hr) was significantly less ($P = 0.001$) in the magnesium group (0.056 ± 0.01) compared to the control group (0.08 ± 0.01) (Table 3).

Average duration of neuromuscular blockage of vecuronium was higher and statistically significant ($P <$

0.001) in the magnesium group (26.89 ± 2.91) compared to the control group (42.28 ± 1.41). Total dose and rate of vecuronium (mg/kg/hr) consumption was reduced during the procedure in the magnesium group and it is statistically significant ($p = 0.001$).

Table 3: Duration of neuromuscular blockade and total dose and rate of vecuronium consumption.

	Group	N	Mean	Std dev	Z/P
Average duration for top up (min)	1	25	26.8925	2.912	5.415 P < 0.001
	2	25	42.28	1.41	
Total dose vecuronium used (mg)	1	25	10.91	2.24	2.658 P = 0.008
	2	25	9.04	1.508	
Vecuronium rate (mg/kg/hr)	1	25	0.0807	0.011	5.255 P = 0.001
	2	25	0.0568	0.0066	

Duration from last dose of vecuronium to reversal of anaesthesia was prolonged in the magnesium group (40.2 ± 3.96) compared to the control group (29.8 ± 6.03) which is statistically significant ($p < 0.001$). Recovery timing from reversal to extubation was significantly more ($P = 0.001$) in the magnesium group (11.2 ± 2.14) compared to the control group (7.55 ± 1.468) (Table 4).

Table 4. Recovery characteristics.

	Groups	N	Mean	Std Deviation	Z/P
Last dose of vecuronium to reversal (min)	1	25	29.80	6.03	4.473 P < 0.001
	2	25	40.20	3.968	
Reversal to extubation	1	25	7.55	1.468	4.622 P = 0.001
	2	25	11.20	2.1425	
Last dose of vecuronium to extubation	1	25	36.30	5.563	5.311 P < 0.001
	2	25	51.25	2.572	

Duration from last dose of vecuronium to reversal of anaesthesia was prolonged in the magnesium group (40.2 ± 3.96) compared to the control group (29.8 ± 6.03) which is statistically significant ($p < 0.001$).

Timing from reversal to extubation was significantly more ($P = 0.001$) in the magnesium group (11.20 ± 2.14) compared to the control group (7.55 ± 1.468).

Discussion

Magnesium sulphate is the drug of choice for various clinical conditions and an anaesthetist who

uses both vecuronium and magnesium sulphate together during surgery should have the knowledge of interaction between them. In our study onset of complete neuromuscular block for intubation was markedly less in the magnesium group. Wang *et al.* observed a synergic action between magnesium sulphate and vecuronium on acetylcholine receptors at neuromuscular junction^[1]. Fuchs Buder *Tet al.* observed a shorter onset of time for vecuronium following magnesium sulphate pre-treatment. They also noted improvement in intubating conditions and predicted that it could serve as an alternative to succinylcholine for rapid sequence intubation^[2]. They found that ED 50 and ED 90 of vecuronium with magnesium sulphate pre-treatment were 25% lower than the control group. Mean onset of time was 147.3 sec in magnesium and vecuronium group compared to 297.3 sec for the control group^[2]. Normal range of serum magnesium is 0.7-1.1 mmol/l. Fuchs Buder *Tet al.* used the bolus dose of 40 mg/kg magnesium intravenously which raised baseline plasma concentration of magnesium from 0.9 mmol/l to 1.08 mmol/l which is significant statistically but still within the physiological range^[2]. Ryu J *Het al.* used bolus dose of 50 mg/kg magnesium followed by 15 mg/kg/hr infusion without increasing serum magnesium level to toxic range^[6]. In our study pre-treatment with MgSO₄ increased the duration of vecuronium block to 42.3 min compared to 26.8 min in the control group which is similar to that noted by Fuchs Buder *T et al*^[2]. They noticed a prolonged duration of neuromuscular block in the magnesium and vecuronium groups (43.3 min) compared to the control group (25.2 min)^[2].

The latter part of our study was about the consumption of vecuronium during the study period. Telci *et al.* observed that the use of magnesium decreases the anaesthetic drug requirement during total intravenous anaesthesia^[7]. Gupta *et al.* found that magnesium has anaesthetic, analgesic, and skeletal muscle relaxation action and it significantly reduces the requirement of anaesthetic drugs^[8]. We also noticed a reduced vecuronium requirement in the magnesium sulphate group (0.05mg/kg/hr) compared to the control group (0.08mg/kg/hr). Okuda *Tet al.* compared the effect of 2 different doses of magnesium (20 and 40 mg/kg) on the potency of vecuronium and found that 40 mg/kg dose enhances vecuronium-induced neuromuscular block^[9]. In our study excellent intubating conditions were obtained within 120.15 seconds in all patients of the magnesium group whereas it was 259.15 sec in the control group.

Park S *Jet al.* also observed a better intubating condition with rocuronium administration following magnesium sulphate pre-treatment^[10]. Limitation of our study is that we did not measure serum magnesium and calcium levels during the study period. Previous studies have used varied doses of magnesium sulphate (20-50mg/kg) without any complications^[2,6]. In the present study, a bolus dose of 40 mg/kg of magnesium was used without any complications. Earliest warning sign of magnesium toxicity is the loss of patellar jerk which is seen when plasma magnesium level exceeds 3.5 mmol/l^[11,12]. We did not encounter any patient with loss of patellar jerk in the immediate postoperative period.

Conclusion

We conclude that magnesium administration before vecuronium significantly accelerated the onset of neuromuscular block necessary for intubation of trachea. It also increased the duration of neuromuscular blockade and can be safely used for surgeries lasting for more than 1 hour. Monitoring of neuromuscular function and reduction in dose of vecuronium are required while using these two drugs in combination.

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Speciality: Anaesthesiology

Conflict of Interest: None

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Conflict of Interest Statement: There is no conflict of interest.

References

1. Wang, H., Liang, Q., Cheng, L., Li, X., Fu, W., Dai, W., Li, S. Magnesium sulfate enhances non-depolarizing muscle relaxant vecuronium action at adult muscle-type nicotinic acetylcholine receptor in vitro. *Acta Pharmacol Sin.* 2011, 32(12): 1454-1459.
2. Fuchs-Buder, T., Wilder-Smith, OH., Borgeat, A., Tassonyi, E. Interaction of magnesium sulphate with vecuronium-induced neuromuscular block. 1995, *Br J Anaesth.* 74:405-9.
3. Krendal, DA. Hypermagnesemia and neuromuscular transmission. *Semin Neurol.* 1990, 10:42-5.
4. McLarnon, JG., Quastel, DM, Postsynaptic

- effects of magnesium and calcium at the mouse neuromuscular junction *J Neurosci.* 1983;3:1626-33
5. DoSH. Magnesium; a versatile drug for anaesthesiologists *Korian j anaesthesiol.* 2013; 65(1):4-8
 6. Ryu, JH., Kang, MH., Park, KS., Do, SH. Effect of magnesium sulphate on intraoperative anesthetic requirements and post operative analgesia in gynaecology patients receiving total intravenous anesthesia. 2008. *Br J Anesth.* 100:397-403
 7. Telci, L.,Esen, E., Akcora, D., Erden, T., Carbolat, T., Akpir, K. . evaluation of effects of magnesium sulphate in reducing intraoperative anaesthetic requirements 2002. *Br JAnesth.* 89(4):594-98
 8. Gupta, K., Vohra, V., Sood, J. The role of magnesium as an adjuvant during general anaesthesia. 2006, *Anaesthesia.* 61(11):1058-63
 9. Okuda, T., Uneda, T., Takemura, M. Pretreatment with magnesium enhances vecuronium induced neuromuscular block. 1998. *Masui.* 47(6):704-708
 10. Park, SJ, Cho, YJ, Oh, JH, Hwang, JW., Do, SH., Na, HS. Pretreatment of magnesium sulphate improves intubating condition of rapid sequence tracheal intubation using alfentanil, propofol, and rocuronium a randomised trail 2013, *Korian j Anesthesiol.* 65(3):221-7
 11. Wacker, WE., Parisi. AF. Magnesium metabolism 1968, *.N Eng J Med .*278:658-63
 12. Lu, JF, Nightingale, CH. Magnesium sulfate in eclampsia and pre-eclampsia: pharmacokinetic principles. 2000, *Clin Pharmacokinetic.* 38(4):-305-14

Assessment of Teaching Ability among University Level Health Science Teachers: Pilot Study

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Abstract

Background: University level teachers were at stress and depression as because of their higher working hours with undergraduate, postgraduate and doctoral students. Which make the teachers to sit for hours and hours in class and stand with blackboard in-order to cover the syllabus hours and to encourage the students to be successful in career? Till now there are no studies done on assessing the cognition and teaching ability of a teacher in relation to the comorbidities they experience as a teaching staff.

Objective: To find out the cognition using ruff figural fluency test.

Procedure: The subjects according to inclusion and exclusion criteria and who were willing to participate in the study will be given a questionnaire of faculty workload survey 2001, Nordic questionnaire to evaluate the musculoskeletal pain and ruff figural fluency test kit to evaluate their cognition.

Results: The teachers inspite of the maximum engagement with curriculum, they have good academic performance, but the cognition is poor as the hours of the day passes by, it is due to the maximum stress they experience in dealing with their musculoskeletal pain.

Keywords: Health science, students, university, Teaching ability.

Introduction

Stress is the cause for work inefficiency and from decades the maximum stress has been experienced by the person who is the sole responsible for the children. Thus the university level teachers were considered to have maximum teaching hours; they were engagement with the curriculum developmental works and also engaged with student developmental programmes¹. They have less time for self analysis and there is a need to look and

examine the cognition and teaching performance and ability level of a university level health science teacher. Cognitive function can be greatly influenced by stress². Importantly, although the majority of studies so far have focused on stress effects on memory function—which will be the main focus of this overview—most cognitive operations (from attention to decision making) are, in fact, susceptible to be affected by stress³. But not all the teachers in the university will be exposed to stress, few will be resistant and others were vulnerable^{2,3}. No human study has done to examine the stress and its impact on cognition, only few animal studies exist.

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It is believed that occupational pain over the muaculoskeletal pain is caused by multiple factors, generally categorized into mechanical and psychosocial ones. Various mechanical factors have been found to be associated with pain in different body regions. Heavy

physical work, heavy or frequent manual operations, repeated rotation of the trunk, whole body vibration, and prolonged sitting were positively associated with low back pain^{3,4}. Working with hands at or above shoulder level, flexion of the neck, static contractions, monotonous or repetitive work with arms, high working pace, and unsuitable work place were responsible for neck and shoulder pain. Psychosocial factors at work have also been shown to play important roles in the development of musculoskeletal pain. Important psychosocial factors included work demands and decision latitude, symptoms of stress, social support, type A behaviour, and psychological distress⁴. After reviewing 59 relevant studies, Bongers and colleagues concluded that monotonous work, high perceived workload, time pressure, low control on the job, lack of social support from colleagues, and stress symptoms were related to musculoskeletal problems. Carayon and colleagues reviewed work organisation, job stress, and work related musculoskeletal disorders, and concluded that work organisation and psychosocial factors at work could contribute to upper extremity disorders⁵⁻⁸. They further indicated that work organisation and ergonomic factors might interact to affect the musculoskeletal system.

Pain and cognition share an inherent overlap owing to the fact that pain itself has a cognitive-evaluative component, requiring learning, recall of past experiences and active decision making⁵. This should be borne in

mind when assessing the effects of pain on cognitive function. Similar studies were majorly done on office workers, school teachers and manual workers. The study is needed as there is no study done on university level staffs

Methodology

We included the teaching staffs of age 50 years, gender both male and female and the information sheet which contained the need to conduct the study has been submitted to the teachers and a written consent form has been signed by the entire faculty. Non-teaching staff were excluded from the study. The staffs that were willing to participate in the pilot study were given with a manual that contains questionnaire that rate the musculoskeletal pain they experience and there is a black space which needs to be addressed by the faculty, which contains type of work, working hours, years of experience and workload. The RFFT is used to analyze the cognitive defects the faculty experience and it contains only line drawing which last 60s and needs maximum attention from the participants. Participants are presented test forms that contain rows of squares and within each is an array of five dots. Participants are then informed that, within each square, they must connect two or more dots by always using straight lines. The goal of the task is to generate as many unique designs as possible without replicating any drawings (Ruff, 1988). The participants were instructed to do so in between their working hours for 1 day.

Data Analysis:

Table 1: Shows the working hours, years of teaching experience, age and gender

	Working Hours	Experience	Ruff Figural Fluency Test	Age	Gender
N	50				
Mean	7.20	7.80	1.04	30.9	2.60
Standard Deviation	.216	1.64	0.64	4.78	.343

Table 2: Shows the musculoskeletal pain experienced by the teachers

	Pain in Neck for last 12 weeks	Pain in neck for last 7 days	Pain in shoulder for past 12 months	Pain in shoulder for past 7 days	Pain in elbow for past 12 months	Pain in elbow for past 7 days	Pain in wrist for past 12 months	Pain in wrist for past 7 days	Pain in upper back for past 12 months	Pain in upper back for past 7 days
N	50									
Mean	5.40	5.60	6.30	4.80	3.50	7.80	3.50	3.70	4.20	5.70
SD	.567	.763	.654	.576	.765	.876	.234	.754	.876	.234

Discussion

When correlation analysis is performed, there exist no correlation between working hours and ruff figural fluency test. Negative correlation exists between age and ruff figural fluency test and there is no correlation between chronic musculoskeletal pain and ruff figural fluency test. The current study documents that musculoskeletal pain experienced by the teaching faculty at the university level will not influence the cognitive ability and it is not going to be a confounding factor in their teaching ability and it will not restrain the administrative role the faculties perform. The total sample selected and recruited from the university was 70, in which 10 were withdrawn from the study due to inadequate time as they were posted in the examination duty, 10 faculties revealed that the questionnaire were filled by the students as they experience inadequate time, thus the forms were rejected. The overall study showed a no or negative correlation between cognition and musculoskeletal pain. According to Richelle et al (2018), in his study concluded that prolonged sitting led to discomfort in lower back, hip and thigh but there was no attention deficit. In contrast to the study of Moriarty et al (2011), concluded that there appears to be sufficient evidence from preclinical and clinical investigations to support the theory that pain is associated with impaired cognitive function. Cognitive deficits in tests with high ethological validity, suggest that cognitive impairment in pain patients may be an obstacle to everyday tasks. As such, this impairment may have a marked impact on patients' quality of life. But the current study has documented that the faculties were not influenced negatively with the increased age, increased working hours and musculoskeletal pain.

Conclusion

This study concludes that there is no relation between Teaching ability and musculoskeletal pain.

References

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4th ed. Washington, DC: American Psychiatric Association; 1994.
2. Grave, de, W.S., De Volder, M.L., Gijsselaers, W.H. & Damoiseaux, V, 'Peer teaching and problem-based learning: Tutor characteristics, group functioning and student achievement', in: Schmidt, H.G., Lipkin Jr. M., de Vries, M.W. & Greep, J.M. (eds.), *Education for Tomorrow's Medicine Today*. New York: Springer. Google Scholar
3. Anderson, L. W., & Krathwohl, D. R. (Eds.). (2001). *A taxonomy for learning, teaching, and assessing: A revision of Bloom's Taxonomy of Educational Objectives (Complete ed.)*. New York, NY: Longman.
4. Archer, M. S. (2013). Reflexivity. *Sociopedia.isa*. <https://doi.org/10.1177/205684601373>. Available from <http://www.sagepub.net/isa/resources/pdf/Reflexivity2013.pdf>
5. Arnstine, B. (1990). Rational and caring teachers: Reconstructing teacher preparation. *Teachers College Record*, 92, 230–247. <https://doi.org/0161-4681-90/9202/230>
6. Bandura, A. (1978). The self-system in reciprocal determinism. *American Psychologist*, 33, 344–358. <https://doi.org/10.1037/0003-066X.33.4.344>
7. Bendixen, L. D., & Feucht, F. C. (2010). Personal epistemology in the classroom: What does research and theory tell us and where do we need to go next? In L. D.
8. Dr.U.Ganapathy sankar, Monisha.R: Evaluation of Cardio-Vascular Risk in Children with Developmental Coordination Disorder in Indian Context- Pilot Study: *Research J. Pharm. and Tech.* 11(12): December 2018

A Critical Study of Women's Health in India from a Socio-Cultural and Gender Perspective

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Abstract

If we conceptualise health in a holistic sense, we would understand that it is not merely about the absence of diseases but essentially a socio-biological concept which hinges upon not just one's physiology but the socio-cultural and psychological variables as well. It is in this context, health issues among women in general and Indian women in particular, as a subset of the larger corpus of health concerns, needs to be inevitably understood and contextualised in the societal and cultural milieu within which women operate. Indian society, with its conservative culture and distinct ascribed social roles, engineers a woman's position in the social hierarchy and personal life experiences. Consequently, socio-cultural attitudes and gender constructs need to be understood as powerful decisive factors of one's health that colludes with other variables like age, family, educational attainment, occupational structure, income and social support etc. Against the backdrop of this social model of health, this paper tries to understand the role played by socio-cultural factors and gender constructs in determining health of women in India. The paper also conclusively, tries to provide various holistic strategies and suggestions for improvement of women's health.

Keywords: *Social model of health, gender, cultural norms, gender mainstreaming, reproductive health.*

Introduction

The World Health Organization's Ottawa Charter for Health Promotion (1986) sees health as multidimensional and espouses a social model of health. It defines health as 'a positive concept emphasising social and personal resources, as well as physical capacities.' In the social model of health, while human biology, physiology and health care are considered as important elements, besides these, it incorporates within its purview a variety of other variables and factors that have the potential to impact the health of an individual. These factors range from social and cultural attributes, political environment, economic and financial factors, psycho-social factors to various other inter-personal and environmental factors as well as their reciprocal communications that might lead to health or illness. Therefore, the concept of health is definitely not unidimensional, it is multifaceted. Such a positive conceptualisation of health necessitates and warrants a discussion and analysis of women's health status and scenario with respect to the role played by the social construct of gender and the various socio-cultural roles and attitudes that flow from it.

Objective and Method

The primary motive of the paper is to study the present scenario of women's health in India. This research paper whilst trying to enquire into the status of women's health, particularly, tries to understand and highlight the role of the contextual socio-cultural factors and gender constructs that operate in Indian society; in serving as determinants of women's health. To this effect, a predominantly qualitative research approach has been adopted to critically inquire into the topic at hand. Data at all stages are secondary in nature and garnered from a variety of published sources. A thorough study of journal articles, newspaper and government health reports, books relevant to the topic has been undertaken. The methodology of data analysis is descriptive, explorative and analytical.

Findings and Discussions

The findings of the study and consequent recommendations have been presented and discussed in various sections dealing with various related observations and ideas.

Indian societal realities and women: It has been evident that women in modern India face a paradoxical situation. While women are increasingly making inroads into erstwhile male-dominated professions and admirably hiking up the corporate hierarchy, there is still a sizeable section of Indian women languishing without any sense of their identity or any form of human rights. Although, the government is striving hard to bring in women-centric legislations and devise policies for women empowerment and uplift, what is happening in ground reality remains unaffected; women still in a very large number and in variegated ways receive systemic discrimination in society. Patriarchy as the basis of India's social functioning operates within a web of norms that possess an inherent tendency to disempower and control women's every aspect of life. The women in India having to survive and grow up in such an environment and simultaneously having to do their best and live up to their own best potential as well as society's expectations from her, proves to be a burdensome toil for all women throughout their life-cycle. The social construct of gender engineers a woman's position in the social hierarchy and also has a prominent bearing on her social and personal life experiences. Consequently, socio-cultural context and gender need to be understood as powerful decisive factors of women's health in India that colludes with other variables like age, family, educational attainment, occupational structure, income and social support etc.

Gender and Health: Crucial Revelations: The effect of the construct of gender is clearly visible in differential allocations of factors of risk and burden of diseases between the genders throughout their cycle of life. A difference between the genders is apparent in risk factors and disease burdens across the lifecycle, from childhood, through adolescence and adulthood, to old age^{1,2}. Data provided by National Family Health Survey(2015-16) shows that boys recorded a higher neonatal mortality rate but post-neonatal mortality rates were higher for girls. This alludes to the fact that there exists gender discrimination leading to improper childcare which ultimately quashes the biological advantage girls enjoy in terms of a lower neo-natal mortality rate as compared to boys¹. Gender gaps are also revealed in nutrition levels with higher rates of anaemia among women and girls. A similar situation prevails in the scenario of immunisation rates. Pregnancy and delivery-related complications in the Indian context also serve as significant reasons for death among 15-19 year old girls. Marriage and

childbirth at an early age further compound the risks to the health of young women which may include mental stress and depression, pregnancy related complications, miscarriage etc³. Studies and statistics reveal that around 50-90% pregnant women in India suffer from iron deficiency which flares up risks of maternal deaths⁴. A typical sort of gender bias is also visible in the pattern of health policy sector where reproductive health services and policies come exclusively to be attached to women and sexual health especially, with reference to HIV/AIDS is prioritised as a sector for males. This makes bare the lack of gender mainstreaming in Indian health policy sector. In the arena of mental health, typically, in the case of women, the construct of gender and other socio-cultural factors have a significant role to play. There appears to be deeper connexion between gender and suicidal behaviour. Factors like childhood abuse, marital rape, domestic atrocities play a significant role in goading suicidal behaviour among women. A socio-cultural variable responsible for female suicide typical to Indian society is the practice of dowry in marriages. "The precipitants for suicide, according to Indian government statistics, among women compared to men are as follows: Dowry disputes (2.9% versus 0.2%); love affairs (15.4% versus 10.9%); illegitimate pregnancies (10.3 versus 8.2); and quarrels with spouse or parents-in-law (10.3% versus 8.2%). The common causes for suicide in India are disturbed interpersonal relationships followed by psychiatric disorders and physical illnesses."⁵ "According to an eye-opening United Nations report, around two-third of married women in India were victims of domestic violence and one incident of violence translated into women losing 7 working days in the country. Furthermore, as many as 70% of married women between the ages of 15 and 49 years are victims of beating, rape or coerced sex."⁶ Female Indian psychiatric patients share a serious concern of sexual coercion. "Sexual coercion was reported by 30% of the 146 women in an Indian study. The most commonly reported experience was sexual intercourse involving threatened or actual physical force (reported by 14% of women), and the most commonly identified perpetrator was the woman's husband or intimate partner (15%), or a person in a position of authority in their community (10%)."⁷

Cultural Norms, Gender Roles and Women's Health: The socio-cultural and gender norms in a conservative society like India has a strong bearing upon women's health. The cultural attitude and social orientations towards the institution of marriage and the

culture ordained role of a woman entering into marriage, the cultural value attached to fertility and the religious importance attached to the sex of the child, the nature of familial organisation and the ideal role coveted of the women by cultural conventions determine a woman's position in a family, her access to healthcare, levels of nutrition, education and her reproductive and overall health.

Marriage in India other than carrying personal significance, also carries tremendous social, cultural and religious significance not only to the individuals tying the knot but the entire sphere of extended families. The cultural insistence on the marriage of women in the ripe phase of their childbearing period leads to a high fertility rate and each additional child is a burden on the mother affecting both her physical and mental health.

Women's reproductive health in India is strongly impinged upon by the culture of preference for sons. Caste-Hindu philosophy as contained in various religious manuscripts like Manusmriti, portrays an exorbitant amount of importance to males and constructs women as 'lesser' human beings. It is a clearly embedded religious worldview in the majoritarian Hindu society that it is only a son that can enable the parents to heaven after their deaths. Moreover, daughters are considered as a liability as they leave their parents' home after marriage and the father as his paternal duty needs to arrange for a dowry to be sent away with the daughter in marriage. Such religion induced practices strengthen a strong preference for sons. This promotes multiple attempts at conception and successive childbirths until a male-child is born creating unnecessary health and mental burden upon the mother. Such a culture of son-preference also leads to crimes like female infanticide, sex-selective abortions etc.

The construction of a woman's personhood and capacity in Indian society contributed by the religious prescriptions, caste and patriarchal dictates brings to fore the image of a subordinate and dependant social identity. From the very early years, a girl is taught to be docile and obedient and in a way systematically internalise her subordinate position in the household and she translates in the same capacity to her husband's house after marriage. The consequences of this subordination incorporates lack of any kind of control over her reproductive rights, lack of equal access to food and nutrition, even access to healthcare.

Patriarchy induced gendered division of labour

forces women to absorb themselves in the domestic sphere of life. In rural areas, the girls from a very young age are made to do strenuous household chores and labour which takes a toll on their health and deprives them of their childhood freedom. Many rural Indian households follow the norm where the male heads of the house eat first while the woman eat last and have to make do with the leftovers. Especially, when it comes to poor families, such a patriarchal norm contributes towards the consistent inadequate nutrition levels in women. This vicious combination of strenuous household labour and inadequate nutrition contributes to poor health of women in India especially, in the rural scene. In the urban scene, situations are not better either. While women are breaking the glass ceiling and entering into the public sphere of workplace, they are not relieved of the gender roles society imposes upon them. As a result, they suffer from a situation called the "double burden" wherein the women have to overwork themselves to play the dual role of breadwinner as well as do strenuous household labour. During the period of pregnancy, childbirth and the consequent period of childrearing, these working women are the ones who go through extreme mental and physical frustration. These unreal societal expectations that women have to live up to naturally take a toll on their mental and physical health.

From their childhood, girls are taught not to complain and to maintain secrecy about their physical troubles. With menstruation, taboos are enforced and restrictions placed on their mobility. They are unable to discuss their health problems, if any, or to visit a doctor. In the later stages of life, as a mother who is more often than not, vested with the entire responsibility of childcare and nurturing, has a strong tendency to hush down any physical or health trouble until the trouble overtakes them.

The Way Ahead: For the improvement of women's health in India, mere policy interventions evidently, would not suffice. A holistic paradigm shift is required in the way women's health concerns are addressed and approached. The aim should be to implement a truly social model of health which emphasises on not just the mere absence of diseases but also improving or eliminating other environmental, social, cultural or personal factors or variables that positively or negatively impact upon one's health. To this end, a five-pronged strategy can be suggested as follows:

- The first step necessarily, would be to formulate such strategies, policies and codes that challenges existing

norms and attitudes that directly harm women's health and ensure stringent implementation.

- Recognise and address differential health needs and concerns of men and women not just basing the understanding on their biological differences but also how their biology interacts with various social norms and gender roles to produce different health vulnerabilities.
- Another potent strategy would be gender-mainstreaming in the entire corpus of health policy sector ensuring women's voices and needs are present in all levels of health policy process.
- Infusing a gendered perspective into the health policy research spectrum. The focus should be on broadening the scope of health research and link biomedical and social dimensions, including gender considerations.
- Transform the gendered politics of health systems by improving their awareness and handling of women's problems as both producers and consumers of health care, improving women's access to health care, and making health systems more accountable to women.⁹

Conclusion

Therefore, it has been made inarguably clear that women's health is not a lone impervious variable, it has to be considered in association with their socio-cultural context and gender roles. Any policy or mere discussion on women's health concern should involve her emotional and mental well-being along with her physical health at all stages of her life. It is a common occurrence where policies in India view women's health very narrowly in terms of reproductive and maternal health solely. Such a constricted policy worldview in India has greatly contributed towards reinforcing the idea that women only exist as mothers and procreators. Moreover, when an individual woman suffering from a certain health concern is focused in isolation as a singular independent biological entity divorcing her condition from her sociological realities, it runs a risk of placing the burden of reformation on the women alone. But as we would agree that change for women is well beyond their control and is possible only with a bigger positive social transformation. Given these realities, it becomes imperative to undertake stratagems and schemes that would target the social factors responsible for having a degrading impact on women's health. Such strategies may involve social policies to reduce gender gaps in

all fields of social existence, enhance women's status in society by giving them their due or at least empower and educate them enough that they are able to voice out their demands and grasp their rights for themselves.

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Ethical Clearance: Data has been collected from medical journals, books, newspaper reports and WHO databases and reports which is related to the topic of women's health.

References

1. International Institute for Population Sciences (IIPS) and ICF. 2017. National Family Health Survey (NFHS-4), 2015-16: India. Mumbai: IIPS.
2. World Health Organization. The Global Burden of Disease 2004 Update. Geneva, Switzerland: World Health Organization; 2008.
3. Santhya, KG, Jejeebhoy, S. Sexual and Reproductive Health Needs of Married Adolescent Girls. *Economic and Political Weekly*; 2003 (38)41: 11-17.
4. George, A. Embodying identity through heterosexual sexuality - newly married adolescent women in India. *Culture, Health, & Sexuality*; 2002 (4)2.
5. Rao V. Suicidology: The Indian context. In: Agarwal SP, editor. *Mental Health: An Indian Perspective 1946-2003*. New Delhi: Directorate General of Health Services/Ministry of Health and Family Welfare Nirman Bhawan; 2004. p. 279-84.
6. Press Trust of India. Two-Third Married Indian Women Victims of Domestic Violence: UN. Posted Online; Thursday, October 13, 2005. Available from: <http://www.expressindia.com/fullstory.php?newsid=56501>.
7. Chandra PS, Carey MP, Carey KB, Shalinianant A, Thomas T. Sexual coercion and abuse among women with a severe mental illness in India: An exploratory investigation. *Compr Psychiatry* 2003;44:205-12
8. Sen, Sujata. *Gender Studies*, 1st Edition, Dorling Kindersley (India), 2012, 172-190
9. Women and Gender Equity Knowledge Network. *Unequal, Unfair, Ineffective and Inefficient Gender Inequity in Health: Why it exists and how we can change it?* September, 2007.

Actions of Riluzole on GLAST and GLT₁ Transporters in Rat Migraine Model

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Abstract

Riluzole exerts a neuroprotective effect through different mechanisms including action on glutamatergic transmission. We investigated whether this drug affect glutamate transporter mediated uptake expressing the rat glutamate transporters GLAST, GLT. We found that riluzole significantly increased glutamate uptake in a dose-dependent manner. This may facilitate the buffering of excessive extra cellular glutamate under pathological conditions suggesting that riluzole's neuroprotective action might be mediated by its activating effect on glutamate uptake.

Keywords: Riluzole, Glutamate transporters, neuroprotective.

Introduction

Glutamate transporters are a family of neurotransmitter transporters proteins that move glutamate -the principal excitatory neurotransmitter – across the membrane. The family of glutamate transporters is composed of two primary subclasses the excitatory amino acid transporter (EAAT) family and vesicular glutamate transporters (VGLUT).¹ In the central nervous system, astrocytes regulate extracellular glutamate concentration via two types of glutamate transporters, glutamate transporters-1 (GLT-1) and glutamate aspartate transporters (GLAST). In physiological conditions, glutamate transporters uptake glutamate from the extracellular space.² However, in pathological conditions such as ischemia, astrocytes release large amounts of glutamate via reverse transport,

and is increased extracellular glutamate participates in neurotoxicity.

Riluzole, a neuroprotective drug approved for ALS, riluzole enhances the activity of glutamate transporters GLAST and GLT₁ and reduces extracellular glutamate concentration in the CNS.³ In the contrast to this glutamate reducing effect in the CNS. Some studies proved that a local injection of riluzole in the locus coeruleus resulted in activation of noradrenergic neurons to induce descending inhibition in rats. The facilitation of glutamate-induced glutamate release from astrocytes.⁴ However, the mechanism by which riluzole might activate glutamate-induced glutamate release from astrocytes in unknown.⁵

Materials and Method

Male albino wistar rats (n=6) of weight ranging from 200g was the histomorphometry in the present study. The rats were obtained from experimental animal; facility of saveetha medical college. The animal were kept in cages with not more than the three animals in one cage. They were maintained at 12hrs:12hrs light/dark cycles with water and food available ad libitum.⁶

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Experimental Design: The rats were divided into three groups

- Group 1 control rats (n=6)- saline treated rats
- Group 2 migraine model rats (n=6)- nitroglycerin (10mg/mg subcutaneous bark of neck) induced rat migraine for 7 days
- Group 3 riluzole treated rats (n=6)- riluzole (6mg/kg i.p) treated nitroglycerin induced rat migraine model for 7 days. Riluzole was given 1h before the administration of nitroglycerin.

Tissue Collection: Fixation was done using 500ml of 4% formaldehyde in 0.1M phosphate buffered saline, through transcardiac perfusion then dissect the rat brain trigeminal ganglion was identified and removed. Tissues were sectioned (20µm) using cryostat and stained with Cresyl violet.

Immunohistochemistry: The antibodies for GLAST and GLT₁ subunits were obtained from sigma laboratories and the standard dilution ratio was determined after repeated histochemical localization

at various dilution ratio. The free-floating sections of trigeminal ganglion were localized for GLAST and GLT₁ subunits focused by JENOPTIK ProgRes capture pro 2.7 (Germany) captured using ProgRes image capture software.

Measurement of Small Neurons: The neurons in the image of immunostained trigeminal ganglion will be measured for the maximum diameter using image j software. The neurons of diameter <22µ were small neurons and the staining pattern of those neurons were studies.

Result

The GLAST and GLT₁ subunits were localized in the cytoplasm of trigeminal ganglion neurons in the control rats and there was upregulation in migraine model rats, especially in the small neurons (Figure 1 and 2). The GLAST subunits expression in the small neurons was decreased after treatment of riluzole (Figure 1). The GLT₁ expression was also seen in satellite glial cells surrounding the neurons but there was no difference in the intensity of expression in all these groups.

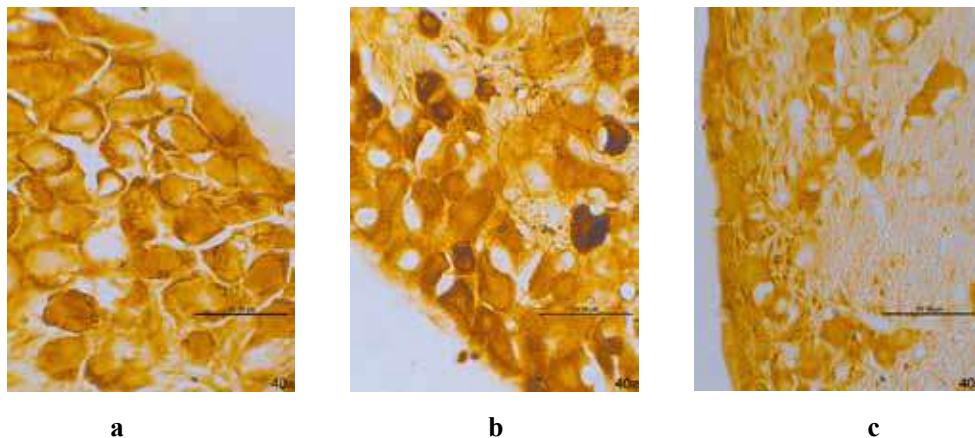


Figure 1: a, b and c: Localization of GLAST in the cytoplasm of the neurons (Figure 1 a), its upregulation in the small neurons (Figure 1 b black arrow). The upregulation has been decreased after riluzole treatment (Figure 1 c).

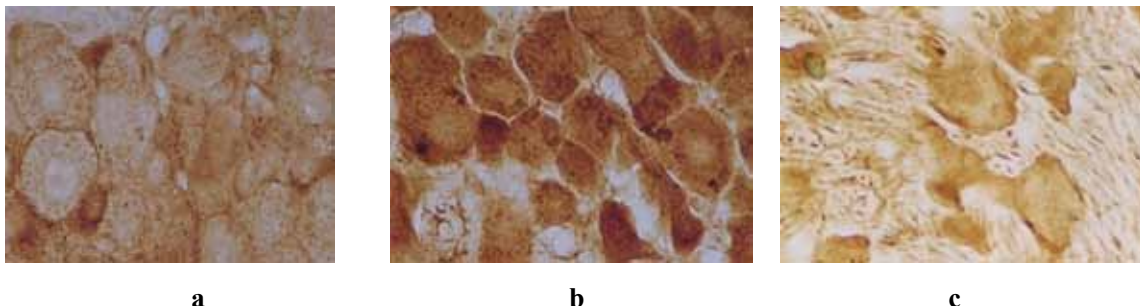


Figure 2: a,b and c: Localization of GLT in the cytoplasm of the neurons (Figure 2 a), its upregulation in the small neurons (Figure 2 b black arrow). The upregulation has been decreased after riluzole treatment (Figure 2 c).

Discussion and Conclusion

Riluzole is a neuroprotective drug acts by blocking glutamatergic cell transmission and controls the neuroexcito-toxic damage. It is though that the neuroprotective action is done by noncompetitive blockage of the NMDA receptors and G protein dependent signals transduction, thus controlling the excitotoxicity.⁷ It was also proved that any neuropathic pain is due to an imbalance between the inhibitory and excitatory synaptic function followed by nerve injuries. riluzole, a novel neuroprotective has been used to prolong the survival of patients with amyotrophic lateral sclerosis.⁸

The neuroprotective effect of riluzole is also known to rely in part on inhibition of sodium channels the inhibition of sodium channels was correlated with post ischemic neuronal protection.⁹ Riluzole had a higher affinity for the inactivity state than the resting state of sodium channels which resulted in a selective block of damaged or depolarised nerve thereby preventing excess stimulation of the glutamatergic receptors.¹⁰

NMDA receptors gate the ion channels present in the presynaptic and postsynaptic regions also in some extra-synaptic locations.¹¹ The amount of glutamate present in the synaptic cleft is very important in deciding stimulatory and excitatory transmission so the maintenance of glutamate concentration between the neurons is very important so that excessive activating of glutamate transporters can lead to various pathological conditions.¹² In this study, after treatment with there is a decrease in the expression of NR2B subunits compared to migraine induced rats. Riluzole a neuroprotectant and with antiglutaminergic activity modulate the neurons and protects from excitotoxicity.¹³ Administration of riluzole increase the uptake of glutamate by increasing the glutamate transporters and reduce its antiglutaminergic action is exerted mainly by blocking the sodium channels by inhibiting the alpha activity and stabilizing the voltage gated calcium channels.¹⁴

So this study was done to prove the changes in the transporters and its counter-regulatory actions of riluzole on GLAST & GLT₁ transporters in a rat migraine model.¹⁵ Also riluzole can be used in the treatment of migraine due to the neuroprotectant and neuromodulatory actions.¹⁶

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Ethical Clearance: Obtained from Institutional Animal Ethical Committee

References

17. Basbaum AI, Woolf CJ: Pain. Recognition and Alleviation of Pain in Laboratory Animals *Curr Biol*, 1999; 9: 429-443.
18. Bensimon, G., Lacomblez, I., Meininger, V. and ALS/Riluzole study group: a controlled trial of riluzole in amyotrophic lateral sclerosis. *N. Engl. J. Med.* 1994; 330: 585-591.
19. Carlton SM, Hargett GL. Colocalization of metabotropic glutamate receptors in rat dorsal root ganglion cells. *J Comp Neurol* 2007; 501:780-789.
20. Danbolt NC: Glutamate uptake. *Prog Neurobiol* 2001; 65:100-105.
21. Doble A, The pharmacology and mechanism of action of riluzole. *Neurology*, 1996; 47: 233-241.
22. Hebert T, Drapeau P, Pradier L, Dunn RJ, Block of the rat brain IIA sodium channel α subunit by the neuroprotective drug riluzole. *Mol Pharmacol*, 1994; 45: 1055-1060.
23. Iversen HK, Olesen J, Tfelt-Hansen P, Intravenous nitroglycerin as an experimental headache model. Basic characteristics. *Pain*, 1989; 38: 17-24.
24. Mizoule, J., Meldrum, B., Mazadier, M, Croucher, M., Ollat, C., Uzan, A., Legrand, 2-amino-6-trifluoromethoxy benzothiazole, a possible antagonist of excitatory amino acid neurotransmission I. *Neuropharmacology*, 1985; 24: 767-773.
25. Messlinger K. Migraine: where and how does the pain originate? *Exp Brain Res.* 2009; 196:179-193.
26. Martin D., Thompson M. A. and Nadler J. V. The neuroprotective agent riluzole inhibits release of glutamate and aspartate from slices of hippocampal area CA1. *Eur. J. Pharmacol.* 1993; 250: 473-476.
27. Moskowitz MA. The visceral organ brain: implication for the pathophysiology of vascular head pain. *Neurology*, 1991; 41:182-186.
28. Malick A, Burstein R, Cells of origin of the trigeminohypothalamic tract in the rat. *J Comp Neurol*, 1998; 400:125-144.

29. Olesen J, Iversen HK, Thomsen LL, Nitric oxide is a key molecule in migraine and other vascular headaches. *Trends Pharmacol Sci*, 1993; 15:149-153.
30. Pardutz A1, Krizbai I, Multon S, Vecsei L, Schoenon J. Systemic nitroglycerin increases Nnos levels in rat trigeminal nucleus caudalis. *Neuroreport*. 2000; 28:11(14):3071-3075.
31. Prenen, G.H. M., Gwan, G.K., Postema, F., Zuiderveen, F. and Korf, J.: Cerebral cation shifts in hypoxic-ischemic brain damage are prevented by the sodium channel blocker tetrodotoxin. *Exp. Neurol*. 1988; 99:118-132.
32. P.K. Sankaran., Histomorphometric study of neurons in the trigeminal ganglion in male wistar albino rats, 2012; 4(6): 28-31.

Factors Affecting Child Development: Highlighting the Facts in the Perspective of Child Abuse in Indian Scenario

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Abstract

Child abuse occurs in all cultural, income and ethnic groups and it can be broadly classified under physical, verbal, sexual, emotional or through neglect. It is often assumed that child abuse is an underlying problem encased in bigger problems like human trafficking, etc. The main objective of the paper is to identify the root causal factors of this problem of Child Abuse. This study has identified seven factors which had some contribution to this problem and they are broadly classified as: health-related problems, physical-abuse-related factors, education-related factors, income-related factors, family-related factors, overall child development and socio-economic improvement. The data was collected with the help of a structured questionnaire using a Likert scale. The reliability as well as validity testing was done for this study. Furthermore, structural equation modeling (SEM) was used for the analysis of the data.

Keywords: Child development, Child Abuse, Indian Scenario, Structural Equation Modeling (SEM).

Introduction

Child Trafficking is also a major crime as it was seen that more than half of the children trafficked for sex and they had experienced sexual violence, along with domestic servitude and labour exploitation. Child Sexual Abuse is also a major segment under Child abuse and it is defined as using children in any kind of sexual activity, often without the consent and understanding of the children (Krishnan, et al., 2017)⁶. It has been also seen that sexual assault to children is not generally reported to the authorities due to social stigmatization

and many other reasons such as guilt, embarrassment, lack of awareness of the victim's rights, the need to keep the event hidden from certain people, unwillingness of the victim to confront the abuser in a legal setting and also fear of not being believed (AlMadani, et al., 2012)². However, it has been seen that the children exhibits first signs of exhibiting sexual abuse by talking to their most trusted adults when they are carefully prompted and asked thoughtfully. Reporting of child abuse to the proper relevant authorities may help in the protection of the children from this evil. A comprehensive public health strategy may go a long way in the prevention of child maltreatment if implemented properly.

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Literature Review: Some of the physical consequences have been defined as thermal injury, Shaking Trauma Syndrome, which is also called STS, blunt trauma, etc. Intentional burns are the most serious kind of child abuse injuries and it must be immediately diagnosed in order to prevent the perpetrator from further harming the child (Pawlik, et al., 2016)⁸. Child

Sexual Abuse, specifically, can be the cause of the child developing internal lacerations and bleeding as a part of most severe physical injuries and in the most severe cases, damage to the internal organs is also seen which can ultimately result in the death of the child (Aboul-Hagag & Hamed, 2012)¹. Though physical maltreatment is very insufferable by the child, emotional maltreatment is also considered as a type of abuse which has many detrimental effects in the long run such as emotional abuse (4.8 per cent) and emotional neglect (6.2 per cent) (Taillieu, et al., 2016)¹¹. Neglect can stem from an unstable family environment wherein the women who encounter Intimate Parental Violence have mental health needs that need to be fulfilled in order for them to show effective improvement (Bowen, 2015)³. Consequently, it has been seen that interventions made to prevent Intimate Parental Violence further explicitly impacts the children’s subjection to violence and can effectively improve parent-children relationship in the long run (Kyegombe, et al., 2015)⁷. A study conducted in Canada revealed that the children or youth who are removed from their parental home due to instances of maltreatment fall under the increased risk group of showcasing Suicide Related Behaviour in the Emergency Departments (Rhodes, et al., 2012)¹⁰. Thus, it is very important to nip this bud right from the very start by identifying the perpetrators, however, the child abusers are people who

are not strangers to the children but they are known to them, they may be family friends, neighbours or some relatives, who have some level of trust in the family (Feng, et al., 2015)⁴. However, certain models have been formulated to assess the risk of maltreatment of the children by looking at certain parameters and stopping the act from escalating further and they can also help the government in formulating certain preventive strategies to permanently stop the recurrence of these events (Prinz, 2017)⁹.

Hypotheses Development:

H1: ‘Physical Abuse Related Factor’ negatively influences the ‘Overall Child Development’.

H2: ‘Education Related Factor’ negatively influences the ‘Overall Child Development’.

H3: ‘Family Related Factor’ negatively influences the ‘Overall Child Development’.

H4: ‘Income Related Factor’ negatively influences the ‘Overall Child Development’.

H5: ‘Health Related Factor’ negatively influences the ‘Overall Child Development’.

H6: ‘Overall Child Development’ positively influences the ‘Socio-Economic Improvement’.

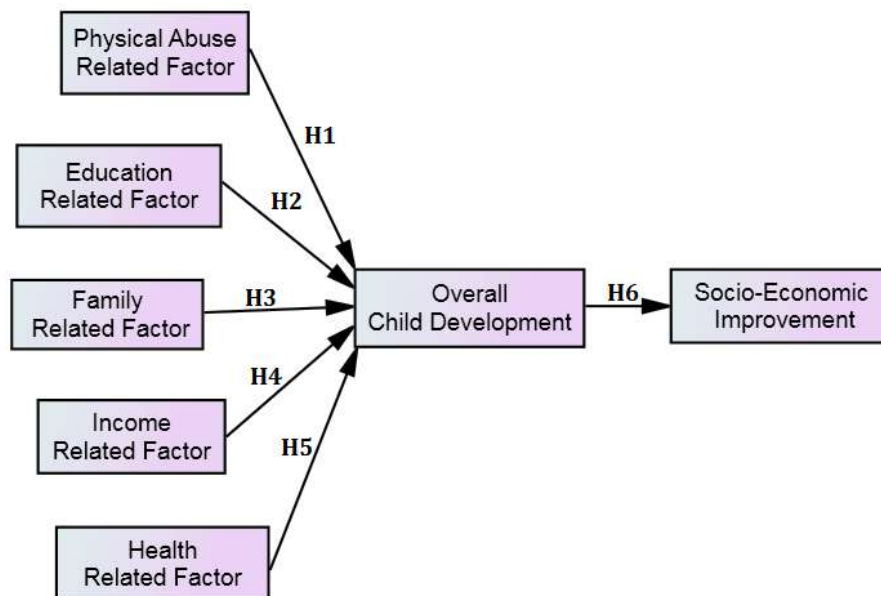


Figure 1: Hypothesized Research Model Establishment

Figure 1 showcases the hypothesized Research Model Establishment of the factors.

Research Methodology: The ‘Hypothesized Research Model’ (Figure 1) was developed by collected factors from literature review. A structure questionnaire was framed with related variables for survey. 5 point Likert scale is used for measuring the responses of people related with child abuse related issues. 250 responses were finally collected for this study. The data was collected in two stages using non-probabilistic sampling techniques. In the first stage, three states were decided from which the samples would be collected by Convenient Sampling. These states were Chhattisgarh, Bihar and Maharashtra. These states were selected for this research study as they contain the largest slums of India from where relevant data pertaining to this study could be collected. As a result, samples were collected

in a relatively short amount of time, that is, 5th August, 2019 to 5th October, 2019. In the second stage of Sampling, simple random sampling was used in order to collect data from the caregivers or guardians or parents of the children who underwent abuse.

Analysis and Results

After collecting the primary data, Structure equation modeling (SEM) was used for developing the model and establishing the hypothesis by the help of AMOS 23 software. Model fitness was judged through structural model. Here, Cronbach alpha value (0.811) for all items which was greater than 0.70, shows the satisfactory range of reliability. The fitness indexes (Table 1) were verified as follows and hypotheses were tested.

Table 1: Fit indices of Confirmatory Factor Analysis for Structural Model

Fit Index	Acceptable Threshold Levels	Structural Model Values
χ^2/df (Chi-square / degree of freedom)	Values less than 3	0.525
RMSEA (Root mean-square error of approximation)	Values less than 0.06	0.001
GFI (Goodness of fit index)	Values greater than 0.90	0.998
AGFI (Adjusted goodness of fit index)	Values greater than 0.90	0.978
NFI (Normed fit index)	Values greater than 0.90	0.991
CFI (Comparative fit index)	Values greater than 0.90	0.999

Here the fit indices of Structural model (Figure 2) indicate the acceptable range and prove a good model fit.

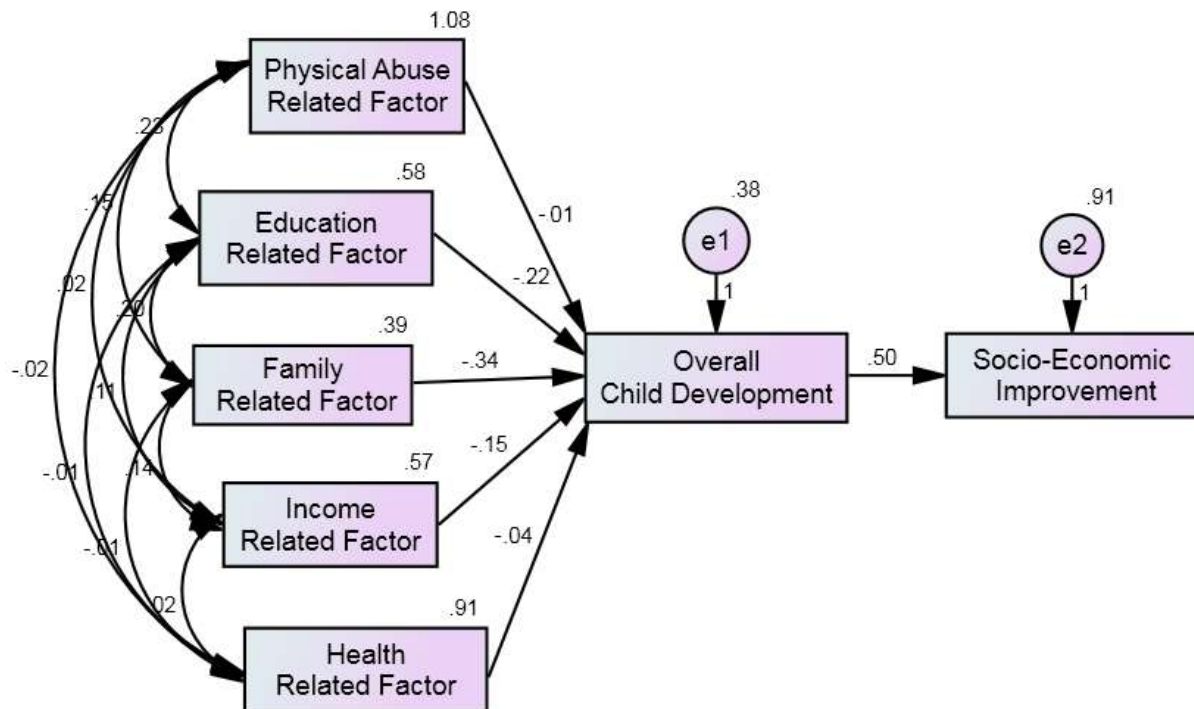


Figure 2: Path diagram of hypothesized structural model

Table 2: Path analysis of Structural Model

Measurement Path		Hypothesis	Estimate	S.E.	C.R.	P	Assessment
Overall Child Development	← Physical Abuse Related Factor	H1	-.010	.045	-.014	.041	Supported
Overall Child Development	← Health Related Factor	H5	-.039	.047	-.841	.028	Supported
Overall Child Development	← Education Related Factor	H2	-.216	.066	-3.256	***	Supported
Overall Child Development	← Income Related Factor	H4	-.150	.062	-2.408	.016	Supported
Overall Child Development	← Family Related Factor	H3	-.345	.082	-4.185	***	Supported
Socio-Economic Improvement	← Overall Child Development	H6	.464	.094	4.934	***	Supported

*Significant Regression co-efficient (P<0.01 and 0.05)

Table 2 represents the Structural Model of the Path Analysis.

Research Findings: Health related factors include HIV and other epidemics, illnesses, alcohol addiction and substance abuse. Victims of Child abuse often suffer from various health issues, be it psychological or physical. There has been some conclusive research in this area and it suggests that the victims of Child Sexual Abuse are very susceptible to a wide range of psychological problems in the long run such as depression, sexual disorders and dissociation symptoms. Adults who have a history of experiencing Child Sexual Abuse also suffer from poor health conditions such as not optimal physical health, psychosomatic physical complaints, DSM disorders, psychosomatic disorders, etc. and the variety of these conditions to be manifested in the victims depends on the kind of abuse that the victim has undergone amongst other factors (Gallo, et al., 2017)⁵. The women who have experienced abuse have more chances of being obese, poor mental health, alcohol dependent and drug dependent. Burns were also identified as one of the most common physical assault injuries in patients. Health factors are also interconnected that might cause the child abuse victims to succumb to the societal pressures and take up certain habits which will prove to be detrimental in the long run. It is evident that the adverse experiences are responsible for various mental conditions; however, it has been shown that they also instigate various physical health problems like risky sexual behaviours and substance abuse and it may also have certain health outcomes like cardiovascular diseases, obesity, diabetes, cancer, etc., furthermore, having certain economic repercussions and social outcomes which hamper the education and subsequently employment of the individual. Sexually Transmitted

Infections were more common in girls who were raped which had further negative effects on the physical health of the victims.

Managerial Implications: The industry might help in a big way by identifying these vulnerable children and help them to equip themselves with sustainable tools such as education, so that they can contribute towards the Indian society. Different organizations can take up this activity as a part of CSR (Corporate Social Responsibility) and they can provide the means for these children to survive these adverse conditions. While interacting with these children, some bright talents could be found who would contribute nicely towards the society, and at large, the economy of the country. This will further have certain deep rooted implications on the productivity of the nation.

Conclusion

This study reveals that exploitation of a child, be it physical or emotional, can have detrimental effects to the child. Children who have been sexually exploited are more prone to substance abuse, cutting behaviours, suicide ideations and also of attempted suicides. Emotional abuse and neglect have a long term effect and negatively influences the overall Child Development. Often, PTSD is seen to be co-occurring with psychosis especially in the population experiencing situations which are likely to cause highly stressful and traumatized situations. This study establishes the fact that abused children share their experience with trusted caregivers when an opportunity is given to them to talk. This helps them to avail therapy for their trauma and it helps in their healing process. Once that is done, overall child development takes place which further helps the child in contributing positively to the society resulting

in affirmative socio-economic development. Mother's parenting and Father's parenting plays a very important role in the overall development of the child which enables them to contribute to the society in the long run.

Ethical Clearance: *Ethical approval for this study has been taken from selected Municipal Authorities from selected states in India for carrying out the data collection procedure smoothly. Also respondents have been assured for maintaining full confidentiality of their feedbacks related to this research.*

Source of Funding: Self

Conflict of Interest: The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

References

1. Aboul-Hagag KE, Hamed AF. Prevalence and pattern of child sexual abuse reported by cross sectional study among the University students, Sohag University, Egypt. *Egyptian Journal of Forensic Sciences*.2012;2(1): 89-96.
2. AlMadani O, Bamousa M, Alsaif D, Kharoshah MAA, Alsowaigh K. Child physical and sexual abuse in Dammam, Saudi Arabia: A descriptive case-series analysis study. *Egyptian Journal of Forensic Sciences*.2012;2(1): 33-37.
3. Bowen E. The impact of intimate partner violence on preschool children's peer problems: An analysis of risk and protective factors. *Child Abuse and Neglect*. 2015;50:141-150.
4. Feng J, Chang Y, Chang H, Fetzer S, Wang J. Prevalence of different forms of child maltreatment among Taiwanese adolescents: A population-based study. *Child Abuse and Neglect*. 2015; 42: 10-19.
5. Gallo EAG, Loret De Mola C, Wehrmeister F, Goncalves H, Kieling C, Murray J. Childhood maltreatment preceding depressive disorder at age 18 years: A prospective Brazilian birth cohort study. *Child Abuse and Neglect*. 2017; 217: 218-224.
6. Krishnan S, Syahirah NF, Syahirah N, Amira N. Study on Child Sexual Abuse. *Human Resource Management Research*. 2017; 7(1): 38-42.
7. Kyegombe N, Abramsky T, Devries KM, Michau L, Nakuti J, Starmann E, Musuya T, Heise L, Watts C. What is the potential for interventions designed to prevent violence against women to reduce children's exposure to violence? Findings from the SASA! Study, Kampala, Uganda. *Child Abuse and Neglect*. 2015; 50: 128-140.
8. Pawlik M, Kemp A, Maguire S, Nuttal D, Feldman KW, Lindberg DM. Children with burns referred for child abuse evaluation: Burn characteristics and co-existent injuries. *Child Abuse and Neglect*. 2016; 55: 52-61.
9. Prinz RJ. Assessing child maltreatment prevention via administrative data systems: A case example of reproducibility. *Child Abuse and Neglect*. 2017; 64: 13-18.
10. Rhodes AE, Boyle MH, Bethell J, Wekerle C, Goodman D, Tonmyr L, Leslie B, Lam K, Manion I. Child maltreatment and onset of emergency department presentations for suicide-related behaviours. *Child Abuse and Neglect*. 2012; 36: 542-551.
11. Taillieu T, Brownridge DA, Sareen J, Afifi TO. Childhood emotional maltreatment and mental disorders: Results from a nationally representative adult sample from the United States. *Child Abuse and Neglect*. 2016; 59: 1-12.

Use of Throat Swab as a Method of Sputum Induction in Suspected Cases of Tuberculosis

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Abstract

Tuberculosis is an infectious disease. It is caused by bacteria Mycobacterium Tuberculosis. It can be diagnosed by demonstrating AFB by either phenotypic method like sputum smear microscopy, culture or by genotypic method like NAAT or LPA. For better results there should be a good quality sputum sample. Induction of sputum is a method for improving the quality of sample. The most commonly used method is induction using 3% saline. It has been seen that during taking throat swab specimen patients usually produce cough. This induced cough can produce better quality of sputum. The following study was done to know about the role of throat swab as a method of sputum induction.

Keywords: AFB, CBNAAT, LPA, Mycobacterium Tuberculosis.

Introduction

Sputum smear microscopy is a very common method for diagnosis of TB but it has limited sensitivity. In RNTCP two method are currently used; one is by ZN staining based microscopy using a regular microscope and secondly is LED based fluorescent microscopy (LED FM).¹ Culture is highly sensitive and specific method for diagnosis of TB but it is very time consuming as it requires 2-8 weeks for results. Newer method of rapid molecular tests like CBNAAT (cartridge based nucleic acid amplification test) and LPA (Line probe assay) have been developed.

According to RNTCP two quality samples should be collected and subjected to microscopy. One of these should be collected early morning empty stomach. Sputum should be 3-5ml in quantity and should be mucoid or muco-purulent preferably. For the success of any diagnostic method like smear examination for AFB,

fluorescent method, CBNAAT, LPA, or culture the quality of sputum specimen is of paramount importance. Even highly sensitive techniques may fail to give the desired results if the quality of sputum specimen is not adequate.

Induction of the sputum can be done for obtaining good quality sputum sample. It can be done by using various method. Most commonly used method is induction of sputum using 3% saline.² But these techniques may not be available at peripheral health institutions. Throat swab is used for obtaining specimen in conditions like H1N1, scarlet fever rheumatic fever, candida albicans, pertusis diphtheria and other respiratory diseases.³ It has been observed that while taking throat swab, once the pharynx is touched, patient starts coughing and produces expectoration. From throat swab the smear can be prepared on slide and induction of cough on touching pharynx may produce sputum expectoration which may give the good quality sputum and thus the higher yield.

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Material and Method

This study was conducted in the department of Respiratory Medicine of MMIMSR, MMDU, Mullana, Ambala. A total of 300 patients of presumptive TB were taken over a period of 12 months for the study. Children

less than 14 years were excluded. Any patient having haemoptysis were excluded. Patients who had cardiac disorder like CHF were excluded. Patients who have undergone recent surgeries of heart, abdomen, eye, ENT were also excluded.

The patients were asked to give the 1st spot sample. The quality and result of the sputum sample was noted. The patient was asked to come the next day and bring early morning sputum sample. Patient who refused to come the next day were offered second spot sputum examination. In this group all the patients were also subjected to induction by throat swab method.

Induction of sputum using throat swab: The steps of the procedure were explained to the patient and consent was taken. After taking personal protective measures using N95 mask and gloves, we first asked the patient to wide open his mouth so that the buccal cavity is fully visualized along with pharyngeal wall and tonsillar pillars etc. Thus a throat swab was taken from the buccal cavity with a swab stick. When the patients who were subjected to throat swab examination, the touching of the buccal cavity pharynx induced cough which yielded the sputum from within the chest. Throat swab was repeated to make the patient cough multiple times and sputum expectorated was collected in container and analysed. A smear was prepared using the throat swab and analysed

The quality of sputum specimen of the 1st spot specimen, second spot specimen, early morning sputum specimen and throat swab expectoration were noted. Sputum smear positivity rates and their grades on 1st spot, 2nd spot examination, sputum smear on throat

swab examination and sputum smear of the cough expectoration produced on throat examination and the next day early morning sample were noted and compared. The grading of all the samples was done according to the RNTCP guidelines. The first spot sample was taken of 272 patients, 28 patients could not spontaneously produce sputum. Second spot sample was obtained from 95 patients. Early morning sample was taken from 157 patients. All 300 patients were subjected to sputum induction by throat swab on the first day.

Results

Table 1: Among sample types in case group, most positive reports were obtained by the early morning sample (11.4%) followed by induction method (8%) and throat swab smear (7%). Positivity rate of spot and second spot sample were 3.3% and 1.1% respectively. Highly positive reports (3+) were seen only in samples taken by induction method and in early morning samples.

Table 2: More positive results were seen in mucoid samples. Highest yield (26 positive) was seen in mucoid samples that were more than 5ml (M3).

Table 3: There was no statistical significance observed between sputum positivity rates of early morning sample given on next day when compared with the induced specimen. Thus instead of calling next day, patients can be subjected to induced sputum specimen on same day this will save the patients of additional cost incurred for food, transport, loss of wages and will also lead to avoidance of failure to get 2nd early morning specimen at all.

Table 1. Results of samples according to sample type in case group

Sample Type	Spot Sample	2 nd Spot	Throat Swab Slide	Induction by Swab Stick	Early Morning Sample
Results					
SCANTY	5	1	18	7	7
1+	3	0	3	10	5
2+	1	0	0	3	2
3+	0	0	0	4	4
Positive Result	9	1	21	24	18
Total Samples	272	95	300	300	157
% Positivity	3.3%	1.1%	7%	8%	11.4%

Table 2. Distribution of samples on the basis of relation between positivity and quality of samples

Quality	Quantity	Positive Cases
Salivary	S1 (<3ml)	0
	S2 (3ml-5ml)	5
	S3(>5ml)	0
Mucoid	M1 (<3ml)	2
	M2 (3ml-5ml)	19
	M3 (>5ml)	26

Table 3. Comparison of samples with induction sample among case group

Types of Sample vs Expectoration After Induction								
Result	Spot	Induction	Early Morning	Induction	2 nd Spot	Induction	Swab	Induction
SCANTY	5	7	7	7	1	7	18	7
1+	3	10	5	10	0	10	3	10
2+	1	3	2	3	0	3	0	3
3+	0	4	4	4	0	4	0	4
Positive Result	9	24	18	24	1	24	21	24
Total Samples	272	300	157	300	95	300	300	300
% Positivity	3.3%	8%	11.4%	8%	1.1%	8%	7%	8%
P Value	0.016*		0.223		0.015*		0.641	

Discussion

Sputum smear microscopy is the most important tool for the diagnosis of PTB. It is reliable inexpensive easily accessible and also a very rapid method to diagnose tuberculosis. All the method for TB diagnosis whether it is genotypic or phenotypic method require a good quality sample for the diagnosis of TB. For any method to give to give desired results the quality of sputum specimen is of paramount importance. It is seen that the yield of sputum is low in females and children. Females and children are in habit of swallowing of sputum. A study was done in which qualitative differences in sputum smear microscopy results for acid fast bacilli by age and sex in four countries Moldova, Mongolia, Uganda and Zimbabwe were studied.⁴ They found striking differences in the low-grade positivity in these four countries. They found that females had lower bacillary counts. The low-grade positivity was more commonly seen in the extremes of the ages. This supports the role of high-quality sputum to improve the yields. Similarly, induction of sputum is helpful in TB diagnosis in children also.

Sputum induction is a method which can lead to increase in quality and quantity of the sputum sample.

There are various method of sputum induction. Most commonly used method is by nebulisation with hypertonic saline. Various other method used are nebulisation with salbutamol, ambroxol, N-acetylcysteine. By using these method yield of sputum can be increased.⁵

Throat swab specimen is standard for obtaining samples in case of H1N1, diphtheria. It is seen that when we touch the pharynx with any object like when taking throat swab sample there is elicitation of cough. When cough is produced it brings out sputum. So it was postulated that sputum induction could be used as a method of sputum induction for diagnosis of tuberculosis.

Five different samples were included in the study from case group including spot sample, second spot sample, an early morning sample, samples after induction by pharyngeal stimulation with throat swab and throat swab slide. Spot sample was taken from all patients who could produce sputum (272 patients). Participants were then asked to come next morning for early morning sample. Second spot sample was taken from those (95 patients in total) who refused to come next day. Sputum induction was done of all 300 patients and sample was taken. A smear slide was also prepared from throat swab

in all 300 patients. Early morning sample was taken from 157 patients as 48 patients did not come despite agreeing. The samples were analysed by FM staining. The positivity rate was highest (11.4%) in early morning sample, followed by induction method (8%). Swab stick smear showed a positivity rate of 75 which was higher than spot sample and second spot sample being 3.3% and 1.1% respectively. Although, the yield was higher with early morning sample than induction sample but this was statistically not significant (p -value $>.05$) The positivity rate of induction method was significantly higher than spot and second spot samples and this was statistically significant with p -value $<.05$. So, we propose that in cases where patients refuse to come for early morning sample on next day or there is high likelihood that patient will not come, the induction method should be used as this method significantly improves the diagnostic yield of smear microscopy.

In order to improve the sputum positivity rate sputum induction using 3% saline, bronchoscopy and gastric lavage are being used. All these method have their limitations. Gastric lavage requires overnight stay so that the secretions from stomach can be collected in the morning and analysed. Sputum induction using 3% saline may cause bronchoconstriction in patients especially with bronchial hyper reactivity.⁵ Bronchoscopy requires highly skilled medical professionals and specialised bronchoscopy suite. Induction using throat swab is a simple process which can be performed anywhere and requires minimal skills. It can also be performed in peripheral health institutes where many facilities are not available and electricity supply may be erratic.

Conclusion

In conclusion, our study shows that although early morning samples have a higher positivity rate for AFB than post-induction sample but induction sample can be useful in cases where early morning sample is not

available. Induction technique can also be useful in cases where sputum production is sparse or in female who usually swallow and don't expectorate.

Conflict of Interest: None

Source of Funding: Self

Ethical Clearance: Ethical Clearance was obtained from the Institutional Ethics Committee (IEC), Maharishi Markandeswar (deemed to be university) Mullana, Ambala.

References

1. Technical and operational guidelines for tuberculosis control, Revised National Tuberculosis Control Programme, New Delhi(IN): Central Tuberculosis Division, Directorate General of Health Services, Ministry of health and family welfare Government of India; 2016.13-4
2. Seong GM, Lee J, Lee JH, Kim JH, Kim M. Usefulness of sputum induction with hypertonic saline in a real clinical practice for bacteriological yields of active pulmonary tuberculosis. *Tuberc Respir Dis*. 2014 Apr;76(4):163-8.
3. Wang WK, Chen SY, Liu IJ, et al. Detection of SARS-associated coronavirus in throat wash and saliva in early diagnosis. *Emerg Infect Dis*,2004;10:1213-9
4. Willy Ssengooba, David P. Kateete, Anne Wajja, et al., "An Early Morning Sputum Sample Is Necessary for the Diagnosis of Pulmonary Tuberculosis, Even with More Sensitive Techniques: A Prospective Cohort Study among Adolescent TB-Suspects in Uganda," *Tuberculosis Research and Treatment*, vol. 2012, Article ID 970203, 6 pages, 2012.
5. Wong HH, Fahy JV. Safety of one method of sputum induction in asthmatic subjects. *Am J Respir Crit Care Med*. 1997 Jul;156(1):299303

mLearning Using Whatsapp Application to Interconnect the Class

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Abstract

E-learning is one such platform used to help students learn with the use of electronic devices like computers and internet. M-learning is one another emerging methodology that follows all the principles of E-learning but with even smaller electronic tools like smartphones, table ts etc. The use of mobile applications in medical and dental education has been shown to increase student participation, enhance the feedback process and improve communication between student and tutor.

Keywords: E-learning, smartphones, M-learning.

Introduction

In Recent times, there has been increased research into mobile learning (mLearning) and specifically the use of instant messaging services.¹ This Application is very addictive and can create a great impact on regular users. Communication has become easier, faster and cheaper with Whatsappmessenger. Mobile phones are banned in selected educational institutions;however, the restriction is only in the campus and not in most of the hostels where the mobiles are used to the most by the students. With our Internet bandwidths growing and the expected freedom to use free internets in the public places and educational campuses, our expectations for the paradigm shift of learning from laptops to mobile devices is not so far. Studies have shown that there are two benefits of Whatsapp for distance learning: mobile learning and context free access to learning resources.² Many researchers have been done in technological profession. Very less data is available in the usage of

WhatsApp as a teaching media in medical colleges. More work needs to be done to explore in detail the advantages and disadvantages of WhatsApp. Hence the study was planned to evaluate the experiences and thoughts of second year pathology students using WhatsApp Messenger discussion group to supplement their learning experience.

Material and Method

The study was conducted in MMIMSR on second year medical students after obtaining Institutional Ethics Committee approval and an informed verbal consent of the students. The study period was 50 days and a whatsapp group named “pathopharma 2014-2015 was created, all the students who had consented (150) were included. Rules & regulations were charted and strict adherence was advised. One girl and one boy who volunteered served as group admin other than the facilitator. Most of the students have the free wifi access in their hostels provided by the university so that the students had not to bear the extra costs. After the conventional lectures being taught in the class about lung pathology the students were sent certain important videos of the patients related to the condition. Since the application supported the internet youtube videos and educational material was also sent on the app. We were even been able to conduct MCQ based class test using a whatsapp based application linked to google drive.

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Analysis: A questionnaire was designed in Google forms to document the perceptions and feedback on this teaching learning methodology. It comprised of both close ended and open ended questions. Quantitative analysis, Likert scale of 5 was used for close ended questions and a qualitative analysis was conducted on the items.

Results

Out of 150 students of second professional MBBS 123(82%) students filled the feedback proforma provided to them. Twenty-seven students did not fill the feedback form. Sixty-eight (55.3%) girls and 55(44.7%) boys responded to it. All the students (100%) have smart phones and internet access on their phones.

All the students are using WhatsApp out of which 97% for both social and academic purposes and 3% for social purposes only.

77% of the students watched the videos. Out of which all the three videos were seen by 17%, maximum students saw the two videos 48% and single video was seen by 12% of students.

Out of 123 students 23% of the students could not see the videos due to lack of interest, could not access easily due to slow internet, problem in buffering of video.

On analysis of 95 students who saw the video for the design and usability of WhatsApp in teaching and it was found that and 65% think that it took reasonable time for watching the video whereas 35% think that it was highly time consumable.

It was a new experience to study pathology this way and 78% of the students enjoyed it very much. Twenty two percent found it long and boring.

The overall presentation and design was rated more than 7 by 58% of the students, 7-5 by 34% and less than 5 by 8%.

Most of the students 89% had a view that both class room and videos suit them best for developing good understanding of the topic.

Qualitative analysis

Theme 1: WhatsApp as a learning medium and usability

They think that by this way topic is better understood,

interesting, it's fun, more interactive session, some find didactic lecture boring, practical learning, creates interest in topic and subject, more retention of the topic. "It has made my understanding regarding chronic lung diseases better. I can be more confident with the patient now" The videos can be seen whenever required.

Theme 2: Content of the videos:

92% found it to be well balanced

84% told that it provided useful information regarding topic

78% feel that it has clear layout

85% found it to be detailed

92% found it to be interesting

It was helpful to the students in implying what is being read. Some students also felt that topic was much stretched.

Theme 3: Better learning

Most of the student like this method of teaching as it is different way of learning, innovative, interactive and helps in more retention. 87% students were of the view that it improves learning as AV aids make more impact. Improves practical learning, pictorial impressions of the topic, better retention, one student feels to self-read the topic from book after watching the videos which is not done by the student otherwise. Few students wanted the videos to be of short duration.

Theme 4: students who could not watch the video due to any of the reasons mentioned:

Classroom lectures more interesting

Could not comprehend and understand

Slow network but wanted to see the videos as they can be paused and be seen again.

Improves understanding and helps in retaining things.

Should be shown in class itself

Time consuming

Theme 5: Feelings about teaching learning methodology

Students feel that the teaching and learning should be informative, interactive as well as few exam oriented things should also be considered. They want all the teachers to incorporate interactive method of teaching in classes. According to a student “interaction makes the topic very familiar and easy to retain.”

Discussion

On the examination and analysis of our research results we found very interesting findings. Hundred twenty-three students participated in this study. All the students have the smart phones which they use for both social and academic purpose. There was an immediate acceptance of our medical students to the new mode of learning. This gave us an understanding that changes in the teaching learning methodology are readily welcomed by our students. Our results were in concurrent with the findings of others who have reported the positive attitude of students over the implementation of M-learning methodology.³ There is a successful integration of social media tool with academics or teaching learning process. It helps in improving the learning concepts among students.

In the journey from memory based schools to the vast medical curriculum, medical students face considerable challenges and hurdles. This scenario worsens further when all the content delivery is primarily based on didactic lectures.⁴ To address this crisis, Medical Council of India (MCI) has revised the medical curriculum which recommends the shift from teacher centered to student centered learning by using various interactive strategies.

WhatsApp used as a social media tool can be successfully integrated with teaching learning methodology. No extra costs incurred so no financial burden on the students. Study by Renu et al had a view that using WhatsApp had a positive effect like making students work like team, improves quality of expression among students and students can learn any anytime anywhere.⁵ The results of this study demonstrate how WhatsApp can be a useful tool for students in the problem based learning process through promoting media sharing, improving communication and generating learning opportunities. It provided a platform for the students to foster a collaborative approach to learning. At present, both the American and British Medical Associations

have recommended guidelines for professional use of social media tools by medical students to promote medical information and education.^{4,5} In spite in Indian Scenario it is in infancy stage and is picking up slowly.

Limitations: Firstly, it was restricted for a single batch of students in Para clinical block. Secondly it only included one section of the subject the assessment could not be done.

Conclusion

Students welcomed and liked the use the Whatsapp in enhancing their learning experience in medicine. It was successful in providing an interactive environment, supplement knowledge and skills by watching videos; we propose that this methodology can be used to enhance student’s learning.

Conflict of Interest: None

Source of Funding: Self

Ethical approval and Informed consent: The study protocol was reviewed by the Ethical Committee of Hospital and was granted ethical clearance. After explaining the purpose and details of the study, a written informed consent was obtained from the participants.

References

1. Raiman L., Antbring R., Mahmood A. WhatsApp messenger as a tool to supplement medical education for medical students on clinical attachment. BMC Medical Education. 2017; 17:7-15.
2. MI M.G., Meerasa. S.S. Perceptions on M-Learning through WhatsApp application. JETH. 2016;3(2): 57-60.
3. Kiviniemi MT. Effects of a blended learning approach on student outcomes in a graduate-level public health course. BMC Med Educ. 2014;14:47.
4. Mazur E. Education. Farewell, Lecture? Science. 2009;323(5910):50–1.
5. Lohitashwa R, Shashikala P, Narendra B, Deshpande K R. Medical teachers becoming technosavy – perception of using Whatsapp as a teaching method. J Educ Res Med Teach. 2015;3(2):20-23.

Mobile Phones of Nursing Staff: A Neglected Source of Cross Infection

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Abstract

Introduction: Inevitable usage of mobile phones by the nursing staff makes them an open admittance for transmission of microorganisms to the patients and other health care-associates specially when used carelessly in intensive care units (ICU).

Methodology: The Study was conducted on 400 samples. Out of which 200 samples were from mobile phones of nursing staff posted in ICU without prior notice and other 200 were from various sites of patients like catheter tip (Urinary & central venous catheters), surgical drains, endotracheal tube and swab from wound of patients after 48hr of admission in ICUs.

Results: Predominant organisms in patient samples were *Escherichia coli* (*E. coli*) (39.2%) followed by *Staphylococcus aureus* (34.6%) and Methicillin Resistant *Staphylococcus aureus* (MRSA) (34.6%) and in mobile phones were Coagulase negative *Staphylococcus* (CONS) (64.1%) which were non-pathogenic and among pathogenic was *E.coli* (50.2%) followed by growth of different types of bacteria.

Conclusion: Mobile phones are cumbersome to clean and we rarely even make an effort to disinfect them. As a result, these devices have the potential for contamination with various bacterial agents. Besides, there are no guidelines for disinfection of mobile phones that meet the set hospital standards.

Keywords: *Klebsiella pneumoniae*, *Escherichia coli*, catheter tip, surgical drains, ET secretions, wound swabs, nosocomial pathogens, nursing staff.

Introduction

In modern era, mobile phones have become an indispensable part of communication.¹ Though the

mobile phones are beneficial but they carry pathogens more than a handle of a public restroom. Since 2005 numerous studies has been published in PubMed, Medline, Google Scholar, Science Citation Index and Scopus on the Mobile Phones of health care workers which has strong circumstantial evidence that mobile phones can be a source of nosocomial infections but the fact has not been definitely proven.² Nursing staff always play a chief role in patient care. The careless use of mobile by them can cause cross infection especially in critically ill or Immuno-compromised patients admitted in ICU which can be diagnosed by

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diverse phenotypic and genotypic method.³In the last few decades, the genotypic method are frequently being used for the identification of bacteria. However major drawback is the expensive nature & requirement of technical staff well-skilled for performing these method. In a developing country like India phenotypic method are still considered mainly for epidemiological typing. Antimicrobial susceptibility (Antibiogram) and bio typing are the mainstay of phenotypic typing method as they are easy to perform, interpret and are reproducible Hence this study was conducted with the aim to determine the cross-transmission of infection from cell phones of nursing staff to the patients.

Unfortunately, such studies have never ever been funded therefore antibiogram was used as a typing method in this study.

Material and Method

The Study was conducted in the department of Microbiology at MMIMSR, Mullana over a period of six months (September 2015-march 2017). A total of 400 samples were taken. Out of which 200 samples were from mobile phones of nursing staff posted in ICU without prior notice and other 200 were from various sites of patients like catheter tip (urinary & central venous catheters), surgical drains, endotracheal tube and swab from wound of patients after 48hr of admission in ICUs.

Sample Collection: A sterilized cotton swab dipped in sterile normal saline was taken. Samples from mobile phones were collected by rotating the wet cotton swabs & patient's samples were collected as per standard procedure. All the samples were cultured on Blood agar & MacConkey agar; incubated overnight at 37°C. Organisms were identified as per standard protocol. The antibiotic sensitivity pattern of the organisms was tested by Kirby Bauer's disc diffusion method following CLSI guidelines 2016 using HiMedia discs.¹⁵ The multidrug resistant strains were identified & further subjected for screening of MRSA and carbapenemase production.

Detection of MRSA strains by Cefoxitin Disc Diffusion Method: Methicillin resistant *Staphylococcus aureus* strains were confirmed by Kirby-Bauer disc diffusion method using cefoxitin (30 µg) disc. The strains of *Staphylococcus aureus* having zone of inhibition of ≤21mm to cefoxitin disc (30 µg) were considered as MRSA strains.

Screening of carbapenemase producing strains by Meropenem Disc Diffusion Method: 10 µg meropenem disc was used for screening of carbapenemase production. The strainshaving zone of inhibition of ≤21mm to meropenem disc (10 µg) were considered as positive for carbapenemase production.

Results

Among 200 samples from mobile phones 112 (56%) revealed more than one organism while 88 (44%) revealed only single isolate, which comprises a total of 424 organisms. Among which 209 (49.3%) were gram positive and 215 (50.7%) were gram negative organisms.

However, from 200 various samples of patient yielded 108 (54%) single pathogenic organisms while 92 (46%) were either sterile or showed growth of nonpathogenic organisms. Out of 108 organisms 52 (48.2%) were gram positive organisms and 56 (51.8%) were gram negative organisms. (Table 1)

The organisms isolated from catheter tip were CONS (3), MSSA (1), MRSA (1), *Candida* sp. (4), *E. coli* (12), carbapenemase producing *E.coli* (4), *Klebsiella* sp. (5), carbapenemase producing *Klebsiella* sp. (3) and *Acinetobacter* sp. (1). From ET secretions MSSA (1), MRSA (1), *E. coli* (3), carbapenemase producing *E. coli* (1), *Klebsiella* sp. (6), carbapenemase producing *Klebsiella* sp. (3), *Pseudomonas* sp. (1) and *Acinetobacter* sp. (1) were isolated. From surgical drains CONS (1), MSSA (6), MRSA (5), *Candida* sp. (2), *E. coli* (4), carbapenemase producing *E. coli* (2), *Klebsiella* sp. (1), carbapenemase producing *Klebsiella* sp. (1) and *Acinetobacter* sp. (1) were isolated. The organisms isolated from wound swabs were CONS (6), MSSA (10), MRSA (11), *E. coli* (3), carbapenemase producing *E. coli* (1), *Klebsiella* sp. (2), carbapenemase producing *Klebsiella* sp. (1).

Surprisingly carbapenemase producing *E. coli* (50%), carbapenemase producing *K. pneumonia* (25%), MRSA (33%)and CONS (33%) from various patient samples showed identical antibiogram with the isolates from the mobile phones of nursing staff. Isolates displaying identical sensitivity pattern (antibiogram) was from surgical drains (40%), endotracheal intubation (30%), wound swabs (20%) and catheter tip (20%).

Discussion

Worldwide increasing incidence of Hospital

acquired infections (HAI) is worrisome to all medical practitioners.⁴ HAI are attributed to transmission of Micro-organisms which can be from person to person or from inanimate items like stethoscopes, aprons, mobile phones and fixed telephones to hand and vice versa. In this study, microbial association of one such inanimate object mobile phone with patient's sample was assessed.⁵

Now days, the mobile phones are multi-utility non-medical devices used in the healthcare facility and in the community with unlimited benefits. Unfortunately, these are used without check in specific, critical areas like the operation room and ICUs, irrespective of their unidentified microbial load.

In current study both gram positive as well gram negative bacterial pathogens were isolated from mobile phones of nursing staff. The findings of this study are in concordance with study by SE Amala et al.⁶ (2015) which showed an overall percentage prevalence rate of 80.6% and 69% pathogen isolates from mobile phones of medical personnel.

Gram-positive and Gram-negative bacteria can persist on dry inanimate surfaces for months or more but humid and lower-temperature conditions prolong their survival. Moisture, optimum temperature of palms and heat generated by mobile phones provide the ideal condition for the bacteria to grow.⁷ In current study from mobile phones of nursing staff among Gram positive organisms majority were CONS (64.1%) and 29.7% gram positive isolates were *Staphylococcus aureus*. While in gram negative organisms *E.coli* (50.2%) and *Klebsiella pneumonia* (17.2%) were isolated. Similar organisms were also reported by Shekhar pal et al.³ (2015) and Raghavendra Rao Morubagal et al.⁵ (2017). Furthermore the great concern was the isolation of *Acinetobacter* (5.6%), carbapenemases producing *Klebsiella pneumonia* (5.1%), carbapenemases producing *E. coli* (15.8%), *P. aeruginosa* (6%) and MRSA (6.2%).

The occurrence of antibiotic-resistant bacteria is a critical issue which hampers prevention and control of hospital acquired infection. The geographic distribution or dissemination patterns of these bacteria differ within and across the region.

In the present study from patients among Gram positive organisms majority were MRSA (34.6%) and (34.6)% gram positive isolates were *Staphylococcus aureus* were isolated. While in gram negative organisms

E.coli (39.2%) and *Klebsiella pneumonia* (25%) were isolated. Furthermore the great concern was the isolation of Carbapenemases producing *Klebsiella pneumonia* (14.3%), Carbapenemases producing *E. coli* (14.3%), *P. aeruginosa* (3.6%), *Acinetobacter* (3.6%) (Table 1) which was similar to the study of Bastola R et al.⁸(2017), Negi V et al.⁹(2015) and Timothy OO et al.¹⁰(2014).

This study is unique in its own way as there are many studies suggesting the role of inanimate objects causing cross contamination of pathogens leading to outbreaks specially in ICUs.^{11,12} However in the present study, taking into consideration that mobile phones can be a chief source of microbial transmission identical pathogens with similar antibiotic sensitivity pattern from patients and mobile phones were isolated which could be a strong evidence suggestive of cross transmission of bacteria. In present study, Carbapenemase producing *E. coli* (50%), Carbapenemase producing *K. pneumonia* (25%), MRSA (33%) and CONS (33%) from various patient samples showed identical antibiogram with the isolates from the mobile phones of nursing staff. To the best of our knowledge none of the researchers till date have shown such relationship but analogous to this Chang HC et al.¹³(2017) has extensively studied the correlation between nasal colonization & bacterial transmission of mobile phone. Although genotypical confirmation of bacterial cross transmission between mobile phones & patient is essential but unfortunately, none of such studies have been financially funded enough thus antibiogram were used as a typing method in this study.

Inanimate surfaces in vicinity of patients can rapidly get contaminated via shedding of microorganisms by patients which may lead to cross transmission because of high-frequency interactions between nurses hands and high-touch surfaces.¹⁴ In current study Isolates displaying identical sensitivity pattern was from surgical drains (40%), endotracheal secretions (30%), swab from wound(20%) and catheter tip (20%). Which are the frequently handled sites of the patients. Calls and answers to call while working are obvious enabling transfer of microbes. In spite of repeated warning the nursing staff receives the phone calls while performing the procedures thus we hypothesized that may be this is the reason for cross transmission of pathogens from patient sites to mobile and vice versa. Although strenuously searched in the literature we still could not found such type of correlation.

Conclusion

This study concludes that nursing staff is disclosed to nosocomial pathogens including multidrug resistant (MDR) species which can be easily transferred to their mobile phones thus acting as a source of infection but further studies are needed to evaluate this correlation. Complete restriction on the use of cell phones in the hospital is not a solution to the concern. Though, there should be controlled use in high risk areas of the hospital

like ICU’s or the modest way out to implement a solution in developing countries (where resources are inadequate) is recurrent cleaning of cell phones with alcohol based disinfectants which should be followed by regular hand washing practices. There should be ultimate Guidelines for Environmental Infection Control in Health Care Facilities which proposes periodic disinfection of mobile phones.

Table I: Frequency of Bacterial Pathogens from Patient Sample and Mobile Phones of Nursing Staff

Nature of Pathogens	Patient Sample (n=52)	Mobile Phones (n=209)
Gram Positive Bacteria		
CONS	10 (19.2%)	134 (64.1%)
S. aureus	18 (34.6%)	62 (29.7%)
MRSA	18 (34.6%)	13 (6.2%)
Candida spp	6 (11.5%)	-
Gram negative Bacteria	(n=56)	(n=215)
E.coli	22 (39.2%)	108 (50.2%)
Carbapenemase producing E.coli	8 (14.3%)	34 (15.8%)
K. pneumonia	14 (25%)	37 (17.2%)
Carbapenemaseproducing K.pneumoniae	8 (14.3%)	11 (5.1%)
Acinetobacter	2 (3.6%)	12 (5.6%)
P. aeruginosa	2 (3.6%)	13 (6%)

CONS: Coagulase Negative Staphylococci, S.aureus: Staphylococcus aureus, MRSA: Methicillin-resistant staphylococcus aureus, Candida spp: Candida species, E.coli: Escherichia coli, K.pneumoniae: Klebsiella pneumonia, P.aeruginosa: Pseudomonas aeruginosa.

Conflict of Interest: None

Ethical Clearance: Taken from institutional ethical committee vide letter no. IEC/2015/133

Source of Funding: Nil

References

- Selim HS, Abaza AF. Microbial contamination of mobile phones in a health care setting in Alexandria, Egypt. *GMS Hyg Infect Control*. 2015;10:1-9
- Fatma Ulger, Ahmet Dilek .Are healthcare workers mobile phones a potential source of nosocomial infections?.*J Infect Dev Ctries*2015; 9(10):1046-1053
- Pal S, Juyal D. Mobile phones: Reservoirs for the transmission of nosocomial pathogens. *Advanced Biomedical Research*. 2015;4:1-18.
- Raziya Bobat, Moherndran Archary, The presence and spectrum of bacteria colonising mobile phones of staff and caregivers in high disease burden paediatric and neonatal wards in an urban teaching hospital in Durban, South Africa, *Southern African Journal of Infectious Diseases*.2016; 32(1):9-11
- Raghavendra Rao Morubagal. Study of bacterial flora associated with mobile phones of healthcare workers and non-healthcare workers. *IRAN. J. MICROBIOL*. 2017; 9 (3):143-151
- S. E. Amala and I. F. Ejikema .Bacteria Associated with the Mobile Phones of Medical Personnel. *Am. J. Biomed. Sci*. 2015; 7(1): 26-32
- Tagoe DN, Gyande VK, Ansah EO. Bacterial Contamination of Mobile Phones: When Your Mobile Phone Could Transmit More Than Just a Call. *Webmed Central Microbiology*. 2011;2(10)

8. Rama Bastola, Pramila Parajuli. Surgical Site infections: Distribution Studies of Sample, Outcome and Antimicrobial Susceptibility Testing. *J Med Microb Diagn.* 2017; 6(1):1-7
9. ViKrant negi, SheKhar Pal, DeePaK Juyal. Bacteriological Profile of Surgical Site Infections and Their Antibigram: A Study From Resource Constrained Rural Setting of Uttarakhand State, India. *Journal of Clinical and Diagnostic Research.* 2015; 9(10): 17-20
10. Timothy OO, Olusesan FJ, Adesola BO, Temitayo AA, David FO, Ige OO. Antibiotic resistance pattern of bacterial isolates from cases of urinary tract infections among hospitalized and out-patients at a tertiary health facility in South Western Nigeria. *Ann Trop Med Public Health.* 2014;7(2):130-135
11. Falk PS, Winnike J, Woodmansee C, Desai M, Mayhall CG. Outbreak of vancomycin-resistant enterococci in a burn unit. *Infect Control.* 2000;21(09):575–82.
12. Seki M, Machida N, Yamagishi Y, Yoshida H, Tomono K. Nosocomial outbreak of multidrug-resistant *Pseudomonas aeruginosa* caused by damaged transesophageal echocardiogram probe used in cardiovascular surgical operations. *J Infect Chemother.* 2013;19(4):677–81.
13. Chang, C. H., Chen, S. Y., Lu, J. J., Chang, C. J., Chang, Y., & Hsieh, P. H. Nasal colonization and bacterial contamination of mobile phones carried by medical staff in the operating room. *PloS one.* 2017;12(5):1-11
14. Hayden MK, Blom DW, Lyle EA, Moore CG, Weinstein RA. Risk of hand or glove contamination after contact with patients colonized with vancomycin-resistant enterococcus or the colonized patients' environment. *Infect Control.* 2008;29(02):149–54.

Comparative Study to Evaluate the Outcome of Sutures Versus Sutureless in Attachment of Conjunctival Autograft for Pterygium Excision

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Abstract

Background: Suturing of conjunctival graft is a traditional technique for pterygium excision surgery. Owing to its many disadvantages & complications many newer techniques like autologous fibrin glue have been introduced & accepted as an alternative method of graft adhesion.

Methodology: The present study was conducted at the Department of Ophthalmology, MMIMSR, Mullana (Maharishi Markandeshwar Deemed to be University) in the time period extending between December 2017 and January 2019. 100 eyes of patients of either sex with primary pterygium were selected and divided into 2 groups of 50 each in Group 1- patient underwent conjunctival auto graft with 10-0 ethilon sutures while in Group 2 suture less conjunctival auto graft was done with patient's own blood fibrin.

Results: Parameters such as mean operating time, presenting complaints like pain, watering, burning and foreign body sensation, complications & recurrence were compared between the two groups on postoperative Day 1, Day 7, 2 weeks, 1 month, 2 month, 3 month & 6th month. Statistical significant difference ($p < 0.01$) was found between the suture and sutureless surgery for pterygium in relation to post-operative discomfort grading. There was a significant difference ($t = 22.149$, $p = 0.001$) in the duration of surgery for GROUP I surgery.

Conclusion: Conjunctival auto graft with autologous serum is a safe and fast method. It is equally effective as conventional sutured autograft technique. Post operative discomfort is significantly less in this method. It also prevents suture related complications

Keywords: Pterygium, sutures, sutureless, duration of surgery postoperative discomfort, complications, recurrence.

Introduction

Pterygium defined as a degenerative disease characterized by triangle shaped fibrovascular growth of bulbar conjunctiva encroaching the cornea^[1]. Etiology includes several environmental factors such as ultraviolet

radiation, geographical location, heat, muddy dust and a arid weather^[2-4]. Though surgical removal remains the treatment of choice^[5] but various conservative treatments like artificial tear drops, vasoconstrictor drops and topical steroid drops have been tried in the early stages because recurrences after pterygium excision are common and aggressive. Conjunctival auto grafting (CAG) with autologous blood (blood fibrin) as it activates the coagulation cascade and eventually leading to fibrin polymerization. It has become the standard procedure of choice for both primary and recurrent pterygium as it offers excellent results with less complication rates & recurrences^[6]. LCAT is also the most popular surgical

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procedure which requires sutures for adhering the graft as it is assumed that addition of limbal stem cells act as a barrier to the migrating conjunctival cells onto the cornea^[7]. This technique requires experience and is allied with certain disadvantages such as increased surgical time, postoperative discomfort, inflammation and granuloma formation etc^[8,9]. India has a geographical location near to the equator suggesting the impact of UV light as well as high grade of the pterygium due to their occupation and lifestyle of people^[10,11,12]. It is being recognized that higher grade act as a risk factor for recurrence^[13]. Anbari AA conducted a comparative study to evaluate efficacy, safety and reliability of autologous cryoprecipitate in comparison with absorbable sutures in pterygium excision surgery & concluded that application of autologous cryoprecipitate glue instead of sutures for attaching the conjunctival auto graft in pterygium surgery resulted in less postoperative pain and shorter surgical time^[14]. In a similar study conducted by Foroutan a et al observed that autologous fibrin was a safe and useful alternative method for graft attachment in pterygium surgery^[15].

Materials and Method

The present study titled “A Prospective Comparative Study To Evaluate Sutures versus Sutureless in Attachment of Conjunctival Autograft For Pterygium Excision” was carried out at the tertiary care hospital in Department of Ophthalmology of Maharishi Markandeshwar deemed to be University (M.M.I.M.S.R.) Mullana, Ambala in a time period between December 2017 to January 2019.

100 eyes of patients of either sex with primary pterygium were selected from those attending the OPD at The Department of Ophthalmology, MMDU (MMIMSR), Mullana.

Patients would be divided into 2 groups of 50 each:

Group 1: Conjunctival auto graft with sutures.

Group 2: Suture less conjunctival auto graft with (patient’s own blood fibrin).

A written informed consent was obtained from each patient explaining them the procedure and the study in detail. Ethical approval for conducting this study was obtained from Institutional Ethics Committee vide letter number 1084.

Inclusion Criteria: Patients with pterygium consenting for surgery & with any of following indications for surgery- encroachment upon visual axis, inducing visually significant astigmatism, causing recurrent irritation or cosmetically bothersome to the patient, Gender i.e males & females, age equal to or more than 20 years

Exclusion Criteria: Recurrent pterygium, Bilateral pterygium, Pseudopterygium, Patients with scarred superior conjunctiva, Patients with cicatricial ocular surface disease, Patients with history of ocular trauma, Patients on anticoagulant therapy, Patients with deranged coagulation profile, Patients with dry eye syndrome, Patients having collagen vascular diseases

50 patients underwent primary pterygium excision and conjunctival auto grafting with autologous fibrin glue (glue group) and 50 with 10-0 ethilon suture.

In Suture Less Group:

- The graft was slid over the cornea without lifting the tissue off the cornea, towards the bare sclera and it was spread and positioned such that the limbal polarity was maintained. The edges of the graft were placed below the undermined edges of the surrounding conjunctiva of the host bed. The graft was allowed to adhere with the help of residual blood. The scleral bed is viewed through the transparent conjunctiva and to ensure residual bleeding does not re-lift the graft. Small central haemorrhages were tamponaded with direct compression using sponge-tipped applicator until haemostasis was achieved, usually within 8–10 minutes.

In Suture Group: The four corners of graft were anchored with episcleral bites to maintain the position of graft. The limbalside of graft were affixed to limbal area and the sides of graft were attached to surrounding conjunctiva at intervals of 1-1.5mm with simple interrupted 10-0 ethilon sutures. The eye was then patched and bandaged for 24 hours with 0.5% moxifloxacin eye drops.

In suture group, sutures were removed approx 2 weeks after surgery. Patients were followed up at day 1, day 7, 2nd week, at 1 month, 2 month, 3 month and then at 6 months. Additional visits were as and when required. Postoperative discomfort, complications related to graft on above described follow up & recurrences were observed & analysed.



Fig. 1: Conjunctival autograft in place using Autologous blood fibrin

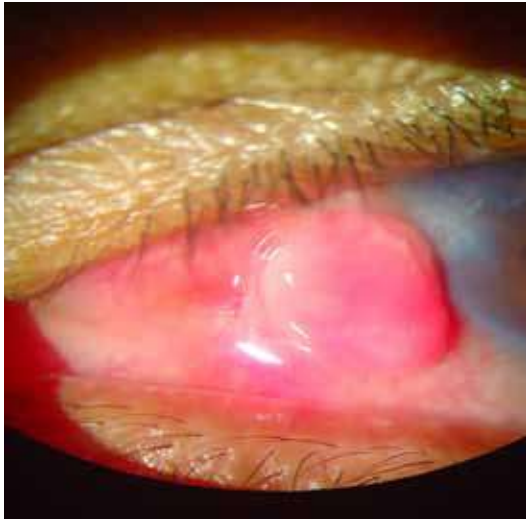


Fig. 2: Conjunctival cyst formation after attaching conjunctival auto graft using 10-0 ethilon sutures (slit lamp view)

Data was collected by using a structured proforma and was entered in MS excel sheet and analysed by using SPSS 19.0 version IBM USA. Quantitative data was expressed in terms of Mean and Standard deviation. Association between two variables was assessed by using Pearson's Chi-square test. Operating time between the two groups was compared using unpaired t test. A p value of <math><0.05</math> was considered as statistically significant whereas a p value of <math><0.001</math> was considered as highly significant.

Results

Majority of patients in both the group were found to

be in between 41-50 years. Overall mean age in group I was estimated to be $45.98 + 12.95$ years while in group II it was estimated to be $48.82 + 11.13$ years.

Maximum patients in both the groups were male.

Significant difference ($p < 0.01$) was found between the suture and sutureless surgery for pterygium in relation to post-operative discomfort grading.

In Group I; 2% patients had conjunctival cyst, 6% patients had conjunctival granuloma, 2% patients had graft displacement, 8% patients had graft edema, 2% patients had graft rejection, 4% patients had recurrence of pterygium. No graft loss was seen in any patient. In Group II; 2% patients had conjunctival cyst; 6% patients had graft displacement, 2% patients had graft edema, 2% patients had graft loss, 2% patient had graft rejection, while no patient had graft granuloma. No statistically significant difference ($p > 0.05$) was found between the suture and sutureless surgery for pterygium in relation to post-operative complications due to less sample size.

Group 1 (SUTURE) had a mean duration of $36.46 + 2.67$ minutes while Group II (SUTURELESS) had a mean duration of $24.88 + 2.55$ minutes. Overall mean duration of surgery was noted to be $30.67 + 6.37$ minutes. There was a significant difference ($t = 22.149, p = 0.001$) in the duration of surgery for GROUP I surgery.

In Group I maximum rate of complication were observed at 3 months i.e. 6%. In Group II maximum complications were seen on day 1 i.e. 6% & day 7 i.e. 4%.

Both the groups had recurrence of pterygium. In Group I 3 patients had recurrence after pterygium surgery while in Group II only 1 patient had recurrence. No statistically significant difference ($p > 0.05$) was found between the suture and sutureless surgery for pterygium in relation to recurrence of the disease.

Overall complication rate in Group I was 20% with 4% patients having recurrence while in Group II was 16% with 2% patients having recurrence.

Table 1: Association of type of surgery and post-operative complications.

Type of surgery	Post-operative complications								Total	Chi-Square Value	p-Value	Inference
	Cc	CG	GD	GE	GL	GR	Recurr	None				
Suture	1	3	1	4	0	1	2	38	50	6.114	0.527	Non-significant
	(2)	(6)	(2)	(8)	0	(2)	(4)	(76)	(100)			
Sutureless	1	0	3	2	1	1	1	41	50			
	(2)	0	(6)	(4)	(2)	(2)	(2)	(82)	(100)			
Total	2 (2)	3 (3)	4 (4)	6 (6)	1 (1)	2 (2)	3 (3)	79 (79)	100 (100)			

(Figures in parentheses indicate percentage-%)

Table 2: Association of type of surgery and post-operative discomfort grading.

Type of surgery	Post-operative discomfort grading				Total	Chi-Square Value	p-Value	Inference
	1	2	3	4				
Suture	0	12	29	9	50	21.643	0.001	Significant
	0	(24)	(58)	(18)	(100)			
Sutureless	6	28	11	5	50			
	12	(56)	(22)	(10)	(100)			
Total	6 (6)	40 (40)	40 (40)	14 (14)	100 (100)			

(Figures in parentheses indicate percentage-%)

Table 3: Association between type of surgery and duration of surgery.

Type of Surgery	Mean	Standard deviation	Standard error Mean	t- value	p-value	Inference
Suture	36.46	2.674	0.378	22.149	0.001	Significant
Sutureless	24.88	2.553	0.361			

(Figures in parentheses indicate percentage-%)

Table 4: Association of type of surgery and recurrence of the disease.

Type of surgery	Recurrence		Total	Chi-Square Value	p-Value	Inference
	Yes	No				
Suture	3	47	50	1.042	0.617	Non-significant
	(6)	(94)	(100)			
Sutureless	1	49	50			
	(2)	(98)	(100)			
Total	4 (4)	96 (96)	100 (100)			

(Figures in parentheses indicate percentage-%)

Discussion

In the present study statistically significant difference was found between the suture and sutureless surgery for pterygium in relation to post-operative discomfort grading. Similar results were seen in a study conducted by G.D. Donepudi, et al.(2019) & Anita Minj et al (2018)¹⁶⁻¹⁷ in early post-operative period there was remarkable pain and discomfort in

group A (sutures) than in group B(sutureless). There was a significant difference in the duration of surgery for suture (M= 36.46, SD= 2.674) and sutureless (M= 24.88, SD= 2.553) surgery; $t = 22.149$, $p = 0.001$. In a study conducted by Sucharita das et al (2018)¹⁸ there was statistically significant difference in the mean operating times between the two groups with results favouring the autologous blood group ($p < 0.05$). Similar type of

study by donepudi et al (2019)¹⁶ concluded that average duration of surgery was significantly less in Group I than in Group II. In our study maximum rate of complication in Group I was seen at 3 months i.e. 6% .In GP II maximum complications were seen on day 1 ie 6% & day 7 ie 4%. Similar study conducted by harpalsingh et al (2017) shows the complications following both groups of pterygium excision. In group A (sutureless), the graft displacement was found in 2 (7.1%) patients, whereas in group B, there was no graft displacement seen. While in group B(sutures), 2 (9.1%) patients had granuloma formation and also the recurrence of pterygium, which was high (22.7%) in group B as compared to group A (3.6%). Mohammed Moizuddin et al (2019)¹⁹ conducted a similar study & found that 40% patients had graft oedema & 10% had graft displacement in autologous blood group while 10% patients had graft oedema & granuloma formation in sutures group. Recurrence was also noticed in both the groups in our study. In both the groups recurrence was seen after 3 & 6 months. No statistically significant difference was found between the suture and sutureless surgery for pterygium in relation to recurrence of the disease. In a study conducted by maiti et al(2017)²⁰ no significant difference was found in the recurrence rate between FG and ABC, but graft stability was found to be better with fibrin glue compared with autologous blood coagulum. 1.32% recurrence was noticed in a study conducted by Thatte et al(2019)²¹ over 6 months of followup.

Conclusion

Efficacy wise both the techniques are comparable. However post operative discomfort and surgical time required are significantly less in autologous serum method. Graft loss is one of the major complication seen in this technique, which may be avoided by making a thick film of blood over recipient bed and by taking thin and uniform graft without tenon's capsule.

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References

1. D. Coster, Pterygium—an ophthalmic enigma, *Br. J. Ophthalmol.* 79 (4) (1995 Apr) 304–305
2. S.M. Saw, D. Tan, Pterygium: prevalence, demography and risk factors, *Ophthalmic Epidemiol.* 6 (3) (1999 Sep) 219–228
3. D.J. Moran, F.C. Hollows, Pterygium and ultraviolet radiation: a positive correlation, *Br. J. Ophthalmol.* 68 (5) (1984 May) 343–346
4. R. Detels, S.P. Dhir, Pterygium: a geographical study, *Arch. Ophthalmol.* (Chicago, Ill 1960) 78 (4) (1967 Oct) 485–491
5. G. Koranyi, S. Seregard, E.D. Kopp, Cut and paste: a no suture, small incision approach to pterygium surgery, *Br. J. Ophthalmol.* 88 (7) (2004 Jul) 911–914
6. K.R. Kenyon, M.D. Wagoner, M.E. Hettlinger, Conjunctival autograft transplantation for advanced and recurrent pterygium, *Ophthalmology* 92 (11) (1985 Nov) 1461–1470
7. K.P.S Malik, R. Goel, A. Gutpa, S.K Gupta, S. Kamal, V.K Mallik, et al., Efficacy of sutureless and glue free limbal conjunctival autograft for primary pterygium surgery, [Internet]. [cited 2019 Jan 27], *Nepal J. Ophthalmol.* 4 (2) (2012) 230–235.
8. S. Choudhury, J. Dutta, S. Mukhopadhyay, R. Basu, S. Bera, S. Savale, et al., Comparison of autologous in situ blood coagulum versus sutures for conjunctival autografting after pterygium excision, *Int. Ophthalmol.* 34 (1) (2014 Feb 4) 41–48
9. P. Prabhasawat, K. Barton, G. Burkett, S.C. Tseng, Comparison of conjunctival autografts, amniotic membrane grafts and primary closure for pterygium excision, *Ophthalmology* 104 (6) (1997 Jun) 974–985
10. R. Asokan, R.S. Venkatasubbu, L. Velumuri, V. Lingam, R. George, Prevalence and associated factors for pterygium and pinguecula in a South Indian population, *Ophthalmic Physiol. Opt.* 32 (1) (2012 Jan) 39–44
11. S. Marmamula, R.C. Khanna, G.N. Rao, Population-based assessment of prevalence and risk factors for pterygium in the South Indian State of Andhra Pradesh: the Andhra Pradesh eye disease study, *Investig. Ophthalmol. Vis. Sci.* 54 (8) (2013 Aug 9)
12. J. Khoo, S.M. Saw, K. Banerjee, S.E. Chia, D. Tan, Outdoor work and the risk of pterygia: a case-control study, *Int. Ophthalmol.* 22 (5) (1998) 293–298
13. P.S. Mahar, N. Manzar, Pterygium recurrence

- related to its size and corneal involvement, *J. Coll. Physicians Surg. Pak.* 23 (2) (2013 Feb) 120–123
14. Anbari AA. Autologous cryoprecipitate for attaching conjunctival autografts after [5] pterygium excision. *Middle East Afr J Ophthalmol.* 2013;20:239-43.
 15. Foroutan A, Beigzadeh F, Ghaempanah MJ, Ashghi P, Amirizadeh N, Sianati [6]H, et al. Efficacy of autologous fibrin glue for primary pterygium surgery with conjunctival autograft. *Iranian J Ophthalmol.* 2011;23:39-47.
 16. Minj A, Satapathy J. Conjunctival Autograft using Autologous Serum versus Suturing Technique. *JMSCR.* 2018; 06(04), 1219-1224
 17. Devi G, Ramesh S, Govindarajulu M, Dhanasekaran M, Moore T, Ganekal S, et al. Early postoperative outcomes of pterygium surgery: Sutures versus autogenous serum in-situ fixation of limbal conjunctival autograft. *Life Sci [Internet].* 2019;221,93–8.
 18. Das S, Pai V, Shetty J, Amin H, Bhat SK, Kotian V. Comparison of Conjunctival Autograft with Suture versus Autograft with Patient's Own Blood (without Suture) in Pterygium Surgery: A Pilot Study. *Journal of Clinical and Diagnostic Research.* 2018, 12(8), NC13-NC16.
 19. Moizuddin M, Khadher SA. A comparative study of post-operative outcomes of pterygium excision with autograft using autologous blood and sutures. *Indian Journal of Clinical and Experimental Ophthalmology.* 2019; 5(1): 23-26
 20. Maiti R, Mukherjee S, Hota D. Recurrence rate and graft stability with fibrin glue compared with suture and autologous blood coagulum for conjunctival autograft adherence in pterygium surgery: A meta-Analysis. *Cornea* 2017; 0: 1–10.
 21. Thatte S, Dube AB, Sharma S. Efficacy of autologous serum in fixing conjunctival autografts of various sizes in different types and grades of pterygium. *J Ophthalmic Vis Res.* 2019; 14: 136-43.

Reported Adverse Drug Reactions in Off-Label Use of Azathioprine in Dermatology: A Review

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Abstract

The skin is one of the largest organs in the human body. Majority of skin diseases requires lifelong treatments since they are chronic in nature. Thereby, appropriate diagnosis by the physicians and rational prescription of drugs becomes a vital component of drug therapy. ADR monitoring is considered to be mandatory as they become severe and potentially life-threatening. Primarily, in off-label setting, patients are treated with drugs which are not registered for that specific indication. Dermatologists have been at the forefront of the application of azathioprine and have thus been using the immunosuppressant for treating patients over several years.

Keywords: Azathioprine, off-label, adverse drug reaction.

Introduction

The skin is one of the largest organs in the human body. It is thus exposed to injury by various extrinsically based factors such as chemical, environmental, infectious agents as well as the intrinsic factors comprising of the metabolic, immunological and genetic. Majority of skin diseases requires lifelong treatments since they are chronic in nature. Thereby, appropriate diagnosis by the physicians and rational prescription of drugs becomes a vital component of drug therapy.¹ While a prescription is determined as a message conveyed by the physician to the patient.² Adverse drug reaction (ADR) is described as the unintended effects of drugs occurring during the use of drugs. ADR monitoring is considered to be mandatory as they become severe and potentially life-threatening. Azathioprine is widely used in medicine today as an immune-modulating drug. This drug in the United States is used in dermatology as an off

label. Although in most European countries the use of azathioprine is licensed for the treatment of pemphigus vulgaris and dermatomyositis, it is extensively used off-label. Primarily, in off-label setting, patients are treated with drugs which are not registered for that specific indication.³ Dermatologists have been at the forefront of the application of azathioprine and have thus been using the immunosuppressant for treating patients over several years. Moreover, azathioprine is discerned to be substantially more affordable.⁴ For decades, physicians have utilized azathioprine and it is available in relatively inexpensive and generic formulation. Since azathioprine is no longer patented and not as lucrative as newer, more costly medications, the pharmaceutical industry appears to have lost interest in scrutinizing azathioprine. The effectiveness of azathioprine in dermatology is supported by numerous studies, reports and expert opinion. However, by the strictest evidence-based medicine standards, the level of evidence supporting the off-label use of azathioprine for many conditions is not as strong as for some newer medications. Thereby, there is a lack of strong evidence due to the time-honoured recognition of the efficacy of azathioprine and the relative newness of evidence-based medicine to the field of dermatology. For instance, dermatologists have been using azathioprine to treat immunobullous diseases for nearly 35 years successfully.

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Overview of off-label drugs: Off-label is determined as the medication that is being used in a manner not prescribed by the Food and Drug Administration as an approved packaging label. Despite the prominence of off-label drug use, few patients as per the experts are aware that they are receiving a drug off-label and hence doctors are not required to tell that the drug is being used as an off-label. Therefore, when a prescription is formed by the doctor for an unapproved use, it is then determined as an “off-label” prescription.⁵ For dermatologists, the use of “off-label” is a common practice for treating dermatologic conditions. According to a study r drugs that have both well acceptable therapeutic value in the medical community and also the proven efficacy on the basis of results of clinical trials, these off-label prescriptions are being used.⁶ As per the reports conducted, in the United States, the largest review conducted of outpatient prescribing patterns discerned that 21% of the prescriptions were off-label based.⁷ Due to the potential benefits associated with the off-label use and prescribing, it is commonly used worldwide. Off-label use may benefit the patients, in particular to those with a life-threatening illness, as off-label use might turn out effective where no standard treatments are available or existing treatments have failed; in some cases, off-label uses may also be perceived as the standard of care.⁸ Despite the benefits, there are also concerns associated with the off-label use of a drug. Few of the potential concerns include adverse reactions, lack of public or private drug coverage for off-label uses^{9, 10} liability for healthcare professionals and the illegal promotion of off-label uses by manufacturers.¹¹ There are numerous reasons for off-label use. Firstly, the FDA-approved therapies might not be discerned to exist for the treated population’s specific disease. Secondly, physicians might replace within a class of medication if in case one medication is approved for a particular use while the others are not. Thirdly, the features of the two conditions might be perceived to be similar and physicians may accept one approved drug for both the conditions.¹² To quote an example, off-label psychiatric drug use is a common practice in children due to the reason that mental illnesses are challenging to diagnose. Moreover, the children are rarely included in clinical trials for drug approval.¹³

Indications for Azathioprine: For over 40 years, azathioprine has been available as an immunosuppressive agent. Moreover, the current routine use of azathioprine in dermatology is not restricted to the licensed indications.

Azathioprine is an immuno-modulating drug for the control of graft rejection during the transplant surgery.¹⁴ As per the licensed indication, dermatomyositis, pemphigus vulgaris and systemic lupus erythematosus are included. Either it is used for these conditions alone, or they are used in combination with corticosteroids. Moreover, the therapeutic effect is typically delayed for weeks or even 2-3 months and includes a steroid-sparing effect that reduces the long-term toxicity of corticosteroids. Azathioprine is also used more frequently as monotherapy in non-licensed indications including atopic eczema. Additionally, 15-28% of patients have adverse drug reactions with azathioprine and includes myelosuppression, rash, nausea and vomiting, hypersensitivity and pancreatitis. As per the study polymorphism in thiopurinemethyltransferase (TPMT) gene predicts haematological adverse drug reactions in 5–10% of patients treated with thiopurinedrugs.¹⁵ While the remaining adverse drug reactions are unexplained and may be further perceived to be mediated by immune mechanisms or by other variables affecting the metabolic fate of the drug. Therefore, it is essential to continue monitoring blood counts throughout treatment with azathioprine.¹⁶ Azathioprine is approved by the Food and Drug Administration (FDA) for the symptomatic treatment of active rheumatoid arthritis.¹⁷

Off-Label uses of Azathioprine: According to a study the off-label uses of azathioprine in dermatology was asserted in a systematic review paper.¹⁸ Evidence pertaining to the effectiveness, efficacy and safety of off-label azathioprine utilized in dermatology was summarized in the paper. In a study conducted the researcher aimed to explore and highlight the off-label uses of Azathioprine (AZA).¹⁷ The study manifested the uses of AZA in the treatment of inflammatory bowel disease,²⁰ autoimmune hepatitis (for maintenance treatment along with steroids),²¹ Churg-Strauss syndrome, chronic ITP (second-line agent), connective tissue disease-associated ILD,²² severe myasthenia gravis, multiple sclerosis, recurrent pericarditis,²³ non-infectious uveitis,²⁴ psoriasis, relapsing polychondritis,²⁵ erythema multiforme, dermatomyositis/polymyositis, severe and refractory atopic dermatitis, pyoderma gangrenosum, chronic actinic dermatitis, pityriasis rubrapilaris, Behcet disease, lichen planus, cutaneous vasculitis, pemphigus vulgaris and bullous pemphigoid. It was asserted that AZA or 6-MP are used for the treatment options of Crohn disease in children in the form of maintenance treatment.²⁶ Strong clinical recommendation was

rendered for the use of azathioprine as an alternative treatment in atopic dermatitis.³ The researcher presented high quality of evidence for a moderate therapeutic response. Azathioprine can be considered an alternative treatment option for severe atopic dermatitis although the efficacy is not as pronounced as for cyclosporine (SASSAD improvement of 39% to 57%).²⁰ The study also concluded in the major findings that azathioprine is discerned to be a corticosteroid-sparing agent which can reduce the corticosteroid-related adverse events. Comparative effectiveness research was elucidated of azathioprine on the clinical and serological response in *Pemphigus vulgaris*.²⁷ It was concluded from the study that azathioprine has a slower onset of action with a statistically significant improvement seen by 6 months ($P = 0.016$). In a study it was contemplated that azathioprine is an immunomodulator that is associated with several serious adverse effects. Susceptibility to its toxicity further varies with the age, medication dosage and the genetic differences.¹⁷ In the patient's compliance, the adverse effects are a limiting factor. Therefore, the physicians and the pharmacists must be aware of the potential adverse effects with AZA, even in patients with asymptomatic. Pharmacists must thus verify that dosing is appropriate to a condition treated.

Monitoring and evaluating off-label use of Azathioprine in dermatology: According to a study the researcher reviewed the short-term nature, with the limited populations and often incomplete or missing reports of AEs, probably because of the emphasis on efficacy in the study design.¹⁸ Thereby, conclusions pertaining to the (long-term) safety could not be drawn. The study concluded that a strong clinical recommendation was rendered for the azathioprine in atopic dermatitis. Thereby, pertaining to the safety in an off-label setting could not be reached because of scarce and incomplete data. As per the research, it was asserted that for several decades, dermatologists had utilized azathioprine for the numerous treatments with regards to the skin disease.¹⁹ The most recognized uses deliberating to the azathioprine are for immunobullous diseases, photodermatoses and generalized eczematous disorders. It was manifested that physicians have successfully employed azathioprine to treat myriad conditions, including inflammatory bowel disease (IBD; ulcerative colitis and Crohn disease), myasthenia gravis, multiple sclerosis, autoimmune conditions and malignancies.²⁸ It was elucidated that off-label use is denoted for the use of the drugs outside of licence applied for and

evaluated and approved by the national and European licensing agencies. The study conclusively asserted that there is an urgent need for a data bank to include off-label therapies in dermatology as well as a dermatologic diagnosis for which no other therapy option beyond off-label use exists. Off-label use occurs, especially when licensed therapy options are missing or when sufficient data for approval are not available.²⁹ This is especially true among children and pregnant women.

Findings and Discussion

Overall, the study asserted the off azathioprine is efficacious for the treatment of severe dermatitis problems; however, a robust data on adverse drug reactions in "off-label" use of azathioprine in dermatology needs to be explored and highlighted. Azathioprine is metabolized by the enzymes by the enzyme thiopurine-S-methyltransferase (TPMT) and causes immunosuppression via inhibition of the lymphocyte cell cycle.¹⁹ Although azathioprine is generally a well-tolerated and as a favourable therapeutic index in comparison to many other traditional immunosuppressant. From the review of the literature, it is concluded that the most common symptomatic side effects of azathioprine comprised of gastrointestinal, ranging from diarrhoea to nausea. Within the first ten days of the treatment, it is not uncommon for patients to experience vomiting, mild nausea and gastrointestinal discomfort. Case reports of patients with the symptoms imitating viral gastroenteritis (nausea, vomiting, anorexia, diarrhoea and fever) hours after a single dose of 25 mg have been discerned. Thereby, azathioprine must be discontinued immediately in those patients' with severe gastrointestinal symptoms, as they may be developing an intolerant or hypersensitivity reaction. While some patients may also experience fatigue and malaise that may necessitate the reduction of dose or discontinuation within a few weeks of initiating therapy. Azathioprine hepatotoxicity may also be developing in some of the patients; however, this side effect is generally not common. Furthermore, bone marrow depression is also a well-known concern pertaining to azathioprine. Therefore, laboratory monitoring of complete blood count is vital to avert hematologic toxicities during the initial weeks of therapy. In addition to this, these known dermatologic problems are discerned to be more frequent in the process of transplantation than in the non-transplantation patients on azathioprine. Some of the significant risk factors in the development of skin lesions include excess sun exposure, pale skin types and

also the duration of the allograft. While a few common skin factors include verrucae, zoster increased skin colour, alopecia and malignant neoplasms.¹⁹

Conclusion

Conclusively, throughout the current review paper, the adverse drug reactions in 'off-label' use of azathioprine in dermatology is explored and highlighted. By reviewing the prior studies in azathioprine, off-label drugs, monitoring and evaluating off-label use of azathioprine in dermatology and indications for azathioprine are elucidated.

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References

- Motgahre VM, Bajait CS, Turankar A, Pimpalkhute SA, Dholpure M. Prescription pattern and adverse drug reaction profile of drugs prescribed with focus on NSAIDs for orthopedic indications at a tertiary care hospital. *Indian Journal of Pharmacy and Pharmacology*. 2016;3(4):178-81.
- Bennett PN, Brown MJ. Prescribing, consumption, economics and patient compliance. *Clinical Epidemiology*. 2005;9:15-22.
- Schram ME, Borgonjen RJ, Bik CM, van der Schroeff JG, van Everdingen JJ, Spuls PI. Off-label use of azathioprine in dermatology: a systematic review. *Archives of dermatology*. 2011 Apr 1;147(4):474-88.
- Martin JE, Daoud AJ, Schroeder TJ, First MR. The clinical and economic potential of cyclosporin drug interactions. *Pharmacoeconomics*. 1999 Apr 1;15(4):317-37.
- Al-Faris HH. Unlicensed and off-label medication uses in dermatology: a systematic review of literatures
- Sugarman JH, Fleischer Jr AB, Feldman SR. Off-label prescribing in the treatment of dermatologic disease. *Journal of the American Academy of Dermatology*. 2002 Aug 1;47(2):217-23.
- Gillick MR. Controlling off-label medication use. *Annals of Internal Medicine*. 2009 Mar 3;150(5):344-7.
- Loder EW, Biondi DM. Off-label prescribing of drugs in specialty headache practice. *Headache: The Journal of Head and Face Pain*. 2004 Jul;44(7):636-41
- Boos J. Off label use—label off use?.
- Leveque D. Off-label use of anticancer drugs. *The lancet oncology*. 2008 Nov 1;9(11):1102-7.
- Leghorn J, Brophy E, Rother PV. The First Amendment and FDA restrictions on off-label uses: the call for a new approach. *Food & Drug LJ*. 2008;63:391.
- Wittich CM, Burkle CM, Lanier WL. Ten common questions (and their answers) about off-label drug use. In *Mayo Clinic Proceedings* 2012 Oct 1 (Vol. 87, No. 10, pp. 982-990). Elsevier.
- Lee MS, Chiang PS, Luo ST, Huang ML, Liou GY, Tsao KC, Lin TY. Incidence rates of enterovirus 71 infections in young children during a nationwide epidemic in Taiwan, 2008–09. *PLoS neglected tropical diseases*. 2012 Feb 14;6(2):e1476.
- Anstey AV, Wakelin S, Reynolds NJ. Guidelines for prescribing azathioprine in dermatology. *British Journal of Dermatology*. 2004 Dec;151(6):1123-32.
- Lennard L. TPMT in the treatment of Crohn's disease with azathioprine. *Gut*. 2002 Aug 1;51(2):143-6
- Holme SA, Duley JA, Sanderson J, Routledge PA, Anstey AV. Erythrocyte thiopurine methyl transferase assessment prior to azathioprine use in the UK. *Qjm*. 2002 Jul 1;95(7):439-44.
- Mohammadi O, Kassim TA. Azathioprine. [Updated 2019 Jul 17]. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2019 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK542190>
- Schram ME, Borgonjen RJ, Bik CM, van der Schroeff JG, van Everdingen JJ, Spuls PI. Off-label use of azathioprine in dermatology: a systematic review. *Archives of dermatology*. 2011 Apr 1;147(4):474-88.
- Patel AA, Swerlick RA, McCall CO. Azathioprine in dermatology: the past, the present and the future. *Journal of the American Academy of Dermatology*. 2006 Sep 1;55(3):369-89.
- Schmidt C, Herrlinger K, Siegmund B, Bokemeyer B, Schreiber S, Stallmach A. Azathioprine in Crohn's disease therapy--guidance against the

- background of recent studies. *Zeitschrift Fur Gastroenterologie*. 2014 Dec;52(12):1423-30.
21. Aljumah AA, Al Jarallah B, Albenmoussa A, Al Khathlan A, Al Zanbagi A, Al Quaiz M, Al-Judaibi B, Nabrawi K, Al Hamoudi W, Alghamdi M, Fallatah H. The Saudi Association for the Study of Liver Diseases and Transplantation clinical practice guidelines for management of autoimmune hepatitis. *Saudi journal of gastroenterology: official journal of the Saudi Gastroenterology Association*. 2018 Nov;24(Suppl 1):S1.
 22. Oldham JM, Lee C, Valenzi E, Witt LJ, Adegunsoye A, Hsu S, Chen L, Montner S, Chung JH, Noth I, Vij R. Azathioprine response in patients with fibrotic connective tissue disease-associated interstitial lung disease. *Respiratory medicine*. 2016 Dec 1;121:117-22.
 23. Imazio M, Lazaros G, Brucato A, Gaita F. Recurrent pericarditis: new and emerging therapeutic options. *Nature Reviews Cardiology*. 2016 Feb;13(2):99
 24. Touhami S, Diwo E, Sève P, Trad S, Bielefeld P, Sène D, Abad S, Brézin A, Quartier P, KonéPaut I, Weber M. Expert opinion on the use of biological therapy in non-infectious uveitis. *Expert opinion on biological therapy*. 2019 May 4;19(5):477-90.
 25. Mathian A, Miyara M, Cohen-Aubart F, Haroche J, Hie M, Pha M, Grenier P, Amoura Z. Relapsing polychondritis: a 2016 update on clinical features, diagnostic tools, treatment and biological drug use. *Best practice & research Clinical rheumatology*. 2016 Apr 1;30(2):316-33.
 26. Ruemmele FM, Veres G, Kolho KL, Griffiths A, Levine A, Escher JC, Amil Dias J, Barabino A, Braegger CP, Bronsky J, Buderus S. European Crohn's and Colitis Organisation; European Society of Pediatric Gastroenterology, Hepatology and Nutrition. Consensus guidelines of ECCO/ESPGHAN on the medical management of pediatric Crohn's disease. *J Crohns Colitis*. 2014 Oct;8(10):1179-207.
 27. Sardana K, Agarwal P, Bansal S, Uppal B, Garg VK. A comparative effectiveness research of azathioprine and cyclophosphamide on the clinical and serological response in pemphigus vulgaris. *Indian journal of dermatology*. 2016 Jul;61(4):418.
 28. Rosman M, Bertino JR. Drugs five years later: Azathioprine. *Annals of internal medicine*. 1973 Nov 1;79(5):694-700.
 29. Brockmeyer NH, Brucklacher U, Potthoff A, Reich-Schupke S. Off-label use in dermatology in Germany: What has changed since 2004?. *J Dtsch Dermatol Ges*. 2009 Nov;7(11):938-45.

Evaluation of Technique Using Pressurized Metered dose Inhaler and its Determinants among COPD Patients: A Cross Sectional Study

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Abstract

The aim was to evaluate the inhalation technique among COPD patients using pressurized metered dose inhaler and determinants of incorrect inhalation technique. In this hospital based cross-sectional study, total 92 COPD patients were enrolled. Basic socio-demographic information was collected. The inhalation technique was visually observed and scored on checklist. Statistical Analysis Used: Chi-square test and Fisher exact test. Among the 92 patients observed, 69 (75.0%) were males. The mean age of the patients was 45.8 ± 1.4 years. Correct technique was observed in only 22 (23.9%) patients step at which maximum number of patients committed mistake was exhalation 65.2% followed by breath holding 45.7% and multiple actuations were seen in 44.5%. It was found that substantial errors were made in the inhalation technique hence proper training and follow-up of the patients is required to achieve the desired effects of the inhaled medications.

Keywords: COPD, pMDI, Inhalation technique.

Introduction

COPD is a disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases.¹

Chronic respiratory diseases which include asthma and chronic obstructive pulmonary diseases, it is responsible for an estimated burden of more than 100 million people in India.² Chronic obstructive pulmonary disease progresses over many decades and tends to present in advanced stages, thus most treated patients are middle aged or elderly. Chronic obstructive pulmonary

disease is the fourth leading cause of death worldwide resulting in more than 2.7 million deaths in 2000.³

Over the years, inhalation therapy has become the backbone in the treatment of these disorders, although new inhalers have been intended to improve ease of use, significant rates of incorrect use have been reported among COPD and bronchial asthma patients, even among regular adult users.⁴

Incorrect use not only undermines the patient acquiescence, but also hampers the effectiveness of these devices on a large scale which leads may leads to poorer control of symptoms due to insufficient drug delivery and inefficient lung deposition and higher rates of asthma instability and increased burden on emergency services. Our study evaluates the inhalation technique in COPD patients using pressurized metered dose inhalers (pMDI) attending a tertiary care hospital in Ambala, India.

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Materials and Method

Study Design, Study Duration, Study Population and Study area: A cross-sectional study was carried out

among indoor and outdoor patients of COPD in a tertiary care hospital in Ambala, India.

Inclusion Criteria:

Subjects fulfilling the eligibility criteria of

- Voluntary participation
- Those patients using pMDI
- Patients above 18 years of age who had been using pMDI for at least 6 months

Exclusion Criteria:

- Those not willing to participate in the study
- Those patients with recurrent exacerbations, chronic infections and
- Those using spacer devices or other inhalation devices

Sample Selection: The sample size was calculated based on the study by Sehajpal R et al.⁵ using a prior type of power analysis by G* Power Software Version 3.0.1.0 (Franz Faul, Universitat Kiel, Germany). The minimum sample size was calculated, following these input conditions: power of 0.90 and $P \leq 0.05$ and sample size arrived were 92 participants.

Training and Calibration: Before the commencement of the study, the examiner was standardized and calibrated in the by the senior faculty member to ensure uniform interpretations and understanding of the steps of inhalation. The kappa value was 0.88, which denoted substantial level of agreement between the examiners.

Data Collection: The study involved collection of the basic socio-demographic information and visual observation of the inhalation technique of the patients and scoring of their technique on the inhaler specific checklist simultaneously by the examiner.

Inhalation Technique: The technique of inhalation was divided into 7 steps, namely shaking, positioning, exhalation, actuation, hand mouth coordination, slow deep inhalation, breath holding. With a view, that each of these steps is crucial for effective delivery of the drug to the lung and also for instant onset of action. Note was also made of the person who taught the patient the technique at first place and a correlation between efficiency of the technique and guide was looked for.

Statistical Analysis: The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2010) and then exported to data editor page of SPSS version 19 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics included computation of percentages and mean. The statistical tests applied for the analysis were Pearson’s chi-square test (χ^2) and fisher exact test. For both the tests, confidence interval and p-value were set at 95% and ≤ 0.05 respectively.

Results

Present study was conducted among 92 patients of COPD 57 (61.9) patients had age more than 35 years, 69 (75.0%) were males. The mean age of the patients was 45.8 ± 1.4 years. 57.6% of the patients were from the rural background and the number of illiterate patients was 51 (56.5%). 55 (59.8%) were using the device for more than 1 year.

Table 1: revealed that only 22 (23.9%) of the patients were able to perform inhalation technique correctly and a total of 70 (76.1%) patients performed at least one step incorrectly. In this study, the step at which maximum number of patients committed mistake was exhalation 65.2% followed by breath holding 45.7%, multiple actuations were seen in 44.5% of the patients, Hand-Mouth coordination 40.2%, Slow deep inhalation 39.1%, shaking 35.0% and positioning 24.0%.

Table 2: depicted that patients who had been using the device for longer duration performed the technique correctly ($P = 0.04$). No significant correlation found between age, sex, education level, area of residence and the correctness of the inhalation technique.

Table 1: Distribution patients according to incorrectly following the technique

Inhalation technique steps checklist	Incorrect (%)
Shaking	35
Positioning	24
Exhalation	65.2
Actuation	44.5
Hand-Mouth co-ordination	40.2
Slow deep inhalation	39.1
Breath holding	45.7

Table 2: Correlation of patient characteristics with correctness of the inhalation technique

Variables	p-value
Age (In years)	
<35	0.42 (NS)
>35	
Gender	
Male	0.33 (NS)
Female	
Literacy	
Literate	0.20 (NS)
Illiterate	
Residence	
Rural	0.29 (NS)
Urban	
Duration of use (In years)	
<1	0.04*
>1	

Statistical tests applied: chi-square test and Fisher exact test.

*indicates statistically significant difference at $p \leq 0.05$

Discussion

To the most effective of our information the current study is that the 1st of its kind performed in Ambala, India and highlights not solely the importance of demonstration of correct technique to the patients however calls attention to the essential steps that the patient may well be playing wrong, in order that these specific steps in inhalation technique will be corrected and stressed for higher relief of the symptoms. This might not solely assist in raising the patient compliance however also enhance the patient still as a physician's confidence within the medical care.

We found that solely 22 (23.9%) of the patients were able to perform inhalation technique properly as we evaluated the technique by visual observation and scored it on the listing. 70 (76.1%) patients performed a minimum of one essential step incorrectly. The controlled metered dose inhalator presents a transparent challenge for a patient with respiratory illness which needs to comprehend and execute the steps that involve synchronous coordination of metabolic process and motor movements.

The substantial variety of mistakes relating to inhalation technique as discovered in our study is in line with previous literature. Study done by Buckley⁶ reportable that solely 18 out of 71 patients (25%) had

excellent technique, twenty six (37%) had adequate technique and twenty seven (38%) had poor technique and therefore the patients presumably to own poor technique were those employing a nongovernmental organization. Molimard et al.⁷ conjointly reported similar results that a minimum of 76 of the pMDI users created more than one mistake.

In this study, the step at which maximum number of patients committed mistake was exhalation: 65.2% followed by breath holding 45.7%, multiple actuations were seen in 44.5% of the patients, Hand-Mouth coordination 40.2%, slow deep inhalation 39.1%, shaking 35.0% and positioning 24.0%. A study conducted in Trivandrum, authors found that the key incorrect steps were, not breathing properly before inhalation (62%), not holding breath properly (57%), not properly shaking the inhalator (55%) and not inhaling properly (17%) for pMDI.⁸ In another study by Rootmensen et al.,⁹ for the pMDI the steps concerning hand-lung coordination; that is, "activate canister in beginning of a slow inhalation" and "continue to inhale slowly and deeply," were most frequently performed incorrectly (respectively, 72 and 31%).

In a study conducted in Turkey also it was found that the most common basic error associated with inhalation maneuvers was failure to exhale before inhaling through the device (18.9%).¹⁰ Research studies show that it is very important for patient to exhale normally until functional residual capacity is reached and then take a slow, but deep breath and hold it for at least 10s for maximum drug penetration into the airways. Multiple actuations do not provide any benefit as the subsequent pumps do not carry medicine as the necessary pressure does not build up and also patient ends up exhaling medicine from first actuation before inhaling deeply.^{11,12}

Limitation: There are varied factors which may influence the patient's adaptation to the inhalation technique like accomplishment level of the patient that affects the comprehension of the technique, variety of pedagogue who instructed the technique that affects the correctness of technique at the preliminary level. Another limitation was; analysis setting was dissimilar to the house surroundings, which can have affected task performance. However, this qualitative study style is common for exploring inhalation devices and allowed discussion with participants to explore the foundation causes of determined errors.

Conclusion

Our study shows that a considerable proportion of COPD patients in health care setting create mistakes once breathing medication using pMDI because the inhalation device. Although it's the first responsibility of the physician prescribing the dispenser to produce patient with correct directions for utilizing the device, however the responsibility may even be branched among the health care team like pharmacists who could play an important role in teaching and reinforcing the technique. Teaching correct technique won't solely improve patient's compliance however conjointly can result in higher un-wellness management and lesser price and stress on emergency medical services.

Conflict of Interest: None

Source of Funding: Self

Ethical Approval and Informed Consent: The study protocol was reviewed by the Ethical Committee of Hospital and was granted ethical clearance. After explaining the purpose and details of the study, a written informed consent was obtained from the patients who participated in the study. It was emphasized that strict confidentiality would be maintained at all times and the patients could withdraw at any time without being penalized.

References

1. Pauwels RA, Buist AS, Calverley PMA, Jenkins CR, Hurd SS. Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease: NHLBI and WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD): executive summary. *Respiratory Care* 2001;46(8):798-825.
2. Vijayan VK. Chronic obstructive pulmonary disease. *Indian J Med Res* 2013;137:251-69.
3. Decramer M, Wim Janssens, Marc Miravittles. Chronic Obstructive Pulmonary Disease, *Lancet* 2012; 379: 1341–51 Published Online February 6, 2012
4. Melani AS, Bonavia M, Cilenti V, Cinti C, Lodi M, Martucci P, et al. Inhaler mishandling remains common in real life and is associated with reduced disease control. *Respir Med* 2011;105:930-8.
5. Sehajpal R, Koolwal A, Koolwal S. Assessment of inhalation technique of bronchial asthma and chronic obstructive pulmonary disease patients attending tertiary care hospital in Jaipur, Rajasthan. *Indian J Allergy Asthma Immunol* 2014;28:78-82.
6. Buckley D. Assessment of inhaler technique in general practice. *Ir J Med Sci* 1989;158:297-9.
7. Molimard M, Raheison C, Lignot S, Depont F, Abouelfath A, Moore N. Assessment of handling of inhaler devices in real life: An observational study in 3811 patients in primary care. *J Aerosol Med* 2003;16:249-54.
8. Nair S, Anitha Kumari K, A Fathahudeen, Win BR, Sreekala C, Nair RS, et al. Technical Errors in Usage of Inha Lers Among Adult Patients with Obstructive Airway Disease Presenting to a Tertiary Care Center in Trivandrum, Kerala. *Pulmon; 2012*. p.14. Available from: http://www.pulmononline.org/article.php?art_id=310
9. Rootmensen GN, van Keimpema AR, Jansen HM, de Haan RJ. Predictors of incorrect inhalation technique in patients with asthma or COPD: A study using a validated videotaped scoring method. *J Aerosol Med Pulm Drug Deliv* 2010; 23:323-8.
10. Yildiz F, Asthma Inhaler Treatment Study Group. Importance of inhaler device use status in the control of asthma in adults: The asthma inhaler treatment study. *Respir Care* 2014; 59:223-
11. Newman SP, Pavia D, Clarke SW. How should a pressurized beta-adrenergic bronchodilator be inhaled? *Eur J Respir Dis* 1981;62:3-21.
12. Armour C, Bosnic-Anticevich S, Brilliant M, Burton D, Emmerton L, Krass I, et al. Pharmacy Asthma Care Program (PACP) improves outcomes for patients in the community. *Thorax* 2007;62:496-502.

Glue Free and Suture Free Conjunctival Autograft in Pterygium Excision: A North Indian Perspective

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Abstract

Aim: To study postoperative outcome & related complications of Glue free and suture free conjunctival autograft in pterygium excision in Haryana-A North Indian state.

Materials and Method: The present study was conducted at the Department of Ophthalmology, MMIMSR, Mullana (Maharishi Markandeshwar Deemed to be University) in the time period extending between December 2017 and January 2019. 50 eyes of patients of either sex with primary pterygium were selected and pterygium was excised & sutureless & glue free conjunctival autograft was done with patient's own blood fibrin. Parameters such as mean operating time, presenting complaints, grade, complications & recurrence were observed on postoperative Day 1, Day7, 2 weeks, 1 month, 2 month, 3 month & 6th month.

Results: The mean age of the study population was 48.82 + 11.13 years... Out of 50 eyes only 1 (2%) had conjunctival cyst, 2 (4%) graft edema and 3 (6%) had graft displacement, 1(2%) had graft lost, 1(2%) had graft rejection & 1(2%) had recurrence at 6 month follow up. The mean operation time was 24.88 minutes. Regarding type of the pterygium, out of 50 patients 9(18%) were grade 1, 26(52%) were grade 2, 11(22%) were grade 3 and 4(8%) were grade 4.

Conclusion: Conjunctival autograft using patients own blood technique is a safe, cheaper, effective, with less surgical time & has minimal postoperative discomfort.

Keywords: Complications, pterygium, recurrence, suture free, glue free conjunctival autograft.

Introduction

Historically, pterygium and its treatment was first described in 1000 BC by Susruta.¹⁻² Thereafter, though many surgical options for pterygium have come out and develop through three centuries, complications like recurrence after surgery have been troublesome. The bare sclera technique which was popular from 1960 to the early 1980s has been discarded due to the unacceptable recurrence rate, often as high as 60%–80%.³ The logical

approach is a safe method with low recurrence rate and less complications. Conjunctival autograft (CAG) fulfils the above criteria and gained popularity in the 1980s following the landmark article by Kenyon et al.⁴ in 1985 who reported a low recurrence rate of 5.3%. Prabhawat et al.⁵ (1997) reported that autologous CAG is the best method, with a low recurrence rate and higher safety margin. Thereafter, several prospective randomised trials of CAG for pterygium surgery have reported higher recurrence rates of 16%–39% in high-risk population.⁶⁻⁷ Nonetheless, CAG has now been in vogue for more than 3 decades and has stood the test of time as the standard of care in pterygium surgery.

The use of fibrin glue was first described by Cohen et al.⁸ in 1993. This is faster and simpler. There is less post-operative pain and discomfort.⁹⁻¹⁰ Disadvantage with fibrin glue is that it is expensive & difficult to

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obtain than sutures. Fibrin glue also has a potential risk of transmitting viral disease along with hypersensitivity reactions as it is a blood derivative.¹¹ The latest approach is fixation of the graft with autologous blood, a technique also known as suture and glue free autologous graft.¹² Patient's own blood is used as a bioadhesive or fixative.¹³ Autologous blood is natural, has no extra cost, no associated risk and can overcome postoperative irritation, redness and foreign body sensation.

Our study intended to evaluate the technique of securing the CAG with fibrin, using the normal physiological clot from the patient's own blood at the surgical site acting as a bioadhesive.

Materials and Method

Type of study was prospective study. The present study was conducted in M.M.I.M.S.R. (Maharishi Markandeshwar Deemed to be University) Department of Ophthalmology, 50 patients of nasal pterygium were included in the group. All the patients underwent pterygium excision with suture free and glue free autologous graft. Subjects included in the study were from 20 to 75 years of age having pterygium (primary) involving any eye. Necessary approval from Institute was obtained beforehand. Written informed consent was taken from each patient. Preoperative ocular examination included refraction and assessment of best-corrected visual acuity, slit lamp biomicroscopy, fundus examination and photographic documentation of the pterygium. Surgeries were done from December 2017 to January 2019. Grading of the pterygium was done as:

Grade I- pterygium head up to the limbus

Grade II- head between the limbus and a point midway between limbus and pupillary margin

Grade III- head between a point midway between limbus and pupillary margin and pupillary margin

Grade IV- crossing pupillary margin. Inclusion criteria were primary nasal pterygium and recurrent pterygium.

Exclusion criteria were temporal pterygium, patients taking oral nonsteroidal anti-inflammatory drug (NSAID) and anticoagulant, active infection or inflammation, symblepharon, past ocular surgery within last 6 months, trauma, systemic diseases such as diabetes mellitus, collagen vascular disease, pregnancy, bleeding disorders.

Indications of Surgery:

1. Pterygium causing foreign body sensation
2. Defective vision
3. 3 to 4 mm encroachment on the cornea
4. Cosmetic intolerance
5. Diplopia due to interference with ocular movements

Surgical Technique: All surgical procedures were done under peribulbar anesthesia. All the surgeries were done under amicroscope by the same single surgeon using the same technique. Taking all aseptic precautionary, eyelid was then separated by a speculum and sub-conjunctival and sub-ptyerygial 0.5 ml lignocaine solution (xylocaine 2%) was injected. Gentle massage over the lesion was applied by cotton-tipped applicator for few seconds. The neck of the pterygium was then lifted up with the help of fine toothed forceps, while the head of the pterygium was gently avulsed from the cornea by placing closed tips of a curved corneal scissors or Iris repository underneath the neck of the pterygium mass, keeping the same constant tractional force throughout. Gentle dissection was then carried out in-between the conjunctiva and the sclera with the help of crescent knife, to resect at least 4-5 mm the pterygium mass that included both the superior and inferior border. Neither cautery nor saline irrigation was used throughout the surgery, except active bleeding, with bi-polar cautery whenever required to check excess hemorrhage. The size of the bare sclera defect was then measured with Castroviejo calipers. Corneal care was taken by applying wet cotton throughout the procedure. Now, approximately 0.5 ml xylocaine 2% was used to balloon up a conjunctival flap. Corneal scissor was used to make a fine film of 0.5 mm oversized, free conjunctival graft, carefully avoiding inclusion of tenon, or making buttonhole within it. The graft was then laid over the bare sclera ensuring same limbus to limbus orientation. We waited for 5 to 10 min for hemostasis to occur. In cases, where the surgeon appreciated the lack of adequate amount of blood at the recipient site, episcleral blood vessel was intentionally punctured to create bleeding. The eye was then patched for 24hrs. The eye was assessed for symptom, graft adherence, or any complication (s) under slit lamp. Postoperatively, patient was put on topical antibiotic and steroid combination for first 2 weeks thereafter tapered over next 4 weeks. Thereafter, an attempted follow-up of cumulative 6 months (at postoperative day 1, 1 week, 2 week, 1 month, 2 month 3 month, 6 month) was done to

every patient. At each postoperative visit, thorough slit lamp examination and any recurrence, complication (s), or any complaints were recorded. The primary outcome measure was the recurrence and the secondary measures were complication (s) and surgical time.

Results

Table 1: Distribution of the Study Population According to Age Groups.

Age Group (Years)	Frequency (N=50)	Percentage (%)
20-30	4	8
31-40	6	12
41-50	21	42
51-60	11	22
61-70	7	14
>71	1	2
Total	50	100

Table 2: Distribution of the Study Population According to Grade of Pterygium.

Grade	Frequency, N=50 (%)
1	9(18)
2	26(52)
3	11(22)
4	4(8)
Total	50(100)

Table 3: Distribution of study population according to the post-operative complications.

Complications	Frequency, N=50 (%)
Conjunctival cyst	1(2)
Conjunctival granuloma	0
Graft displacement	3(6)
Graft edema	2(4)
Graft lost	1(2)
Graft rejection	1(2)
Recurrence	1(2)
Nil	41(82)
Total	50(100)

A total of 50 cases were included in the study. The mean age of the study population was 48.82 + 11.13 years. The male and female distribution was 28 and 22 respectively. All the patients were examined after 24hrs following operation for graft dislodgement, recession, edema subconjunctival hemorrhage. Out of 50 eyes only 1(2%) had conjunctival cyst, 2(4%) graft edema and 3(6%) had graft displacement, 1(2%) had graft lost,

1(2%) had graft rejection & 1(2%) had recurrence at 6 month follow up. The mean operation time was 24.88 minutes. Regarding type of the pterygium, out of 50 patients 9(18%) were grade 1, 26(52%) were grade 2, 11(22%) were grade 3 and 4(8%) were grade 4.

Table 4: Distribution of study population according to the post-operative complications w.r.t time.

Complications	No. of cases, N=50 (%)
Day 1	3(6)
Day 7	2(4)
Week 2	1(2)
1 Month	0
2 Months	1(2)
3 Months	1(2)
6 Months	1(2)
Nil	41(82)
Total	50(100)

Discussion

Pterygium surgery should ideally have a low or no recurrence, minimum complications and should be cosmetically acceptable. Conjunctival autograft using sutures used to be a standard procedure. The grafts were stable with acceptable cosmetic results. Suture related complications like postoperative inflammation, granuloma formation, pain, foreign body sensation were observed. Suture's presence may lead to prolonged healing and fibrosis. Later, complications such as formation of symblepheron, forniceal contracture, restriction of ocular movements, diplopia, scleral necrosis and infection are much more difficult to manage and may be sight threatening.¹⁴ Fibrin glue usage is quicker and easier with less postoperative complications. But fibrin glue is expensive and difficult to obtain. Foreign materials or Plasma derived products such as fibrin glue may produce possible hypersensitivity reactions or anaphylaxis in susceptible individuals and transmission of viral diseases.¹¹ Recent introduction of auto graft technique using patient's own blood as bioadhesive substance on the excised bed of the pterygium have become popular. It has minimized the surgical time, trauma to the conjunctiva, cost of surgery and recurrence rate. In our series, the operation time was only 24.88 minutes and there was only 1 case of pterygium recurrence after 6 months of surgery though we had 3 cases of graft displacement with one patient of conjunctival cyst, graft loss & graft rejection each. The technique is cost effective and easy to perform with less

discomfort to patient. The result was comparable to other studies with similar techniques.¹⁵ Sutureless and glue free conjunctival auto graft using blood clot as a bioadhesive is a useful alternative method for graft fixation in pterygium surgery. We found the new procedure of auto grafting free of any untoward complications. Suture and glue free autologous graft has no extra cost or associated risks and can overcome the post-operative irritation, pain and foreign body sensation to a great extent. The procedure was cosmetically better. The opposition of the lids to the bulbar conjunctiva provides a natural biological dressing and confers a unique wound healing environment.¹¹ The main disadvantage of this method is the risk of graft getting lost in the immediate post-operative period. Graft loss is usually seen in first 24 to 48 hours. These complications were associated with larger grafts. This could be due to inadequate excision of the pterygium tissue or leaving too much tenon's tissue on the graft.⁹ Meticulous dissection of the sub-epithelial graft tissue is required.¹¹

Conclusion

Pterygium excision and conjunctival auto graft with autologous blood is a viable and better surgical option for management of primary as well as recurrent pterygium. The probability of attachment of graft without glue and sutures is promising. The risks associated with the use of fibrin glue and suture related problems can be avoided in this technique. This technique has excellent outcome. It is cheaper, time saving, has less surgical time and safe for the patients with good cosmetic output.

Conflict of Interest: None

Source of Funding: Self

Ethical Clearance: Ethical Clearance was obtained from the Institutional Ethics Committee (IEC), Maharishi Markandeswar (deemed to be university) Mullana, Ambala.

References

- Rosenthal JW. Chronology of pterygium therapy. *Am J Ophthalmol* 1953;36:1601–16.
- Singh G. Pterygium and its surgery. In: Foster CS, Azar DT, Dohlman CH, eds. *Smolin and Thoft's The Cornea: scientific foundations and clinical practice*. 4th edn. Vol 4. Philadelphia: Lippincott Williams & Wilkins, 2005:999–1017.
- Hirst LW. The treatment of pterygium. *Surv Ophthalmol* 2003;48:145–80.
- Kenyon KR, Wagoner MD, Hettinger ME. Conjunctival autograft transplantation for advanced and recurrent pterygium. *Ophthalmology* 1985;92:1461–70.
- Prabhasawat P, Barton K, Burkett G, et al. Comparison of conjunctival autografts, amniotic membrane grafts and primary closure for pterygium excision. *Ophthalmology* 1997;104:974–85.
- Manning CA, Loess PM, Diaz MD, et al. Intraoperative mitomycin in primary pterygium excision. *Ophthalmology* 1997;104:844–8.
- Mahar PS. Conjunctival autograft versus topical mitomycin C in the treatment of pterygium. *Eye* 1997;11:790–2.
- Cohen RA, Mc Donald MB. Fixation of conjunctival autograft with an organic tissue adhesive. *Arch ophthalmol*. 1993; 111:1167-8.
- G Koranyi, S Seregard, ED Kopp. Cut and paste; A no suture, small incision approach to pterygium surgery. *British Journal of Ophthalmology*. 2004; 88:911-914.
- Harvey S Uy, John Micheal G Reyes, John DG flores, Ruben, Lim-Bon-Siong. Comparison of fibrin glue and sutures for attaching conjunctival autograft after pterygium excision. *Ophthalmology*. 2005 April;112(4):667-6.
- D de Wit, I Athanasiadis, A Sharma, J Moore. Suture less and glue free conjunctival autograft in pterygium surgery. *Eye* (2010) 24,1474-1477.
- Jean Shaw, LW Hirst, Santanu Mitra, Jonathan E Moore. American academy of Ophthalmology. A new approach emerges for pterygium surgery. *Clinical update. Cornea*. 2012 Feb; Eye net: 27-29.
- Singh PK, Singh S, Vyas C, Singh M. Conjunctival autograft without fibrin glue or sutures for pterygium surgery. *Cornea*. 2013 Jan;32 (1):104-7.
- BD Allan, P Short, GJ Crawford, GD Barrell, IJ Constable . Pterygium excision with conjunctival autografting; an effective and safe technique. *British Journal of Ophthalmology*. 1993 Nov; 77(11): 698-701.
- Sharma A, Raj H, Gupta A, Raina AV. Sutureless and glue-free versus sutures for limbal conjunctival autografting in primary pterygium surgery: a prospective comparative study. *J ClinDiag Res*. 2015;9(11): NC06NC09

Effect of Change in Position of Finger on SpO₂ Value by Pulse Oximetry: A Cross Sectional Study

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Abstract

Background: Pulse oximetry is widely used in patients of respiratory diseases for monitoring the oxygen saturation in blood. First commercial pulse oximetry was used in 1975. Although there have been many improvements in its design since then, still there are a few limitations. The limitations of pulse oximetry include mechanical artefacts accuracy, electromagnetic interference, calibration, delay, pulse dependence-volume and rhythm, abnormal haemoglobins, other absorbents, pulsatile veins, pigmentation.

Objective: Despite so many studies on the pulse oximetry, there still isn't any study on pulse oximetry which focused changes in the readings of pulse oximeter with respect to position of finger in relation to the sensor. So in this study we tried to analyse the effect of anatomical plane of finger on O₂ saturation as measured by pulse oximetry.

Material and Method: This study was done on 400 patients and included both healthy and unhealthy patients. Portable pulse oximeter was used in the study. Pulse oximetry was done on the subjects with finger in supine, prone and lateral position in respect to the probe, while the patient was in sitting position with a waiting period of 1 min between each reading.

Results: The study shows no significant difference (p value > 0.05) between SpO₂ value obtained from any position of finger in relation to the sensor while applying the pulse oximeter.

Conclusion: Pulse oximetry is a very safe, non-invasive and inexpensive way of continuous O₂ saturation monitoring in critical patients. Mal-positioning of sensors can be potentially dangerous as it may give erroneous high or low readings. The ways to prevent mal-positioning of the sensor are good design of pulse oximeter and ensuring that it is properly visible to the clinician.

Keywords: Pulse oximetry, oxygen saturation variation, sensor mal-positioning.

Introduction

Pulse oximetry is widely used for patients who require monitoring of oxygen saturation in variety of clinical settings. Its main purpose is the early detection of hypoxemia in diverse situations and the monitoring of

perfusion and circulation. The prototype pulse oximeter¹ made use of a halogen incandescent lamp as a light source and the broad band of energy is passed to a fingertip probe through a glass fibre bundle. There were many disadvantages to this prototype e.g. it had a heavy probe; the fiberoptic cable was unhandy; there were instances of finger burns by unwanted wavelengths passing through the finger; it was insensitive to even moderately low pulse pressure; and its analogue electronics were error prone.

The first commercial pulse oximeter was available in 1975. All currently available conventional pulse

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oximeters use a combination of two wavelengths, normally 660 nm and 940 nm, generated in the probe by combining light-emitting diodes with a miniature semiconductor photodetector, thus providing a compact probe for attachment to the ear or fingertip. A small lightweight cable connects the probe to the main unit.

Conventional pulse oximeters function by comparing the absorption of energy at two wavelengths, usually 660 nm and 940 nm, passed through an extremity. A value, SpO₂, which is approximately equal to arterial haemoglobin saturation, SaO₂, is determined from the ratio of the absorption of the energy at the two wavelengths.

However, there are several limitations to the pulse oximetry which include mechanical artefacts, accuracy, electromagnetic interference, calibration, delay, pulse dependence- volume and rhythm, abnormal haemoglobins, other absorbents, pulsatile veins,

pigmentation. Various studies have been done on pulse oximetry but to the best of our knowledge none has focused on the position of finger in relation to the sensor. In this study we tried to analyse the effect of anatomical plane of finger on O₂ saturation as measured by pulse oximetry.

Material and Method

This study was done on 400 patients and included both healthy and unhealthy patients. Portable pulse oximeter was used in the study. Pulse oximetry was done on the subjects with finger in supine, prone and lateral position in respect to the probe, while the patient was in sitting position with a waiting period of 1 min between each reading. The sensors were placed appropriately on index finger and reading was taken with stable plethysmograph. The statistics were calculated using repeated ANOVA test. Significance was calculated using p value and significance level was set at 0.05.

Results

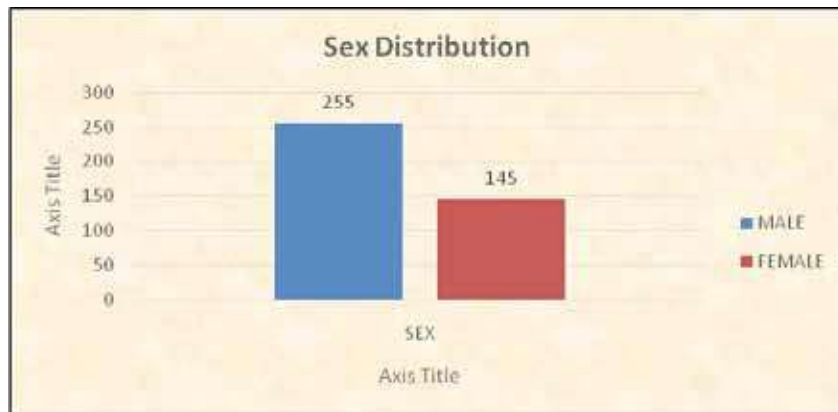


Chart 1. Sex Distribution

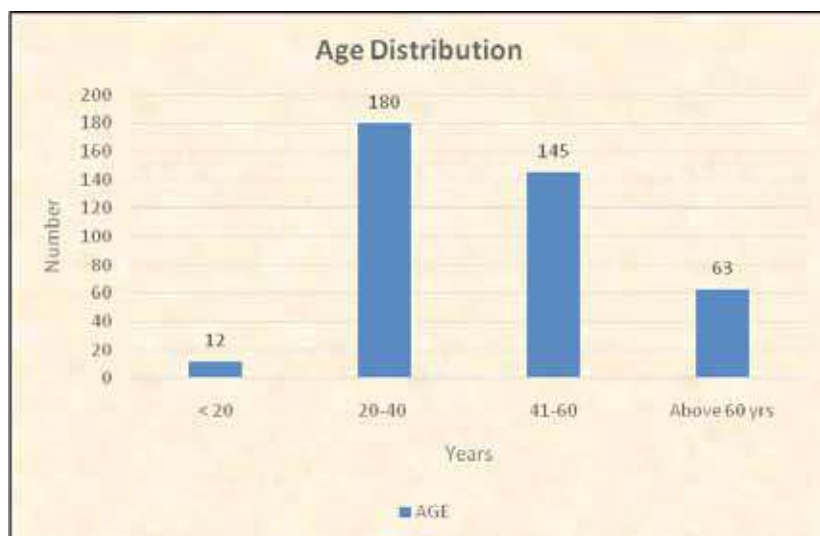


Chart 2. Age distribution

There were 255 males and 145 female subjects in the study. The age distribution of subjects is given in Chart 2. The mean and standard deviation value for various parameters are given in Table 1. The study shows no significant difference (p value > 0.05) between SpO_2 value obtained from any position of finger in relation to the sensor while applying the pulse oximeter.

Table 1. Different Parameters with mean values and standard deviation

Parameter	Mean±SD	p value
Hb	12.7±1.83 g/dl	
Pulse	84±1.83/min	
AP diameter (Distal Phalanx)	12.3±1.09 cm	
Transverse Diameter	14.95±1.49 cm	
SpO ₂ in Prone finger	96.91±4.06%	0.41
SpO ₂ in Supine finger	96.91±3.80%	
SpO ₂ in Lateral finger	96.87±3.93%	

Discussion

The mal-positioning in terms of improper application of sensor is significant as shown by various studies but the position of finger while the sensor is appropriately placed has not been studied. We did this study to see if position of sensor in relation to the anatomical position of finger affects the SpO_2 value but the results showed no significant difference. The penumbra effect refers to an erroneously low SpO_2 reading when the probe is mal-positioned.

The penumbra effect and the errors due to mal-positioning of the pulse oximeter probe are a combination of technical and physiological problems. This may be caused by there being a finite distance between the red and infrared light-emitting diodes and hence different path lengths for the two wavelengths, especially with babies and children. The penumbra effect has also been noted in adults, which may be due to different path lengths or to pulsatile venules at the tips of the extremities. In a study by Kim et al.,² the investigators suggested that the pulsatile venules are a result of the rich arteriovenous anastomoses in the cutaneous circulation at these sites. Cutaneous blood flow may vary from 1 ml/min/100 g of skin to as much as 150 ml/min/100 g in response to thermoregulatory and other vasodilatory stimuli. Cutaneous venules may be pulsatile owing to the arteriovenous anastomoses or the close proximity of pulsatile arterioles. Kelleher and Ruff³ also speculated that these cutaneous venules might contain desaturated blood from the cutaneous capillaries

and that as the arteriovenous anastomoses render these venules pulsatile, inaccurately low SpO_2 readings are therefore displayed. They also suggested that if the pulse oximeter probe is poorly applied then most of the pulsatile signal is generated by the cutaneous blood flow, with its pulsatile venous component. This would explain why the penumbra effect is less common in conditions causing vasoconstriction, such as hypothermia and peripheral shutdown, when the cutaneous arteriovenous anastomoses are closed, thus reducing the pulsatility of the venules.

Barker et al.⁴ investigated about the effect of mal-positioning of the pulse oximeter probe and reported that improperly placed or displaced probes may cause pulse oximeters readings to become erroneous. Most pulse oximeters under-read, a failsafe condition because it prompts urgent medical attention, but some either overread or failed to follow trends in saturation. The possible explanations include the penumbra effect and that a weak plethysmograph signal.

Conclusion

The pulse oximetry is a very safe, non-invasive and inexpensive way of continuous O_2 saturation monitoring in critical patients. Mal-positioning of sensors can be potentially dangerous as an erroneous high reading may give false sense of security while an erroneous low reading may result in excessive financial burden on the patient in terms of unnecessary and more invasive investigations. The ways to prevent mal-positioning of the sensor are good design of pulse oximeter and ensuring that it is properly visible to the clinician. Finally it doesn't make any clinically significant change in spo_2 level with relation to the position of finger be it supine, prone or lateral.

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References

1. Yoshiya I, Shimada Y, Tanaka K. Spectrophotometric monitoring of arterial oxygen saturation at the fingertip. *Med Biol Eng Comput* 1980; 18:27–32.

2. Kim J-M, Arakawa K, Benson KT, Fox DK. Pulse oximetry and circulatory kinetics associated with pulse volume amplitude measured by photoelectric plethysmography. *Anesth Analg* 1986; 65:1333–9.
3. Kelleher JF, Ruff RH. The “penumbra effect”: pulse oximeter artefact due to probe malposition is attenuated by vasoconstriction. *Anesthesiology* 1991;71:A372.
4. Barker SJ, Hyatt J, Shah NK, Kao J. The effect of sensor mal-positioning on pulse oximeter accuracy during hypoxaemia. *Anesthesiology* 1993; 79:248-54.

Use of Custom-Made Antibiotic Coated Intra-Medullary Nail in Treatment of Infected Non-Union of Long Bones

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Abstract

Introduction: In cases of infected Nonunion of long bones Antibiotic coated nail provides mechanical support for the affected bone with delivery of high concentration of antibiotics for infection control and a conducive environment for fracture healing. The aim of the study was to observe and study the treatment of infected non-union of long bones with antibiotic coated nailing in infection control and bony union.

Material and Method: The study was conducted on 30 patients (male and female between the age of 18-70 years). All patient on admission were subjected to detailed history, relevant investigations and thorough clinical examinations. Minimum follow-up period was 6 months. Radiological and blood investigations were done for infection control and bony union.

Result: In the current study of 30 patients with mean age of 43.67 years, Infection control and bony union was achieved in 27 patients without any need for subsequent procedures. Current study provides an alternative to external fixation alone as a means of stabilizing non-unions while providing a high concentration of antibiotic locally for combating this difficult problem.

Conclusion: The clinical results and final outcome after antibiotic coated I.M. nailing in infected nonunion of long bones are both satisfactory and reproducible as evident by the comparison of this present study with the previous literature available.

Keywords: *Infected nonunion, antibiotic coated nail.*

Introduction

Infected non-union of long bones is one of the most challenging clinical situations faced by orthopedic surgeons. It presents with dual problems of controlling infection and providing stability. Various local (Infection at or around the fracture site, Implant failure, Fracture

fragments, Inadequate immobilization of the fracture) and systemic factors (Age, nutrition, Immunodeficient states, smoking) contribute to infected nonunion. The presence of poorly vascularized tissues, adherence of bacteria to bone and implant, along with slow bacterial replication rate contribute to persisting infection¹⁻². The method of treatment proposed here provides a combination of fracture stability and local antibiotic delivery for infection control in a single procedure.

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Patients and Method

The study was conducted on 30 patients (male and female between the age of 18-70 years) in the Department of Orthopedics, Tertiary Care Centre, MMIMSR,

Mullana. Infected nonunion of the long bones of upper and lower limbs were included in this study after informed consent was obtained. Patients included in this study had compound diaphyseal fractures of long bones, Bone gap less than 3 cm, age more than 18 years and No radiological signs of union despite previous mode of treatment used. Patients excluded from study - Patient with large bone gaps (>3 cm), Infection involving the joint and patients with allergy to the antibiotic (to be used in cement) were excluded.

Surgical Steps: The surgical technique involved a series of steps. The first step was evaluation of pre-op culture and sensitivity results and radiographs. Samples were taken after 72 hours of stopping antibiotics. Pre-operative measurements of the length of the bone femur, tibia, humerus were taken. Surgery began with exploration and excision of sinus tracks followed by removal of any metal work present at the nonunion site.

Second step was Debridement of infected tissues such as skin, soft tissues and bone, was done until bleeding viable tissue was present at the margins (in case of bone- Paprika sign). The fracture site and surrounding soft tissues were irrigated with saline and samples were sent for gram staining and culture.

Third step was preparation of the Intramedullary canal for nail insertion as per standard procedure according to the bone involved i.e. femur/tibial/humerus. Length of the nail required was calculated using the scale under C-Arm. Appropriate size of nail was determined and then used accordingly. Fracture was reduced and a flexible guide wire inserted in medullary cavity. Then reaming was done with the flexible power reamer in graded sequential manner. This was done one or two sizes (1-2mm) more than that of the intramedullary nail removed. In cases where there was no intramedullary nail in-situ, reaming was done to 1.5-2mm more than size of antibiotic coated nail. On a separate table Required antibiotic cement-impregnated nail according to culture and sensitivity was prepared. If the culture was sterile then gentamicin impregnated cement (40 g) along with 4 g vancomycin was used. Custom made molds and nails were used. The size of the mold varied from 9-10 mm for tibia nails and 10-11 mm for femoral nails. For tibia, nails with diameter 7 to 8mm and for femur nails with diameter 8 to 9mm were used. Before putting the cement, molds were coated with a thin layer of sterile lubricant gel and sprinkled with powdered cement to facilitate easy removal of the cement-coated nail from the molds. The

bone cement was mixed with culture specific antibiotics and was put on the mold with the help of cement gun in semiliquid state. The nail was put in mold. The locking sites of the nail were covered with cut pieces of chest tube which were subsequently removed. The nail with antibiotic cement coating was removed after the cement sets (usually in 8 to 10 minutes). The interlocking sites were left free without any bone cement when the cut ends of chest tube were removed. Figure-1. The nail was inserted into the intramedullary canal using standard entry point for the respective bones which were already prepared, the fracture was reduced and nail was inserted into the distal fragment. In cases where interlocking I.M nail couldn't be used because of narrow intermedullary canal, K-nail was used. It was prepared using measuring scale method. The k-nail was covered with antibiotic. Impregnated cement with hands and then the nail was passed through a nail measuring scale for uniformity. Wound closure was done in layers and appropriate postoperative splint were given accordingly. Patients were kept on follow up at 2, 6,12 weeks and 6 months. Routine investigations as required such as CBC, ESR, CRP and X-rays were done to assess rate of union, and control of infection. Non weight bearing walking was started first followed by partial weight bearing depending upon healing on X-rays and clinical assessment.

Results

30 patients of infected nonunion of long bones were treated using Antibiotic cement-coated IM nails. Minimum follow-up period was 6 months. 9 female and 21 male patients (age range, 18–70 years) with a mean age of 43.6 years were included in the study. In current study 9 femur, 20 tibia and one humerus were treated. When the fracture occurred primarily 20 were open and 10 were closed. The primary procedures performed in these patients were as follows

Table 1 Open fractures are more commonly associated with infected non-union. In 17 patients, the organism isolated was Staph. Aureus out of which 10 patients had MRSA. 2 patients had klebsiella, 3 patients had pseudomonas aeruginosa, in 4 patients signs of infection were present but no organism was isolated in rest of the patient's multiple organisms were isolated.

Table 2 depicts pre-operative organisms, their sensitivity and antibiotics used. In 21 cases interlocking I.M nail was used while K-nail was used in 9 cases. Infection Control was successfully achieved in 90%

(27 patients) of the cases. In 3 patients discharge was present for more than 8 weeks. In rest of the patient's average time for infection control was around 3.3 weeks. The clinical assessment of the union was mainly based on complete absence of pain and tenderness at the fracture site. Radiological criteria for union are evidence of bridging periosteal and endosteal callus formation in minimum 3 cortices. Bony union was achieved in 90% of the cases with average mean time of union at 27.27 weeks of time. The mean time of bony union of femur was more than tibia at 29.66 weeks. The mean time for union of tibia was 26.17 weeks in 17 patients. Figure 2 shows a tibia patient. In humerus bony union

was achieved by 24 weeks. Deformity was present in 3 patients. In 3 patients were no signs of bony union were present secondary procedure, Ilizarov^{3,4,5} was done after nail removal. In 2 out of these 3, infection control and bony union was successfully achieved

Table 1: Primary Procedure

Primary Procedure	No. of Cases	Percentage
Conservative	3	10.0%
External Fixator	11	36.7%
I.M Nailing	16	53.3%
Total	30	100.0%

Table 2: Pre-operative organism isolated, culture sensitivity and combination used. Culture specific antibiotics vancomycin 4 gm + gentamicin impregnated cement or tobramycin 2.4 gm + vancomycin 2 gm in 40gm of cement.

Pre-Op pathogen Isolated	No. of Cases	% Age	Antibiotic Sensitivity	Combination Used
Klebsiella	2	6.7	Vancomycin Gentamicin	Vancomycin, Gentamicin cement
Not Identified	4	13.3		Vancomycin, Gentamicin cement
Pseudomonas Aeruginosa	3	10.0	Vancomycin Gentamicin	Vancomycin, Gentamicin cement
Pseudomonas Aeruginosa + Klebsiella + Staph. Aureus	1	3.3	Vancomycin, Gentamicin Tobramycin	Vancomycin, Tobramycin
MRSA	10	33.3	Vancomycin	Vancomycin, Gentamicin cement
Staph. Aureus	7	23.3	Vancomycin,	Vancomycin, Gentamicin cement
Staph. Aureus + Bacillus Cereus	1	3.3	Vancomycin, Gentamicin	Vancomycin, Gentamicin cement
Staph. Aureus + Klebsiella	1	3.3	Vancomycin, Gentamicin	Vancomycin, Gentamicin cement
STAPH. Aureus + Pseudomonas Aeruginosa	1	3.3	Vancomycin, Tobramycin	Vancomycin, Tobramycin
Total	30	100		

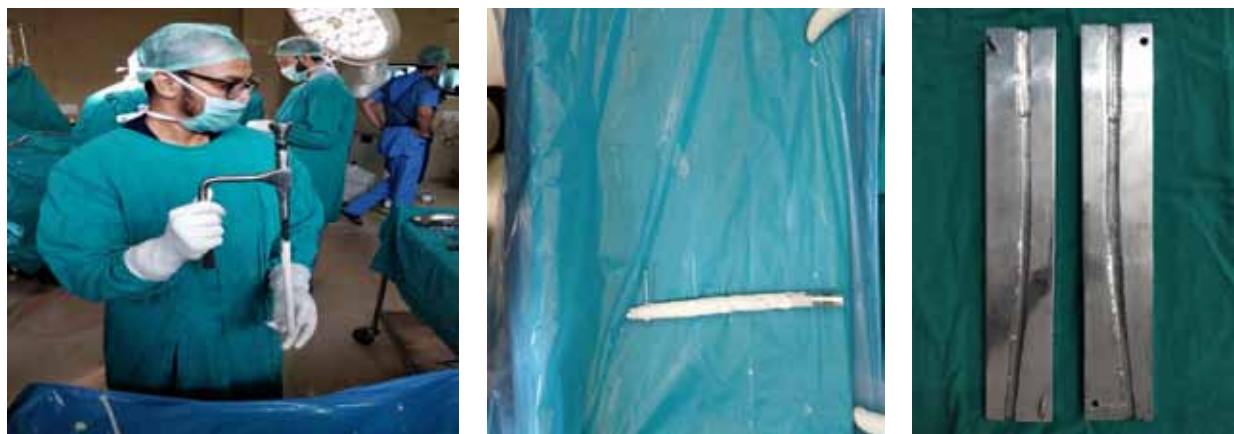


Image 1: Shows Custom made Molds and Prepared Interlocking I.M nail



Image 2: Shows pre-op, post op 2 months and post op 8 months radiographs of a patient of infected Non-union of tibia.

Discussion

Infective non-union of long bones require treatment method that offer control of infection and provide stability to the bone to promote union.⁶ There is no single universally accepted modality of treatment presently available for the management of infected non-union. Thorough debridement, rigid fixation and prolonged antibiotics are the mainstay in treatment of infected non-union of the long bone.^{7,8} The infected foci within the bone are surrounded by a sclerotic, relatively avascular bone covered by a thickened periosteum, scarred muscle and subcutaneous tissue. This avascular envelope of scar tissue leaves systemic antibiotics essentially ineffective.⁹ Osteomyelitis^{7,10} is polymicrobial in majority of patients. The most common infecting organism in the literature and in our study is *Staphylococcus aureus*.^{11,12} The choice of antibiotic is culture dependent heat stable broad-spectrum antibiotic such as gentamicin and vancomycin. Main advantage is Local concentration of antibiotics is far higher than what can be achieved with systemic antibiotics. Clinical and experimental studies show them to have good elution properties from bone cement and no deleterious effects on bone healing.^{6,13} In order to cure biofilm-related infection, four principles formulated by Cierny and Mader must be observed: (1) Complete surgical debridement with dead space management (2) Fracture/nonunion stabilization (3) Soft tissue coverage and (4) Adequate antibiotic levels.² Antibiotic cement has been shown to elute antibiotic at the local sites for up to 36 weeks thus having a therapeutic effect on refractory infection.^{1,14} Various studies have reported success with

the use of intramedullary antibiotic-impregnated bone cement rods for the management of infected non-unions of long bones.^{6, 15-19}

Culture specific antibiotics gentamycin, vancomycin and tobramycin were used for their broad spectrum of activity, heat stability and low allergenicity. We used custom made molds for I.M nails and chest tube for K-nail. Patients were advised for implant removal once infection control and bony union was achieved. We removed implant in 3 patients. Paley and Herzenberg also retained their cement-coated rods for up to 753 days without any major complication except rod fracture in one patient.²⁰ It is advantageous over external fixators, as it eliminates the complications of external fixators and has good patient compliance.

Conclusion

Antibiotic cement impregnated nailing provides effective infection control and good stability to promote union, traditionally provided by two separate procedures. It is advantageous over external fixators, as it eliminates the complications of external fixators and has good patient compliance.

Antibiotic cement impregnated nailing is a simple, economical and very effective procedure than the traditional method in management of infected nonunion of long bones.

Conflict of Interest: None

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References

- Nelson CL, Hickmon SG, Harrison BH. Elution characteristics of gentamicin-PMMA beads after implantation in humans. *Orthopedics* [Internet]. 1994 May [cited 2019 Sep 24];17(5):415–6.
- Cierny G, Mader JT EC. *Surgery of the musculoskeletal system*. New York, Churchill-Livingston. 1983;15-35.
- Baltimore CM-C and treatment of nonunion., 1991 undefined. *Operative principles of Ilizarov by ASAMI group*.
- Yin P, Ji Q, Li T, Li J, Li Z, Liu J, et al. A systematic review and meta-analysis of Ilizarov method in the treatment of infected nonunion of tibia and femur. Vol. 10, PLoS ONE. Public Library of Science; 2015.
- Hosny G, Shawky MS. The treatment of infected non-union of the tibia by compression-distraction techniques using the Ilizarov external fixator. *Int Orthop*. 1998;22(5):298–302.
- Thonse R, Conway J. Antibiotic cement-coated interlocking nail for the treatment of infected nonunions and segmental bone defects. *J Orthop Trauma*. 2007 Apr;21(4):258–68.
- Jain AK, Sinha S. Infected nonunion of the long bones. *Clin Orthop Relat Res* [Internet]. 2005 Feb [cited 2019 Aug 28];(431):57–65. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/15685056>
- Motsitsi NS. Management of infected nonunion of long bones: the last decade (1996-2006). *Injury* [Internet]. 2008 Feb [cited 2019 Sep 24];39(2):155–60. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/18234202>
- Shyam AK, Sancheti PK, Patel SK, Rocha S, Pradhan C, Patil A. Use of antibiotic cement-impregnated intramedullary nail in treatment of infected non-union of long bone. *Indian J Orthop*. 2009 Oct 1;43(4):396–402.
- Ostermann PA, Seligson D, Henry SL. Local antibiotic therapy for severe open fractures. A review of 1085 consecutive cases. *J Bone Joint Surg Br* [Internet]. 1995 Jan [cited 2019 Aug 28];77(1):93–7. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/7822405>
- Costerton JW, Lewandowski Z, Caldwell DE, Korber DR, Lappin-Scott HM. Microbial Biofilms- Annual Review of Microbiology, 49(1):711. *Annu Rev Microbiol* [Internet]. 1995 Jan 28 [cited 2019 Sep 12];49:711–45. Available from: <http://www.annualreviews.org/doi/pdf/10.1146/annurev.mi.49.100195.003431>
- Costerton JW, Cheng KJ, Geesey GG, Ladd TI, Nickel JC, Dasgupta M, et al. Bacterial Biofilms in Nature and Disease. *Annu Rev Microbiol* [Internet]. 1987 Oct [cited 2019 Sep 15];41(1):435–64. Available from: <http://www.annualreviews.org/doi/10.1146/annurev.mi.41.100187.002251>
- Masri BA, Duncan CP, Beauchamp CP. Long-term elution of antibiotics from bone-cement: an in vivo study using the prosthesis of antibiotic-loaded acrylic cement (PROSTALAC) system. *J Arthroplasty* [Internet]. 1998 Apr [cited 2019 Sep 15];13(3):331–8. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/9590645>
- Nizegorodcew T, Palmieri G, Marzetti E. Antibiotic-coated nails in orthopedic and trauma surgery: state of the art. *Int J Immunopathol Pharmacol* [Internet]. [cited 2019 Sep 24];24(1 Suppl 2):125–8. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/21669150>
- Gallucci G, Donndorff A, Boretto J, Constantini J, De Carli P. Infected nonunion of the humerus treated with an antibiotic cement rod. Case report. *Chir Main* [Internet]. [cited 2019 Aug 29];26(4–5):242–6. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/17904402>
- Dhanasekhar R, Pj J, Francis J. Antibiotic cement impregnated nailing in the management of infected non-union of femur and tibia [Internet]. Vol. 26, Kerala Journal of Orthopaedics. 2013. Available from: www.kjoonline.orgwww.kjoonline.orgQuickresponsecode
- Kanakaris N, Gudipati S, Tosounidis T, Harwood P, Britten S, Giannoudis P V. The treatment of intramedullary osteomyelitis of the femur and tibia using the Reamer-Irrigator-Aspirator system and antibiotic cement rods. *Bone Jt J*. 2014;96 B(6):783–8.
- Barger J, Fragomen AT, Rozbruch SR. Antibiotic-Coated Interlocking Intramedullary Nail for the Treatment of Long-Bone Osteomyelitis. *JBJS*

- Rev [Internet]. 2017 [cited 2019 Aug 30];5(7):e5. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/28719401>
19. Bhatia C, Tiwari AK, Sharma SB, Thalanki S, Rai A. Role of Antibiotic Cement Coated Nailing in Infected Nonunion of Tibia. *Malaysian Orthop J* [Internet]. 2017 Mar [cited 2019 Aug 30];11(1):6–11. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/28435567>
20. Paley D, Herzenberg JE. Intramedullary infections treated with antibiotic cement rods: preliminary results in nine cases. *J Orthop Trauma* [Internet]. [cited 2019 Aug 28];16(10):723–9.

Role of Tranexamic Acid in Controlling Blood Loss in Major Orthopaedic Surgeries (TRAMOS): A Comparative Study

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Abstract

Introduction: Tranexamic Acid has been used in major surgeries in various fields of medicine. It has shown to be effective in reducing the blood loss during surgery. But its use in orthopaedic surgeries was limited due to concern regarding efficacy and safety.

Material and Method: 54 patients were included in the study during the study period. Patients were randomly allotted to 2 groups of equal participants. The first group (Group A) received Tranexamic Acid. The second group (Group B) was given placebo. The Total Blood Loss and Fall in Haemoglobin levels were measured post-operatively at 24 and 72 hrs of post-operative period.

Result: The group A had showed significantly reduced total blood loss and fall in Haemoglobin, thus, requiring less blood transfusions. No complications were noted with tranexamic acid use.

Conclusion: We conclude that Tranexamic acid can be effective in reducing blood loss and subsequent fall in haemoglobin. Its judicious use may thus reduce allogenic blood transfusions in major orthopaedic surgeries.

Keywords: TRAMOS, Tranexamic acid, Bleeding, Major Orthopaedic surgeries.

Introduction

Major orthopaedic surgeries like Total Hip Arthroplasty, Total Knee Arthroplasty, Major Spine Surgery are associated with significant perioperative blood loss.¹⁻³ The amount of blood loss in such surgeries can be significant necessitating allogenic blood transfusion.^{4,5} Allogenic blood transfusion is inherently associated with potential risks like infections, immunologic reactions, apart from increasing the cost of care. Reducing the blood loss and thus the need for blood transfusion remains a major concern.

Tranexamic Acid (TXA), a synthetic analog of Lysine, binds to lysine binding site on plasminogen

thereby blocking its activation to plasmin. It thus prevents degradation of blood clot resulting in reduced blood loss. It has proved to be effective in reducing the perioperative bleeding in various surgeries like Liver Transplantation, Cardiac Surgeries, Maxillofacial Surgeries.^{6,7} The efficacy of Tranexamic Acid in Major Orthopaedic Surgeries is being established. The ideal dose for maximum effect is still under evaluation.^{8,9} It has recently been shown to control the perioperative blood loss.¹⁰ But its widespread use has been affected by concerns regarding its safety, especially the propensity to precipitate an VTE.¹¹ On the promising side, use of such pharmacological agents to control perioperative bleeding can significantly reduce healthcare costs and prevent potential risks of blood transfusion.

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Material and Method

The study was conducted in Department of Orthopaedics at Maharishi Markandeshwar Institute

of Medical Sciences and Research, Mullana-Ambala, Haryana.

Period of study: 1st July 2018 – 30th June 2019.

Inclusion Criteria:

1. Age: 18-70 years
2. Gender: Both
3. Primary Total Hip Replacement
4. Primary Knee Replacement
5. Major Spine Surgeries–Decompression with Instrumentation.

Exclusion Criteria:

1. Revision arthroplasty
2. Revision Spine Surgery
3. Presence of comorbid medical conditions like coronary disease, bleeding disorders, chronic renal failure, previous thromboembolism.
4. Active Infection

Study Design:

Type: Double Blind Randomised Parallel Placebo Control Trial

Method of Randomisation: Simple Random Sampling–Random number generator in Microsoft Excel.

Intervention Agent: The first group (Group A) received Tranexamic Acid 500mg intravenous bolus just before skin incision and 500mg slow intravenous infusion which was started just before the surgery.

Comparator Agent: Normal Saline

Primary Outcome Measures: Total Blood Loss

Fall in Haemoglobin levels

Time points of Outcome Measure:

- Primary Endpoint: 72 hours after closure of skin incision.
- Secondary Endpoint: 24hours after closure of skin incision.

The study was approved by institutional review board. A total of 72 patients were screened for the study. of these, 18 patients were excluded due to comorbid

conditions. Total of 54 patients who underwent major orthopaedic surgical interventions in the institute who satisfied the inclusion criteria during the study period were enrolled into the study. Informed Consent was taken for the same.

The intervention group (Group A) received Tranexamic Acid 500mg intravenous bolus and 500mg slow intravenous infusion which was started just before the surgery. The control group (Group B) did not receive any Tranexamic Acid during surgery, instead control agent i.e Normal Saline was administered in similar method as to intervention group. The drug was packed into an envelope by an OT nurse. The drug administered by the operating team anaesthetist by opening the envelope. Both the operating surgeon and the anaesthetists were blinded for the content of the envelope.

Surgical Technique: All the arthroplasties were performed by a single surgeon. Spine surgeries was performed by another surgeon.

Total Hip Arthroplasty: A standard posterior approach was used. Cemented and Uncemented THR was decided according to patient profile.

Total Knee Athroplasty: Performed with medial parapatellar incision.

Spine Decompression and Instrumentation was performed with standard midline posterior approach.

Standard Bipolar electro-cautery was used for haemostasis during surgery. Wound was closed in anatomical layers with vacuum suction drain placed in-situ. Wound dressing was done on post-op day 2.

Estimating the Total Blood Loss: Total Blood Loss was estimated intraoperatively and post-operatively. Total Blood Loss was estimated to be the sum of Intra-op and Post-op estimated blood losses.

Intra-Op blood loss estimated by weighing all the mops used during surgery (whose dry weight had been standardised and documented using an electronic weighing scale) and total blood loss in the suction drain.

Post-op Blood loss was calculated by the soakage of the incision site dressing at first post op dressing (done using pre-weighed cotton pads) and negative pressure suction drain collection wherever applicable. Suction drain was removed on 2nd post-operative day.

The formula for calculation of total blood loss was derived as follows:

- Blood loss in suction drain = Total amount of suctioned fluid – amount of normal saline used during lavage.
- Blood loss in mops = Total weight of mops used – n x (standardised dry weight of a single mop), where “n” is the total number of mops used.
- Post Op Blood Loss = Amount of blood in negative pressure suction drain + [weight of dressing pads – dry weight of pads].

Total blood loss calculated by adding all three.

$$\text{Total Blood Loss} = a + b + c$$

Comparison Variables: The two study groups were compared based upon:

- Total blood loss
- Fall in Hb

Results

The results were compiled in Microsoft Excel and the Statistical relation between the two groups was analysed using SPSS software. Paired Student T-Test was applied for the compiled data. P-value of <0.05 was considered significant.

The average of patients in Group A was 59.1 years whereas 57.7 years in Group B. Male predominance was seen with 59% in Group A and 55% in group B. (Table 1).

The intraoperative blood loss in Group A was 160.1±23.3ml and 203.7±33.7ml for the Group B. The postoperative blood loss measured in suction drain was 371.3±464ml in group A and 455.5±66.8ml for group B. Mean reduction of the intraoperative blood loss was 43.5ml which was statistically significant (p value <0.05). Mean reduction in the postoperative blood loss was 84.2ml which was also significant (p value <0.04).

Mean Total Blood Loss in group A was 531.5±48.8 ml and 659.2±72.5ml in Group B. There was 19% reduction in the total blood loss. Total blood loss in patients receiving tranexamic acid, i.e. Group A was significantly lower compared to the Group B which did not receive tranexamic acid (p value < 0.008).

Mean Loss in Haemoglobin in group a was 2.38±0.26mg/dl and 3.72±0.29mg/dl in group B. There was 36% improvement in Haemoglobin values. Group A had significantly less drop of haemoglobin values compared to group B (p value <0.001). Requirement of blood transfusion was also lower in the group A.

None of the patients in both groups had any complications.

Table 1

Demographic Characteristics	Group A	Group B
Age (Years)	59.1	57.7
Sex – Male (Female)	16 (11)	15 (12)
Height (cm)	161.7	163.5
Weight (kg)	66.6	64.7
Mean Intraoperative Blood Loss (ml)	160.2	203.7
Mean Postoperative Blood Loss (ml)	371.3	455.6
Mean Total Blood Loss (ml)	531.5	659.3
Mean decrease of Haemoglobin (mg/dl)	2.4	3.7

Discussion

Tranexamic acid has been used to control the blood loss during major surgeries. However, the efficacy and safety of its usage in Orthopaedics Surgeries is being established. The concerns regarding prothrombotic effects lead to avoidance of its use in orthopaedic surgeries.

Recently various researchers have tried to study the efficacy and safety of tranexamic acid. In a recent meta-analysis, Huang F. et al¹² had reported significant reduction in blood loss in major orthopaedic surgeries. It was observed that there was significant reduction in intra-operative (125.65ml) and postoperative (214.58ml) blood loss in tranexamic acid group. The results of the present study show a mean reduction of 43.52ml in the intraoperative period and 84.26ml in the postoperative period.

It is noted that the effect of tranexamic was seen to be greater if the dose of the tranexamic acid was increased.¹³ This explains the results obtained in our study, where the mean difference in total blood loss was 127.8ml between the two groups. Blood loss could further be reduced by increasing the dose of Tranexamic acid but evidence regarding the safety of the higher dose treatment is lacking. He had established the

effectiveness of tranexamic acid in reducing the need for blood transfusion.

Kagoma et al.¹⁴ in a meta-analytical study had concluded that tranexamic acid, including other antifibrinolytics had reduced the blood loss and thus need for blood transfusion. However, they also reported inadequate evidence regarding the safety of these agents in the major surgeries. They reported no increased incidence of VTE in the perioperative period.

There are now reports of safety and efficacy of tranexamic acid in the major surgical procedures.^{15,16} There is not much reported data in Indian subcontinent. Although the present study has smaller sample size, it is established that TXA can be effectively and safely reduce the blood loss in Orthopaedic Surgeries.

Conclusion

We thus conclude that tranexamic acid can be an effective tool to reduce blood loss in major orthopaedic surgeries and prevents gross fall in haemoglobin levels thus contributing to the early recovery in the postoperative period. This in-turn limits the adverse effects associated with blood transfusions and reduces cost of patient care.

Conflict of Interest: None

Source of Funding: Self

Ethical Clearance: Ethical Clearance was obtained from the Institutional Ethics Committee (IEC), Maharishi Markandeswar (deemed to be university) Mullana, Ambala.

References

1. Willner D, Spennati V, Stohl S, Tosti G, Aloisio S, Bilotta F. Spine Surgery and Blood Loss: Systematic Review of Clinical Evidence. *Anesth Analg* 2016;123:1307–15..
2. Danninger T, Memtsoudis SG. Tranexamic acid and orthopedic surgery-the search for the holy grail of blood conservation. *Ann Transl Med* 2015;3:77.
3. Poeran J, Rasul R, Suzuki S, Danninger T, Mazumdar M, Opperer M, et al. Tranexamic acid use and postoperative outcomes in patients undergoing total hip or knee arthroplasty in the United States: Retrospective analysis of effectiveness and safety. *BMJ* 2014;349:1–10..
4. Gibon E, Courpied J-P, Hamadouche M. Total joint replacement and blood loss: what is the best equation? *Int Orthop* 2013;37:735–9.
5. Levine BR, Haughom B, Strong B, Hellman M, Frank RM. Blood management strategies for total knee arthroplasty. *J Am Acad Orthop Surg* 2014;22:361–71.
6. Ker K, Prieto-Merino D, Roberts I. Systematic review, meta-analysis and meta-regression of the effect of tranexamic acid on surgical blood loss. *Br J Surg* 2013;100:1271–9.
7. Henry DA, Carless PA, Moxey AJ, O’Connell D, Stokes BJ, Fergusson DA, et al. Anti-fibrinolytic use for minimising perioperative allogeneic blood transfusion. *Cochrane Database Syst Rev* 2011:CD001886.
8. Hourlier H, Fennema P. Single tranexamic acid dose to reduce perioperative morbidity in primary total hip replacement: A randomised clinical trial. *HIP Int* 2014;24:63–8.
- 9] Yoo JS, Ahn J, Karmarkar SS, Lamoutte EH, Singh K. The use of tranexamic acid in spine surgery. *Ann Transl Med* 2019;7:S172.
10. Pinzón-Florez CE, Vélez Cañas KM, Díaz Quijano DM. Efficiency of tranexamic acid in perioperative blood loss in hip arthroplasty: A systematic literature review and meta-analysis. *Rev Española Anestesiología y Reanimación (English Ed)* 2015;62:253–64.
11. Myers SP, Kutcher ME, Rosengart MR, Sperry JL, Peitzman AB, Brown JB, et al. Tranexamic acid administration is associated with an increased risk of posttraumatic venous thromboembolism. *J Trauma Acute Care Surg* 2019;86:20–7.
12. Huang F, Wu D, Ma G, Yin Z, Wang Q. The use of tranexamic acid to reduce blood loss and transfusion in major orthopedic surgery: A meta-analysis. *J Surg Res* 2014;186:318–27.
13. Zufferey P, Merquiol F, Laporte S, Decousus H, Mismetti P, Auboyer C, et al. Do Antifibrinolytics Reduce Allogeneic Blood Transfusion in Orthopedic Surgery? *Anesthesiology* 2006;105:1034–46.
14. Kagoma YK, Crowther MA, Douketis J, Bhandari M, Eikelboom J, Lim W. Use of antifibrinolytic therapy to reduce transfusion in patients undergoing orthopedic surgery: A systematic review of randomized trials. *Thromb Res* 2009;123:687–96.
15. Poeran J, Rasul R, Suzuki S, Danninger T, Mazumdar M, Opperer M, et al. Tranexamic acid use

and postoperative outcomes in patients undergoing total hip or knee arthroplasty in the United States: retrospective analysis of effectiveness and safety. *BMJ* 2014;349:g4829.

16. Dahuja A, Bhowmik S, Kaur R, Shayam R, Jindal S. Antifibrinolytic in reducing postoperative blood loss in total hip replacement and its effect on coagulation profile: A prospective randomized study. *J Orthop Allied Sci* 2018;6:3.

Repair of Chronic Achilles Tendon Rupture by Modified Bosworth Technique

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Abstract

Introduction: The Tendo-achilles, also known as the calcaneal tendon is a strong fibrous tissue structure that connects muscles of the calf to the heel (calcaneus). The calf muscles-gastrocnemius and the soleus muscle along with the plantaris muscle, unites into a strip of tissue and becomes the Tendo-achilles at the lower end of the calf and acts as a main flexor of the ankle joint. The Achilles tendon rupture is considered to be chronic if the injury is past 4-6weeks of duration.

Materials and Method: From May 2016 to May 2018, 15 Patients with long-standing rupture of the Achilles tendon were treated with the operative technique mentioned below, in MMDU, Mullana, Ambala. All the patients gave informed consent prior to being included in the study. Results All patients were evaluated according to The American Orthopedic Foot and Ankle Society (AOFAS) Ankle-Hindfoot Score. 8 patients had excellent results, 4 patients had good results, 2 had fair results and 1 patient had poor result. All patients resumed work at 6 months postoperatively.

Conclusion: Our technique is ideally suitable for chronic ruptures in zone I (where there is no distal stump available for repair) and ruptures that have a large gap of more than 5-6 cms. This is accomplished with a single long incision, with a good post-operative range of ankle motion and function and no major post op complications.

Keywords: Chronic TA Rupture, Modified Bosworth Technique, Zone I Ruptures.

Introduction

The Tendo-achilles/Calcaneal tendon is a strong fibrous tissue structure that connects muscles of the calf to the heel (calcaneus). The calf muscles-gastrocnemius and the soleus muscle, along with the plantaris muscle, unites into a strip of tissue and becomes the Tendo-achilles at the lower end of the calf. The gastrocnemius,

the soleus and the plantaris muscles mainly functions as the ankle flexors, while the gastrocnemius also functions as a knee flexor.^{1,2}

The Tendo-achilles is considered as one among the strong structures, a large and a thick tendon in the human body.^{1,3,4} The Achilles Tendon measures about 15 cms in length, ranges from 10 to 25 cms, is about 6.8 cms in width (ranges from 4.8–8.8 cms) at its origin and it gradually decreases in size at the mid-section (1.8 cms, ranges from 1.2–2.4 cms). The Achilles tendon then turns into rounded structure at an average of about 4 cms above its insertion into the calcaneus and has a width of about 3.4 cms (ranges from 2.0–4.8 cms) at its site of insertion over the posterior surface of the calcaneus.^{1,5} Hence the aim of this study was to observe and study the

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treatment of chronic tendo-achilles rupture by modified Bosworth technique.

Materials and Method

From May 2016 to May 2018, 15 Patients with long-standing rupture of the Achilles tendon were treated with the operative technique mentioned below, in MMIMSR, Mullana, Ambala. All the patients gave informed consent prior to being included in the study. The study was approved by the Ethics committee of our Institution.

The duration of the symptoms ranged from 3 to 12 months. None of the cases were compound ruptures. All the patients had difficulty in walking and pain around the ankle which was of moderate severity. 8 of 15 patients were manual laborers, 5 patients were students and the other 2 patients were homemakers. (Table-1)

Because of the chronicity of the symptoms, none of the patients had ecchymosis, swelling and point tenderness, which are most commonly associated with an acute tendon rupture. There was only moderate swelling and edema around the posterior aspect of the ankle, but all patients had complaints of inability to do active plantar flexion and Difficulty in walking (a limp), Difficulty in Climbing Stairs & Difficulty in getting up from Squatting position. In 12 patients, the defect in the Achilles tendon was visible or palpable. Usually there was some tenderness about the proximal and distal stumps of the ruptured tendon. The Thompson test was positive in all patients (that is, squeezing of the calf did not result in plantar flexion of the foot). Plain radiographs revealed Achilles tendon rupture by the gap between the tendon ends and presence of calcification in the distal portion of the proximal stump of the Achilles tendon.

All patients had undergone an ultrasound scan of the Achilles tendon to confirm the rupture. 9 patients had a rupture in zone I (rupture within 2 cm of the calcaneal insertion). 6 patients had a rupture in zone II (rupture 2 to 6 cm from the calcaneal insertion). The patients who received steroid injection had an avulsion of the tendon from the calcaneum. Intraoperatively, Calcification of the tendon along with necrosis was seen in a few patients.

Operative Technique: After Administering, Epidural/Spinal Anesthesia, the patient was made to lie down in prone position over the operating table. Next step was to inflate the lower limb tourniquet. The back of the leg over the affected side was prepared with aqueous

iodine based solution from popliteal fossa till the heel and covered with sterile drapes. We used A straight long midline incision extending proximally about 10–12 cms below the knee joint and this incision was continued distally, distal to the site of insertion of the Achilles tendon up to the heel. The length of the incision was about 15–20 cms. After performing the skin incision, two important structures viz., the short saphenous vein and the sural nerve were secured and isolated. Then a wide strip of Achilles tendon measuring about 1-1.5 cms was cut and freed of from the central portion of the aponeurosis. The aponeurosis was then left attached (about 1.5-2 cms) proximal to the ruptured end. The hole was made in calcaneus from lateral to medial direction and strip was passed through it, taking care that there is free movement of the tendon raphe inside the bony tunnel (Figure-1). The strip was then sutured back to the main Achilles tendon in Zone-1 Ruptures (Figure-2). The strip was passed through the calcaneum and through distal stump for better anchorage and stability (in Zone-2 Ruptures).

While suturing, a proper amount of tension was maintained in the tendon by plantar flexing the ankle. The precautions that were taken during the surgery were (1) without any subcutaneous dissection, making the skin incision up to the Achilles tendon, (2) to prevent wound dehiscence, by doing a tight continuous subcutaneous suturing, (3) by suturing back the Para-tenon to provide stability.

In the post-op period, a long, non-weight-bearing above knee cast with the ankle in plantar flexion (Equinus) and the knee in 30° flexion was applied for 4 weeks. Wound dressing was done through a window created over the cast 2 days after surgery. The sutures were removed 14 days after surgery. After 4 weeks, the knee was freed from the cast and a short leg cast with the ankle in 20° plantar flexion was applied for 4 weeks. A walking short leg cast with the ankle Plantigrade was applied for 4 more weeks and completely freed from casting after 3 months. After 3 months, gradual calf strengthening and stretching exercises were started along with weight bearing.

Follow Up and Result Evaluation: Ankle pain was Assessed using, The American Orthopedic Foot and Ankle Society (AOFAS) Ankle-Hindfoot Score. Patient was followed up in the OPD after two weeks post operatively, then on monthly basis for 6 months. The scoring included subjective factors such as pain,

Activity Limitations, Maximum walking distance (in Blocks), walking surface, as well as objective factors such as Gait Abnormality, Sagittal Motion (Flexion plus Extension), Hind-Foot (Inversion plus Extension), Ankle-Hindfoot Stability (Antero-Posterior, Varus-Valgus), Alignment. The maximum number of points achievable was 100. The results were classified as Excellent (≥ 90 points), Good (75–89 points), Fair (60–74 points) or Poor (< 60 points). The patients were asked to give answers to a Non-Validated subjective Symptoms Questionnaire.

Results

All patients were evaluated according to The American Orthopedic Foot and Ankle Society (AOFAS) Ankle-Hindfoot Score. Data collected was entered into Microsoft Excel worksheet and Analyzed Statistically by using SPSS (Statistical Package for Social Sciences). 8 patients had excellent results, 4 patients had good results, 2 had fair results and 1 patient had poor result.

All patients resumed work at 6 months postoperatively. 2 patients had mild pain at the end of 1 year at the ankle joint, but this did not hinder their daily or recreational activities. However, 1 patient had moderate pain that limited them from Sports activities but not from daily activities. Slight Gait Abnormality was noted in 1 patient at the end of 1 year, but this did not limit their daily or recreational activities. 2 Patients complained of Moderate Restriction In Sagittal motion. Almost all the patients had normal walking and stair climbing. There was significant improvement in the range of ankle motion postoperatively. There was an equal range of motion in both ankles in 13 out of 15 patients during follow-up of patients at the end of 1 year. 2 patients were unable to raise their heels from the floor equally when on tiptoe because of other unrelated causes such as old age and obesity.

Table 1: Study Design

Characteristics	Value
Total Number of patients	15
Sex ratio M:F	7:8
Duration of follow-up	1 Year
Zone I ruptures	9
Zone II ruptures	6
Mechanism of injury	
Steroid intake	8
Severe trauma	4
Trivial trauma	3

Complications in this study included Scar Hypertrophy (in 1 patient), superficial infection (in 1 patient) and delayed wound healing (in 1 patient, Due to Co-morbidities like Type-2 Diabetes Mellitus). Superficial infection was treated with oral antibiotics and regular dressings. In 1 patient, there was delayed healing and it took nearly 1 month to heal completely with regular dressings. Fortunately, none of the patients had an episode of re-rupture of the Achilles tendon Post Surgery.



Figure 1: Tendon RAPHE being passed through the hole made in the calcaneum



Figure 2: STUMP Then sutured back to the main achilles tendon with ankle in plantar flexion.

Discussion

The cause of Tendo-Achilles rupture is still unknown, whereas in certain studies it has been proven that the most common cause from samples sent for histological studies is chronic degenerative changes.^{6,7} In various studies it has been mentioned that failure the diagnose Achilles tendon rupture in the first visit

of the patient is the most common reason of delayed intervention. Hence, patient is unable to get the required treatment in time and thus showing a wide range of presentation.⁴ Patients with Achilles tendon ruptures face problems like not able to maintain posture on the toes on the ruptured side, but patients can perform active plantar flexion due to the following reasons viz., (A) partial ruptures, (B) an intact plantaris muscle and (C) recruitment of plantar flexors. No obvious loss of plantar flexion and the lack of pain can be misleading and this may be reason due to which in up to 20-25% of cases the diagnosis of Achilles tendon rupture is being missed during the initial presentation.^{8,9}

In 1956, Bosworth devised the repair of the neglected tendoachilles tears with a long strip of proximal aponeurosis of the Achilles tendon passed through the proximal and distal tendon stumps. This repair is ideally not suitable for Zone 1 ruptures.¹⁰

Langergran and Lindholm (1958), based on vascularity, divided the tendoachilles into three zones (based on vascularity). Zone I is around <3 cms away from the insertion, zone II 3–6 cms away from the insertion and zone III >6 cms away from the insertion.¹¹

In 1972, In A study conducted by Bala subramaniam et al. it is stated that the main reason for necrosis of Achilles tendon and a delayed healing is because of the injection of steroids into the insertion site of Achilles tendon.¹² The symptoms of tendon damage like pain may be masked due to the analgesic and anti-inflammatory properties of corticosteroids, provoking the patients to continue their routine day-to-day activities though the tendon is ruptured.¹³

In 1991, Mann et al. conducted a study in which FHL tendon was taken from Mid-foot and the distal portion of the ruptured tendon was sutured to FHL. The proximal end of the ruptured tendon being attached to the calcanei by pullout wire technique. But the above-mentioned method is not applicable, when the distance across the two ruptured parts is >5cms.^{14,15}

In 2013, Pavan Kumar A et al. modified the Bosworth technique by passing a part of aponeurosis of gastrocnemius muscle which was taken and then made into a tendon-like structure and inserted through the calcaneum by making a hole in it, which is then attached back to the proximal end of the tendon. This method is ideal for Zone 1 ruptures also.¹⁵

In 2016, Yangjing Lin et al. did a study on 29 subjects who had chronic tendoachilles rupture and had used flexor hallucis longus tendon transfer, gastrocnemius fascia turndown flap, or V-Y advancement based on the presence or absence of achilles tendon stump, gap that prevails between the ruptured ends and the length of the rupture and all the subjects of the study had the opportunity once again to participate in sports activities of preinjury level.¹⁶

In our Study, we have used the aponeurosis of the gastrocnemius itself, thereby not needing any tendon transfers, which would compromise the function of that tendon. As we were using the same tendon aponeurosis, the strength remained balanced. Our technique would be ideal for a gap of more than 5-6 cms that needs tendon transfer with additional synthetic grafts.

Conclusion

Our technique was ideally suitable for chronic ruptures in zone I (where there is no distal stump available for repair) and ruptures that have a large gap of more than 5-6 cms. This is accomplished with a single long incision, with a good post-operative range of ankle motion and function and no major post op complications.

Conflict of Interest: None

Source of Funding: Self

Ethical Clearance: Ethical Clearance was obtained from the Institutional Ethics Committee (IEC), Maharishi Markandeswar (deemed to be university) Mullana, Ambala.

References

1. Del Buono A, Chan O, Maffulli N. Achilles tendon: functional anatomy and novel emerging models of imaging classification. *Int Orthop*. 2013;37(4):715-21.
2. Grumbine NA, Santoro JP. The tendo Achillis as it relates to rearfoot position. A new classification for evaluation of calcaneal stance position. *Clin Podiatr Med Surg*. 1990;7(2):203-16.
3. Doral MN, Alam M, Bozkurt M, Turhan E, Atay OA, Dönmez G, Maffulli N. Functional anatomy of the Achilles tendon. *Knee Surg Sports Traumatol Arthrosc*. 2010;18(5):638-43.
4. Ahmed P, Usmani Y, Garg AM. Repair of Chronic Tendoachilles Rupture-Bosworth technique

- versus Peroneus Brevis Transfer technique – A Retrospective Study and Prospective Study. *JBJD*.2017;32(2):17-23.
5. Apaydin N, Bozkurt M, Loukas M, Vefali H, Tubbs RS, Esmer AF. Relationships of the sural nerve with the calcaneal tendon: an anatomical study with surgical and clinical implications. *Surg Radiol Anat*. 2009;31(10):775-80.
 6. Barfred T. Experimental rupture of the Achilles tendons. *Acta OrthopScand*. 1971; 42 (6): 528-43.
 7. Kannus P, Jozsa L. Histopathological changes preceding spontaneous rupture of tendon. *J Bone Joint Surg Am*. 1991;73(10):1507-25.
 8. Maffulli N. Clinical tests in sports medicine: more on Achilles tendon. *Br J Sports Med*. 1996;30(3):250.
 9. Nillius SA, Nilsson BE, Westlin NE. The incidence of Achilles tendon rupture. *Acta Orthop Scand*. 1976;47(1):118-21.
 10. Bosworth DM. Repair of defects of the tendoachillis. *J Bone Joint Surg Am*. 1956;38-A(1):111-4.
 11. Langergran L, Lindholm A. Vascular distribution in the Achilles tendon. *Acta Chir Scand*. 1959;116(5-6):491-5.
 12. Balasubramaniam P, Prathap K. The effect of injection of hydrocortisone into rabbit calcaneal tendons. *J Bone Joint Surg Br*. 1972;54(4):729-34.
 13. DiStefano VJ, Nixon JE. Ruptures of the Achilles tendon. *J Sports Med*. 1973;1(2):34-7.
 14. Mann RA, Holmes GB Jr, Seale KS, Collins DN. Chronic rupture of the Achilles tendon: a new technique of repair. *J Bone Joint Surg Am*. 1991;73(2):214-9.
 15. Pavan Kumar A, Shashikiran R, Raghuram C. A novel modification of Bosworth's technique to repair zone I Achilles tendon ruptures. *J Orthop Traumatol*. 2013;14(1):59-65.
 16. Lin Y, Yang L, Yin L, Duan X. Surgical Strategy for the Chronic Achilles Tendon Rupture. *Biomed Res Int*. 2016;2016:1416971.

Comparative Evaluation of Conventional Media with Bactec MGIT 960 for Detection of Mycobacterium Tuberculosis in Clinically Suspected Cases of Pulmonary and Extra-Pulmonary Tuberculosis

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Abstract

Background: Tuberculosis (TB) is a leading cause of morbidity and mortality worldwide, despite being a treatable and preventable disease. The emergence of Multi Drug Resistant (MDR) TB had exacerbated the situation further. To prevent the spread of infection & to accelerate the administration of Anti-tubercular treatment, early detection of TB is required.

Methodology: This Cross-sectional study was carried out on 236 samples clinically suspected cases of Pulmonary & Extra-Pulmonary Tuberculosis processed for Direct Ziehl-Neelsen Staining, Decontamination by NALC-NaOH and Culture in MGIT tubes & Lowenstein-Jensen Medium.

Results: Out of 60 samples, 60(25.42%) were culture positive cases showed highest isolation rate by BACTEC MICRO MGIT as compared to LJ Medium 42(17.79%) with time of detection by BACTEC MICRO MGIT was 17 days and LJ Medium was 33.72 days. The Diagnostic accuracy of BACTEC MICRO MGIT when LJ Medium considered to be gold standard was also exhibited which showed sensitivity of 95.24%, Specificity of 89.69% while Negative Predictive value (NPV) & Positive Predictive value (PPV) was 98.86% and 66.67% respectively. The BACTEC MICRO MGIT detects mycobacteria early, with less contamination rates and has good sensitivity & specificity as compared to LJ Medium.

Conclusion: So it can be concluded that BACTEC MICRO MGIT can be used as method of isolation of Mycobacterium tuberculosis either alone or in combination with LJ Medium.

Keywords: Tuberculosis, Pulmonary, Extra-Pulmonary, Lowenstein-Jensen Media, Mycobacterial.

Introduction

Tuberculosis is a global public health problem with significant incidence and mortality rates predominantly in developing countries. According to a World health organization report, approximately 1.7 million cases of

TB were notified and 0.42 million TB deaths occurred in 2018.¹ The early diagnosis of tuberculosis can play a major role in reducing the mortality rate and economic burden.² However the most common presentation is pulmonary tuberculosis but Extra Pulmonary Tuberculosis (EPTB) is also the emerging clinical problem.³ The diagnosis of Extra pulmonary tuberculosis infections are difficult due to paucibacillary nature.⁴

The Lowenstein Jensen (LJ) culture and the AFB microscopy remains the basis of diagnosis of tuberculosis, but the traditional method has very low sensitivity, especially in samples containing few number of microorganisms.⁵ Specifically, In order to reduce

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the time to detect and identify Mycobacteria in clinical specimens, a variety of manual and automated systems have been developed.⁶ MGIT 960 (mycobacterial growth indicator tube) is a non-radioactive detection system which uses fluorochrome based method for early detection (7-12 days) of Mycobacteria.⁴

This study was conducted to evaluate the capability, efficiency and reliability of MGIT in comparison to Lowenstein Jensen (LJ) Media for detection of Mycobacteria from Pulmonary and Extra-Pulmonary specimens.

Materials and Method

A Cross-sectional study for duration of 2 year (2016-2018) was carried out in the Department of Microbiology, MMIMSR, Mullanaon 236 samples from clinically suspected cases of Pulmonary & Extra-Pulmonary tuberculosis. The ethical clearance was taken from the institutional ethical committee.

All samples from clinically suspected cases of tuberculosis were includes while patients on Anti-tubercular treatment (ATT), diagnosed cases of lower respiratory tract infection were excluded from the study.

Sample Processing:

The Samples were subjected to:

- i. Direct Ziehl-Neelsen Staining of Sample.
- ii. Decontamination of sample by NALC-NaOH as recommended by the CDC’s Public Health Mycobacteriology: A Guide for the Level III Laboratory.
- iii. Culture
 - (a) Inoculation in MGIT tubes.
 - (b) Inoculation on Lowenstein-Jensen Medium

LJ Medium was incubated at 37°C for 8 weeks as per standard guidelines. The culture was first examined after 1 week followed by 15 days up to 8 weeks. Growth was confirmed by Ziehl-Neelsen staining and Gram staining.

MGIT tubes were incubated at 37°C for 2-8 weeks. The reading was taken thrice in a week till up to 2 weeks then twice in a week up to 8 weeks. Reading of MGIT tubes was taken by BACTEC micro MGIT instrument and positive tubes were sub-cultured on LJ Medium and Acid fast smears were also prepared. Also to rule out contamination, positive tubes were also sub-cultured on Blood Agar and gram staining was also done.

Table I: Frequency of Mycobacterial isolates in clinically suspected cases of pulmonary and extra-pulmonary tuberculosis

Number of samples studied	Number of culture positive cases					
	236	60 (25.42%)	<table border="1" style="width: 100%;"> <tr> <td>Pulmonary</td> <td>54</td> </tr> <tr> <td>Extra-Pulmonary</td> <td>6</td> </tr> </table>	Pulmonary	54	Extra-Pulmonary
Pulmonary	54					
Extra-Pulmonary	6					

Table II: Sample wise distribution and positivity rate of ZN staining, BACTEC MICRO MGIT & Lowenstein Jensen Medium

Samples	Total no. of samples	ZN staining	Growth of Mycobacterium		p-value
			BACTEC MICRO MGIT	Lowenstein Jensen Medium	
Sputum	158	28	54	36	0.041
BAL	18	2	2	1	
Pleural Fluid	15	1	1	2	
Urine	15	0	1	1	
Pus aspirate	13	1	1	0	
CSF	5	0	0	0	
Endometrial Biopsy	12	1	1	2	
Total	236	33(13.98%)	60(25.42%)	42(17.79%)	

*The result is significant at p < .05. By Chi-Square Test.

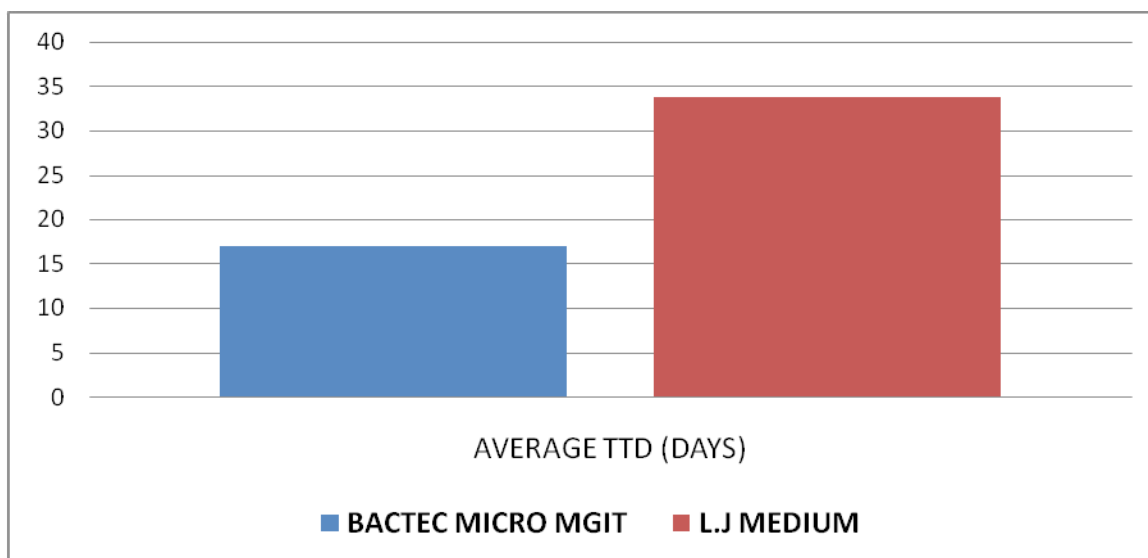


Fig. I: Average Time of Detection

		BACTEC MICRO MGIT (N=236)					
		+VE	-VE	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
L.J MEDIUM (N=236)	+VE	40	2	95.24	89.69	66.67	98.86
	-VE	20	174				

Table III: Diagnostic accuracy of BACTEC MICRO MGIT in comparison to L.J Medium (Gold standard) in detection of Mycobacteria in clinically suspected cases of pulmonary and extra-pulmonary tuberculosis

Result

Out of 236 clinically suspected cases of pulmonary and extra-pulmonary tuberculosis, 60 (25.42%) samples were positive by MGIT, 42(17.79%) samples showed growth on L.J Medium while Z.N Staining detected 33(13.98%) samples positive. [Table-I & II].

The average time of detection in MGIT was 17days while on L.J Medium was 33.72 days. [Figure I].

The Diagnostic accuracy of MGIT was also calculated considering L.J Medium as gold standard which showed 95.24% sensitivity, 89.69% specificity, 66.67% Positive predictive value and 98.86% Negative predictive value. [Table-III]

Discussion

Tuberculosis has been affecting humankind for thousands of years and still is one of the most deadly infectious diseases in the world. The emergence of Multidrug resistant (MDR) and extensively drug resistant

tuberculosis (XDR) has agitated the situation further. Hence, the early diagnosis of tuberculosis is critical in appropriate management of Tuberculosis. Culture still is considered as Gold standard.⁷

In Present study total culture positive cases were 60 (25.42%) which is supported by the studies conducted by Sebastian G et al⁸(2016) (22%) while lower percentage was reported by Bunger R et al⁹ (2015) (11%). The High positivity rates were also reported by Rodrigues C et al¹⁰ (2009) (42%). The rate of positivity varies from region to region and depends on many other factors.

Under the Revised National Tuberculosis Control Program (RNTCP), priority is given to the smear-positive cases. Every smear positive person, if left untreated, has potential to infect 10–15 persons per year. Ziehl-Neelsen staining technique for sputum microscopy is employed as the standard case-finding tool. Although advances in diagnostics are leading to the introduction of new tests, the backbone of TB diagnosis worldwide continues to be smear microscopy.

In Present study, 33 (13.98%) cases were found to be AFB positive with ZN Microscopy (Table II). The Present finding was found to be in concordance with studies conducted by Saini D et al⁴ (2017) (15.15%).

The present finding was found to be higher than the studies conducted by Roy A et al¹¹ (2016) (6.67%) while the higher positivity rate was found in studies conducted by Tortoli E et al¹² (1999) (54%). The detection rate of Mycobacteria by Direct AFB smear examination in Extra-Pulmonary samples is significantly less as compared to the pulmonary samples.

Even though AFB microscopy and the LJ Medium are the cornerstones of diagnosis of tuberculosis but the sensitivity of these conventional method is quiet low, especially in samples with less number of organisms. There is a need of rapid, accurate and sensitive method for the early detection of these organisms in clinical specimen so as to prevent the cross-infection among community & accelerate the appropriate antimycobacterial therapy for the infected persons.

In Present study, 60 (25.42%) of Mycobacteria were isolated from BACTEC MICRO MGIT (Table IV). The Present finding was found to be in concordance with studies conducted by Roy A et al¹¹ (2016) (18%). The present finding was found to be higher than the studies conducted by Siddiqui MAM et al¹³ (2013) (15%). The higher positivity rate was found in studies conducted by Rishi S et al¹⁴ (2007) (50.6%). The average time of detection by MGIT was 17 days which is supported by studies conducted by A Oberoi et al¹⁵ (2004) which showed mean time to be 16 days.

In Present study, 42 (17.79%) of mycobacteria were isolated on LJ Medium (Table IV). The Present finding was found to be in concordance with studies conducted Siddiqui MAM et al¹³ (2013) (15%). The Present finding was found to be higher than the studies conducted by Roy A et al¹¹ (2016) (8%). The higher positivity rate was found in studies conducted by Rodrigues C et al¹⁰ (2009) (24%). The Average time of detection by L.J Medium was 33.72 days which is supported by study of Nor MF et al¹⁶ (2009) (33 days).

The less average time of detection by MGIT is due to growth supplements like Bovine Albumin, Dextrose, Polyoxyethylene stearate, Catalase & Oleic acid which are absent in LJ Medium. Thus BACTEC MICRO MGIT detects Mycobacteria more rapidly than LJ Medium.

Higher Contamination rates are the major drawback of fully automated system but in our present study, the contamination rate was found to be lower with BACTEC MICRO MGIT (7%) as compared to L.J Medium (9%). The results are in concordance with the study conducted

by Bunger R et al⁹ (2013) (6%). The BACTEC MICRO MGIT is a liquid media which is supplemented with antimicrobial agents like PANTA (Polymyxin B, Amphotericin B, Nalidixic acid, Trimethoprim & Azlocillin) while LJ medium contains only Malachite green to reduce the contamination. Thus more the number of Antimicrobial agents lesser are the chances of contamination.

Conclusion:

The results of this study demonstrated that the MGIT system provided better recovery of Mycobacteria than the traditional LJ slant. The average time of detection, Contamination rate in MGIT was significantly less as compared to the conventional culture method i.e. L.J Medium. So it can be concluded that MGIT can be used as method of isolation of Mycobacterium tuberculosis either alone or in combination with LJ Medium.

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References

1. World Health Organization. Global tuberculosis report 2018. [http://www.who.int/tb/publications/global_report/en/\(2014\)](http://www.who.int/tb/publications/global_report/en/(2014)). Accessed 10 July 2019.
2. Chan WC, Li LK, Yung PT. Wearable patch for the electrical, durometry and optical skin measurements in tuberculin skin test. In: Biomedical and health informatics (BHI), 2012 IEEE-EMBS international conference on 2012. IEEE.
3. Fanning A. Tuberculosis-extrapulmonary disease. CMAJ. 1999; 160:1597-603.
4. Saini D et al. Comparison of BACTEC MGIT with conventional method for detection of Mycobacteria in clinically suspected patients of extra pulmonary tuberculosis in a tertiary care hospital. Int J Res Med Sci. 2017;5(8):3530-3533
5. Hawkinds JOE. Antibacterial susceptibility tests. Manual of clinical Microbiology. Ed5 American Society for Microbiology. Washington DC.1991:1138.
6. Hanna BA, Ebrahimzadeh A, et al . Multicentre evaluation of BACTEC MGIT 960 system for recovery of Mycobacteria. J Clin Microbiol 1999; 37 :748-52
7. Golden MP, Vikram HR. Extrapulmonary

- tuberculosis: an overview. *Am Fam Physician*. 2005;72(9):1761-68.
8. Sebastian G, Tripathy SK, Vishwanatha T, Kumar P. BACTEC MGIT 960 liquid culture system from sputum samples of presumptive pulmonary tuberculosis patients. *World Journal of Pharmacy and Pharmaceutical Sciences*. 2016;5(8):1646-1653.
 9. Ruhi Bunger, VarshaA Singh et al: Evaluation of BACTEC Micro MGIT with Lowenstein Jensen Media for Detection of Mycobacteria in Clinically Suspected Patients of Extra-Pulmonary Tuberculosis. *J Med MicrobDiagn* 2013, 2:3
 10. Rodrigues C, Shenai S et al. Evaluation of the Bactec MGIT 960TB System for recovery and identification of Mycobacterium tuberculosis Complex in a high through put tertiary care center. *Indian J Med Microbiol*. 2009 Jul-Sep;27(3):217-21.
 11. Roy A, Baveja CP, Kumar S. Comparison of recoveries of Mycobacterium tuberculosis using the Automated BACTEC MGIT 960 System and Lowenstein-Jensen Medium in clinically suspected cases of tubercular meningitis in children. *International Journal of Biomedical and Advance Research* 2016; 7(2): 094-096
 12. Tortoli E, Cichero P et al. Use of BACTEC MGIT 960 for recovery of mycobacteria from clinical specimens: multicenter study. *J ClinMicrobiol*. 1999 Nov;37(11):3578-82
 13. Siddiqui MAM, Anuradha PR, Nagamani K, Vishnu PH. Comparison of conventional diagnostic modalities, BACTEC culture with polymerase chain reaction for diagnosis of extra-pulmonary tuberculosis. *J Med Allied Sci* 2013;3(2):53-58.
 14. Rishi S, Sinha P, Malhotra B PN. A comparative study for the detection of Mycobacteria by BACTEC MGIT 960, Lowenstein Jensen media and direct AFB smear examination. *Indian J Med Microbiol*.2007;25(4):383–386
 15. AOberoi, H Kaur. Comparison of rapid colorimetric method with conventional method in the isolation of mycobacterium tuberculosis. *Indian J Med Microbiol*. 2004;22(1):44-46.
 16. Nor MF et al. The manual MGIT system for the detection of M tuberculosis in respiratory specimens: an experience in the University Malaya Medical Centre. *Malaysian J Pathol* 2009; 31(2): 93-97.

Nontuberculous Mycobacterium in Pulmonary & Extrapulmonary Tuberculosis: Still a Neglected & Underdiagnosed Pathogen in Developing Countries

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Abstract

Non-tuberculous mycobacterium (NTM) has been identified in human pulmonary and extra pulmonary diseases and is of great concern for clinicians and microbiologists because of their increasing global incidence. They are now increasingly recognized as important pathogens in both immunocompromised and immunocompetent population. They should be identified rapidly and should be carefully differentiated as contamination, colonization or disease. Cultures were made on conventional LJ and LJ with PNB media. Growth was confirmed as AFB (acid fast bacilli) by ZN staining. NTM were identified by growth on LJ with PNB media, colony morphology, rate of growth, pigmentation, catalase activity and confirmed by MPT 64 antigen rapid test (using SD Bioline TB Ag MPT 64 test kit). Data was analysed statistically using SPSS software. Out of total 500 processed samples (250 pulmonary & 250 extrapulmonary), 12(21.05%) and 7(21.8%) NTM were isolated from pulmonary and extrapulmonary samples respectively. Maximum pulmonary NTM (41.7%) were isolated from > 60 years age of patients in contrast to extrapulmonary NTM isolates which were more in 20-40 years of age group. There was 16.7% previously treated patients in pulmonary while 100% were newly diagnosed patients in extrapulmonary TB cases. This study highlights the importance of early diagnosis and differentiation among *Mycobacterium tuberculosis* and NTM so that these NTM are not underestimated in routine diagnostic procedures merely as environmental or laboratory contaminants.

Keywords: Non-tuberculous mycobacterium, p-nitrobenzoic acid, Pulmonary TB, extrapulmonary TB, MPT64 antigen.

Introduction

Of all infectious diseases pulmonary tuberculosis is the leading killer and is endemic in India but extrapulmonary TB is also emerging rapidly. The primary

causative agent of these infections is *Mycobacterium tuberculosis* (M.tb) however, rising prevalence of NTM draws attention as an important pathogen in both immunocompromised and immunocompetent persons gaining importance for clinicians, microbiologists & epidemiologists¹. In immunocompetent persons especially in individuals with chronic obstructive pulmonary disease it causes pulmonary fibrosis or cavitary lung disease while in immunocompromised hosts it produces systemic infection which may or may not mimic MTBC but the treatment regimen of both are different. The NTMs are often resistant to drugs used for treating *Mycobacterium tuberculosis complex* (MTBC) which helps falsely conclude the patients as 'multidrug

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resistant tuberculosis (MDRTB) who correspondingly take the treatment of 'MDRTB'. Indicating clearly that early and accurate identification of NTM is essential for precise treatment and management of patient. However in India it is still the tip of iceberg, may be because of unavailability of comprehensive data depicting occurrence of NTM in pulmonary and extrapulmonary diseases. As very less number of studies are available from this region therefore, this study was conducted with aim (1) to determine the frequency of NTM in pulmonary and extrapulmonary TB cases (2) to assess the NTM from newly diagnosed and previously treated cases of pulmonary and extrapulmonary TB (3) to assess the age wise distribution of NTM in pulmonary and extrapulmonary TB.

Material and Method

Study Design & Period: The cross sectional study was conducted in the Department of Microbiology at MMIMSR, Mullana, Ambala during 2017-2019 after taking approval of Ethical Committee of the Institute.

Clinical specimens & Data collection - A Total 500 samples were analysed for laboratory diagnosis of nontubercular mycobacterial infection from pulmonary & extrapulmonary cases. The pulmonary patients were selected as per ATS (American Thoracic Society) criteria² i.e clinically and radiologically suspected tuberculosis cases. Two samples were collected from each patients (either two sputum samples or one sputum and one BAL sample). 2-10 ml. of nonrepeated samples were collected from suspected cases of extrapulmonary TB.

The specimens were included as lymph node aspirate, pleural fluid, cerebrospinal fluid, ascetic fluid, pus, endometrial biopsy materials, menstrual blood and endotracheal secretions. All the patients signed due consent for sample collection.

RNTCP defined, Newly diagnosed and previously treated TB patients were also included in the study³. The clinical history regarding present and past history of antitubercular treatment (ATT) and family history of tuberculosis and any other associated disease were taken in prescribed performa.

Processing and Microbiological Analysis of Specimens: Samples were subjected for concentration and decontamination by standard NALC-NaOH technique⁴ except sterile specimens which were centrifuged & processed directly. After concentration

sediment was subjected to smear microscopy by Ziehl-Neelsen (ZN) staining method & inoculated simultaneously over the slants of LJ media and LJ with PNB (p-nitrobenzoic acid) media as per Koneman EW and Mackie & Maccartini practical medical microbiology book⁴. The LJ medium slopes were incubated at 37⁰ C. Growth was checked daily during first week for Rapid growers and then weekly for a maximum of six weeks. Growth was confirmed by smear microscopy for the presence of acid fast bacilli (AFB). No growth after 6 weeks of incubation was treated as negative for mycobacteria. NTM were identified on the basis of growth on LJ with PNB media, colony morphology, rate of growth, pigmentation, catalase activity⁴ and confirmed by SD Bioline TB Ag MPT 64 kit which is a rapid immunochromatographic test to differentiate NTM from *Mycobacterium tuberculosis complex* (MTBC).

Result

The present study was conducted on 500 samples (which includes 250 pulmonary & 250 extrapulmonary). The pulmonary samples includes 244 sputum and 6 bronchoalveolar lavage (BAL) while extra pulmonary samples were pleural fluid (70/250), pus (56/250), CSF (45/250), endometrial biopsy (35/250), menstrual blood (15/250), lymph node aspirates (14/250), ascetic fluid (10/250) and endotracheal secretion (5/250).

Out of total 500 samples 57(22.8%) & 32(12.8%) mycobacteria were isolated from pulmonary and extrapulmonary samples respectively. The frequency of NTM among Mycobacterial isolates of pulmonary samples was 12(21.05%) while of extrapulmonary was 7(21.8%) which was statistically insignificant (p-value 0.701) (table 1).

In pulmonary isolates, 41.7% were from > 60yrs followed by 33.4% from 41-60 years and 16.5% from 20-40 years of age group with male predominance (75%). In contrast, extrapulmonary isolates which have female predominance (57.14%) with 71.4% of 20-40 years followed by 14.2% of 41-60 years and 14.2% of > 61 years of age group suffered from EPTB caused by NTM (table 2).

As per sample wise distribution was concern, pulmonary isolates, 12(100%) were from sputum samples whereas in extrapulmonary, 4(57.14%) isolates were from pus, 2(28.6%) isolates were from endometrial samples and 1(14.3%) isolate was from pleural fluid (fig 1).

Among pulmonary cases, (83.4%) NTM were from newly diagnosed & (16.7%) were previously treated patients in contrast to it, in extrapulmonary tuberculosis 100% isolates were from newly diagnosed cases (table 3).

Table I: Frequency of Non Tubercular Mycobacteria (NTM) in pulmonary and extra-pulmonary TB isolates

Mycobacterial isolates Total no. of Non Tubercular mycobacteria (NTM)	
Pulmonary (n=57)	12 (21.05%)
Extra-pulmonary (n=32)	7 (21.8%)
Total isolates (n=89)	19 (21.3%)

By Chi square test: Statistically not significant (p value 0.701)

Table II: Age wise distribution of NTM isolates in pulmonary and extrapulmonary TB patients.

Age Group	Pulmonary TB		Extrapulmonary TB	
	M	F	M	F
20-40 years	3(33.4%)	-	3(100%)	2(50%)
41-60 years	2(22.3%)	2(66.7%)	-	1(25%)
>61 years	4(44.5%)	1(33.3%)	-	1(25%)
Total	9	3	3	4

Table III: Frequency of NTM in previously treated & newly diagnosed patients of pulmonary & extrapulmonary tuberculosis.

Site Involved	Previously Treated Patients	New Patients
Pulmonary (n=12)	2(16.7%)	10(83.4%)
Extrapulmonary (n=7)	0	7(100%)

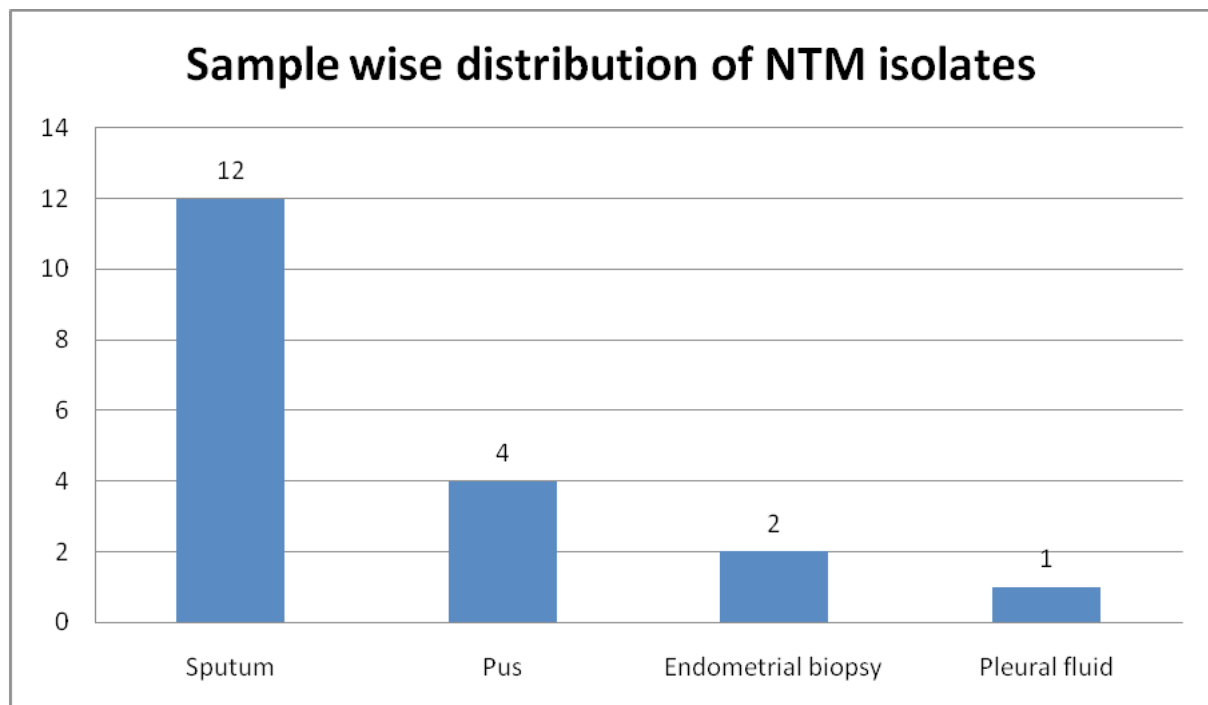


Fig. 1

Discussion

Prevalence of NTM is unknown in India as NTM disease is not reportable and there is lack of awareness among clinicians coupled with lack of laboratory capacity to diagnose these infections. Identification of NTM is of clinical relevance as most of the NTM are notably resistant or only partially susceptible to the standard anti-tubercular drugs and the treatment strategies and the duration of these infections differs from MTB. In the current study, from pulmonary samples out of 57 mycobacterial isolates, 21.05% NTM were detected (Table I) which is in concordance with Eliane Picoli et al⁵ who detected 23% NTM and M.J.Nasiri et al⁶ (15.1%) in their study whereas higher rate was detected by Sarika Jain et al⁷ (69.2%) in 2014. Lesser isolation rate of NTM in pulmonary samples were observed by Yan Shao et al⁸ (3.37%) in their study. Similarly, 21.8% NTM were detected in extrapulmonary mycobacterial isolates, which is supported by Sarika Jain et al⁷ (30.8%) and Archana. B. Wankhade et al⁹ who observed 15.9% NTM in pus samples. Lesser isolates were detected by V.P.Myneedu et al¹⁰ (0.38%) in their study. In India prevalence rate of NTM increases every year. According to study conducted by Sarika Jain et al⁷, prevalence rate of NTM in India was 1.0% in 2005, 3.5% in 2008 and upto 88.6% of NTM isolation rate is clinically relevant.

In current study, as age wise prevalence of NTM is concern, maximum 41.7% patients were from >60 years of age group with male predominance were suffered from pulmonary tuberculosis caused by NTM whereas maximum 71.4% of 20-40 years of age group with more of females were revealed diseased from extrapulmonary TB by NTM. Similar results were observed by Maura J. Donohue¹¹ and Hywoon Lee et al¹² in their study. They also found that NTM effects more to older age group (>60 years) with female predominance. In contrast Pooja Sharma et al¹³ reported 41-60 years of age group infected more with NTM in their study. Pulmonary NTM were more isolated from old patients, may be due to age related immunosuppression or underlying lung disease like COPD (common in rural people due to use of hukka habit). In contrast, NTM from Extrapulmonary TB were more isolated from reproductive age group with female predominance presented mainly as infertility and cervical lymphadenitis.

Relapse of tuberculosis (TB) is defined as re-emergence of clinical symptoms after stopping anti-

TB treatment, while this treatment appeared effective initially. Relapse of TB can occur in patients that are therapy-compliant, but the risk of relapse is dramatically increased when patients are non-compliant. Also TB caused by NTM is falsely reported as relapse or MDR TB as drugs used to treat MTBC are not effective for the treatment of NTM. Some epidemiological factors like age, sex, smoking, immunosuppression, history of contact, HIV co-infection etc. are also related with recurrence of pulmonary and extrapulmonary TB. In this study, 83.7% patients were newly diagnosed whereas 16.4% were previously treated patients for pulmonary tuberculosis caused by non tubercular mycobacteria (NTM). Results were in concordance with study conducted by Mu-Lu Wu et al¹⁴ (12%) in 2018. Higher relapse rate of NTM was observed by Daniel. P. Boyle et al¹⁵ (25%) and Bo Young Lee et al¹⁶ (31.6%) in their study. In this study, no relapse was found in case of extrapulmonary TB caused by NTM. In India, NTM infections usually get undiagnosed due to overwhelmed cases of MTb and poor diagnostic resource settings. After exhaustive search no relevant reference was found to support the result.

Conclusion

Due to scarcity of literature and unawareness of clinicians, usually NTM remain unreported or misinterpreted as MDR TB. Therefore, there is need for awareness regarding appropriate NTM diagnosis among physicians. NTM should be differentiated between colonization and disease by following the ATS diagnostic criteria. Every sample in the laboratory coming from clinically suspected pulmonary and extrapulmonary tuberculosis cases should be inoculated on LJ and LJ with PNB media specially in low budget set ups where molecular method are not available for NTM detection. Therefore, Growth on LJ with PNB media should be confirmed by at least with biochemical tests and MPT 64 antigen test.

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Conflict of Interest: The authors declare that there is no conflict of interest.

Ethics Statement: Maharishi Markendeshwar (Deemed to be University) Ethical Committee approved the study protocol (IEC No./MMIMSR/17/995) and informed consent was obtained from all the study participants.

References

1. Myneedu VP, Verma AK, Bhalla M, Arora J, Reza S, Sah GC, Behera D. Occurrence of nontuberculous mycobacterium in clinical samples—a potential pathogen. *Indian Journal of Tuberculosis*. 2013;60(2):71-6.
2. Griffith DE, Aksamit T, Brown-Elliott BA, Catanzaro A, Daley C, Gordin F, Holland SM, Horsburgh R, Huitt G, Iademarco MF, Iseman M. An official ATS/IDSA statement: diagnosis, treatment and prevention of nontuberculous mycobacterial diseases. *American journal of respiratory and critical care medicine*. 2007 Feb 15;175(4):367-416.
3. TB India Annual, 2018. (internet) Report. Central Tuberculosis Division, Ministry of Health & Family Welfare, Government of India, 2018
4. Mackie & Maccartini. *Book of practical medical microbiology*. Edt. 2013.
5. Bensi EP, Panunto PC, Ramos MD. Incidence of tuberculous and non-tuberculous mycobacteria, differentiated by multiplex PCR, in clinical specimens of a large general hospital. *Clinics*. 2013;68(2):179-84.
6. Nasiri MJ, Dabiri H, Fooladi AA, Amini S, Hamzehloo G, Feizabadi MM. High rates of nontuberculous mycobacteria isolation from patients with presumptive tuberculosis in Iran. *New microbes and new infections*. 2018 Jan 1;21:12-7
7. Jain S, Sankar MM, Sharma N, Singh S, Chugh TD. High prevalence of non-tuberculous mycobacterial disease among non-HIV infected individuals in a TB endemic country—experience from a tertiary center in Delhi, India. *Pathogens and global health*. 2014 Mar 1;108(2):118-22.
8. Shao Y, Chen C, Song H, Li G, Liu Q, Li Y, Zhu L, Martinez L, Lu W. The epidemiology and geographic distribution of nontuberculous mycobacteria clinical isolates from sputum samples in the eastern region of China. *PLoS neglected tropical diseases*. 2015 Mar 16;9(3):e0003623.
9. Wankhade B Archana, Ghadage Dhyaneswari, Bhore AV. Isolation and identification of mycobacterium from pus samples from various lesions. *Indian journal of research*. 2013 March. ISSN - 2250-1991
10. Myneedu VP, Verma AK, Bhalla M, Arora J, Reza S, Sah GC, Behera D. Occurrence of nontuberculous mycobacterium in clinical samples—a potential pathogen. *Indian Journal of Tuberculosis*. 2013;60(2):71-6.
11. Donohue MJ, Wymer L. Increasing prevalence rate of nontuberculous mycobacteria infections in five states, 2008–2013. *Annals of the American Thoracic Society*. 2016 Dec;13(12):2143-50.
12. Lee H, Myung W, Koh WJ, Moon SM, Jhun BW. Epidemiology of Nontuberculous Mycobacterial Infection, South Korea, 2007–2016. *Emerging infectious diseases*. 2019 Mar;25(3):569.
13. Sharma P, Singh D, Sharma K, Verma S, Mahajan S, Kanga A. Are We Neglecting Nontuberculous Mycobacteria Just as Laboratory Contaminants? Time to Reevaluate Things. *Journal of pathogens*. 2018;2018.
14. Wu ML, Aziz DB, Dartois V, Dick T. NTM drug discovery: status, gaps and the way forward. *Drug discovery today*. 2018 Aug 1;23(8):1502-19.
15. Boyle DP, Zembower TR, Qi C. Relapse versus reinfection of Mycobacterium avium complex pulmonary disease. Patient characteristics and macrolide susceptibility. *Annals of the American Thoracic Society*. 2016 Nov;13(11):1956-61.
16. Lee BY, Kim S, Hong Y, Lee SD, Kim WS, Kim DS, Shim TS, Jo KW. Risk factors for recurrence after successful treatment of Mycobacterium avium complex lung disease. *Antimicrobial agents and chemotherapy*. 2015 Jun 1;59(6):2972-7.

Clinical Evaluation of Pyuria, Bacteriuria and Culture for Diagnosis of Urinary Tract Infection

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Abstract

Background: Culture remains the gold standard for the diagnosis of urinary tract infections (UTIs). However, the diagnosis of UTIs can be potentially enhanced when clinical characteristics of UTI, pyuria and bacteriuria are considered.

Methodology: To evaluate the relationship between pyuria, bacteriuria and clinical characteristics with culture, un-centrifuged urine samples (N=817) were subjected to direct wet mount, direct Gram staining and semi-quantitative culture and the results were compared.

Results: The direct wet mount and direct gram staining showed an overall sensitivity, specificity, positive predictive value and negative predictive value of 11.08%, 88.88%, 87.96%, 29.28% and 34.21%, 96.55%, 91% and 38.89%, respectively, as compared to semi-quantitative culture. Alternatively, the overall sensitivity, specificity, positive predictive value and negative predictive value of clinical characteristics of both upper and lower UTIs (most sensitive and specific symptoms combined) were found to be 55.14%, 76.06%, 71.29%, 31.47%, respectively. Conclusion: Both the direct wet mount and direct Gram staining could be considered as screening tests for diagnosis of UTI due to its low sensitivity and high specificity. However, integrated approaches wherein clinical characteristics of UTI combined with culture results would be of high diagnostic value in the diagnosis of UTI.

Keywords: Urinary tract infection, significant bacteriuria, pyuria, semi quantitative urine culture.

Introduction

Urinary tract infections (UTI) are one of the most common bacterial infections that constitute major public health problem across the world. UTIs are the second most common infection in both hospitalized and community practices¹. UTIs are most common among females of reproductive age². UTI is a heterogeneous disease, which may be of various types such as acute and

chronic, complicated and uncomplicated, asymptomatic bacteriuria and recurrent cystitis³. Patients having lower UTI generally have symptoms like burning micturition, dysuria, frequency urgency, suprapubic pain. Upper UTI (e.g. pyelonephritis) may be characterized by fever with or without chills, flank pain, nausea, vomiting, diarrhoea, haematuria, fatigue and change in mental status. It is difficult to differentiate indubitably between upper and lower UTI due to the low sensitivity of these symptoms in diagnosing UTI⁴

Literature indicates that both pyuria (the presence of polymorphonuclear leukocytes (PMNs) in urine) and bacteriuria (presence of bacteria) are good indicators of bacterial infection other than genitourinary symptoms. Alternatively, the dipstick leukocyte esterase test is a simple technique having the advantage of detecting

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leukocyte esterase activity from both intact and lysed PMNs; however, when it is used alone, the sensitivity, specificity and positive predictive value are relatively low⁵. Significant bacteriuria increases the diagnostic value of UTI. The significant bacteriuria is defined as the presence of 10^5 or more colony forming units (CFU) per ml of urine⁶. This suggests that the presence of both pyuria and bacteriuria may markedly increase the probability of UTI⁷. However, currently, no published data are available to evaluate the significance of these parameters. Therefore, the current study was designed to evaluate the significance of pyuria, bacteriuria and clinical features of UTI with culture in the diagnosis of UTI.

Material and Method

The study was carried out (between October 2017 and March 2018) in the Department of Microbiology, M.M.I.M.S.R, Ambala). Mid-stream urine samples (5-10ml) were collected from patients having symptoms of UTI. Further, catheterized patients, post-chemotherapy and all other patients who were receiving or received antibiotics in the last one month were excluded from the current study. The clinical histories of all consecutive patients were collected. Immediately after the specimen collection, urine samples were transported to microbiology laboratory (most of the urine samples were processed within 2 hr. of the collection). This midstream urine sample was subjected to direct wet mount examination, direct gram staining and, semi-quantitative urine culture.

Laboratory Method: Direct wet mount; Direct wet mount was prepared by taking 50 μ l of an uncentrifuged urine sample on a glass slide (25x75 mm) and covered with a coverslip (22x22mm)⁸.

Gram stain; Each un-centrifuged urine sample was mixed and Gram-stained as per standard laboratory protocol⁹.

Microscopic examination; All the smears were examined using 40x high power objective (Nikon E100 - magnification 400x) for a minimum of seven fields and the cells per field were noted. For gram staining, a minimum of 20 microscopic fields was examined using 100x oil immersion objective (Nikon E100 - magnification 1000x) and the average number of organisms per field was recorded. The Gram stain was considered positive if one or more organisms per microscopic field were seen⁸.

Semi-quantitative urine culture: Uncentrifuged urine samples were cultured on cystine-lactose-electrolyte-deficient agar using calibrated loop technique as suggested by Clarridge et al¹⁰. Growth was recorded as $<10^2$, 10^2 - $<10^3$, 10^3 - $<10^4$, 10^4 - $<10^5$, or $\geq 10^5$ CFU/ml. Samples were considered positive (significant growth) if it contained $\geq 10^2$ - $\geq 10^5$ CFU/ml along with symptoms of UTI as mentioned in patient inclusion criteria of the current study.

Results

In the current study, urines samples were collected from all the patients recruited (N=841). The study profile, demographics and clinical characteristics of the study participants are presented in Table-1. The male-female ratio was 1:3.4(184/633). The most commonly affected age group was 34.5 (SD=15.5). Further, of the 69.76% (570/817) significant isolates obtained, 92.81% (529/570) isolates were having growth of a single type organism and the remaining 7.19% (41/570) showed multiple organisms (mainly two types organisms). However, for data analysis, each urine culture isolates (even multiple organisms) was considered as growth of single organism.

Table-2 demonstrates the comparison of the direct wet mount and Gram staining results with culture. of the 570 significant isolates obtained in culture, direct Gram staining could detect the presence of bacteria in 68.42% (390/570) cases. of these 68.42% isolates, 59.23% (231/390), 37.63% (147/390), 2.56% (10/390) and 0.5% (2/390) were having CFU of $\geq 10^5$, 10^4 - $<10^5$, 10^3 - $<10^4$ and 10^2 - $<10^3$ respectively. Similarly, of the 570 significant isolates obtained in culture, the direct wet mount could demonstrate the presence of WBCs in 98.25% (560/570) cases. of the 98.25% cases, 42.32% (237/560), 29.82% (167/560) and 18.57% (104/560) and 9.28% (52/560) were having significant growth of $\geq 10^5$, 10^4 - $<10^5$ and 10^3 - $<10^4$, 10^2 - $<10^3$, respectively. However, of these 98.25% (560/570) specimens, direct gram staining could detect the presence of bacteria in 68.04% (381/560) urine specimens.

Table-3 illustrates the diagnostic accuracy of the direct wet mount and direct Gram staining with culture. It is apparent from Table 3 that the difference between sensitivities of ≥ 5 bacilli/field and ≥ 1 - <5 bacilli/20 fields were not statistically significant (Fishers Exact test, p=0.5623). The urine specimens having six to ten WBCs per high power field (HPF) in the direct wet

mount of urine (Table-3) demonstrated relatively higher sensitivity and specificity than culture in the diagnosis of UTI. The direct wet mount and direct gram staining showed an overall sensitivity, specificity, positive predictive value and negative predictive value of

11.08%, 88.88%, 87.96%, 29.28% and 34.21%, 96.55%, 91% and 38.89%, respectively, as compared to semi-quantitative urine culture. It is evident from Table-3 that sensitivity of Gram staining was relatively higher than that of the direct wet mount.

Table 1: Comparison of demographics and clinical characteristics of patients with culture

Characteristics of Patients	Total number N=817 (%)	Culture				
		$\geq 10^5$ N=237 (%)	10^4 - $<10^5$ N=169 (%)	10^3 - $<10^4$ N=109 (%)	10^2 - $<10^3$ N=55 (%)	$<10^3$ N=247 (%)
Out patients	789 (96.57)	230 (97.04)	155 (91.72)	107 (98.17)	55 (100)	242(97.98)
In patients	28 (3.42)	7(2.95)	14 (8.28)	2 (1.83)		5 (2.02)
Gender						
Male	184 (22.52)	78(32.91)	23 (13.61)	11 (10.09)	13 (23.64)	59 (23.89)
Female	633 (77.47)	159 (67.09)	146 (86.39)	98 (89.91)	42 (76.36)	188 (76.11)
Age	34.5 (SD=15.5)	44.56 (SD=11.29)	26.69 (SD=4.49)	28.75 (SD=4.8)	32.89 (SD=5.2)	33.43 (SD= 17.96)
Infections in pregnancy (not included asymptomatic bacteriuria)	76 (9.30)	1 (0.42)	22 (13.01)	8 (7.34)	4 (7.27)	41 (16.6)
Infections due to any anatomical anomalies (e.g. an obstruction, hydronephrosis, renal tract calculi)	57 (6.98)	3 (1.27)	15 (8.88)	1 (0.92)		38 (15.38)
Genital tract infection***	42 (5.14)	3 (1.27)	15 (8.88)	1 (0.92)	2 (3.64)	21 (8.50)
Infections due to immune compromised (e.g. diabetes, elderly population)	114 (13.95)	60 (25.32)	3 (1.78)	13 (11.93)		38 (15.38)
Recurrent UTI (Recurrent infections despite adequate treatment)	16 (1.96)	-	-	2 (1.83)		14 (5.67)
Symptoms of UTI						
Upper UTI						
Fever with or without chills and rigors	473 (57.89)	165 (69.62)	90 (53.25)	46 (42.21)	21 (38.18)	151 (61.13)
Flank pain	540 (66.09)	174 (73.42)	98 (57.99)	72 (66)	29 (52.73)	167 (67.61)
Vomiting	307 (37.58)	112 (47.26)	74 (43.79)	44 (40.37)	15 (27.27)	62 (25.11)
Diarrhea	217(26.57)	94 (39.66)	71 (42.01)	16 (14.68)	7 (12.73)	29 (11.74)
Fatigue (Generalized weakness)	453 (55.45)	135 (56.96)	104 (61.54)	46 (42.21)	28 (50.91)	140 (56.68)
Hematuria	73 (8.93)	38 (16.03)	29 (17.16)	-	-	6 (2.43)
Change in mental status (Confusion)	114 (13.95)	19 (8.01)	6 (3.55)	6 (5.51)	4 (7.27)	79 (31.99)
Lower UTI						
Burning micturition	374 (45.77)	129 (54.43)	72 (42.6)	76 (69.72)	16 (29.09)	81 (32.79)
Painful micturition (dysuria)	257 (31.46)	108 (45.57)	53 (31.36)	43 (39.45)	22 (40)	31 (12.55)
Increased frequency	359 (43.94)	96 (40.51)	80 (47.33)	60 (55.05)	35(63.64)	88 (35.62)
Urgency	211 (25.83)	33 (13.92)	42 (24.85)	17 (15.6)	22(40)	97 (39.27)
Suprapubic pain	287 (35.12)	107(45.15)	37 (21.9)	21 (19.27)	19(34.54)	103 (41.71)

Table 2: Comparison of direct wet mount and Gram staining with culture results

Method	Culture (CFU/ml)				
	≥10 ⁵ (N= 237)%	10 ⁴ -<10 ⁵ (N= 169)%	10 ³ -<10 ⁴ (N=109)%	10 ² -<10 ³ (N=55)%	<10 ² (N= 247)%
No WBC/7 HPFs (N=10)	-	2(1.18)	5(4.59)	3(5.45)	-
0-1 WBC/7 HPFs (N=69)	9(3.79)	17(10.06)	14(12.84)	5(9.09)	24(9.72)
1-5/HPF(N=375)	53 (22.36)	73(43.2)	30(27.52)	-	219(88.66)
6-10/HPF(N=195)	45(18.99)	43(25.44)	60(55.05)	47(85.45)	-
11-15/HPF(N=33)	29(12.24)	4(2.37)	-	-	-
16-25/HPF(N=42)	24(10.13)	18(10.65)	--	-	-
26-50/HPF(N=43)	31(13.08)	12(7.11)	-	-	-
51-75/HPF (N=21)	20(8.44)	-	-	-	1(0.41)
75 and above/HPF(N= 29)	26(10.97)	-	-	-	3(1.21)
Direct Gram staining		-	-	-	-
≥5 bacteria/field, (N= 209)	135(56.96)	71(42.01)	3(2.75)	-	-
≥1- <5 bacteria/20 fields (N=198)	96(40.51)	76(44.97)	7(6.42)	2(3.64)	17(6.88)
No bacteria/20 fields (N=410)	6(2.53)	22(13.01)	99(90.83)	53(96.36)	230(93.11)

Table 3: Diagnostic accuracy of direct wet mount and direct with culture results

Wet Mount (40x High Power Field)	Culture*(CFU/ml) N= 817			Sensitivity %	CI%	Specificity %	CI%	PPV%	CI%	NPV%	CI%
	+	-									
No WBC/7HPFs	+	10	0	1.7	0.8-3.3	100	98-100	100	65.55-100	30.6	27.46-33.94
	-	560	247								
0-1 WBC/7 HPFs	+	45	24	7.8	5.8-10.49	90.28	85.76-93.5	65.2	52.71-76.01	29.8	26.58-33.25
	-	525	223								
1-5/HPF	+	156	219	27.36	23.79-31.26	11.33	7.7-16.12	41.6	36.59-46.78	6.3	4.32-9.13
	-	414	28								
6-10/HPF	+	195	0	34.21	30.34-38.28	100	98.09-100	100	97.59-100	39.71	35.86-43.68
	-	375	247								
11-15/HPF	+	33	0	5.7	4-8.11	100	98-100	100	87.01-100	31.5	28.2-34.9
		537	247								
16-25/HPF	+	42	0	7.36	5.42-9.9	100	98.09-100	100	89.56-100	31.87	28.62-35.3
		528	247								
26-50/HPF	+	43	0	7.54	5.57-10	100	98.09-100	100	89.79-100	31.91	28.66-35.34
	-	527	247								
51-75/HPF	+	20	1	3.5	2.21-5.46	99.59	97.41-99.9	95.23	74.12-99.7	30.9	27.73-34.26
		550	246								
75 and above/HPF	+	26	3	4.56	3.05-6.7	98.78	96.2-99.68	89.65	71.5-97.2	30.96	27.77-34.34
	-	544	244								
Gram Staining (100x Oil Immersion/)	Culture*(CFU/ml) N=817										
≥5 bacilli/field	+	+	-	36.67	32.72-40.78	100	98.09-100	100	97.75-100	40.63	36.71-44.66
	-	209	0								
		361	247								
≥1- <5 bacilli/20 fields	+	181	17	31.75	27.98-35.78	93.11	89-95.8	91	86.38-94.7	37.15	33.38-41.6
	-	389	230								

*Number of significant growth (≥10³ to ≥ 10⁵ CFU/ml), N=570 and insignificant growth (<10³ CFU/ml), N=247)

Discussion

Accurate diagnosis of UTI is challenging because of the lack of both sensitive and specific laboratory tests. The current study was conducted to evaluate the relationship between direct wet mount (for WBCs in urine), direct Gram staining (for bacteria in urine) and genitourinary symptoms with semi-quantitative urine culture (the gold standard for diagnosis of UTI)¹¹. The other vital features of the study design were the inclusion of patients with a minimum of at least two symptoms of either upper or lower UTI (or symptoms of both). Further catheterized patients, post chemotherapy and all other patients who were receiving antibiotics or received antibiotics in last ten days were excluded from the study as any kind of antibiotic intake may affect the growth of bacteria in culture. These criteria helped in excluding most of the patients receiving antibiotic particularly inpatients. In the current study, most predominant organism isolated was *Escherichia coli* (55.79%), *Klebsiella pneumonia* (9.12%) and *Enterococcus* species (8.42%), respectively. This distribution was comparable with previous workers wherein the incidence of *Escherichia coli*, *Klebsiella* species and *Enterococcus* species varied between 53-72%, 6-12%, 1.7-12%, respectively¹²⁻¹³.

Pyuria is a condition wherein an increased number of polymorphonuclear leukocytes (PMNs) are excreted in the urine. This excretion of PMNs may be an indication of an inflammatory response in the genitourinary tract¹⁴. In the current study, it is evident from the Table-3 that urine specimens having six to ten WBCs per HPF in the direct wet mount demonstrated relatively higher sensitivity (34.21%) and specificity (100%) with culture for the diagnosis of UTI. This clearly explains that the presence of WBCs is more specific but relatively less sensitive for the diagnosis of UTI. It is also evident from Table-3 that urine samples containing 1-5 WBCs/HPF were having low sensitivity and specificity when compared with urine samples containing 6-10 WBCs/HPF. However, the sensitivity of direct wet mount (for diagnosis of UTI) was decreasing for urine specimens containing a comparatively higher number of WBCs per HPF (>11 or more). This low sensitivity of pus cells in direct wet mount reaffirms the high specificity of WBCs for diagnosis of UTI. Further, it is evident from Tables (2 and 3) that four urine specimens were positive for sterile pyuria. This may be substantiated due to the fact that sterile pyuria is usually seen in patients having renal tuberculosis, sexually transmitted diseases, or inflammatory diseases like interstitial nephritis,

indicating pyuria itself is not a marker for diagnosis of UTI and is not effective in differentiating symptomatic and asymptomatic UTI.

It is estimated that the presence of one or more bacteria per oil immersion field reciprocates with most of the significant bacteriuria cases and thus suggest the presence of active UTI^{9,11,15-16}. In the current study, it is evident from Table-2 that direct Gram staining could detect the presence of bacteria in 68.42% (390/570) cases of significant growth. However, this low detection rate may be attributed to the low sensitivity of Gram stain to detect the presence of bacteria, particularly in urine specimens having <10³CFU/ml¹⁷⁻²¹. Further, it is apparent from Table-3 that there was no difference between sensitivities of ≥ 5 bacilli/field and ≥ 1 - <5 bacilli/20 fields. This clearly substantiates the fact that one or more bacteria per field indicate significant bacteriuria. Further, it was also observed that the sensitivity of Gram staining was relatively higher than that of the direct wet mount. This may be attributed to high specificity and low sensitivity of direct wet mount in the diagnosis of UTI. The presence of any bacteria in midstream urine may indicate bacteriuria. The other advantages of Gram staining include; rendering instant information about the nature of the infecting organisms and thus assisting the physician for choosing appropriate empirical therapy²¹.

Conclusion

Both direct wet mount and direct Gram staining (from uncentrifuged urine) were having comparatively low sensitivity but high specificity for the diagnosis of UTI as compared to culture. Therefore, direct wet mount or direct gram staining may be considered as screening tests for the diagnosis of UTI. However, an integrated approach wherein clinical characteristics of UTI (having both higher sensitivity and specificity) when combined with culture would be of high diagnostic value in the diagnosis of UTI.

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Ethics Statement: Ethical Committee approved the study protocol (IEC No./MMIMSR/17/156).

Reference

1. Rowe TA, Juthani-Mehta M. Diagnosis and management of urinary tract infection in older

- adults. *Infect Dis Clin North Am.* 2013, 28:75-9.
2. Minardi D, d'Anzeo G, Cantoro D, et al. Urinary tract infections in women: etiology and treatment options. *Int J Gen Med.* 2011,4:333-43.
 3. Wilson ML, Gaido L. Laboratory diagnosis of urinary tract infections in adult patients. *Clin Infect Dis.* 2004,38:1150-158.
 4. Najjar MS, Saldanha CL, Banday KA. Approach to urinary tract infections. *Indian J Nephrol.* 2009,19:129-39.
 5. Stamm WE, Counts GW, Running KR, et al. Diagnosis of coliform infection in acutely dysuric women. *N Engl J Med.* 1982, 307:463-8.
 6. Kass EH. Asymptomatic infections of the urinary tract. *Trans Assoc Am Physicians.* 1956, 69:56-64.
 7. Loveday HP, Wilson JA, Pratt RJ, et al, UK Department of Health. epic3: national evidence-based guidelines for preventing healthcare-associated infections in NHS hospitals in England. *J Hosp Infect.* 2014,86:S1-S70.
 8. Washington J A, C M White, M Laganieri and L H Smith. Detection of significant bacteriuria by microscopic examination of urine. *Lab Med.* 1981,12:294-296.
 9. Tille M P. Bailey and Scott's diagnostic microbiology, In: Role of microscopy, St. Louis, Missouri: Elsevier Mosby; 2014, p. 68-70.
 10. Baron EJ, Miller JM, Weinstein MP, et al. A guide to utilization of the microbiology laboratory for diagnosis of infectious diseases: 2013 recommendations by the Infectious Diseases Society of America (IDSA) and the American Society for Microbiology (ASM)(a). *Clin Infect Dis.* 2013, 57(4):e22-e121.
 11. Hooton TM, Stamm WE. Diagnosis and treatment of uncomplicated urinary tract infection. *Infect Dis Clin North Am.* 1997, 11:551-81.
 12. Grude N, Tveten Y, Kristiansen B-E. Urinary tract infections in Norway: bacterial etiology and susceptibility. A retrospective study of clinical isolates. *Clin Microbiol Infect.* 2001, 7:543-547.
 13. Gupta K, Sahm DF, Mayfield D, et al. Antimicrobial resistance among uropathogens that cause community-acquired urinary tract infections in women: a nationwide analysis. *Clin Infect Dis.* 2001, 33:89-4.
 14. Stamm WE. Measurement of pyuria and its relation to bacteriuria. *Am J Med.* 1983, 75(Suppl 1B):53-8.
 15. Jenkins, R D, J P Fenn and J M Matsen. Review of urine microscopy for bacteriuria. *JAMA.* 1986, 255:3397-403.
 16. Pollock, H M 1983. Laboratory techniques for detection of urinary tract infections and assessment of value. *Am. J. Med.* 75(Suppl. 1B):79-84.
 17. Marques AG, Doi AM, Pasternak J, et al. Performance of the dipstick screening test as a predictor of negative urine culture. *Einstein (Sao Paulo).* 2017;15(1):34-9.
 18. Cardoso CL, Muraro CB, Siqueira VL, et al. Simplified technique for detection of significant bacteriuria by microscopic examination of urine. *J Clin Microbiol.* 1998, 36(3):820-3.
 19. Goswitz JJ, Willard KE, Eastep SJ, et al. Utility of slide centrifuge gram's stain versus quantitative culture for diagnosis of urinary tract infection. *Am J Clin Pathol.* 1993, 99(2):132-6.
 20. Jorgensen, J. H. and P. M. Jones. Comparative evaluation of the limulus assay and the direct Gram stain for detection of significant bacteriuria. *Am J Clin Pathol.* 1975, 63:142-48.
 21. McNair RD, MacDonald SR, Dooley SL, et al. Evaluation of the centrifuged and Gram-stained smear, urinalysis and reagent strip testing to detect asymptomatic bacteriuria in obstetric patients. *Am J Obstet Gynecol.* 2000, 182:1076-79.

Detection and Enumeration of Parasitic Infections in Stool Samples from Tertiary Care Hospital of Rural Setting

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Abstract

Background: Parasitic infections are the major public concern particularly in developing countries like India. Routinely used microscopy method for the detection of parasitic infections have compromised sensitivity.

Materials and Method: The study was carried out on 500 stool samples received in Department of Microbiology MMIMSR, Mullana (Haryana) for a period of 6 months (August 2017 to January 2018). Stool samples for detection of ova and cyst were included.

Result: Of these 500 samples examined, 235 (47%) stool samples showed positive results for ova/cyst after the use of simple salt floatation technique while it was merely 33% (n-165) without using the salt floatation method. of the 235 positive samples 29.8% were cyst of *Giardia lamblia* followed by eggs of *Ascaris lumbricoides* (Fertilized and unfertilized) and cyst of *Entamoeba histolytica* each of 19.1%, *Ancylostomoduodenale* 14.9%, *Hymenolepis nana* 10.6%, *Entamoeba coli* 4.2% and *Trichuris trichiura* 2.1% were also identified.

Conclusion: There is a need for more tests that do not sacrifice sensitivity and that can be used in poor resource field settings.

Keywords: Parasitic infection diagnosis, Ova/cyst, stool samples.

Introduction

Parasitic infections remain the major global health problem particularly in developing countries.¹ Prevalence of parasitic infections varies in different geographical area. It depends upon a number of factors like level of sanitation, socioeconomic status, malnutrition, population density of the area, low health status, unavailability of potable drinking water and lack of personal hygiene.^{2,3} Intestinal parasitic infections are recognized as neglected tropical diseases because of lack of adequate research, inability to prevent by

immunization as no effective vaccine is available against them, compromised investigative modalities for the diagnosis of parasitic infections are among the major drawbacks to fight against this neglected public health problem.^{4,5}

The infirmities caused by parasitic diseases vary from mild discomfort to severe manifestations. Some parasites may lead to anaemia and protein malnutrition which can be the cause of growth retardation in children.³ Amoebiasis, ascariasis, hookworm infection are the most common infections responsible for iron-deficiency anaemia, chronic diarrhoea and impaired physical development in children along with other comorbidities.^{5,6}

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The routinely used method for the detection of Ova/cysts in diagnostic laboratories are wet mounts like saline wet mount and iodine wet mount. But the sensitivity of this method is compromised i.e. false negative results

which affects the treatment adversely and leads to worsening of symptoms and spread of infection in the community.⁷

The burden of intestinal parasitic infections needs to be cautiously monitored in the developing countries. Several studies have been undertaken in different parts of India. In India, the overall prevalence rate ranges from 12.5% to 66%. The prevalence rate for individual parasite varying from region to region.^{3,7,8,9} These infections still continue to predominate and similar studies would definitely add to the existing knowledge of parasitic infections in patients suffering from gastrointestinal problems.

According to literature detection rate of parasite can be improved by use of staining method like Lactophenol cotton blue and various concentration techniques.¹⁰

Lactophenol cotton blue stains internal structure of parasites and facilitates their detection and identification.^{11,12} Lacto-phenol cotton blue preparation is made by using glycerol which is hygroscopic in nature, which help to absorb the water molecules from the environment and prevents the drying the wet mount preparation.¹⁰

Addition use of concentration techniques can detect parasites which are present in small numbers which can be missed easily by using direct wet mounts.³ Various concentration techniques are available and can be used for the detection of the parasitic infections depending upon availability of resources. So there is dire need of simple, economical, reliable and sensitive diagnostic method for the detection of these parasitic infections.

By keeping in mind the above facts, we have planned a study with following objectives:

- To detect parasitic infections by using wet mount preparations like saline, iodine and staining method like lacto phenol cotton blue wet mount before and after applying concentration technique.
- To see the effect of concentration technique for the detection of ova/cyst from stool samples over microscopy alone without concentration techniques.

Materials and Method

The prospective study was carried out on 500 stool samples received in Department of Microbiology MMIMSR, Mullana (Haryana) for a period of 6 months

(August 2017 to January 2018). Ethical Clearance: Taken from Institutional ethical committee. Stool samples for detection of ova and cyst were included.

Methodology

The patients were provided wide mouthed clean, dry, properly labelled plastic container for collection of samples. The stool samples were examined within 1-2 hours of collection. The stool samples which were contaminated with the patient's urine were rejected. Both the formed and the unformed stools were examined freshly. After the macroscopic examination of the stool including colour, consistency, presence of blood and mucus were noted. The stool specimens were examined for the presence of worms like segments of *Taenia*, adult Hookworm, round worm either with the naked eye or with the aid of a hand lens.⁴

Each stool specimen was processed by the direct microscopy including Saline wet mount, Iodine wet mount, Lactophenol cotton blue and concentration technique using simple salt floatation method.^{13,14}

Results

A total of 500 stool samples were examined. of these 500 samples examined, 235 (47%) stool samples showed positive results for ova/cyst after the use of simple salt floatation technique while it was merely 33% (n-165) without using the salt floatation method. (Table 1).

Of the total 235 positive samples 42.5% was from the age group 6-14 years, followed by 21.28% from the age group 0-5 years, followed by 17.1% in the age group above 60 years, followed by 10.6% and 6.4% in the age group 15-30 years and 46-60 years respectively and the least positivity rate was seen in the age group 31-45 years. (Figure I).

Of the 235 positive samples 29.8% were cyst of *Giardia lamblia* followed by eggs of *Ascaris lumbricoides* (Fertilized and unfertilized) and cyst of *Entamoeba histolytica* each of 19.1%, *Ancylostoma duodenale* 14.9%, *Hymenolepis nana* 10.6%, *Entamoeba coli* 4.2% and *Trichuris trichiura* 2.1% were also identified. (Table II).

Photographs showing *Hymenolepis nana* in saline (P1a), Iodine (P1b) and Lactophenol Cotton blue wet mount (P1c).

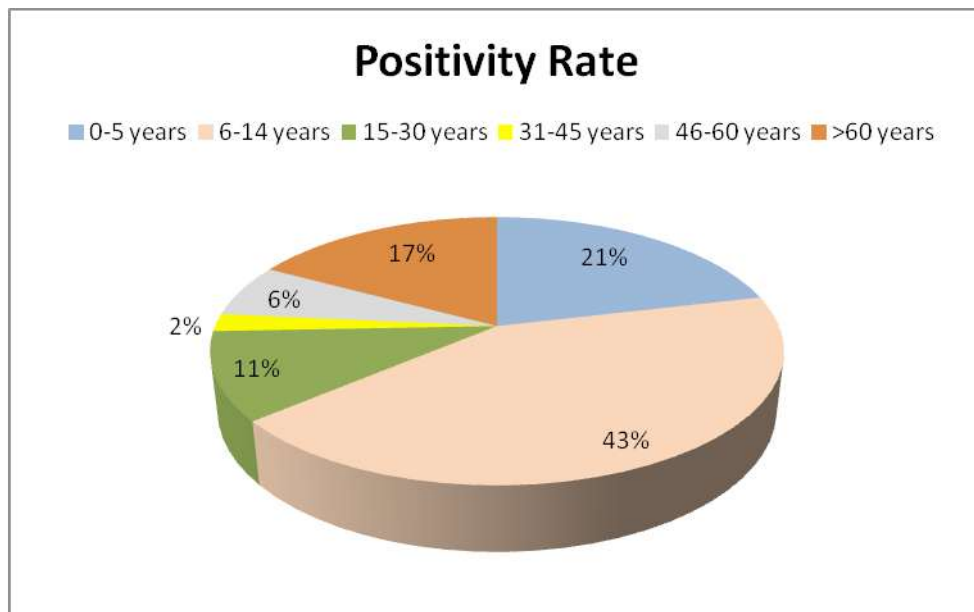


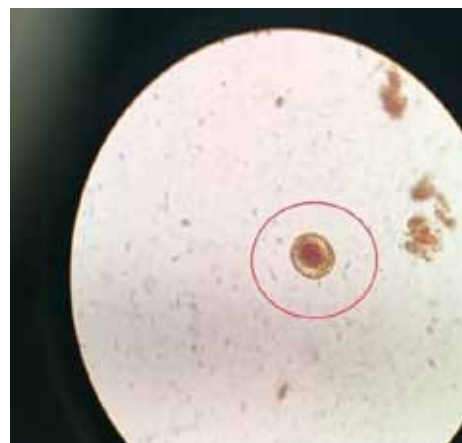
Figure I: Age wise prevalence of parasitic infection

Table I: Positivity rate before and after concentration technique

Total Sample	Positivity Before Salt Floatation Method	Positivity After Salt Floatation Method
500	165	235

Table II: Distribution of Parasites in total Positive Sample

Parasite	Number	Percentage
Giardia lamblia cyst	70	29.8%
Ascaris lumbricoides eggs (Fertilized and unfertilized)	45	19.1%
Entamoeba histolytica cyst	45	19.1%
Ancylostoma duodenale egg	35	14.9%
Hymenolepis nana egg	25	10.6%
Entamoeba coli cyst	10	4.2%
Trichuris trichiura egg	5	2.1%



Photograph I (a) and (b): Saline and Iodine wet mount showing Hymenolepis nana egg



Photograph I (c): Lactophenol cotton blue wet mount showing Hymenolepis nana egg



Discussion

Parasitic infections are the significant cause of morbidity and mortality in developing countries like India. Method for the diagnosis of parasitic infections have stagnated in the past three decades. Labor-intensive method such as microscopy still remain the mainstay of several diagnostic laboratories.¹⁵ There is a need for more tests that do not sacrifice sensitivity and that can be used in poor resource field settings. In our study we had used lacto-phenol cotton blue staining technique in addition to routine wet mounts which helped demonstration of better morphology so made identification easier and also used simple salt floatation technique; by this technique we were able to diagnose 70 more positive samples as compared to wet mount examination alone.

In the present study positivity rate was 47%. Previous study in our department showed slightly lower positivity rate.³

Of the total 500 samples maximum positivity rate was 43% from the age group 6-14 years and least was 2% in the age group 31-45 years. A study done by Parameshwarappa et al, showed highest prevalence of parasitic infection between age group 10-20 years.¹⁷ The reason for higher rate of prevalence of intestinal parasitic infection in these age groups may be due to lack of awareness, lack of health care, education level.¹⁶

In the present study the maximum positivity i.e. 29.8% was shown by *Giardia lamblia*, followed by *Ascarislumbricoides* eggs (Fertilized and unfertilized) and *Entamoeba histolytic* cyst i.e. 19.1% each which was followed by *Ancylostomaduodenale* egg i.e. 14.8%, followed by *Hymenolepisnana* egg 10.7% and *Entamoeba coli* cyst 4.2%. And least positivity was shown by *Trichuristrichiura* (2.3%). A study done by Rajvir Singh et al. showed higher prevalence for *Giardia lamblia* 58.5%.¹⁷ In another study done by Kang et al.; commonest parasitic infection was hookworm followed by *Giardia* and *Cryptosporidium*.¹⁸ Sorevalence of different ova/cyst differs from area to area which can be due to different food habits in different regions, differences in geographical conditions and culture practices accounts for variations in parasitic prevalence

Of the 500 samples positivity rate before salt floatation was 33% (n-165) and 47% (n-235) with the addition of salt floatation method, showing higher prevalence of intestinal parasites by including simple salt floatation method, related to the study done by

Parameshwarappa KD et al., 38% was positivity rate before salt floatation method and 42% with simple salt floatation method.⁷

This study also showed advantage of Lactophenol cotton blue wet mount above iodine wet mount and saline wet mount. This was in accordance with the study done S.C. Parija et al in their study they concluded that Lactophenol cotton blue helps to stain the internal organs of the ova and cyst and easy to identify the internal parasites.⁸

Conclusion

Intestinal parasitic infection is on the rise and remains the cause of concern. Improvements in sanitation, limiting open defecation by provisions of sanitary latrines for all and hygiene and health education are the required interventions that will be helpful in preventing these infections. Such types of hospital-based studies are always helpful in accessing the present burden of parasitic infections in patients suffering from gastrointestinal diseases. Our study would surely add to the existing knowledge of parasite prevalence in such type of patients and serve as a measure of their inclination toward the health indicators.

Conflict of Interest: None

Source of Funding: None

Ethical Clearance: Taken from Institutional ethical committee of MMIMSR, Mullana, Ambala.

References

1. Norhayati M, Fatmah MS, Yusof S, Edariah AB. Intestinal parasitic infections in man: a review. *Med J Malaysia*. 2005; 58(2):296-305.
2. Chandrashekar V. Detection and Enumeration of the Commonest Stool Parasites Seen in a Tertiary Care Center in South India. *ISRN Tropical Medicine*. 2013 Jun 23; 2013.
3. Garg R, Singh V.A. Identification of parasitic infections in stool samples by different method: a study emphasizing the use of concentration technique- India. *Sch. J. App. Med. Sci*. 2017; 5(1C):159-161.
4. Sahimin N, Lim YAL, Ariffin F. Migrant workers in Malaysia: current implications of sociodemographic and environmental characteristics in the transmission of intestinal parasitic infections.

- PLoS Neglected Tropical Diseases. 2016; 10(11) : e0005110.
5. Shobha M, Bithika D, Bhavesh S. The prevalence of intestinal parasitic infections in the urban slums of a city in Western India. *Journal of infection and public health*. 2013; 6:142-149.
 6. Kumar S, Nag VL, Dash S, Maurya AK, Hada V, Agrawal R, et al. Spectrum of parasitic infections in patients with diarrhoea attending a tertiary care hospital in Western Rajasthan, India. *Journal of Clinical and Diagnostic research*. 2017;11(8):DC01-DC04.
 7. Parameshwarappa KD, Chandarkanth C, Sunil B. The Prevalence of Intestinal Parasitic Infestations and the Evaluation of Different Concentration Techniques of the stool examination. *J clinical and Diagnostic Research*. 2012; 6(7): 1188-1191.
 8. Ramesh GN, Malla N, Raju GS, Sehgal R, Ganguly NK, Mahajan RC, et al. Epidemiological study of parasitic infestations in lower socio-economic group in Chandigarh (North India). *Indian J Med Res* 1991; 93:47-50.
 9. Singh S, Raju GV, Samantaray JC. Parasitic gut flora in a north Indian population with gastrointestinal symptoms. *Trop Gastroenterol* 1993; 14:104-8.
 10. Parija SC, Prabhakar PK. Evaluation of Lacto-Phenol cotton blue for wet mount preparation of feces. *J Clin Microbiol*.1995; 33(4):1019-1021.
 11. Goncalves ML, Araujo A, Ferreira LF. Human intestinal parasites in the past:new finding and review. *Mem Inst Oswaldo Cruz*.2003; 98:103-18.
 12. Donaldson SR. An easy and rapid method for detecting protozoal cysts in feces by mean of wet stained preparations. *Lancet*.1917; 1:571-573.
 13. Sastry AP, Bhat SK. Laboratory diagnosis of parasitic infections In *Essentials of Medical Parasitology*,1st edition, 2014: 295-296.
 14. Chatterjee KD. Diagnostic procedures In *Parasitology (Protozoology and Helminthology)*, 13th edition, 2009: 293.
 15. Ricciardi A, Ndao M. Diagnosis of parasitic infections: What's Going On? *Journal of biomolecular screening* .2015;20(1):6-21.
 16. Tandukar S, Sherchan J B, Thapa P, Malla D, Bhandari D, Ghaju R et al. Intestinal Parasitic infection among school children- Kathmandu. *Austin J Pediatr*. 2015; 2(2): 1022.
 17. Singh R, Singla P, Sharma M, Aparna, Chaudhary U Prevalence of intestinal Parasitic infections in a Tertiary care hospital- Rohtak, India. *Int J Microbiolo Appl Sci*. 2013; 2(10):112-117.
 18. Kang G, Mathew MS, Rajan DP, Daniel JD, Mathan MM, Mathan VI et al. The prevalence of intestinal parasites in rural southern Indans. *Trop Med and Int Health* 1998; 3(1): 70-75.

Evolution Proof-Antibiotics: A Hopeful Future to Combat Antibiotics Resistance

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Abstract

Over the years we have seen many antibiotics have been developed, each one supposedly better than the previous, but still we have not been able to overcome the persistent problem of antibiotic resistance regardless of the potency of the drug. There is an urgent need to develop new antibiotic strategies to overcome this problem that is different from previous efforts. Hence a method should be focused on the area of inhibition of bacterial evolution for resistance-“evolution proof Antibiotics”.

Keywords: Antibiotics, miracle molecules, Anti microbial resistance (ARM), Evolution proof molecules, evolvability factor.

Introduction

Evolution is cleverer than we are. Over the years hundreds of “miracle” molecules- (antibiotics) have been discovered that have brought many pernicious infections to heel. But every time researchers identify a new drug, resistance arises regardless of the nature or potency of the drug. Anti microbial resistance (ARM) is global problem; causes of which may be: over-population, enhanced global migration, wildlife spread, excessive use of antibiotics in humans as well in animals, over-the-counter sale of antibiotics, selection pressure, poor sanitation, poor sewerage disposal system, release of nonmetabolized antibiotics or their residues into the environment through feces etc.^{1,2} There is increasing evidence that directly associates antibiotic use with

the emergence of resistant bacteria such as methicillin-resistant staphylococcus aureus (MRSA), vancomycin resistant enterococcus, resistant gram negative bacilli and clostridium difficile. This often lead to development of superbugs and will limit the therapeutic options in the treatment of even minor infections making them life threatening ones.³ We thrust; they (bacteria) parry. In vitro development of resistance to last resort drug colistin in *Pseudomonas aerogenosa* has shown the power of adaptive mutations in response to increasing dose of drug due to the network of genetic changes.⁴ These bacteria evolve rapid resistance and also express an additional factor of cross-resistance. This shows the inherent capacity of the bacteria to overcome the huge spectrum of antibiotics and further flourishing the problem of antibiotic resistance.⁵

1930s to 1960s remained the “golden era” of antibiotics which gave rise to many antibiotics. Unfortunately, this era came to the end because scientists were unable to maintain the pace of antibiotic discovery with regards to emerging resistant pathogens.⁶ Estimates suggest that antimicrobial resistance causes at least 700,000 deaths every year worldwide, a figure that could rise to 10 million by 2050 and surpass cancer as the primary global cause of death. Organizations like the Centers for Disease Control and Prevention (CDC)

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and World Health Organization (WHO) have declared antibiotic resistance to be a “global public health concern.”^{7,8}

Analysis of bacterial genomes concluded that over 20,000 potential resistance genes (r genes) are present. However, the functional resistance determinants are far less in number.^{6,9}

Discussion

Although many recommendations and resolutions have been proposed, several reports have also been written, the increase in antibiotic resistance is a persistent issue. Most of our strategies against pathogenic bacteria have focused on developing new antibiotic drugs, but the resistance has arisen to every antibiotic. There should be an alternate strategy to resolve this problem: inhibiting evolution. Lowering mutation rates in bacteria might be a way to hinder the emergence of antimicrobial pathogens. There can be two kinds of ‘evolution-proof’ antibiotics. The first category can literally be evolution-proof antibiotics to which bacteria cannot become resistant by mutation or horizontal gene transfer. The second category can be of molecules to which resistance may arise, but so rarely that it does not become epidemic.¹⁰

To overcome this hurdle we need to understand the molecular trajectories and the biochemical pathways associated with the development of resistance. A major success has been achieved with the identification of Mfd; an evolvability factor. The term evolvability factor refers to the protein that has the ability to increase mutation rate and so accelerates the bacterial evolution. Mfd is a highly conserved ATP dependent DNA translocase that mediates the role of Transcription-Coupled-DNA-Repair (TCR) in bacteria. Mfd enhance mutations at genetic level leading to hypermutator alleles which eventually result in development of resistance in bacteria and that this holds true for multiple classes of antibiotics. Mfd promotes mutagenesis in bacteria both during laboratory growth and during infection of eukaryotic cells. Researchers have found that disabling the protein Mfd reduced mutation rate and the ability of pathogenic bacteria such as *Mycobacterium tuberculosis* (Mtb) and *Salmonella typhimurium* to develop resistance to antibiotics. Tests were done using wild-type and Mfd-deficient *M. tuberculosis* which showed marked differences in the ability of bacteria to develop resistance to rifampicin drug. The bacterial strains lacking Mfd protein had 1,000-fold lower resistance to

the drug. In *S. typhimurium* Mfd was seen to promote hypermutation—a key mechanism that leads to rapid AMR development. About half of the strains studied developed hypermutator alleles during the course of developing resistance towards the drug trimethoprim. In contrast, strains lacking the protein Mfd didn’t form hypermutator alleles.¹¹

At present, while developing new drugs our target is mainly essential proteins but this approach has its own limitations. The alarming rate at which the microorganisms are adapting to our present drugs, the need is to address the problem at its core level i.e. developing drugs which will function as “anti-evolution” drugs that specifically block evolvability factors like Mfd or other evolvability factors that promote mutagenesis could be a revolutionary strategy to alleviate the problem of chromosomally acquired mutations that promote AMR.^{11,12}

Conclusion

To fight the growing number of antibiotic-resistant bacteria; researchers are focusing on the need for new approach to find novel antibiotics. Inactivate the evolvability factors is an unexplored route towards “battling the AMR crisis.” This concept of an “evolution-proof” antibiotic seems more of a dream rather than a reality. In the present scenario, it may be a stepping stone to more rigorous and concrete models in the hopeful future.

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References

1. Singer AC, Shaw H, Rhodes V, Hart A. Review of antimicrobial resistance in the environment and its relevance to environmental regulators. *Front Microbiol.* 2016;7:1728.
2. Marshall BM, Levy SB. Food animals and antimicrobials: impacts on human health. *Clin Microbiol Rev.* 2011;24(4):718–733.
3. Lipsitch M, Samore MH. Antimicrobial use and antimicrobial resistance: a population perspective. *Emerg Infect Dis.* 2002 Apr;8(4):347-54.

4. Mehta HH, Prater AG, Shamoo Y. Using experimental evolution to identify druggable targets that could inhibit the evolution of antimicrobial resistance. *J Antibiot (Tokyo)*. 2018 Feb;71(2):279-86.
5. Barbosa C, Trebosc V, Kemmer C, Rosenstiel P, Beardmore R, Schulenburg H, Jansen G. Alternative Evolutionary Paths to Bacterial Antibiotic Resistance Cause Distinct Collateral Effects. *Mol Biol Evol*. 2017 Sep 1;34(9):2229-44.
6. Nathan C, Cars O. Antibiotic resistance-problems, progress and prospects. *N Engl J Med*. 2014;371(19):1761-1763.
7. Michael CA, Dominey-Howes D, Labbate M. The antimicrobial resistance crisis: causes, consequences and management. *Front Public Health*. 2014;2:145.
8. Spellberg B, Srinivasan A, Chambers HF. New societal approaches to empowering antibiotic stewardship. *JAMA*. 2016;315(12):1229-1230
9. Davies J, Davies D. Origins and evolution of antibiotic resistance. *Microbiol Mol Biol Rev*. 2010;74(3):417-433
10. Bell G, MacLean C. The Search for 'Evolution-Proof' Antibiotics. *Trends Microbiol*. 2018; 26(6): 471-483.
11. Ragheb MN, Thomason MK, Hsu C, et al. Inhibiting the Evolution of Antibiotic Resistance. *Mol Cell*. 2019;73(1):157-65.e5.
12. Luria S.E., Delbrück M. Mutations of Bacteria from Virus Sensitivity to Virus Resistance. *Genetics*. 1943;28:491-511.

Violence Against Doctors. Doctors: Earlier Demigods; Now Culprits?

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Abstract

Violence against medical professionals at the workplace is not a new phenomenon. In recent times, the reports of doctors getting thrashed by patients or their relatives have made headlines around the world. Almost every doctor has experienced some kind of violence whether physical or verbal at certain stage of their profession. This article aims to discuss the risk factors associated with violence against doctors and the possible steps that are needed to prevent such incidents.

Keywords: *Violence, medical professionals, Health care setting.*

Introduction

Earlier Doctors were given respect and were treated as equivalent to God and now they are not even treated as human beings, so where is the humanity??

Violence against doctors is certainly not India specific. It is a global phenomenon. The US, Britain, China, Bangladesh, Pakistan have all had victims of violence.¹ A few years ago, a paediatrician in China's Fujian province was injured after leaping out of a fifth-floor window to escape angry relatives of a newborn baby who had died under his care.² This year, large numbers of cases have been reported related to violence on doctors. To protest against this, large number of doctors was on strike and candle march was done in various parts of our country. Even doctors wore helmet in order to protect themselves from the anger of mob

and to save their life. Similarly in 2017, More than 2000 junior doctors from 17 government-run hospitals in India's largest city, Mumbai, went on strike for 4 days in March, to protest a recent spate of violence against doctors.³ At least four separate incidents of assault on a junior doctor at a government hospital were reported in the week preceding the strike in the state of Maharashtra of which Mumbai is the capital.⁴ The chief demand of the striking doctors was better security from the government to protect them at hospitals. So, every year violence against doctors is increasing.

Violence against doctors in India is not new and a 2015 survey by the Indian Medical Association suggests that as many as 75% of doctors in India have faced some form of violence at work.⁵ How doctor can serve humanity if he will not survive?

Now even doctors are thinking not to make their children doctors, only to save their life and doctors are thinking to opt non-clinical branches for their postgraduation.

There arises a question...

There are many cases for medical negligence but how many cases have been registered on the patients and

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their relatives under the prevention of violence against doctors act?

Looking towards the assessment of reasons behind violence against doctors?

Causes of Violence:

- **Psychology of Family:** Violence is an outburst of anger mixed with the frustration among the relatives of the people. Whenever we face the demise of any of our dear and near one, we go through phasic alterations in our mind and pass through five main stages of grief, denial, anger, bargaining, depression and finally acceptance. People exhibit the displacement of anger and denial to cope with the situation and it is the emotion transfer from a situation or person to another that is the main reason for violence against doctors and other health staff.
- **Advanced Medical Care Technology:** Has revolutionized medical care outcomes on the one hand; however, it has led to high expectations for 100% cure among patients and relatives. The difference between these high expectations and actual ground realities is the main root cause of this curse.
- **Doctor-Patient Relationship:** Doctor–patient mistrust, changing dynamics of the doctor–patient relationship although the other factors cannot be ignored.
- **Social Factors:** Giving more importance to medical negligence. As all the fingers of the hand are not alike, then how can all doctors are the same?? The mistakes of some of the doctors are made sensational by media people and that further leads to damaging the image of doctors in the society.
- **Less Budget for Health and Poor Quality Healthcare:** Of the total GDP of India, only 1.5% is for healthcare. So, there is pathetic condition of health in government sector. There is overcrowding, long waiting time to meet doctors, absence of a congenial environment, multiple visits to get investigations done as well as consult doctors, sharing a bed by two and sometimes three patients and poor hygiene and sanitation.
- **Lack of Faith in the Judicial Process:** As judicial cases take a long time for their hearings as there are a lot of cases in queue and a person with a grievance does not trust the mechanisms of redressal provided

by law.⁶

- **Mob Mentality:** Mob mentality frequently snowballs into a violent crisis in hospitals. In China mobs, called ‘yinao’, regularly protest at hospitals or harass hospital administrators in exchange for money.⁷ In India, emotional turmoil due to death of a loved one is sometimes used by local politicians as an opportunity to demonstrate their political relevance by orchestrating violence at the clinical establishment.
- **Cost of Healthcare:** The rising cost of healthcare is the key reason for the breakdown of the bond between doctors and their patients. As, in private sector the patient is paying a lot of expenses then, they think they have just to pay rest doctors have to see. But doctors are not God, they can give treatment then, its patient who will respond or not, they can’t say. So, only blaming doctor for everything is not wise.

Various studies on risk factors associated with violence against doctors found the following⁸

- Younger doctors face more physical violence, as they think that they are much experienced that’s why they suffered loss.
- Female doctors are more likely to face violence.
- Department of obstetrics and gynaecology reported the highest rates of violence, followed by the paediatrics and medicine department with allied specialties and surgery with allied specialties.
- Verbal violence was the most common form of violence. In the emergency department, 100% of doctors reported some kind of verbal violence.

Due to the rising rates of violence, doctors are reluctant to take up serious cases, compromising health-care delivery. Thus, there is an urgent need to make health-care facilities safe for doctors as only then can they work with complete dedication. This needs to be done at various levels by the government, media and medical professionals alike.

- Higher authorities (government level)-As the saying goes, “health is wealth.” Policymakers need to understand that the overall health of the people contributes to the efficiency of the workforce, in turn, contributing to the growth of the economy. More health budget spending would translate to better facilities and increased doctor–patient ratio,

leading to a decrease in violence related to these factors.

- Social levels (Media)-Doctors are almost always portrayed negatively by the media. There are sensational news reports of death and sting operations against doctors. Media needs to understand that the practice of medicine is not a black-and-white subject. Diagnosis of a patient is essentially a hypothetico-deductive process and with the appearance of new evidence through investigations and knowledge, the diagnosis of some of the cases continues to be questioned and refined.
- Doctor role- Modern medicine is reaching new frontiers, but at the same time, a negative public perception of doctors is leading to an increase in litigations. Thus, every doctor should follow the cardinal principle “do not overreach,” i.e., do not treat beyond the scope of one’s training and facilities to prevent both violence and litigations against themselves. Second, all doctors should ensure that a valid and informed consent is taken properly and not just considered a formality.
- Medical institutions- Hospitals can do much to reduce the violence. In government hospitals, this can be done as a part of general reform for the hospital services in the form of: (i) Improvement of services in a global fashion (ii) employment of adequate number of doctors and other steps to ease the rush of patients and long waiting hours (iii) use of computer and internet technology (iv) hospital security should be strengthened and it needs to be properly interlocked with nearby police station (v) no arms/ammunition by patient or their relatives should be allowed inside the hospital (vi) there should be transparency on rates of different investigations, rents and other expenses in the hospital and (vii) there should be a proper complaint redressal system in the hospital.

It is important to be vigilant and look for early warning signs of violence by using the STAMP approach as follows⁹:

- Staring is an important early indicator of potential violence. Nurses have felt that staring was used to intimidate them into prompter action—when they responded to this cue violence tended to be avoided.
- Tone and volume of voice has been associated with violent episodes. Most instances involve raised

voices and yelling but also involved sarcastic and caustic replies.

- Many people who attend the emergency department are anxious and nurses are aware of how stressful such a visit can be. They should intervene before anxiety reaches dangerous levels, but sometimes patient’s anxiety does escalate to violence.
- A majority of patients who become violent have been observed to be mumbling, using slurred or incoherent speech or repeatedly asking the same question or making the same statements. Mumbling has been perceived to be a sign of mounting frustration and a cue for violence.
- Pacing was seen as an indication of mounting agitation and has been observed in instances that resulted in violence. Other physical indicators include staggering, waving arms or pulling away from healthcare personnel attempting to treat them.
- Restrict entry- The most important step in preventing mob violence in a hospital is restricting entry of the public. Entry should be strictly by passes and this must be implemented through good security, preferably by deploying ex-army personnel. Security guards must be placed inside the hospital at sensitive areas such as intensive care units, operation theatres and casualty.
- Standard operating procedure (SOP)-All clinical establishments should develop an SOP for violence. Mock drills need to be conducted and each member of the staff should be clear about his role if the situation of impending or actual violence does arise.
- Insurance- Insure the establishment against mob violence, damage to property and injury to workers to at least mitigate the financial losses that are incurred in the aftermath of violence.

Conclusion

Although violence against doctors and other health workers is not uncommon, the incidence in India seems to be increasing. Doctors need to pressurize the government to equate assault on a doctor with assault on a public servant on duty. Necessary changes should be made urgently in the IPC and Criminal Procedure Code (CrPC) to have a deterrent effect and prevent future incidents of violence against doctors. However, for this to happen a coordinated effort is needed. We hope no more healthcare personnel lose their lives to violence

before action is initiated by their associations and the government.

Let the doctors live and work freely, only then they are able to serve the humanity and save life of others....

Swachh Bharat mission is going on- why not swachh mentality of citizens for doctors too??

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Ethical Clearance: The ethical clearance from institutional ethical committee has been taken.

References

1. Mirza NM, Amjad AI, Bhatti AB, Tuz-Zahra, Shaikh KS, Kiani J, et al. Violence and abuse faced by junior physicians in the emergency department from patients and their caretakers: A nationwide study from Pakistan. *J Emerg Med* 2012;42:727-33.
2. Anonymous. Chinese doctors are under threat. *Lancet*. 2010;376:657.
3. Doshi V. Thousands of Mumbai doctors strike after assaults on hospital staff. *The Guardian* (London). [Internet]. [assessed 20 oct 2019]. Available from: <https://www.theguardian.com/world/2017/mar/21/doctors-strike-mumbai-assaults-on-hospital-staff-india>.
4. Vora P. India's hospital assaults: patients blame doctors while doctors blame the broken health system. *Scroll.in* (Mumbai). [Internet]. [assessed 21 oct 2019]. Available from: <https://scroll.in/pulse/832349/hospital-violence-patients-blame-doctors-while-doctors-blame-the-broken-health-system>.
5. Dey S. Over 75% of doctors have faced violence at work, study finds. *Times of India* 4 May 2015.
6. Madhok P. Violence against doctors. *Bombay Hosp J*. 2009;51:301-2.
7. Hesketh T, Wu D, Mao L, Ma N. Violence against doctors in China. *BMJ*. 2012;345:e5730.
8. Kumar M, Verma M, Das T, Pardeshi G, Kishore J, Padmanandan A. A study of workplace violence experienced by doctors and associated risk factors in a Tertiary care hospital of South Delhi, India. *J ClinDiagn Res*. 2016;10:LC 06-10.
9. STAMP- System can help professionals to identify potentially violent individuals. *Eurek Alert!* The global source for science news. Washington, DC: Black Lack Publishing. [Internet]. [assessed 2 oct 2019]. Available from: https://www.eurekalert.org/pub_releases/2007-06/bpl-ssc062007.php.

Microbiological Profile of Diabetic Wound Infection

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Abstract

Introduction: Diabetic wound infections is a dreaded complication of diabetes and often the leading cause of hospitalization for patients with diabetes worldwide. Infection if not treated timely and properly can even lead to amputation of the infected part. The present study was conducted as an attempt to evaluate the different microorganisms infecting diabetic wounds and to find out the antibiotic susceptibility patterns.

Material and Method: A total of 128 patients of diabetic wound infections were included in this study from September 2018 to August 2019. Samples were processed as per standard guidelines, the microorganisms (bacterial and fungal) were isolated and further antibiotic susceptibility pattern for bacterial isolates was studied.

Results: Out of 128, 106 (82.82%) yielded growth of microorganisms on culture. Predominance of bacterial growths (73.58%) as a causative etiology in diabetic wound infections were noticed over fungal (26.42%). Gram positive bacterial growths accounted to 39.74%, whereas 60.27% were gram negative growths. Staphylococcus aureus (29.49%) was the most predominant organism isolated, followed by Escherichia coli (25.64%) and Pseudomonas aeruginosa (24.36%). of the Staphylococcus aureus, 73.92% were methicillin resistant while 72.34% among gram negative isolates were ESBL producers with Escherichia coli accounting the highest degree of ESBL production. Linezolid, vancomycin and teicoplanin were the most sensitive drugs for Staphylococcus aureus and Gram-negative isolates were mostly sensitive to imipenem based on our susceptibility results. Candida species (89.28%) was noted to be the most dominant fungal pathogen in diabetic wound infections.

Conclusion: A good knowledge about the microbiological profile of diabetic wound infections and antimicrobial susceptibility patterns of the isolates can be helpful in guiding the clinicians to promptly and effectively treat diabetic wound infections.

Keywords: Diabetic wound infections, Bacterial isolates, Fungal isolates, Antimicrobial Susceptibility, Extended spectrum beta-lactamase (ESBL), Methicillin resistant staphylococcus aureus (MRSA).

Introduction

Diabetes mellitus, a chronic disease, affects a large segment of population and is now a worldwide

epidemic. Among all the WHO member states, India has the highest number of people with diabetes.¹

A variety of factors related to diabetes weaken wound healing, together with wound hypoxia, infection and nutrition deficiencies.² It is estimated that about 12%–25% of diabetics across the world will develop a foot ulcer at some time during their life, thus contributing to a major public health issue even to the endpoint amputation as 85% of major leg amputations begin with a foot ulcer.^{3,4,5}

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Diabetic neuropathy and micro- or macro-angiopathy

leading to ischemia are the two main risk factors that cause foot ulcers.⁶ The most common cause of morbidity and mortality associated with foot ulcers is infections, which are seen in 40%–80% of the cases.⁷ Exposed subcutaneous tissue supplies a favorable substratum to the broad variety of microorganisms to contaminate and colonize, causing devitalization of the involved tissue and the host immune response is compromised, the conditions become best for microbial growth⁸ Impaired micro vascular circulation and elevated blood sugar levels further reduces the effectiveness of bacteria fighting cells to the infected areas hence necessitating limb amputation.⁹

These problems are largely preventable and successful treatment depends on the correct evaluation of the patient, diagnosis, proper and timely management of infection. Wound infections in diabetics are largely mixed infections in nature with a combination of both bacterial and fungal isolates.¹⁰ Thus, the present study was an attempt to evaluate the different microorganisms infecting diabetic wounds and to know the antibiotic susceptibility patterns to the bacterial isolates.

Material and Method

One hundred and twenty-eight patients (OPD and IPD) of diabetic wound infections were included in this study. The prospective and observational hospital-based study was conducted from September 2018 to August 2019 in the Department of Microbiology of a tertiary care hospital. The Institutional Ethical Committee's clearance was obtained prior to conducting the study.

Inclusion Criteria: Diabetic patient who had wound infection or developed deep tissue wound infection leading to ulceration were included.

Exclusion Criteria: Non diabetic patient with wound infection were excluded.

After obtaining informed consent from the patients, the samples such as wound swab, pus or tissue debris were collected in a sterile container and transported to our microbiology lab within 10 to 15 minutes for further processing. The samples were first microscopically

examined by Gram staining and Potassium hydroxide wet mount. Further, aerobic microbial culture and fungal culture were performed.

For aerobic cultures, the samples were inoculated on blood agar and MacConkey's agar and plates were then incubated at 37°C for 24-48 hours. Bacterial isolates were identified as per the standard operating procedures.¹¹ Antibiotic susceptibility testing was done by Kirby-bauer disc diffusion method and the susceptibility patterns of the bacterial isolates were detected following the antimicrobial agent's panel recommended by Clinical and Laboratory Standards Institute (CLSI) guidelines, 2018 and 2019.^{11,12,13}

For fungal cultures, the scrapings were directly inoculated into two slants of Sabouraud's dextrose agar with chloramphenicol and cyclohexamide. The slants were incubated at 22-25°C and the other at 37°C with periodic observations for about 4 weeks. Identification was made based on the colony characteristics, rate of growth and microscopic examination by lactophenol cotton blue stain, KOH (10%) and gram staining.¹⁴ Antifungal susceptibility testing was however not performed in our laboratory.

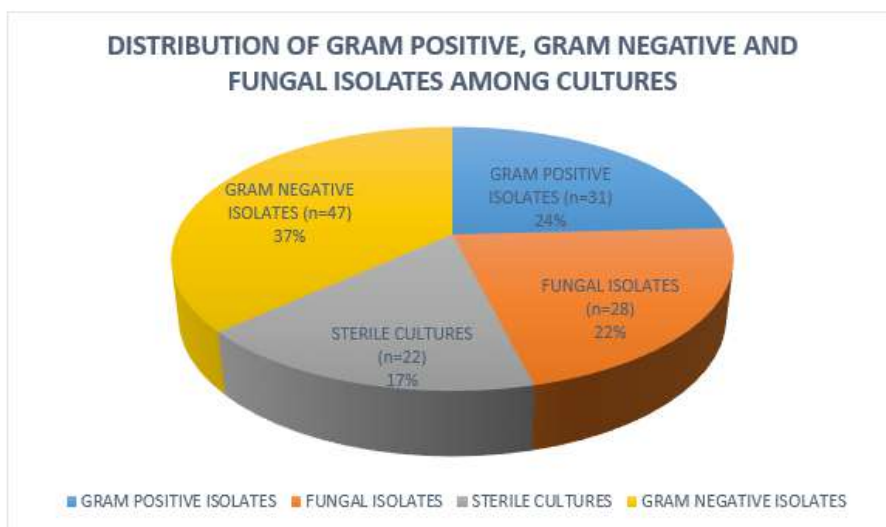
Results

A total of 128 diabetic patients presenting with diabetic wound infections attending our hospital in the period from September 2018 to August 2019 were included in this study.

Of 128 patients, 72 (56.25%) were males and 56 (43.75%) were females. Most patients (64.1%) in this study belonged to age group 51-70 years, while relatively less patients belonged to age groups 30-50 years (14.8%) and 71-90 years (21.1%) respectively.

In this study, the total numbers of patients showing culture positivity were 106 (82.82%) [Figure-1], out of which there were 73 (68.87%) monomicrobial cases and 33 (31.13%) polymicrobial cases. Predominance of bacterial growths as a causative etiology in diabetic wound infections were noticed over fungal.

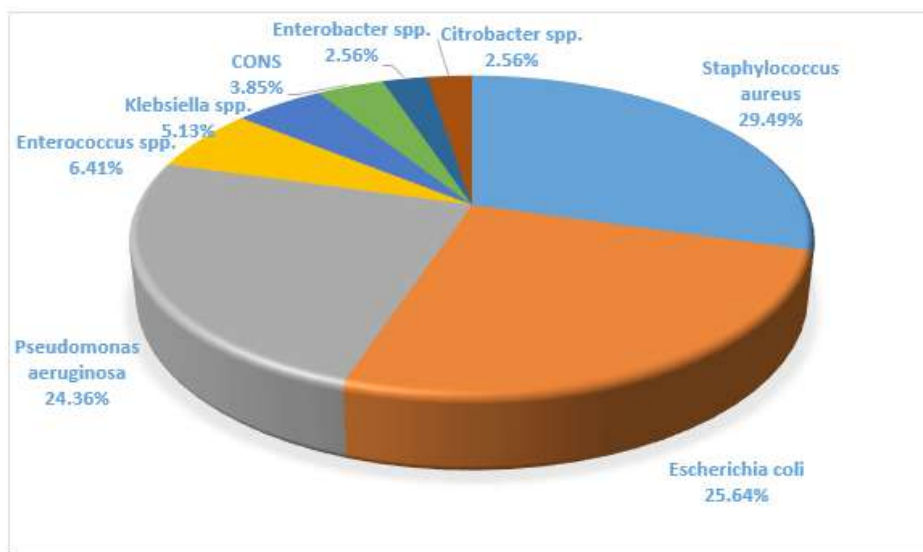
FIGURE 1: MICROBIOLOGICAL PROFILE OF CULTURE GROWTHS IN PATIENTS WITH DIABETIC WOUND INFECTION (n=128)



The positivity rate of bacterial isolates was 73.58% and 26.42% for fungal isolates. Among the bacterial isolates, gram positive bacterial growths were present in 31 (39.74%) cases, whereas gram negative growths

were seen in 47 (60.26%) cases. [Figure-1]. The most predominant bacterial growth was that of *Staphylococcus aureus* (29.49%), followed by *Escherichia coli* (25.64%) and *Pseudomonas aeruginosa* (24.36%). [Figure-3].

FIGURE 3: DISTRIBUTION OF VARIOUS BACTERIAL ISOLATES



In the present study, most of the *Staphylococcus aureus* were sensitive to Linezolid (100%), Vancomycin (95.65%) and Teicoplanin (91.30%). [Table-1] Nearly 73.92% of *Staphylococcus aureus* were methicillin-resistant *Staphylococcus aureus* (MRSA). [Figure-4]

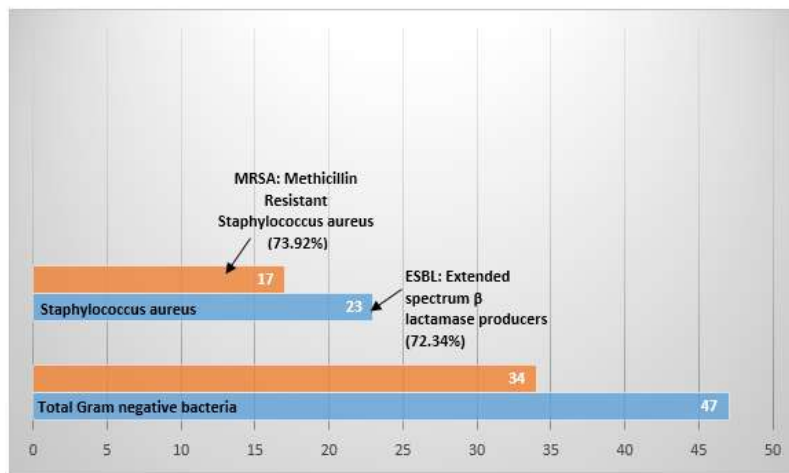
Imipenem showed to be most sensitive antibiotic among the gram negative bacterial isolates, 72.34% of these were ESBL producers with *Escherichia coli* accounting the highest degree of production of ESBL. [Table-2, Figure-4].

TABLE 2: ANTIMICROBIAL SUSCEPTIBILITY PATTERNS OF GRAM NEGATIVE BACTERIA

ORGANISM (n=47)	AMP	AMC	CTX	CTR	CAC	CPM	COT	CFS	PIT	LEV	OF	AK	GEN	NET	IMP	MRP
Escherichia coli (n=20)	19 (95%)	1 (5%)	3 (15%)	1 (5%)	10 (50%)	11 (55%)	20 (100%)	9 (45%)	14 (70%)	11 (55%)	3 (15%)	11 (55%)	10 (50%)	13 (65%)	19 (95%)	11 (55%)
Pseudomonas aeruginosa (n=19)	0 (0%)	1 (5.26%)	0 (0%)	1 (5.2%)	14 (73.6%)	11 (57.9%)	0 (0%)	15 (78.9%)	17 (89.4%)	11 (57.9%)	9 (47.3%)	9 (47.3%)	7 (36.8%)	11 (57.9%)	17 (89.4%)	13 (68.4%)
Klebsiella spp. (n=4)	4 (100%)	2 (50%)	0 (0%)	0 (0%)	1 (25%)	2 (50%)	4 (100%)	1 (25%)	3 (75%)	4 (100%)	2 (50%)	3 (75%)	2 (50%)	4 (100%)	3 (75%)	1 (25%)
Enterobacter spp. (n=2)	2 (100%)	1 (50%)	1 (50%)	1 (50%)	1 (50%)	0 (0%)	1 (50%)	1 (50%)	1 (50%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (50%)	2 (100%)	1 (50%)
Citrobacter spp. (n=2)	1 (50%)	1 (50%)	1 (50%)	1 (50%)	1 (50%)	1 (50%)	2 (100%)	1 (50%)	1 (50%)	1 (50%)	0 (0%)	1 (50%)	1 (50%)	1 (50%)	2 (100%)	2 (100%)

AMP: Ampicillin (10 µg), AMC: Amoxicillin-clavulanic acid (30/10 µg), CTX: Cefotaxime (30 µg), CTR: Ceftriaxone (30 µg), CAC: Ceftazidime-clavulanic acid (30/10µg), CPM: Cefipime (30 µg), CFS: Cefoperazone-sulbactam (75/30 µg), PIT: Piperacillin-tazobactam (100/10 µg), LE: Levofloxacin (5 µg), OF: Ofloxacin (5 µg), AK: Amikacin (30 µg), GEN: Gentamicin (10 µg), NET: Netilmicin (30 µg), IMP: Imipenem (10 µg), MRP: Meropenem (10 µg).

FIGURE 4: ADDITIONAL RESISTANCE PATTERN OF GRAM NEGATIVE BACTERIA AND STAPHYLOCOCCUS AUREUS



Among the fungal isolates in our study, Candida species (89.28%) was noted to be the most dominant in diabetic wound infections. [Table-3].

TABLE 3: FUNGAL PATHOGENS ISOLATED FROM DIABETIC WOUND INFECTION

FUNGAL SPECIES	FREQUENCY (NO. OF ISOLATES)	PERCENTAGE (%)
Candida albicans	21	75%
Candida tropicalis	03	10.71%
Candida parapsilosis	01	3.57%
Aspergillus Niger	02	7.15%
Aspergillus flavus	01	3.57%
Total	28	100%

Discussion

Diabetic foot infections are a rising problem worldwide affecting millions of people. Patient care for Diabetic wound infections is complex and necessitates a multi professional collaborative approach to provide comprehensive wound care. The constant non healing wounds are more susceptible to infection further leading to decrease in the healing procedure and often may result in amputations.

Among the 128 patients in the present study,

72/128 (56.25%) were males and 56/128 (43.75%) were females. Similar figures indicating higher male prevalence have been reported by Jain and Barman.¹⁵ This could be attributed to outdoor occupation in males as a consequence of which males are more vulnerable to trauma as compared to females.

In this study, most patients (64.1%) belonged to age group 51-70 years. This could be an indication of increased level of physical activity among this age group as well as the higher prevalence of comorbidities such

as peripheral neuropathy, peripheral vasculopathy, etc. in males. Similarly, studies by Nithyalakshmi et al and Gadepalli et al, mentioned that the majority of patients with diabetic wound infections were in 50-70 years' age range.^{16,17}

The data of present study showed a culture positivity of 82.82% which was comparable to the report of Khare et al¹⁸ (90.32%) who quoted this data from a Tertiary care centre in South India. However, around 17.18% were culture negative and showed no microbial growth which could be attributed to prior antibiotic therapy.

Diabetic wound infections are unique as it can be caused by single organism or in combination suggesting mixed etiology.^{19,20} In current study, the prevalence of monomicrobial infection (68.87%) was seen over polymicrobial infection (31.13%). Our findings are comparable to various studies by Otta et al (62.2%)²¹, Kavitha et al (58.73%)²², Ali et al (55%)²³ where higher prevalence of monomicrobial infection has been documented over polymicrobial infection.

Predominance of bacterial isolates are observed over fungal in this study with positivity rates of 73.58% (bacterial) and 26.42% (fungal) similar to study reported by Chellan et al.²⁴

Our study indicates gram negative isolates (60.26%) as the most predominant infection in patients with diabetic wound infections over gram positive isolates (39.74%), which is in accordance with earlier studies by Zubair et al,²⁵ Umadevi et al²⁶ and Shanmugam et al.²⁷ Few other studies, however reported that gram positive bacteria were more frequently isolated in comparison to gram negatives.^{21,28}

Staphylococcus aureus (29.49%) was the predominant organism in the present study, followed by *Escherichia coli* (25.64%) and *Pseudomonas aeruginosa* (24.36%). Similar pattern has also been observed by other studies.^{15,29,30}

In our study, like many others,^{21,31,32} Linezolid (100%), Vancomycin (95.6%) and Teicoplanin (91.3%) were the most susceptible antibiotics for *Staphylococcus aureus* and other gram positive bacteria isolated. Susceptibility pattern for gram negative isolates demonstrated that Imipenem was the most effective antimicrobial agent which was in accordance to other studies.³³⁻³⁵

With the emergence of multidrug resistant bacteria, treatment of diabetic wound infection gets difficult resulting in poor outcome, longer hospital stays and further deteriorating the wound condition. In the present study, we demonstrated additional resistance pattern for *Staphylococcus aureus* and noticed that nearly 73.92% of *Staphylococcus aureus* were methicillin-resistant *Staphylococcus aureus* (MRSA). Various other studies^{21,29,31} also showed similar rates of MRSA (77.8%, 66.7% and 60%) respectively. Preliminary detection of Vancomycin resistant gram positive bacteria was also noted by Kirby-Bauer's method, however since Minimum Inhibitory Concentration (MIC) was not performed it could not be confirmed. Hence, our study lacks data on important resistance mechanisms like Vancomycin-resistant *Staphylococcus aureus* (VRSA) and Vancomycin-resistant *Enterococcus* species (VRE).

In our study, ESBL production was noted in 72.34% of gram negative isolates in our study with *Escherichia coli* as the highest ESBL producer (52.94%) followed by *Pseudomonas aeruginosa* (38.23%). Similarly, in a study by Jain and Barman,¹⁵ ESBL producing gram negative bacteria were seen in 79.16% of patients and highest prevalence of ESBL was observed in *Escherichia coli*.

The present study depicts *Candida* species (89.28%) as the most frequently occurring fungi in diabetic wound infections. A similar study showed that among the fungal isolates, 76.6% were *Candida* species.²⁴ Furthermore, our study showed 84% *Candida albicans* and 16% *Candida non-albicans* respectively. This observation was comparable to the study of J. Nithyalakshmi et al¹⁶ and Saba Fata et al.³⁶ Our data also revealed the occurrence of *Aspergillus* species (10.72%) which was similar to a study by Chellan et al (5% *Aspergillus* species).²⁴

Conclusion

The emerging menace associated with MDR pathogens and their associated complications worsen the problems of Diabetic wound as infections with these isolates are more difficult to manage and treat. It is to help guide the clinicians by postulating our study data about the microbiological profile of these infections, prevalence of isolates and their antimicrobial susceptibility patterns. These are important findings related to good patient management and for development of empirical antimicrobial guidelines.

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References

1. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care* 2004;27:1047–1053.
2. Mohan V, Shah SN, Joshi SR, Seshiah V, Sahay BK, Banerjee S et al. Current status of management, control, complications and psychosocial aspects of patients with diabetes in India: Results from the Diab Care India 2011 Study. *Indian J Endocr Metab* 2014;18:370-8.
3. Huang Y, Cao Y, Zou M, Luo X, Jiang Y, Xue Y, et al. A comparison of tissue versus swab culturing of infected diabetic foot wounds. *Int J Endocrinol* 2016; 2016: 8198714.
4. Andersen CA, Roukis TS. The diabetic foot. *SurgClin North Am* 2007;87:1149-77.
5. Lipsky BA. Medical treatment of diabetic foot infections. *Clin Infect Dis* 2004;39 Suppl2:S104-14.
6. Ismail K, Winkley K, Stahl D, Chalder T, Edmonds M. A cohort study of people with diabetes and their first foot ulcer: The role of depression on mortality. *Diabetes Care* 2007;30: 1473-9.
7. Richard JL, Sotto A, Lavigne JP. New insights in diabetic foot infection. *World J Diabetes* 2011;2:24-32.
8. Bowler PG, Duerden BI, Armstrong DG. Wound microbiology and associated approaches to wound management. *ClinMicrobiol Rev.* 2001;14(2):244–269.
9. Hena J and Growther L. Studies on bacterial infections of diabetic foot ulcer. *African J. Clin. Experimental Microbiol.*2010;11(3): 146-149.
10. Zubair M, Malik A, Ahmad J. Clinico-bacteriology and risk factors for the diabetic foot infection with multidrug resistant microorganisms in North India. *Biol Med* 2010;2:22-34.
11. Collee JG, Miles RS, Watt B. Test for identification of bacteria. In: Collee JG, Fraser AG, Marmion BP, Simmons A, editors. *Mackie and McCartney Practical Medical Microbiology*. 14th ed. London: Churchill Livingstone Inc.; 1996. p. 435.
12. CLSI. Performance Standards for Antimicrobial Susceptibility Testing. 28th ed. CLSI Supplement M100. Wayne, PA: Clinical and Laboratory Standards Institute; 2018.
13. CLSI. Performance Standards for Antimicrobial Susceptibility Testing. 29th ed. CLSI Supplement M100. Wayne, PA: Clinical and Laboratory Standards Institute; 2019.
14. Chander J. Lab Diagnosis of Fungal Infections in Textbook of Medical Mycology. 4th ed. Jaypee Brothers Medical Publishers (P) Ltd.; India; 2018.
15. Jain SK, Barman R. Bacteriological profile of diabetic foot ulcer with special reference to drug-resistant strains in a tertiary care center in North-East India. *Indian J Endocr Metab* 2017;21 :688-94.
16. Nithyalakshmi J, Nirupa Sand Sumath G: Diabetic foot ulcers and Candida co-infection: a single centered study. *Int J CurrMicrobiol App Sci* 2014;3(11) :413-419.
17. Gadepalli R, Dhawan B, Sreenivas V, Kapil A, Ammini AC, Chaudhry R. A clinico-microbiological study of diabetic foot ulcers in an Indian tertiary care hospital. *Diabetes Care* 2006;29:1727-1732.
18. Khare J, Srivastava P, Khare J, Wadhwa J, Deb P. Microbiological Profile of Diabetic Foot Ulcers- Experience from a Tertiary care centre in South India. *Int J Gen Med Surg* 2017; 1: 109.
19. Viswanathan V, Jasmine JJ, Snehalatha C, Ramachandran A. Prevalence of pathogens in diabetic foot infection in South Indian type 2 diabetic patients. *J Assoc Physicians India* 2002;50: 1013-6.
20. Chincholikar DA, Pal RB. Study of fungal and bacteriological infections of the diabetic foot. *Indian J PatholMicrobiol* 2002;45:15-22.
21. Otta S, Debata NK, Swain B. Bacteriological profile of diabetic foot ulcers. *CHRISMED J Health Res* 2019;6:7-11.
22. Kavitha Y, Khaja Mohiddin S. Bacteriological profile of diabetic foot infections in a tertiary care teaching hospital; *Indian J Basic and App Med Res* 2014; 3(4) :260-266.
23. Ali O, Ali HA, Southy HE, Khirallah S. Microbiological Profile of Diabetic Foot Ulcer and Use of IL6 as a Predictor for Diabetic Foot

- Infection. *Int J Curr Microbiol App Sci* 2016;5(12): 1-10.
24. Chellan G, Shivaprakash S, Karimassery Ramaiyar S, et al. Spectrum and prevalence of fungi infecting deep tissues of lower-limb wounds in patients with type 2 diabetes. *J Clin Microbiol* 2010;48:2097–2102.
 25. Zubair M, Malik A, Ahmad J. Clinico-bacteriology and risk factors for the diabetic foot infection with multidrug resistant microorganisms in North India. *Biol Med* 2010;2: 22-34.
 26. Umadevi S, Kumar S, Joseph NM, Easow JM, Kandhakumari G, Srirangaraj S, et al. Microbiological study of diabetic foot infections. *Indian J Med Specialities* 2011;2:12-7.
 27. Shanmugam P, M J, Susan S L. The bacteriology of diabetic foot ulcers, with a special reference to multidrug resistant strains. *J Clin Diagn Res.* 2013;7(3):441–445.
 28. Dang CN, Prasad YD, Boulton AJ, Jude EB. Methicillin resistant *Staphylococcus aureus* in the diabetic foot clinic: A worsening problem. *Diabet Med* 2003;20: 159-61.
 29. Amini M, Davati A, Piri M. Determination of the resistance pattern of prevalent aerobic bacterial infections of diabetic foot ulcer. *Iran J Pathol* 2013;8:21-6.
 30. Chopdekar K, Chande C, Chavan S, Veer P, Wabale V, Vishwakarma K et al. Central venous catheter-related blood stream infection rate in critical care units in a tertiary care, teaching hospital in Mumbai. *Indian J Med Microbiol* 2011 :29(2): 16971.
 31. Mehta V J, Kikani K M, Mehta S J. Microbiological profile of diabetic foot ulcers and its antibiotic susceptibility pattern in a teaching hospital, Gujarat. *Int J Basic & Clin Pharmacol* 2017; 3(1): 92-95.
 32. Suresh A, Muthu G, Srivani R, Moses A. Aerobic bacterial resistance in diabetic foot ulcer from Chennai. *Int J Pharma and Bio Sci* 2011;2: B517-28.
 33. Mohanasoundaram KM. The microbiological profile of diabetic foot infections. *J Clin Diag Res* 2011; 5:1-3.
 34. Banashankari G, Rudresh H, Harsha A. Prevalence of gram negative bacteria in diabetic foot-a clinico-microbiological study. *Al Ameen J Med Sci* 2012; 5:224-32.
 35. Hefni AA, Ibrahim AM, Attia KM, Moawad MM, El-ramah AF, Shahin MM, et al. Bacteriological study of diabetic foot infection in Egypt. *J Arab Soc Med Res* 2013;8:26-32.
 36. Fata S, Saeed-Modagheh MH, Faizi R, Najafzadeh MJ, Afzalagheh M, Ghasemi M, et al. Mycotic infections in diabetic foot ulcers in Emam Reza hospital, Mashhad, 2006-2008. *Jundishapur J Microbiol* 2011;4:11–6.

Correlation between Bio-Film Formation and Carbapenem Resistant Enterobacteriaceae Isolates Obtained from Various Clinical Specimens

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Abstract

Introduction: The ability to form bio-film is a universal trait of bacteria by attaching to the surfaces. Carbapenem resistance in Enterobacteriaceae might be endorsed by bio-film formation which augmented colonization of pathogens.

Aim: To correlate between bio-film formation and carbapenem resistant Enterobacteriaceae isolates obtained from various clinical specimens and to compare the qualitative and quantitative assay for bio-film production.

Method: Study was conducted on 150 strains of Enterobacteriaceae isolates. of these, carbapenem resistant Enterobacteriaceae isolates were subjected for bio-film formation by Modified Congo red agar method, tube adherence method and Tissue culture plate method.

Results: Carbapenem resistant Enterobacteriaceae strains were found to be 60.66% and the rate of bio-film producers was 75.53% by any of the phenotypic method. Tissue culture plate method was found to be (67.6%) better than Modified Congo Red agar method (54.9%) and Tube adherence method (39.4%). The highest number of bio-film producers was isolated from urinary tract infections (36.61%).

Conclusion: TCP method is most reliable, precise and sensitive method for detection of bio-film formation by Enterobacteriaceae isolates and is ideal to use as a general screening tool to detect bio-film production.

Keywords: Carbapenem resistant Enterobacteriaceae; bio-film; qualitative; quantitative assays.

Introduction

The ability to form bio-film is a universal trait of bacteria by attaching to the surfaces. Bio-films

significantly increase the capability of the pathogen to evade host defenses as well as antibiotics. Such bio-film phenotype leads to emergence of multi-drug resistant organisms and consequently treatment failure.⁽¹⁾

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Development of bio-film is a survival strategy for fungi and bacteria to adjust to their living atmosphere. The microbial cells under bio-film protection turn out to be tolerant and resistant to immune responses and antibiotics, thereby increasing difficulties in treatment.⁽²⁾

The Enterobacteriaceae are the most frequent pathogen detected among gram negative bacteria

contributing to majority of infections. Enterobacteriaceae resistance to broad spectrum antibiotics is an increasing problem worldwide. Carbapenem resistant Enterobacteriaceae (CRE) are emerging as tremendously drug resistant bacterial pathogens. These organisms are typically resistant to almost all existing antibiotics and risk of mortality has increased due to infections caused by them. Overuse of antibiotic, hygienic practices and improper sanitation has led to huge extent rate of these multidrug resistant strains.⁽³⁾

In recent years, carbapenem-resistant Enterobacteriaceae (CRE) have been acknowledged more gradually as a cause of healthcare associated infections and outbreaks of disease also reported from several countries.^(4,5,6,7,8)

Bio-films pose a serious trouble for public health because of the increased resistance of bio-film-associated organisms to antibiotics.⁽⁹⁾ Carbapenem resistant Enterobacteriaceae further possess several resistance mechanisms which makes them extremely difficult to treat and almost impossible in a few cases.⁽¹⁰⁾

Carbapenem resistant in Enterobacteriaceae might be endorsed by bio-film formation which augmented colonization of pathogens. So, to develop more effective treatment for Enterobacteriaceae infections, perceptive of the development of bio-films and intercellular interactions within the bio-films is of great significance.⁽¹¹⁾

Considering the above issues, the current study was designed to correlate bio-film formation and carbapenem resistant in Enterobacteriaceae isolates obtained from various clinical specimens.

Material and Method

Study Period: It was a cross-sectional study conducted at the Department of Microbiology, MMIMSR, Mullana, Ambala, over a period of one year i.e. from 2018 to 2019.

Bacterial Isolates: A total of 150 isolates of Enterobacteriaceae were obtained from a total of 1250 various clinical specimens such as Urine, Blood, Pus, Sputum, Wound, HVS, Drain, Stool, Foley's Tip and ET Secretion. All the isolates were identified to species level by Gram staining and a battery of biochemical tests. Antibiotic susceptibility testing was done by Modified Kirby Bauer disc diffusion method

according to CLSI guidelines using antibiotics which were obtained from Hi-Media, such as - Ciprofloxacin (5 mcg), levofloxacin (5 mcg), Ampicillin-Sulbactam (10/10 mcg), Piperacillin/Tazobactam (100/10 mcg), Amoxycylav (30 mcg), Cefepime (30 mcg), Ceftriaxone (30 mcg), Imipenem (10 mcg), Meropenem (10 mcg), Co-Trimoxazole (25 mcg), Sulphafurazole (300 mcg), Gentamicin (10 mcg), Amikacin (30 mcg).

Detection of Bio-Film Formation: Carbapenem resistant Enterobacteriaceae isolates were screened for bio-film production by quantitative and qualitative assays, using *Escherichia coli* (ATCC 25922) as a positive control and *Klebsiella pneumonia* (ATCC 700603) as a negative control.

Modified Congo Red Agar Method: It is a qualitative method described by Freeman DJ *et al* ⁽¹²⁾ 1989 to detect bio-film production by using Modified Congo Red Agar (MCRA) medium which is composed of BAB-2, Glucose and Congo red dye. Enterobacteriaceae isolates were inoculated onto MCRA plates and the medium was incubated aerobically at 37°C for 24 to 48 hours. Positive and negative results were interpreted by observing black colored colonies with dry crystalline consistency and red colored colonies respectively.

Tube Adherence Method: A qualitative estimation of bio-film formation was described by Christensen *et al* ⁽¹³⁾ Enterobacteriaceae isolates were inoculated in a glass tube containing Brain heart infusion (BHI) broth with 2% sucrose and incubated at 37 °C for 24 hours. After 24 hours the supernatant was decanted and the sediment was washed with PBS (Phosphate Buffer Saline, Ph7.3) so as to remove non-adherent cells. Dried tubes were stained with 0.1% crystal violet and the excess stain was removed. Then, tubes were washed three times with distilled water and kept in inverted position to dry. Bio-film formation was observed by ring formation indicating positive result and the absence of ring was considered as negative result.

Tissue Culture Plate Method: It is most widely used quantitative assay described by Christensen *et al* ⁽¹⁴⁾ to detect bio-film formation. Enterobacteriaceae isolates were inoculated in BHI (Brain heart infusion) broth with 2% sucrose and incubated for 24 hours at 37 °C. The broth was diluted with fresh medium to 1:10 and then 20 µl pipetted to each well of 96 wells microtiter plate and incubated overnight at 37°C. After incubation, plate was washed thrice with PBS, pH 7.2 to remove free

floating bacteria. After washing, fixed with 2% sodium acetate for 15 minutes, decanted and stained with 0.1% crystal violet for 20 minutes. The wells were washed with distilled water to remove excess stain and dried. Optical density (OD) of stained adherent bacteria was established with a micro ELISA auto reader (model 680, Bio rad) at 570 nm wavelength (OD 570 nm). These OD values were taken as an indicator of bacterial adherence to the surface and bio-film formation.

Data analysis was performed using both descriptive and inferential statistical analysis.

Results

During the study period, 1250 samples (urine, pus, blood, sputum, wound, HVS, drain and others) were processed and a total of 150 Enterobacteriaceae isolates were obtained. of these 150, maximum numbers were *Escherichia coli* (79) followed by *Klebsiella* spp. (48), *Citrobacter* spp. (15), *Proteus* spp. (5) and *Enterobacter* spp. (3).

Antibiotic sensitivity pattern of Enterobacteriaceae isolates is shown in Table 1. All the 150 isolates were found to be multi drug resistant Enterobacteriaceae (resistant to ≥3 classes of antibiotic).

Table 1: Antibiotic sensitivity pattern of Enterobacteriaceae isolates screened for bio-film production

Antimicrobial Agents		Percentage of Sensitivity						
		Escherichia Coli (79)	Klebsiella spp. (48)	Citrobacter spp. (15)	Proteus spp. (5)	Enterobacter spp. (3)	P value	
Quinolones	CIP	0%	0%	0%	0%	0%	NA	
	LE	0%	0%	0%	0%	0%		
Pencillins	AMP	1(1.26%)	1(2.08%)	3(20%)	1(20%)	1(33.33%)	NA	
β-lactam/β-lactamase inhibitors	β-lactam/β-lactamase inhibitors	PIT	34 (43.03%)	22(45.8%)	5(33.33%)	3(60%)	3(100%)	0.212*
		AMC	16(20.2%)	2(4.16%)	3(20%)	2(40%)	1(33.33%)	
	Cephalo-sporins	CPM	3(3.79%)	1(2.08%)	3(20%)	1(20%)	1(33.33%)	NA
		CTR	0%	0%	0%	0%	0%	
	Carba Penems	IMP	25 (31.64%)	19(39.58%)	4(26.66%)	3(60%)	3(100%)	0.996*
		MRP	24 (30.37%)	20(41.66%)	3(20%)	3(60%)	3(100%)	
Sulfonamides	COT	11(13.9%)	8(16.6%)	3(20%)	1(20%)	1(33.33%)	0.874*	
	SF	14(17.72%)	7(14.58%)	6(40%)	2(40%)	2(66.66%)		
Aminoglycosides	GEN	29(36.7%)	14(29.16%)	6(40%)	3(60%)	3(100%)	0.9152*	
	AK	19(24.05%)	16 (33.33%)	4(26.66%)	3(60%)	3(100%)		

*P value is statistically not significant at < 0.05 using Chi square test

CIP: Ciprofloxacin, LE: levofloxacin, AMP: Ampicillin-Sulbactam, PIT: Piperacillin/Tazobactam, AMC: Amoxyclav, CPM: Cefepime, CTR: Ceftriaxone, IMP: Imipenem, MRP: Meropenem, COT: Co-Trimoxazole, SF: Sulphafurazole, GEN: Gentamicin, AK: Amikacin

Out of 150 Enterobacteriaceae isolates, 91 (60.66%) showed resistance to carbapenems. These carbapenem resistant Enterobacteriaceae were then subjected for detection of bio-film production by three phenotypic method namely Tissue culture plate method, Tube

adherence method and Modified Congo red agar method. The rate of bio-film producers among carbapenem resistant Enterobacteriaceae was found to be 75.53% by all phenotypic method (Table 2).

Table 2: Distribution of strains showing resistance to Carbapenems and the no. of bio-film producers

Carbapenem resistant Enterobacteriaceae (CRE)	Bio-film producers and percentage	p value
91	71 (75.53%)	<0.0001
One proportion z test used to calculate significant level, the result is significant (*p value < 0.001)		

Quantitative tissue culture plate method (TCP) showed 67.6% isolates positive for bio-film production, which were further categorized as strong, moderate and non/weak bio-film producers (figure 1). Strong and moderate bio-film producers were 10 and 14 respectively, while weak or non-bio-film producers were 24 (50%).

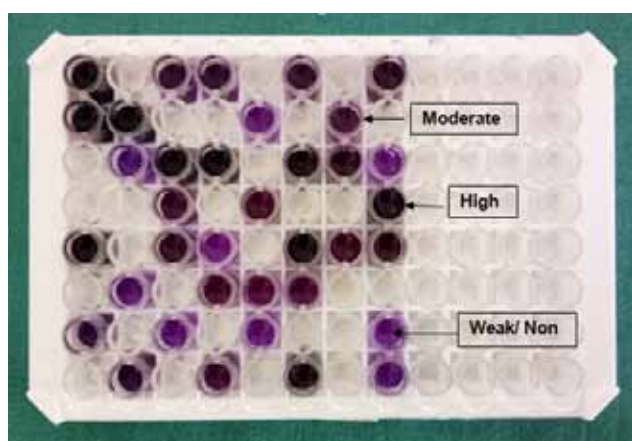


Figure 1: Quantitative assay for bio-film detection, showing high, moderate and weak/non bio-film producers.

Qualitative Tube adherence method (TAM) and Modified Congo red agar method (MCRA) of bio-film detection showed 39 (54.9%) and 28 (39.4%) bio-film producers respectively. The positive isolates in tube adherence method showed blue colored ring formation at the liquid-air interface (figure 2). While in MCRA method, positive isolates showed black colored colonies and negative isolates showed red colored colonies as shown in figure 3.



Figure 2: Qualitative Tube Adherence Method showing Biofilm producer (ring formation) and Non- biofilm producer (absence of ring formation)

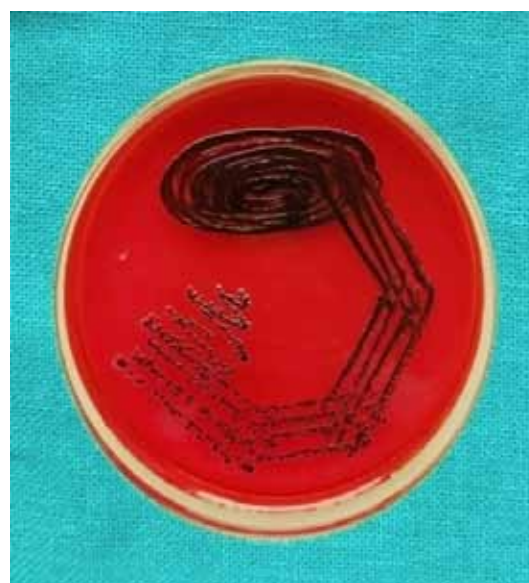


Figure 3: Qualitative Modified Congo Red Agar Method showing Biofilm producer (black colonies) and Non biofilm producer (pinkish-red colonies)

The maximum number of bio-film producers were isolated from urinary tract infection (36.6%) followed by wound infection (19.7%) as shown in Table 3.

Table 3: Distribution of bio-film producers according to clinical diagnosis

Clinical Diagnosis	Total CRE (n=91)	No. of Bio-film Producers (n=71)	Percentage of Bio-Film Producers
Urinary tract infection	30	26	36.61%
Wound infection	16	14	19.71%
Pneumonia	11	9	12.6%
Otitis media	9	6	8.45%
Abscess	8	7	9.8%
Endocarditis	6	4	5.63%
Bronchitis	4	2	2.8%
Vaginitis	3	2	2.8%
Biliary tract infection	2	0	0%
Intestinal infection	2	1	1.4%

Chi-square value (with Yates correction) is 0.529, p value is 0.9999. The result is not significant at $p < 0.05$

In our study the rate of bio-film formation was highest by tissue culture plate method 48 (67.6%) followed by tube adherence method 39 (54.9%) and modified congo red agar method 29 (39.4%) (Table 4).

Table 4: Detection of bio-film production in Carbapenem resistant Enterobacteriaceae isolates (71) by three method

Method	No. of bio-film producers	Percentage of bio-film Producers
Tissue culture plate method	48	67.6%
Tube adherence method	39	54.9%
Modified Congo red agar method	28	39.4%

Interestingly, the rate of bio-film production in our study by combination of all three method was highest 24 (33.8%), also the results of tube adherence method correlate well with tissue culture plate method (Table 5).

Table 5 : Rate of bio-film production by three method in combination

Total no. of Positive Strains N= 71	No. of bio-film producers	Percentage
MCRA + TAM+TCP	24	33.8%
MCRA + TAM	3	4.22%
TAM+TCP	8	11.26%
MCRA+TCP	0	0%

TCP: Tissue culture plate method, MCRA: Modified congo red agar method, TAM: Tube adherence method

Discussion

Enterobacteriaceae are amongst the most common human pathogens causing wide ranging infections. They cause hospital and community-acquired infections as well as device-associated infections.

Carbapenem resistant Enterobacteriaceae (CRE) have been reported worldwide and has become a major

health threat across the world due to their emerging resistance to nearly all existing antibiotics via acquisition of carbapenemase genes. This resistance is probably associated with the capability of these organisms to form bio-film.. In our study the rate of bio-film production in Carbapenem resistant Enterobacteriaceae isolates was 75.53%. The association has been found to be highly significant statistically with p value < 0.0001 . Our results

were in accordance to the study done by Swarna SR⁽¹⁵⁾ who showed that 74.50% isolates were positive for carbapenem resistance as well as bio-film production.

There are many studies who also reported that bio-film formation was highest by tissue culture plate method.^(16,17,18,19)

Since the best results were obtained by combination of all the method, we highly recommend that all the laboratories must include these tests for bio-film production to assess the better positivity rate.

In our study maximum no. of bio-film producers were isolated from Urinary tract infections (36.61%) followed by Wound infections. None of the clinical conditions has been found to be statistically significant (p value 0.9999) for bio-film production. This is contrary with the study done by R Srinivasa Rao *et al*⁽¹¹⁾ who reported that higher number of bio-film producing isolates were isolated from wound infection (44%) followed by 30% from nosocomial pneumonia patients. The contradiction was obvious as in our study the maximum number of isolates was that of hospitalized patients, so it directly increases the chances of Urinary tract infections rather than wound infections which were possibly associated with urinary catheters.

Conclusion

The present study highlights the need to detect bio-film production among Carbapenem resistant Enterobacteriaceae isolates. Also, there is a need to institute standard guidelines on the care of indwelling medical devices in the hospital to prevent bio-film formation as bio-film formation depends on the adherence of bacteria to various surfaces.

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References

1. Sritharan M, Sritharan V. Emerging problems in the management of infectious diseases: The bio-films. *Indian J Med Microbiol.* 2004; 22(3):140-2.
2. Wu H, Claus M, Wang H Z, Hoiby N and Song Z. Strategies for combating bacterial bio-film infections. *Int J Oral Sci.* 2014; 7(1): 1-7.
3. Ekadrishi R, Rajpurohit V, Rathore PK, Shikhar D, Khatri PK. Bio-film formation by carbapenem-resistant Enterobacteriaceae strains isolated from surveillance cultures in Intensive Care Unit patients: A significant problem. *J Health Res Rev* 2018; 5:147-52.
4. Chmelnitsky I, Navon-Venezia S, Leavitt A et al. Emergence of KPC-2 and KPC-3 in carbapenem-resistant Klebsiella pneumoniae strains in an Israeli hospital. *Antimicrob Agents Chemother* 2007; 51(8):3026-9.
5. Cuzon G, Naas T, Demachy MC, Nordmann P. Nosocomial outbreak of Klebsiella pneumoniae harbouring bla (KPC-3) in France subsequent to patient transfer from Italy. *Int J Antimicrob Agents* 2012; 39(5):448-9
6. Papadimitriou M, Voulgari E, Ranellou K, et al. Emergence of VIM-1 metallo- β -lactamase-producing Escherichia coli in a neonatal intensive care unit. *Microb Drug Resist* 2011; 17(1): 105-8.
7. Patel G, Bonomo RA "Stormy waters ahead": global emergence of carbapenemases. *Front Microbiol* 2013;4:48-17.
8. Gupta N, Limbago BM, Patel JB, Kallen AJ. Carbapenem-resistant Enterobacteriaceae: epidemiology and prevention. *Clin Infect Dis* 2011;53(1):60-7.
9. Jamal M, Tasneem U, Hussain T and Andleeb S. Bacterial Bio-film: Its Composition, Formation and Role in Human Infections. *J Chin Med Assoc.* 2018; 81(1):7-11.
10. Leski T A, Taitt C R, Bangura U, Stockelman M G, Ansumana R, Cooper W H, et al. High prevalence of multidrug resistant Enterobacteriaceae isolated from outpatient urine samples but not the hospital environment in Bo, Sierra Leone. *BMC Infect Dis.* 2018; 16:167.
11. Rao R S, Karthika U, Singh SP, Shashikala P, Kanungo R, Jayachandran S et al. Correlation Between Bio-film Production And Multiple Drug Resistance In Imipenem Resistant Clinical Isolates of Acinetobacter Baumannii. *Indian Journal Med. Microbiol.* 2008; 26(4): 333-7.
12. Mariana NS, Salman SA, Neela V, Zamberi S. Evaluation of modified Congo red agar for detection of bio-film produced by clinical isolates

- of methicillin resistance *Staphylococcus aureus*. *African J of Microbiology Research*. 2009; 3(6):330-8.
13. Christensen GD, Simpson WA, Bisno AL, Beachey EH. Adherence of slime-producing strains of *Staphylococcus epidermidis* to smooth surfaces. *Infect Immun* 1982;37:318–26.
 14. Christensen GD, Simpson WA, Younger JJ, Baddour LM, Barrett FF, Melton DM, et al. Adherence of coagulase-negative *Staphylococci* to plastic tissue culture plates: A quantitative model for the adherence of staphylococci to medical devices. *J Clin Microbiol* 1985;22:996-1006.
 15. Swarna SR, Swedha and Gomathi S. Bio-film Production in Carbapenem Resistant Isolates from Chronic Wound Infections. *International Journal of Medical Research & Health Sciences*. 2017; 6(2):61-67.
 16. Deka N. Comparison of Tissue Culture plate method, Tube Method and Congo Red Agar Method for the detection of bio-film formation by Coagulase Negative *Staphylococcus* isolated from Non-clinical Isolates. *Int. J. Curr. Microbiol. App. Sci*. 2014; 3(10): 810-815.
 17. Mathur T, Singhal S, Khan S, Upadhyay DJ, Fatma T, Rattan A. Detection of bio-film formation among the clinical isolates of *Staphylococci*: an evaluation of three different screening method. *Ind. J Med Microbio*. 2006; 24(1):25-29
 18. Trivedi L. and Gomathi S. Detection of bio-film formation among the clinical isolates of *Enterococci*: An evaluation of three different screening method. *Int.J. Curr. Microbiol. App. Sci*. 2016; 5(3): 643-650.
 19. Panda PS, Chaudhary U, Dube SK. Comparison of four different method for detection of bio-film formation by uropathogens. *Indian J Pathol Microbiol* 2016; 59:177-9.

Role of DLCO in Differentiation or Subtyping of Obstructive Lung Disease Beyond Spirometry and CT Scan

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Abstract

Introduction: Spirometry helps us to differentiate between obstructive and restrictive disease, body plethysmography tells about lung volumes and DLCO about diffusion defect. Determining which tests to do depends on the clinical question to be answered i.e. whether test is being done to diagnose a disease or for evaluation for lung surgery or some other reason.

Material and Method: 46 patients coming to department of respiratory medicine, who were diagnosed with obstructive lung disease by PFT as per GOLD guidelines were considered for the study. Chest X-ray and CT chest were also done. Then DLCO was performed in every patient. Single breath hold method was used in the study. The report of the DLCO was interpreted according to the American Thoracic Society/European Respiratory Society statement on PFT interpretation.

Results: Male preponderance was seen in study cases with 65.2% males to 34.8% females. Mean age of the study group was 54.39 years with most cases (18) from 31-50 years of age group. Most common diagnosis was COPD emphysema (22) followed by chronic bronchitis (12), bronchial asthma (10) and bronchiectasis (2). Among obstructive lung diseases, B. asthma had the highest mean DLCO percentage predicted of 102.20 ± 14.36 followed by COPD-Bronchitis (76.33 ± 5.57), COPD-Emphysema (37.80 ± 13.41) and bronchiectasis (62 ± 4.48).

Conclusion: DLCO can be helpful beyond spirometry in classification of obstructive lung diseases. DLCO values in COPD Emphysema variant are decreased, COPD bronchitis variant remains normal or slightly reduced and asthma either normal or increased. So, DLCO can help in differentiation or sub categorization of obstructive disease more than spirometry.

Keywords: DLCO, Obstructive diseases, Lung function test, COPD, Emphysema, Bronchial Asthma.

Introduction

Carbon monoxide diffusing capacity is the least understood pulmonary function test in clinical practice

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worldwide, even among experienced pulmonologists. There are lot of different tests used for evaluation of lung functions. These tests may be performed individually or in combination with other tests. Pulmonary function test report includes spirometry, diffusing capacity, lung volumes and airway resistance (R_{aw}) measurements in a commonly used format. Spirometry help us to differentiate between obstructive and restrictive disease, body plethysmography tells about lung volumes and DLCO about diffusion defect. Determining which tests to do depends on the clinical question to be answered

i.e. whether test is being done to diagnose a disease or for evaluation for lung surgery or some other reason. Measuring the diffusing capacity of lungs for carbon monoxide is 2nd most important pulmonary function test that is done after spirometry.

The single breath test of carbon monoxide (CO) uptake has a long history, from its birth (Krogh and Krogh, 1909)¹ to the first publication by Ogilvie et al describing a standardized technique for the diffusing capacity measurement (DLCO) in 1957.² The DLCO was devised originally as a physiological tool to test the notion that the lung, like the swim bladder of some deep-sea fish, could secrete oxygen against the normal tension gradient provided by inspired air by Bohr in 1900 although this notion is now long abandoned.

As a clinical test DLCO was introduced in 1915 by Marie Krogh, but the measurement never caught on because method of measuring carbon monoxide were so cumbersome.³ But now a day's single breath technique is in common use. DLCO measures the transfer of a diffusion-limited gas (CO) across the alveolocapillary membranes.

DLCO is increased in the circumstances when pulmonary capillaries are recruited, as occurs during exercise, during a Mueller (reverse Valsalva) manoeuvre, pulmonary hemorrhage, polycythemia, obesity, asthma etc. DLCO is decreased in cases of lung resection, pulmonary emphysema affects capillary or alveolar bed, pulmonary vascular disease including PAH and chronic venous thromboembolism, interstitial lung diseases, anemia, drugs induced fibrosis e.g. bleomycin, amiodarone, pulmonary lymphangitic carcinomatosis.

Material and Method

23 patients coming to department of respiratory medicine of MMIMSR, who were diagnosed with obstructive lung disease by PFT, Chest X-ray or CT chest, were considered for the study. At baseline, patient's medical history was recorded and thorough physical examination was done. The medical history chiefly included history of symptoms related to respiratory system, namely shortness of breath, cough, weight loss, fatigue, expectoration and any other symptom related to other systems. Obstructive disease was categorized as post-bronchodilator FEV1/FVC <0.70 for COPD and post bronchodilator change in FEV1 by >12% and 200ml in case of Bronchial asthma. Chronic bronchitis defined clinically as the presence of a chronic productive

cough for 3 months during each of 2 consecutive years after excluding other causes of cough. Then DLCO was performed in every patient. Single breath hold method was used in the study. The report of the DLCO was interpreted according to the American Thoracic Society/European Respiratory Society statement on PFT interpretation and is as follows – normal - >80% predicted DLCO, mild reduction - 79% to 60% of predicted DLCO, moderate reduction - 59% to 40% of predicted DLCO, severe reduction - < 40% of predicted DLCO.

In this present study we aimed to find out the importance of DLCO in differentiation of obstructive disease beyond spirometry and CT evidence as some of the COPD patients may also show post-bronchodilator reversibility.

Results

Male preponderance was seen in study cases with 65.2% males to 34.8% females. Mean age of the study group was 54.39 years with most cases (18) from 31-50 years of age group. Most common diagnosis was COPD emphysema (22) followed by chronic bronchitis (12), bronchial asthma (10) and bronchiectasis (2). 14 (30.4%) patients were smokers, 12 (26.1%) were non-smokers and 20 (43.5%) patients were ex-smokers. Among obstructive lung diseases, B. asthma had the highest mean DLCO percentage predicted of 102.20± 14.36 followed by COPD-Bronchitis (76.33±5.57), COPD–Emphysema (37.80±13.41) and bronchiectasis (62±4.48).

Table 1: Distribution of study cases as per Diagnosis

Diagnosis	N	%
Chronic Obstructive Pulmonary Disease – Emphysema	22	47.82%
Chronic Obstructive Pulmonary Disease – Bronchitis	12	26.08%
Bronchial Asthma	10	21.73%
Bronchiectasis	2	04.34%
Total	46	100%

Table 2: DLCO value in Obstructive lung disease

	N	Mean	SD
B. Asthma	10	102.2	14.32
COPD – E	22	37.80	13.41
COPD – B	12	76.33	5.57
Bronchiectasis	2	62	4.48
Total	46	62.39	29.44

Discussion

DL_{CO} measurement is very reliable and sensitive. DL_{CO} is determined by the amount of blood recruited in the alveolar capillary bed and the alveolo-capillary surface available for diffusion.

The decrease in DL_{CO} is probably more closely related to the loss of lung volume, alveolar surface area, or capillary bed than to the thickening of the alveolocapillary membranes. DLCO also decreases when there is loss of lung tissue or replacement of normal parenchyma by space-occupying lesions such as tumours. DLCO may also be decreased in pulmonary oedema as in congestive heart failure. Surgical lung resection for cancer or other reasons also reduce DLCO except in LVRS and bullectomy because the resected areas generally have little to no blood flow.

In acute and chronic obstructive lung disease also DLCO may be decreased. But other obstructive diseases (e.g., chronic bronchitis, asthma) may not reduce DLCO unless they result in markedly abnormal patterns. Some asthmatic patients may have an increased DLCO, but the cause is not completely understood.

Obstructive lung diseases in our study included B. Asthma, Chronic obstructive pulmonary disease-emphysema and bronchitis variants and bronchiectasis. The mean value of DLCO in obstructive lung diseases was 62.39 ± 29.44 . In specific diseases, B. asthma had the highest mean DLCO percentage predicted of 102.20 ± 14.36 . Saydain G⁴ et al did a study on clinical significance of elevated DLCO in 245 patients who had elevated DLCO values. He found that most patients with elevated DLCO had the diagnosis of obesity, asthma or both. Our study also showed COPD- bronchitis patients had the mean DLCO of 76.33 ± 5.57 while COPD-emphysema patients had a mean predicted DLCO value of 37.80 ± 13.41 . There were only two bronchiectasis patients in the study and the mean DLCO value was 62 ± 4.48 .

To summarize, DLCO is a very good tool for early identification of lung diseases. It can be used to differentiate between COPD and asthma as percentage predicted DLCO is usually decreased in emphysematous patients while it may be normal or increased in asthmatic patients. Bronchitis patients may also show normal or slightly decreased DLCO values.

Conclusion

DLCO can be helpful beyond spirometry in classification of obstructive lung diseases. DLCO values in COPD Emphysema variant are decreased, COPD bronchitis variant remains normal or slightly reduced and asthma either normal or increased. So DLCO can help in differentiation or sub categorization of obstructive disease more than spirometry.

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References

1. Krogh A, Krogh M. 1909. Rate of diffusion into lungs of man. *Skand. Arch. Physiol.* 1909;23: 236-47.
2. Ogilvie CM, Forster RE, Blakemore WS, Morton JW. A standardized breath holding technique for the clinical measurement of the diffusing capacity of the lung for carbon monoxide. *The Journal of clinical investigation.* 1957;36(1):1-7.
3. Krogh M. 1915. The diffusion of gases through the lungs of man. *J. Physiol. Lond.* 1915; 49:271-96.
4. Saydain G, Beck KC, Decker PA, Cowl CT, Scanlon PD. Clinical significance of elevated diffusing capacity. *Chest.* 2004;125(2):446-52.

Time Lag in Reporting of CBNAAT Under RNTCP in Rural Tertiary Health Care Centre

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Abstract

Introduction: CBNAAT is a very useful rapid diagnostic test for the early diagnosis of DS and DR TB. Report of sample can be available in just 2 hours. But the results of these tests are not available for many days to weeks which results in delay in diagnosis and treatment initiation.

Material and Method: This study was conducted for a period of 4 months from mid-April to mid-August 2018 in MMIMSR, Mullana. A total of 535 samples were sent for CBNAAT to TB Hospital, Ambala and the time taken from sending of samples to the receiving of report was analysed and time lag was calculated.

Results: Out of 535 samples, 429 samples were negative, 104 were positive for MTB and 2 samples resulted as invalid/error. Out of 104 positive samples, 95 were rifampicin sensitive and 9 were rifampicin resistant MTB. The average time lag in reporting of CBNAAT samples was 11.1 days with shortest time being 2 days and longest being 33 days.

Conclusion: CBNAAT is a very useful modality in TB diagnosis and should be made available to all eligible patients especially so in high DR-TB prevalence areas. But delay in reporting undermines the purpose of the test i.e. rapid diagnosis and treatment. There is an urgent need to establish more centres with CBNAAT facility throughout India so that there is no delay in reporting and early treatment can be started.

Keywords: RNTCP, CBNAAT, Tuberculosis, NIKSHAY, TB prevalence.

Introduction

TB has been an important challenge for India from last century. From diagnosis to treatment, challenges have been posed that have remained unresolved for many years. The implementation of National Strategic Plan (NSP) 2017-2025 envisions a TB-Free India with zero deaths, disease and poverty due to tuberculosis.

The goal of the NSP 2017-2025 is to achieve a rapid decline in burden of TB, morbidity and mortality while working towards elimination of TB in India by 2025.¹ The requirements for moving towards TB elimination have been integrated into the four strategic pillars of “Detect – Treat – Prevent – Build” (DTPB).¹

The NSP intends to detect Drug sensitive and drug resistant TB by universal implementation of high sensitivity rapid diagnostic tests for diagnosis of TB. These tests like CBNAAT (Cartridge Based Nucleic Acid Amplification Test) is a very useful in early diagnosis of drug resistance and sensitivity patterns of TB. These tests have been incorporated into the TB diagnostic algorithm and are being increasingly used under the RNTCP for diagnosis of TB and drug resistance. But the

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facilities where these tests are available are very few and the number of samples are increasing day by day. There is a considerable gap between the potential of CBNAAT for early diagnosis of TB within 2 hrs and that being achieved in the field.

CBNAAT takes about 2 hours for the reporting. But from the rural and remote centres the sample has to be sent to these centres which are usually available only in district headquarters. This process takes time and resources and it is usually seen that there is delay in reporting of these tests ranging from days to weeks. This results in delay in diagnosis as well as initiation of treatment. This leads to transmission of TB which in some cases may be drug resistant TB.

This study was undertaken in the department of respiratory medicine, MMIMSR, Mullana to find out the average number of days taken after giving sample by the patient till their reporting of CBNAAT samples and to analyse the cause for this delay.

Material and Method

This study was conducted in the department of respiratory medicine in MMIMSR, Mullana, Ambala. Sputum samples of suspected TB patients attending OPD of respiratory medicine department and patients admitted in respiratory medicine ward were collected in the hospital DMC and sent by courier to Ambala District TB Hospital for CBNAAT test. Samples were collected over a period of 4 months from mid-April to mid-August 2018 and 535 patients were included in the study. The reports were received through e-mail in the month of April through mid-August 2018 and the average number of days lapsed between sending of samples from our hospital to receipt of the report through e-mail was calculated.

Results

Out of 535 samples, whose report was received during study period, MTB was detected in 104 (19.4%) samples. Out of these 104 samples, 95(91.2%) samples were rifampicin sensitive MTB (RS-TB) and 9 (8.8%) were detected as rifampicin resistant MTB(RR-TB). 1 sample was reported as invalid and 1 as having erroneous result. (Table 1). The rate of CBNAAT positivity was 19.4% in the study.

Out of 104 samples that were positive for MTB, 96 were Pulmonary TB and 8 were EPTB. Out of total PTB cases, 88 (91.6%) were rifampicin sensitive TB (RS-TB) and 8 (8.4%) were rifampicin resistant TB (RR-TB). Out of 8 EPTB cases, 7 cases (87.5%) were RS-TB and 1(12.5%) was RR-TB. From positive cases 4 (50%) were pleural TB, 1 (12.5%) TB meningitis and 3 (37.5%) cold abscess. In EPTB group 1 RR-TB case was pleural TB. (Table 2)

The average time lag between collecting the sample from the patient in our hospital DMC to receiving the report of that sample was calculated as 11.1 days. The longest duration for receiving a report was 33 days for 1 sample while the shortest duration was of 2 days that was for 8 samples out of 535 total samples sent. Maximum number of samples 58(10.8%) were in the 11 days lag bracket followed by 10 days lag for 57(10.6%) samples. (Table 3).

71.4% of samples had a delay of more than 1 week, 26.5% (142) of samples had a delay of more than 2 weeks, 10% of sample reports were received after a delay of more than 3 weeks. 1.32% reports were received after 4 weeks of delay. (Table 4).

Maximum number of samples consisted of sputum specimen [n = 435 (81.34%)] followed by pleural fluid samples [n= 34 (6.35%)]. Remaining samples included pus, ascitic fluid, Cerebrospinal fluid (CSF), Lymph node (LN), Endometrial tissue, Gastric aspirate, Broncho alveolar lavage (BAL) fluid and 3 other samples. Only a single sample per patient was sent owing to high work load at district CBNAAT lab. Repeat sample was sent only in case of positive result. (Table 5).

Table 1: Distribution of CBNAAT Reports and Sensitivity pattern

S.No.	Result	No. of Cases	Percentage
1.	Total samples sent	535	100%
2.	MTB Not Detected	429	80.2%
3.	Invalid/Error	2	0.4%
4.	MTB Detected	104	19.4% (100%)
5.	RS TB	95	17.7% (91.2%)
6.	RR TB	9	1.7% (8.8%)

Table 2: Site wise distribution of TB

Total TB Cases	EPTB		N = 8	PTB (n)		N = 96
104	8(7.7%)			96(92.3%)		
	RS-TB	7	87.5%	RS-TB	88	91.6%
	RR-TB	1	12.5%	RR-TB	8	8.4%
	TOTAL	8	100%	TOTAL	96	100%
	Site Wise Distribution (n = 8)					
	PLEURAL	4	50%			
		RS = 3	(37.5%)			
		RR= 1	(12.5%)			
	CSF	1	12.5%			
	PUS	3	37.5%			

Table 3: Mean Duration

	Mean Time	Maximum No. of Days	Minimum No. of Days
Duration (Days)	11.1 Days	33 Days	2 Days

Table 4: Summary of Time lag and number of samples

Time Lag (Days)	No. of Samples	Percentage
2	8	1.5%
3	17	3.17%
4	28	5.2%
5	39	7.30%
6	33	6.16%
7	28	5.23%
8	14	2.61%
9	35	6.54%
10	57	10.65%
11	58	10.84%
12	25	4.70%
13	15	2.80%
14	36	6.72%
15	15	2.80%
16	17	3.2%
17	15	2.80%
18	10	1.86%
19	11	2.05%
20	18	3.36%
21	2	0.4%
22	3	0.56%
23	17	3.17%
24	3	0.56%
25	10	1.86%
26	1	0.2%
27	9	1.7%
28	3	0.56%
29	7	1.30%
33	1	0.2%

Table 5: Proportion of type of specimen

S.No.	Specimen Type	Number of Samples	% of Total	Positive	% Positivity of Specimen
1.	Sputum	435	81.34%	96	22%
2.	Pleural Fluid	34	6.35%	4	11.8%
3.	Pus	19	3.55%	3	15.8%
4.	Ascitic Fluid	10	1.86%	-	-
5.	CSF	14	2.61%	1	7.1%
6.	LN Aspirate	8	1.49%	-	-
7.	Endometrial Tissue	5	0.93%	-	-
8.	Gastric Aspirate	4	0.74%	-	-
9.	BAL	3	0.56%	-	-
10.	Other	3	0.56%	-	-
	Total	535	100%	104	

Table 6: Geographical Distribution of samples

S.No.	Area	State/Country	Number of Samples	Percentage
1.	Saharanpur	Uttar Pradesh (UP)	302	56.4%
2.	Ambala	Haryana	91	17%
3.	Yamuna Nagar	Haryana	61	11.4%
4.	Haridwar	Uttarakhand	14	2.61%
5.	Shamli	UP	12	2.24%
6.	Muzaffarnagar	UP	12	2.24%
7.	Kurukshetra	Haryana	9	1.68%
8.	Roorkee	Uttarakhand	6	1.12%
9.	Karnal	Haryana	6	1.12%
10.	Dehradun	Uttarakhand	6	1.12%
11.	Naraingarh	Haryana	5	0.93%
12.	Patiala	Punjab	4	0.74%
13.	Ludhiana	Punjab	2	0.37%
14.	Mandi, Sirmaur, Paonta Sahib	Himachal Pradesh (HP)	3 (1 each)	0.56%(0.18% each)
15.	Fillaur	Punjab	1	0.18%
16.	Nepal	Nepal	1	0.18%
	Total		535	100%

Conclusion

Molecular rapid diagnostic tests have become an integral part of Revised National TB control Program in India. It is recommended for diagnosis of TB in all previously treated patients, Childhood TB and extrapulmonary TB apart from detecting the drug resistant TB. Under National Strategic Plan RNTCP is of the vision that molecular method for diagnosis of TB are to be implemented in country wide manner in all suspected TB cases. But in remote and rural areas CBNAAT facility is not yet available in most centres so the time from sending of samples to receiving the report

is too long. It may range from few days or weeks to a month or more in which time the patient is potentially transmitting the disease to household persons, at occupational place and at social and public places. These delays lead to lack of trust of patients in government TB control program as the same report can be obtained within few hours from private labs despite of it being free of cost in government hospitals.

Delay can occur in the process of sending of samples from the DMC, dispatching of samples by the courier service provider, processing of samples by the receiving district lab, short supply of cartridges or other

accessories, reporting of the test by the lab personnel or due to delay in sending the e-mail by the district hospital or delay in communication of the report to the patient or time taken by the patient to collect the report. All these factors may contribute to the delays in reporting which in turn delays the process of diagnosis and initiation of treatment. A number of patients never show up or show up days or weeks later to collect the report. Delays in diagnosis of drug resistant TB can be very hazardous as this not only results in delay in treatment initiation but also in transmission of DR TB which is already taking up epidemic proportions in India.

In our study the causes of delay are due to several factors including high sample load leading to back log of samples at district lab, high TB incidence in the region, lack of CBNAAT machine at our centre, lack of human resources, delay in sending the samples as they are sent by courier and are sent after a certain number of samples are collected due to financial constraints and delay in opening the e-mail at the receiving end as reports are received by e-mail. But the major part of delay occurred at district lab because the average delay in our study is 11.1 days while samples are usually sent within 1 day of collection from our centre.

The result of our study shows that one of the purposes for which CBNAAT was introduced, i.e. rapid diagnosis of TB, is not being served in most of the remote and rural areas where CBNAAT facility is not available or available too far away. Just implementing a new diagnostic algorithm is not enough; there is an urgent need to set up new centres for molecular testing in remote and rural areas so that this time lag can be reduced if not eliminated.

Conclusion

The effectiveness of the CBNAAT as rapid diagnostic tool does not depend only on the machine but

at each level from collecting the sample up-to receiving of the report. The delay can be reduced by increasing the number of machines at district level and by providing CBNAAT machines in more centres especially in areas of high TB burden, in medical colleges and by provision of adequate workforce and sufficient funding by the government. Apart from these the prompt action of personnel at each level can improve the current appalling state of affairs in rural areas where most of the population lives in India. This will not only result in early diagnosis and treatment initiation but will also prevent transmission of TB and will help in achieving the goal of TB elimination by 2025.

Conflict of Interest: None

Source of Funding: Self

Ethical Clearance: Ethical Clearance was obtained from the Institutional Ethics Committee (IEC), Maharishi Markandeswar (deemed to be university) Mullana, Ambala.

Remarks by the Author: This is the first study of its own kind. After exhaustive search couldn't found the relevant references.

References

1. Revised National Tuberculosis Control Programme, NATIONAL STRATEGIC PLAN FOR TUBERCULOSIS ELIMINATION 2017–2025.
2. NITI Aayog, Govt. of India | Literacy Rate 7+ years(%) 2011 census| link - <http://niti.gov.in/content/literacy-rate-7years>
3. India Census 2011| link - <https://www.census2011.co.in/states.php>
4. Nikshay Notification Report | link - <http://nikshay.gov.in/NotificationReport.aspx>

To Study the Prevalence of Obstructive Airway Disease in Patients of OSA Diagnosed by Polysomnography

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Abstract

Aim: To study the prevalence of obstructive airway disease in patient of OSA diagnosed by polysomnography.

Method: This study is a descriptive cross-sectional and was carried out in patients admitted in the department of Respiratory Medicine who were diagnosed with OSA after polysomnography. Total 41 patients who were diagnosed as cases of obstructive sleep apnea were clinically evaluated and investigated by history taking and final diagnosis were made as either COPD, Asthma on basis of GOLD and GINA guidelines respectively.

Results: Mean age of the study participants was 50.95 years. Prevalence of Asthma and COPD among cases with OSA was 58.5% and 14.6%. Mean AHI and ESS score was 42.45 and 16.80 respectively. The most common co-morbid condition was GERD (19.5%).

Conclusion: Present study concluded that asthma is more prevalent than COPD in patients of obstructive sleep apnea. The main factors associated with Obstructive lung diseases and its pathogenesis is the obesity, hypertension, smoking habits, adenoids, tonsillitis, musculoskeletal changes, weakness and atrophy of muscles of upper respiratory tract.

Keywords: Asthma, COPD, Obstructive Sleep Apnea, Polysomnography.

Introduction

Sleep is a natural periodic state of rest for the psyche and body, where the eyes generally close and cognizance is totally or incompletely lost so that there is a lessening in real development and responsiveness to external stimuli. It is said that "sleep is remunerated for somewhere in the range of, a discipline for others." Obstructive sleep apnea (OSA) is leading medical issue in developed and developing countries.¹

Untreated OSA leads to excessive daytime sleepiness, diminished performance and overall poor

quality of life. Sleep disorder breathing (SDB) includes a spectrum of conditions including snoring, upper airway resistance syndrome (UARS) and OSA. The most severe of which is obstructive sleep apnea syndrome (OSA). It is potentially disabling condition characterized by disruptive snoring, repeated episodes of complete or partial pharyngeal obstruction during sleep resulting in nocturnal hypoxemia, frequent arousals and excessive day time sleepiness.²

Prevalence of OSA varies in different population. In most of the studies it varies from 3-7%. In India prevalence of obstructive sleep apnea is 7.5% in males and that of 4.5% in females.³ Several studies have investigated the association between OSA and obstructive airway disease (OAD), including both asthma and chronic obstructive air way disease (COPD). A high prevalence of OSA has been reported in asthma cases⁴ and asthma may also be common in OSA.⁵ Sleep related symptoms do also occur in patients of COPD.

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Whenever both these condition present together is called “Overlap Syndrome.”

It is not surprising that research attentions have focused on the overlap syndrome between these two highly prevalent conditions with the aim of determining their relationship. In patients with COPD, studies have shown that as the depth of sleep increases, there is a reduction in minute ventilation with an increase in upper airway resistance⁶ with up to 20% patients of severe COPD exhibiting co-existent OSA.⁷ In the previous literature there is some controversy as to whether the association between obstructive lung diseases and OSA is that expected merely on the basis of the conjunction of two relatively common clinical conditions or whether having OSA or obstructive lung diseases confers increased risk for having the other.⁸ In the current study, we explored the prevalence of obstructive airway disease in patients of OSA diagnosed by polysomnography.

Material and Method

Study Design: The present descriptive cross-sectional study was carried out in patients admitted in the department of Respiratory Medicine of our hospital who were diagnosed with OSA after polysomnography. The patients fulfilled the inclusion criteria and exclusion criteria were finally taken up for the study. Total 41 patients who were diagnosed as cases of obstructive sleep apnea, these cases were further clinically evaluated and investigated by history taking and final diagnosis were made as either COPD, asthma on basis of GOLD and GINA guidelines respectively.

Sample Size Calculation: The sample size was calculated using following formulae:

$$n = (Z_{\alpha/2})^2 * (PQ)/E^2$$

n - Sample size

Z_{α/2} – Z value at 5% error (1.96)

E – Absolute error (taken as 20%)

Sample size was found to be 23 by using this formula. However, we decided to take more than 30 cases in the present study.

Inclusion Criteria: All OSA cases diagnosed by polysomnography in department of respiratory medicine will be taken up for the study.

Exclusion Criteria:

1. Patients who were critical ill.
2. Patients who were known cases of CVA.
3. Hemodynamically unstable patients.
4. Pregnant women

Methodology

Patient’s evaluated using polysomnography after taking history clinical examination and investigations were done:

1. Vitals
 - Blood pressure
 - Pulse rate
 - SPO2
 - Respiratory rate
 - Temperature
2. Body mass index
3. Chest x-ray PA view
4. ECG 12 lead
5. Spirometry with reversibility test

Diagnosis of COPD, Asthma and overlap syndrome or any other comorbid condition was established

Statistical Analysis: The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2010) and then exported to data editor page of SPSS version 20 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics included computation of percentages, means and standard deviations.

Table 1: Distribution of gender, clinical symptoms and personal history

Gender	N	%
Male	30	73.2
Female	11	26.8
Clinical Symptoms		
Snoring	40	97.6
Fatigue	29	70.7
Day time Sleepiness	25	61.0
Difficulty in Sleeping	13	31.7
Smoking and Alcohol Intake		
Ex-smoker	1	2.4
Smoker	8	19.5
Alcohol	6	14.6
Alcoholic + Smoker	1	2.4

Table 1: Mean age of the study participants was 50.95 years. Male predominance was seen among study cases with 73.2% males to 26.8% females. Most common presenting symptoms among study population were snoring (70%) followed by day time sleepiness (61.0%) fatigue (70.7%) and difficulty in sleeping (31.7%). Out of all, 19.5% are smokers and 14.6% were alcoholics.

Table 2: Distribution of mean Age, Anthropometry, Spirometry, AHI & ESS

Variables	Mean	Std. Deviation
Age	50.95	11.48
BMI	31.24	5.61
Neck circumference	40.71	1.68
Spirometry	FEV1 (%)	63.19
	FVC (%)	70.82
	FEV/FVC (%)	87.36
AHI	42.45	20.86
ESS	16.80	4.22

Table 2: Mean age of the study participants was 50.95 years. Mean BMI of study participants was 31.24 kg/m² while mean neck circumference was 40.71 cm. Mean FEV1, FVC and FEV1/FVC was 63.19, 70.82 and 87.36. Mean AHI and ESS score was 42.45 and 16.80 respectively

Table 3: Prevalence of COPD, Asthma and COPD/ Asthma Combined

Variables	N	%
Asthma	24	58.5
COPD	6	14.6
Combined	0	0.0
Total	41	100.0

Table 3: Prevalence of asthma and COPD among cases with OSA was 58.5% and 14.6%

Table 4: Distribution of Co-morbidities

Variables	N	%
GERD	8	19.5
HTN	5	12.2
Diabetes	4	9.8
CAD	3	7.3
DNS	2	4.8
Rhinitis	2	4.8
Hypothyroidism	0	0.0

Table 4: The most common co-morbid condition

was GERD (19.5%) followed by hypertension (12.2%), Diabetes (9.8%), CAD (7.3%), DNS and Rhinitis (4.8%) each.

Discussion

Sleep medicine is an emerging field of medical science that has recently become popular due to developments in technology and medical science. Development in the field of sleep medicine has come in leaps and bounds in recent years and it has coincided with its emerging popularity in the developing world. Obstructive and central sleep apneas are two forms of sleep disordered breathing that has received most interest. Obstructive sleep apnea is the most commonly seen sleep abnormality and is the one in which most interest has been shown by the medical fraternity.

In present study we aimed to find out the prevalence of COPD and asthma in patients diagnosed with Obstructive Sleep Apnea. A total of 41 cases of OSA fulfilling the inclusion criteria and exclusion criteria were include in the study. Cases were subjected to physical examination included measurement of height, weight, Body Mass Index (kg/m²), neck circumference and spirometry. Epworth sleepiness scale was applied to the patients and total score was also calculated and severity of OSA was recorded using AHI Index. All patients were subjected to a full night hospital-based sleep study for diagnosis of OSA.

In present study, prevalence of Asthma and COPD (as defined by GOLD and GINIA guidelines) among cases with OSA was 58.5% and 14.6%. The mean AHI and Epworth sleepiness score was 42.45 and 16.80 respectively. Our study supports the notion that there is an association between OLD and OSA. Our findings were in agreement with study conducted by Greenberg-Dotan et al. (2014), COPD was found prevalent in 7.6% patients and asthma was found in 10.4% of the patients.⁹

In the present study the most common presenting symptoms among study population was snoring (70%) followed by day time sleepiness (61.0%) fatigue (70.7%) and difficulty in sleeping (31.7%). Similarly, Snoring is the most frequent symptom of OSAS, occurring in up to 95% of patients, but has poor predictive value because of the high prevalence in the general population.¹⁰ However, the absence of snoring makes OSAS unlikely and only 6% of patients with OSAS did not report snoring in one report.¹¹ Between 30-50% of the general population report significant sleepiness.¹² Other than

EDS, such as fatigue, memory impairment, personality changes, morning nausea, morning headaches, automatic behavior and depression.^{13,14} Although these features may be important in assessing the impact of sleep apnea on a patient and the effectiveness of therapy, there has been no systematic study of the capacity of these features to predict the presence or absence of OSA

The role of smoking and alcoholism has also been studied in OSA. In our study 19.5% were smokers and 14.6% were alcoholics. Scanlan et al. found that alcohol resulted in a small but statistically significant rise in the frequency of obstructive apnoeas and hypopnoeas, without prolonging the apnoea length or worsening hypoxaemia.¹⁵

Proposed mechanisms for the adverse effects of alcohol upon OSA include selective reduction in genioglossus and hypoglossal motor nerve activity, increased nasal mucosa oedema and thereby increased resistance, a reduction in arousal response and a reduced haemoglobin affinity for oxygen.^{16,17} In addition, considerable evidence exists that alcohol fragments sleep, independent of apnoea status, which may further aggravate OSA.^{18,19}

In the present study the most common co-morbid condition was GERD (19.5%) followed by hypertension (12.2%), Diabetes (9.8%), CAD (7.3%), DNS and Rhinitis (4.8%) each Link between sleep apnea and hypertension has been consistently demonstrated in many studies and the finding of hypertension in a patient with symptoms suggestive of OSAS increases the likelihood of the disorder.^{20,21} OSAS also relates independently to diabetes and the metabolic syndrome.^{22,23} Assad et al (2013) indicated that asthma is associated with three components of metabolic syndrome, the abdominal obesity, hypertension and elevated fasting glucose or diabetes in an un-adjusted models.²⁴ From the aforementioned studies, it is understandable that the abdominal obesity, insulin resistance (elevated glucose) and hypertension are the main risk factors that associate metabolic syndrome with asthma. Based on these risk factors, there are several suggestive mechanisms which explain the link between metabolic syndrome and asthma. It can be due to mechanical effect, genetic factors, epigenetic factors, inflammatory effect, mitochondrial dysfunction, hormonal effect and the effect of other co-morbidities.²⁵

Conclusion

The present study concluded that asthma is more prevalent than COPD in patients of obstructive sleep apnea. The main factors associated with Obstructive lung diseases and its pathogenesis is the obesity, hypertension, smoking habits, adenoids tonsillitis, musculoskeletal changes, weakness and atrophy of muscles of upper respiratory tract. ESS can be an important predictor of presence of OSA as well as severity of OSA, when used in combination with patient history, symptoms and physical examination. Studies show that there is improvement in symptoms after CPAP therapy was reported by the patients on follow up visits but this aspect was not analyzed in the current study as our study mainly deals with prevalence of COPD and asthma not with treatment part. But we recommend future prospective studies to evaluate the role of CPAP in these patients.

Conflict of Interest: None

Source of Funding: Self

Ethical Approval and Informed Consent: The study protocol was reviewed by the Ethical Committee of Hospital and was granted ethical clearance. After explaining the purpose and details of the study, a written informed consent was obtained from the patients who participated in the study. It was emphasized that strict confidentiality would be maintained at all times and the patients could withdraw at any time without being penalized.

References

1. The American Heritage® Medical Dictionary Copyright © 2007.
2. Sharma H, Sharma SK. Overview and implications of obstructive sleep apnea. *Ind J Chest Dis Allied Sci* 2008; 50:137-150.
3. Udawadia ZF, Doshi AV, Lonkar SG, Singh CI. Prevalence of sleep disordered breathing and sleep apnea in middle aged urban Indian men. *Am J Respir Crit Care Med* 2004; 169:168-173
4. Auckley D, Moallem M, Shaman Z, Mustafa M. Findings of a Berlin Questionnaire survey: comparison between patients seen in an asthma clinic versus internal medicine clinic. *Sleep Med* 2008; 9:494-499.

5. Alharbi M, Almutairi A, Alotaibi D, Alotaibi A, Shaikh S, Bahammam AS. The prevalence of asthma in patients with obstructive sleep apnoea. *Prim Care Respir J* 2009; 18:328-330.
6. Ballard RD, Clover CW, Suh BY. Influence of sleep on respiratory function in emphysema. *Am J Respir Crit Care Med*. 1995; 151(4):945-51.
7. Brander PE, Kuitunen T, Salmi T, Partinen M. Nocturnal oxygen saturation in advanced chronic obstructive pulmonary disease after a moderate dose of ethanol. *Eur Respir J*. 1992; 5(3):308-12.
8. Hiestand D, Phillips B. The overlap syndrome: chronic obstructive pulmonary disease and obstructive sleep apnea. *Crit Care Clin*. 2008; 3:551-63
9. Greenberg-Dotan S, Reuveni H, Tal A, Oksenberg A, Cohen A, Shaya FT, Tarasiuk A, Scharf SM. Increased prevalence of obstructive lung disease in patients with obstructive sleep apnea. *Sleep Breath*. 2014;18(1):69-75.
10. Gottlieb DJ, Yao Q, Redline S, Ali T, Mahowald MW. Does snoring predict sleepiness independently of apnea and hypopnea frequency? *Am J Respir Crit Care Med* 2000;162:1512–1517.
11. Viner S, Szalai JP, Hoffstein V. Are history and physical examination a good screening test for sleep apnea? *Ann Intern Med* 1991;115:356–359.
12. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. *N Engl J Med* 1993;328:1230–35.
13. Deegan PC, McNicholas WT. Predictive value of clinical features for the obstructive sleep apnoea syndrome. *Eur Respir J* 1996;9:117–124.
14. Whyte KF, Allen MB, Jeffrey AA, Gould GA, Douglas NJ. Clinical features of the sleep apnoea/hypopnoea syndrome. *Q J Med* 1989;72: 659-66
15. Scanlan MF, Roebuck T, Little PJ, Redman JR, Naughton MT. Effect of moderate alcohol upon obstructive sleep apnoea. *Eur Respir J*. 2000;16(5):909-13.
16. Robinson RW, White DP, Zwillich CW. Moderate alcohol ingestion increases upper airway resistance in normal subjects. *Am Rev Respir Dis* 1985; 132: 1238-1241
17. St John WM, Bartlett D, Knuth KV, Knuth SL, Daubenspeck JA. Differential depression of hypoglossal nerve activity by alcohol. Protection by pre-treatment with medroxyprogesterone acetate. *Am Rev Respir Dis* 1986;133: 46-48
18. Landolt HP, Roth C, Dijk DJ, Borbely AA. Late afternoon ethanol intake affects nocturnal sleep and the sleep EEG in middle-aged men. *J Clin Psychopharmacol* 1996; 16: 428-436.
19. Leiter JC, Knuth SL, Bartlett DJ. The effect of sleep deprivation on activity of the genioglossus muscle. *Am Rev Respir Dis* 1985; 132: 1242-1245.
20. McNicholas WT, Bonsignore MR; Management Committee of EU COST ACTION B26. Sleep apnoea as an independent risk factor for cardiovascular disease: current evidence, basic mechanisms and research priorities. *Eur Respir J* 2007;29:156-78.
21. Peppard PE, Young T, Palta M, Skatrud J. Prospective study of the association between sleep-disordered breathing and hypertension. *N Engl J Med* 2000;342:1378-84.
22. Reichmuth KJ, Austin D, Skatrud JB, Young T. Association of sleep apnea and type II diabetes: a population-based study. *Am J Respir Crit Care Med* 2005;172:1590-95.
23. Coughlin SR, Mawdsley L, Mugarza JA, Calverley PM, Wilding JP. Obstructive sleep apnoea is independently associated with an increased prevalence of metabolic syndrome. *Eur Heart J* 2004;25:735–741
24. Assad N, Qualls C, Smith LJ, Arynchyn A, Thyagarajan B, Schuyler M, Jacobs DR Jr, Sood A. Body mass index is a stronger predictor than the metabolic syndrome for future asthma in women. The longitudinal CARDIA study. *Am J Respir Crit Care Med*. 2013;188(3):319-26.
25. Agrawal A, Mabalirajan U, Ahmad T, Ghosh B. Emerging interface between metabolic syndrome and asthma. *Am J Respir Cell Mol Biol*. 2011; 44(3):270-5.

Correlation of Chest Radiography with Microbiological Findings for the Diagnosis of Pulmonary Tuberculosis

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Abstract

Introduction: Tuberculosis is a major health problem faced by mankind since ancient times till date in spite of advances in our knowledge. Recently HIV hastened this & it became the single largest infectious disease-causing high mortality in humans leading to numerous deaths annually.

Early & prompt diagnosis is the only solution to control it. In developing country like India RNTCP depends on chest radiography & smear microscopy but culture is still GOLD standard method. Thus this study was designed to correlate the radiologically suspected tuberculosis cases with Zeihl-Neelsen staining & culture on LJ medium.

Method: A cross-sectional study conducted on 60 radiologically suspected cases of pulmonary tuberculosis to compare the efficacy with conventional LJ medium culture and ZN staining. The samples were chosen using simple random sampling method.

Results: Out of total 60 cases, 40(66.66%) cases showed positive results by any of the method. ZN staining (100%) rendered highest positivity than LJ media (80%) in far advanced with cavity while in minimal lesion LJ media (25%) was more effective than ZN staining (12.5%). Maximum number of Grading 3+ cases were with far advanced with cavity (100%) followed by moderate lesion with cavity (72.7%). Advanced with cavity showed highest and earliest growth i.e. 60% within 2 weeks while in moderate lesion with cavity it was 18.8%

Conclusion: Correlation between radiological and microbiological findings must be the mainstay for the diagnosis in clinical suspected case of pulmonary TB.

Keywords: Tuberculosis, ZN staining, Cavity lesions, LJ media.

Introduction

Tuberculosis (TB) is a global problem that seriously threatens public health causing several deaths annually. Nearly 95% of all tuberculosis cases and 98% of deaths due to tuberculosis are in developing countries and 75%

of tuberculosis cases are in the economically productive age group.¹ In India there are about 500,000 deaths occurring annually due to TB with the incidence and approximately 1.8 million persons develop TB annually of which about 0.8 million are new smear positive highly infectious cases.^{2,3} It affects both sexes and all ages due poverty, overcrowding, low socioeconomic status, multiple pregnancies, active & passive smoking, lack of health education, under-nutrition, poor housing etc.⁴ RNTCP guidelines are based on recommendations of the World Health Organization (WHO) and focus on detection of cases using acid fast bacilli (AFB) smear microscopy.⁵ The mainstay for its control is the rapid

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and accurate identification of infected individuals. This will detect only those patients with the highest number of TB organisms in the sputum, presumed to be the most infectious cases. Although less infectious than smear positive patients, smear-negative patients are capable of transmitting disease and experience substantial morbidity and mortality.⁶ The tools used for diagnosis of TB have remained largely unchanged since the 1880s when sputum microscopy, Mycobacterium tuberculosis culture on solid media tuberculin skin testing and chest radiology were initially developed.⁶ Chest x-ray is one of the most popular and non-expensive imaging tools for the diagnosis of pulmonary TB.⁷ There should be correlation of detection & isolation of Mycobacteria with abnormal x-ray finding in every clinically suspected tuberculosis patient. Therefore this study was designed to compare on the radiologically suspected tuberculosis cases, the culture on LJ medium which is a gold standard.

Materials and Method

Study Design: A prospective cross-sectional test validation study.

Sample Size: A total of 60 radiologically suspected TB patients attending OPD and IPD of M.M. Institute of Medical Sciences & Research Centre were recruited for the study.

Sampling: Systematic random sampling.

Specimen collection and transport: Sputum samples from the patients of suspected pulmonary tuberculosis were collected by standard aseptic precaution as per RNTCP guidelines.

Processing: The sputum samples were processed for

- i. ZN-Staining
- ii. Culture-After digestion/decontamination and concentration (standard NALC-NAOH procedure) sputum samples were inoculated on LJ media.⁸

Results

The rate of mycobacterial species amongst radiologically suspected tuberculosis patients 40 (66.66%) cases showed positive results by any of the method i.e. culture on LJ media and ZN staining (Table 1). Growth of LJ and ZN staining rendered highest positivity in far advanced with cavity, 80% and 100% respectively ensued by moderate lesions with

cavity, where smear was positive for 81.8% and culture for 63.6% of patients (fig 1). It confirms the affirmative relation between extent of radiological lesions and the ZN smear grading (fig 2). The highest number of cases which were positive by radiological findings were seen with grading 3+ and the maximum number of cases (100%) had far advanced with cavity followed by moderate lesion with cavity (72.7%). The cavitary nature of the lesion corroborates with rapidity in growth on LJ media (Table II). For advanced with cavity showed highest and earliest growth i.e. 60% within 2 weeks while in moderate lesion with cavity it was 18.8%

Discussion

India, holding the highest percentage of the Mycobacterium tuberculosis patients & its fatal nature along with the increasing resistance to anti tubercular drugs further worsens the situation. In the current scenario, the diagnostic aspect of the disease has improved manifolds and every day, scientists are out there to invent newer and better diagnostic method. An age old and efficient method to diagnose tuberculosis has been radiology. The images formed on radiograph give a fair idea about the intensity of the disease as well. But the radiological appearances of many other lung diseases also give similar images thereby making it difficult for the accurate detection as far as pulmonary tuberculosis is concerned.

Microbiology, a department dealing right away with the causative agent has been providing a variety of authentic method for the detection. Culture being the gold standard for the diagnosis of mycobacteria tuberculosis is one of the most effective ways. But due to the delay in giving growth, which further delays the initiation of treatment generates a need to involve a relatively rapid technique along with it. Speaking of rapid method, Ziehl – Neelson staining has been one of the most reliable method, which actually show the mycobacteria in microscopy and in addition give the approximate bacterial count as well. As an adjunct, various method like tuberculin testing, ELISA, BactT/3D Alert and PCR have come but some of them are not cost efficient whereas some of them lack specificity, thereby making them able to strengthen the diagnosis only. In view of that the present study is conducted on 60 radiologically suspected patients of pulmonary tuberculosis to traverse the distance of old age till new age by various microbiological detection method viz Growth on LJ media and AFB staining. The samples were received in

the department of Microbiology from different wards and OPD's of MMIMSR, Mullana.

Multiple test increases the overall percentage positivity and many researchers believe in the same. Jena J et al.⁹ (1995) and Kamal Mostafa M A et al.¹⁰ (2009). In their studies rendered the overall positivity rate 47.9% and 44% respectively while in the present study, the rate of mycobacterial species by one or more tests came out to be 66.66% (Table 1) which is on higher side, maybe because of the selection criteria (equal number of samples were positive for ZN staining). While the present study is in accordance with Rao SK et al.² (2010) which illustrated 71.1% positivity.

The radiological picture to diagnose pulmonary TB still considered holding a genuine significance. There is a very strong correlation between the extent of radiographic findings and the prevalence of bacillary disease. In the present study, far advanced lesion with cavity have highest rate of growth on LJ culture as well as smear positivity i.e 80% and 100% respectively, followed by moderate lesions with cavity where growth on LJ culture came out be 54.5% and smear positivity, 81.8% (Fig. I). These findings were quite high when compared to non cavitary lesions (minimal, moderate/far advanced without cavity and fibrotic and calcified). This is further supported by Tupasi ET et al.¹¹ (2000) who observed maximum smear positivity and growth on

LJ media i.e. 90.9% and 90.9% in far advanced lesions with cavity.

The presentation of radiological lesions i.e. minimal, moderate/far advanced without cavity. Moderate with cavity, far advanced with cavity or fibrotic and calcified lesions can be mimicked by many other lung diseases making it unreliable for accurate diagnosis. This is even supported by the American thoracic society. Thus, one of the most rapid reliable microbiological method of diagnosis, ZN Staining can be relied upon for making the diagnosis of pulmonary tuberculosis. The presence of cavitary lesions in radiological findings had high number of mycobacteria because the cavity facilitates spreading of the bacteria and such lesions would show early growth on LJ media as well as the AFB staining of sputum would show higher grade in the present study, 3+ grade is shown by cases which had far advanced lesions with cavity (100%) followed by moderate lesions with cavity (12.5%) (Fig. II).

While in the present study, far advanced lesions with cavity presented highest growth, 80% and that to in 2 weeks followed by moderate lesions with cavity, 54.5%. Moderate lesions with cavity and minimal lesions showed late growth on LJ i.e. 31.25% and 25% and after 4-7 weeks (table II). As per our best of knowledge is concerned, such studies have not been conducted in the past.

Table 1: Detection of mycobacteria species in radiologically suspected patients of pulmonary tuberculosis

Total number of patients	60
Total positive cases by microbiological tests	40(66.6%)

Table 2: Interrelation of radiographic findings with weekly growth on L.J. media in detection of mycobacterium tuberculosis

Lesions	1 Week	2 Week	3 Week	4 Week	5 Week	6 Week	7 Week	Total
Minimal lesion (n=24)	Nil	nil	Nil	nil	3(12.5%)	2(8.3%)	1(4.7%)	6
Moderate without cavity (n=16)	Nil	nil	Nil	2(12.5%)	2(12.5%)	1(6.2%)	nil	5
Moderate with cavity (n=11)	Nil	4(18.2%)	1(27.3%)	1(9.01%)	nil	Nil	nil	6
Far advanced with cavity (n=5)	Nil	3(60%)	1(20%)	nil	nil	Nil	Nil	4
Fibrotic and calcified lesion (n=4)	Nil	nil	Nil	nil	nil	Nil	Nil	nil

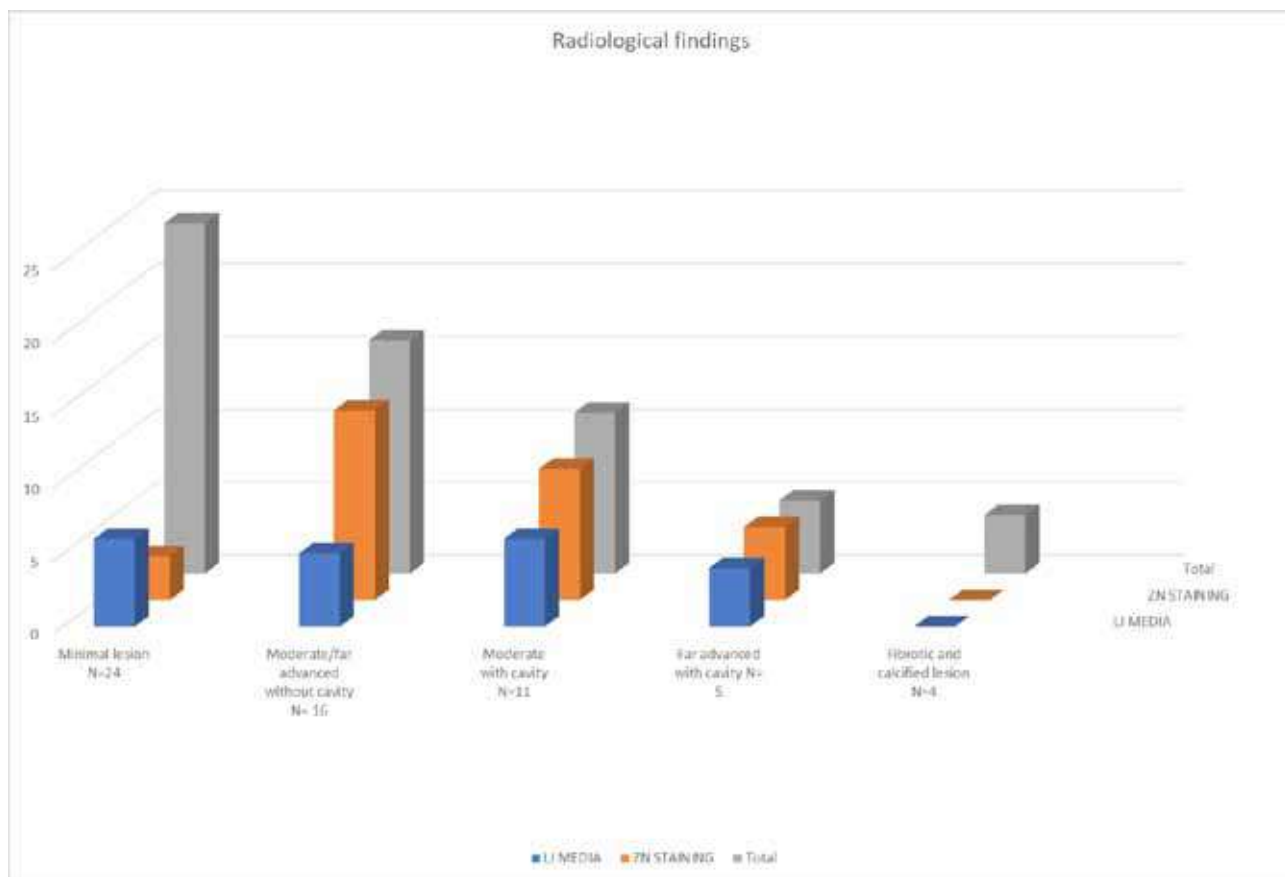


Figure 1: Correlation of radiological findings with LJ Media and ZN staining in detection of Mycobacterial tuberculosis

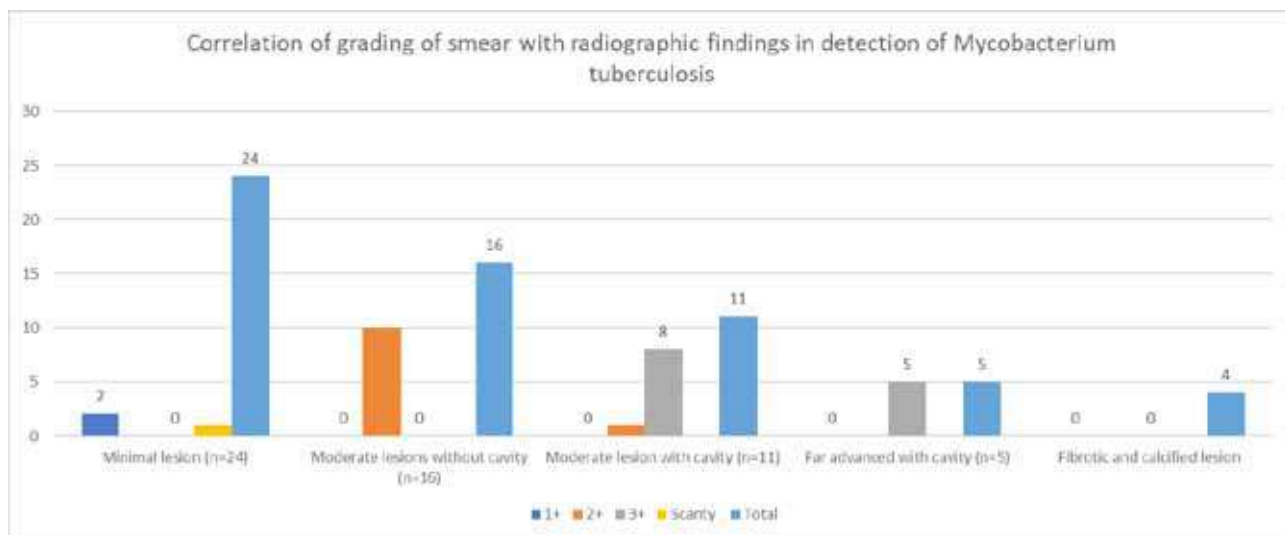


Figure 2: Correlation of grading of smear with radiographic findings in detection of Mycobacterium tuberculosis

Conclusion

To achieve the final diagnosis of Pulmonary TB clinical correlation between radiological and microbiological findings are must. In India, RNTCP also

recommends the sputum smear positivity or cavity lesions in chest X ray to diagnose pulmonary TB before the commencement of ATT. In the current study, correlation between radiological (minimal lesions, moderate lesions

without cavity or with cavity, far advanced lesion with cavity and fibrotic calcified lesion) and microbiological findings were established to empower the diagnosis of pulmonary TB.

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Conflict of Interest: The authors declare that there is no conflict of interest

Ethics Statement: Maharishi Markendeshwar (Deemed to be University) Ethical Committee approved the study protocol and informed consent was obtained from all the study participants.

References

1. Ramachandran R, Paramasivan C. What is new in the diagnosis of tuberculosis? Part 1: Techniques for diagnosis of tuberculosis. *Ind J Tub.* 2003(50):-133-41.
2. Rao SK, Kumar AH, Rudresh BM, Srinivas T, Bhat HK. A comparative study and evaluation of serum adenosine deaminase activity in the diagnosis of pulmonary tuberculosis. *Biomedical Research* 2010; 21(2):189-194.
3. Kanade SR, Nataraj G, Anita R, Mehta PR. Correlation between Smear Positivity Grade at two Month With Culture Positivity and Final outcome in Patients Receiving Anti tuberculosis Treatment. *Bombay Hosp J.* 2010;52(2):401-13.
4. Aziz N, Hasan S, Munir M, Tayyab M, Chaudhry NA. Risk to household contact of tuberculosis patients based on mantoux test and antibody titre. *J Ayub Med Coll Abbottabad.* 2008;20(2):47-50.
5. Wood R. Challenges of TB diagnosis and treatment in South Africa. *SAJHIVMED.* 2007; 44-48.
6. Albert H. Economic analysis of the diagnosis of smear-negative pulmonary tuberculosis in South Africa: incorporation of a new rapid test, FASTPlaque TB, into the diagnostic algorithm. *Int J Tuberc Lung Dis.* 2004;8(2):240-7.
7. Jamzad A, Shahnazi M, Khatami A, Azimi G, Khanbabaee G, Salimi L, Mehrafarin M. Radiographic Finding of Pulmonary Tuberculosis in Tehran in Comparison With Other Institutional Studies. *Iran J Radiol.* 2009; 6(3):131-36.
8. KUBICA GP, DYE WE, COHN ML, MIDDLEBROOK G. Sputum digestion and decontamination with N-acetyl-L-cysteine-sodium hydroxide for culture of mycobacteria. *Am Rev Respir Dis.* 1963;87:775-9.
9. Jena J, Nema KS, Panda NB, Rajan EK. Comparative efficacy of rapid slide culture of M. Tuberculosis and conventional LJ medium culture in diagnosis and management of pulmonary tuberculosis cases. *Ind J Med Res* 2009; 130(5): 561-6
10. Mostofa Kamal SM, Mahmud AM, Ahsan CR, Islam MR, Sarwar G, et al. Use of Mycobacterial Culture for the Diagnosis of Smear Negative TB Cases Among New Outpatients at NIDCH, Dhaka. *Bangladesh J Med Microbiol.* 2009; 3(1):23-26.
11. Tupasi TE, Radhakrishna S, Co VM, Villa ML, Quelapio MI, Mangubat NV, Sarol JN, Rivera AB, Pascual ML, Reyes AC, Sarmiento A, Solon M, Solon FS, Burton L, Mantala MJ. Bacillary disease and health seeking behavior among Filipinos with symptoms of tuberculosis: implications for control. *Int J Tuberc Lung Dis.* 2000;4(12):1126-32.

Perception of Students Regarding Small Group Teaching in Microbiology at Undergraduate Level

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Abstract

Background: Active learning strategies for understanding the subject like microbiology is need of the hour. Small group teaching is considered to nurture active learning by the students. It is a student centered method and promotes active learning. So by keeping in mind the usefulness of the active learning, the present study was planned to assess the perception of students after introducing small group teaching (SGT) in Microbiology.

Materials and Method: The study was conducted on 150 MBBS second year professional students in the department of microbiology of Maharishi Markandeshwar Institute of Medical Sciences & Research, Mullana. Small group teaching method were conducted for all selected topics. At the end of the sessions of SGT, perceptions of students were taken on feedback questionnaire and analysed on 3 point Likert scale.

Result: Total 150 MBBS second Professional Students taken part in Study. Out of 150 students, 142 (94%) students took part in the study. Above 90% stated that it is easy and fun filled method, concepts are clearer and stronger, interaction increased with teachers, retention of the subject increased. Above 80% stated that willingness to study increased, doubts cleared easily, attention in the class increased, increased application of knowledge, sharing of ideas. Above 70% stated that clinical correlation, learn team work, self-directed learning.

Conclusion: By Small group teaching, students will be apply their knowledge and will be able to provide effective diagnostic services in the community. Small group teaching can be easily adopted in curriculum by proper management of time and by cooperation of faculty and students.

Keywords: *Small group teaching, active learning, student centred teaching method.*

Introduction

Active learning occurs when students are given the opportunity to develop interactive relationship with the course content, encouraging them to apply rather than simply receive knowledge.¹ Small group teaching is considered to nurture active learning by the students.² In

current medical education, learning relevant to the health requirements of the community is the need of the hour. Indian Medical Graduate (IMG) should be competent to function aptly and efficiently as a physician of first contact in the community.³

In microbiology, students are taught about infectious diseases, so correlations of infectious agents with the diseases are essential which cannot be achieved by traditional method. By adopting active learning strategies students will be able to apply correlation of infectious agent with the diseases.⁴

Small group discussions for general microbiology and introduction of case in small group teaching for

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applied microbiology improves clinical applications of theoretical knowledge gained about the subject by the student. By keeping in mind the usefulness of the small group teaching method the present study was conducted with following objectives:

1. To evaluate the perception of medical students regarding small group teaching for general microbiology
2. To evaluate the perception of medical students regarding case based small group teaching for applied microbiology
3. To investigate faculty perceptions on small group teaching.

Materials and Method

The cross sectional study was conducted on 2nd Prof Students in microbiology department, MMIMSR, Mullana for period of 4 months. The study was conducted on 150 Second professional MBBS students. Informed consent was taken from students. The faculty of the department was sensitized regarding the method used in the study. Topics for the study were taken from the scheduled time table. Students were taught general microbiology and applied microbiology in small groups. For general microbiology, two topics, Culture media and Antimicrobial susceptibility was selected for the study and for applied microbiology two topics, Urinary Tract infection and Tuberculosis was taken. The questionnaire was designed to document the students' responses. Case based scenarios were prepared to teach applied microbiology and scenarios were validated by faculty of the department. A sample case scenario used for UTI is provided below.

A 31 year old female was admitted with dysuria and increased frequency of micturition for the past 5 days. A urine sample was collected for culture and sensitivity. *Escherichia coli* were isolated from the sample. Patient was treated as per the sensitivity report and responded well to the treatment.

- What was the clinical diagnosis?
- How to collect the urine sample?
- Enumerate etiological agents causing UTI.
- What is the importance of antimicrobial susceptibility testing?

Student's feedback questionnaire Containing 15

questions was prepared and was validated by peer review. Group dynamics was also explained to the students. Practical classes were used for the sessions of small group teaching. As MBBS batch is of 150 students. Whole class is divided into two practical batches of 75 students each. Here Group A is batch A and Group B is batch B. further sub grouping was done for the session of small group teaching. Each batch A & B was divided into further 9 groups (A1-A9) and (B1-B9) containing eight to nine students each for the session. All the groups in batch A and batch B were given a case scenario for applied microbiology one week prior and asked to read about the topic from different sources like books, internet etc. After one week they join together in their respective groups and again discussed the scenario with each other for 20 minutes. Then every group discussed the Case based scenario with their respective teachers. Same method was followed with rest of the topics. In this way all the students was exposed to all the sessions. At the end of the sessions, perceptions of students were taken on a 3 point Likert scale regarding the small group teaching method adopted. Feedback was taken from faculty also. The feedback from faculty was also taken by asking open ended questions.

- a. Is there need of introduction of student centered teaching learning methodologies in microbiology?
- b. What will the impact on students learning and performance?
- c. How it will motivate self-directed learning?
- d. What will be the impact on shy students?
- e. How students will understand the clinical aspect of microbiology better?
- f. What will be the impact on interest in microbiology?

Results

Total 150 MBBS second Professional Students taken part in Study. Out of 150 students, 142 (94%) students took part in the study. 91% students stated that with small group teaching concepts are more clearer and stronger and it is easy, quick and fun filled method of learning. 77% stated that method adopted different views for the same topic help to understand the concept easily, Clinical correlation is more as compared to traditional method, We learn to work together. 79% opined that it motivates for self-directed learning. 82% students felt that doubt are cleared easily, Willingness to study in class is increased, Improved application of

knowledge, 85% students stated that there is Sharing of ideas and knowledge, Shy students get a chance to interact in groups and gain confidence of speaking, 88% students stated good method for recall of prior knowledge and attention in class is improved. 92% stated that retention of topic is increased by discussions with others and 95 felt that more interaction with teachers and classmates [Table/Fig-1).

Faculty Feedback: All the faculty members opined that dire need of introduction of student centered teaching learning methodologies in microbiology, great impact on students learning and performance, Motivates self-directed learning, Shy students gets chance to interact with teachers, students will understand the clinical aspect of microbiology better, Small group teaching helps the students to increase their interest in microbiology. But they also felt that CBL is a tedious and time consuming process so more resources and proper management of time is required.

Table 1: Perceptions of the students regarding small group teaching (%)

Sr No.	Items	Agree	Neutral	Disagree
1.	Concept becomes more clear and stronger with small group teaching	91	7	2
2.	Easy, quick and efficient method of learning	91	8	1
3.	Different views for the same topic help to understand the concept easily	77	17	6
4.	Doubt are cleared easily	82	15	3
5.	Sharing of ideas and knowledge	85	13	2
6.	Good method for recall of prior knowledge	88	9	3
7.	Retention of topic is increased by discussions with others	92	8	0
8.	Motivates us for self -directed learning	79	16	5
9.	Clinical correlation is more as compared to traditional method	77	16	7
10.	Willingness to study in class is increased	82	16	2
11.	Attention in class is more	88	10	2
12.	Shy students get a chance to interact in groups and gain confidence of speaking	85	14	1
13.	More interaction with teachers and classmates	95	5	0
14.	Improved application of knowledge	82	13	5
15.	We learn to work together	77	13	10

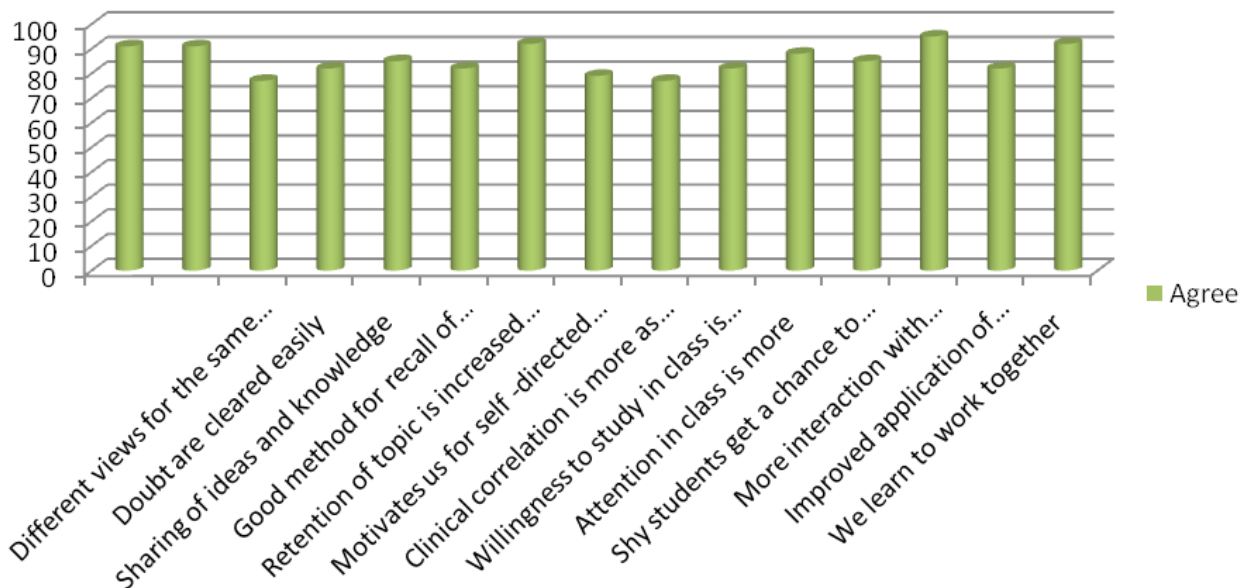


Figure 1: Bar Chart showing students perceptions on small group teaching (%)

Discussion

The present study was conducted on implementation of small group teaching in microbiology at undergraduate level. Feedback given by students on small group teaching clearly indicated that there is improvement of clinical correlation of the microbiology. Above 90% stated that it is easy and fun filled method, concepts are clearer and stronger, interaction increased with teachers, retention of the subject increased. Above 80% stated that willingness to study increased, doubts cleared easily, attention in the class increased, increased application of knowledge, sharing of ideas. Above 70% stated that clinical correlation, learn team work, self-directed learning. Study done by Kassebaum D et al showed that students are more engaged, interested and involved in the class.⁶

In another study above 77% students stated CBL contributed to better understanding of the microbiology learning objectives, helped them retain the relevant information.¹

Kanchan Gupta in her study showed 94.4% students opined that subject effectively illustrated the medical concepts. 78% opined that motivated them to use addition resources. 87.29% feels that stimulated their interest in subject. 89.6% opined that intervention of the teacher was useful, 72% opined that session was better than theory classes.⁷

Neena Bhattacharya et al. in their study “Introducing problem based learning in physiology in the conventional Indian medical curriculum” found that almost all the students found PBL to be useful (96.6%). Most of the students (92.4%) strongly felt that PBL helped in self-directed learning and 87.8% wanted more PBL sessions preferably in combination with conventional learning. Interestingly, 69.3% of the students wanted a complete changeover to PBL.⁸

Kawai et al and Tiwari et al. stated that most students enjoyed case-based teaching and considered that their clinical reasoning, diagnostic interpretation and ability to think logically were improved. They observed that one advantage of this teaching strategy is that students have the opportunity to perform in-depth analyses and apply critical thinking to realistic, complex patient care situations in a safe environment.^{9, 10}

Conclusion

Our study showed that small group teaching for the subject of microbiology used can promote active learning among students. Response from the students was very encouraging and that will motivate teachers to implement learner oriented strategies.

Conflict of Interest: None

Source of Funding: Self

Ethical Clearance: Ethical Clearance was obtained from the Institutional Ethics Committee (IEC), Maharishi Markandeswar (deemed to be university) Mullana, Ambala.

References

1. Ciraj AM, Vinod P, Ramnarayan K. Enhancing active learning in [5] microbiology through case-based learning: Experiences from an Indian medical school. *Indian J Pathol Microbiol.* 2010; 53:729-33.
2. Singh T, Gupta P, Singh D. Teaching and Learning and Taking [1]a Lecture in Principles of Medical Education. Ed 4th. JAYPEE. 2013. Pp:1-8 & 39-44.
3. Medical Council of India Regulations on Graduate Medical Education, 2012- www.mciindia.org
4. Tathe SS, Singh AL. Case based lectures versus conventional lectures for teaching medical microbiology to undergraduate students. *Int J Curr Rev.* 2014; 06(04):35-41.
5. Garg R, Singh VA. Introduction of case based learning in microbiology at undergraduate level. *National Journal of Laboratory Medicine.* 2018, Jul, Vol-7(3): MO06-MO10.
6. Kassebaum D, Averbach R, Fryer G. Student preference for case-based vs. lecture instructional format. *J Dent Educ* 1991;55:781-4.
7. Gupta K, Arora S, Kaushal S. Modified case based learning: Our [18]experience with a new module for pharmacology undergraduate teaching. *Int J Appl Basic Med Res.* 2014;4(2):90-94.
8. Neena Bhattacharya, Nilima Shankar, Farah Khaliq, C.S. Rajesh, O.P Tandon. Introducing problem-based learning in physiology in the conventional Indian medical curriculum *Medical Education* 2005;18.

9. Kawai Y, Yazaki T, Matsumaru Y, Senzaki K, Asai H, Imamichi Y, et al. Comparative analysis of learning effect for students who experienced both lecture-based learning and problem based learning in a complete denture course *Nihon Hotetsu Shika Gakkai Zasshi* 2007; 51: 572-581.
10. Tiwari, P. Lai, M. So, K. Yuen A comparison of the effects of problem-based learning and lecturing on the development of students' critical thinking *Med Educ*, 40 (2006), pp. 547–554.

Proximal Fibular Osteotomy—A Novel Technique for Decompression of Isolated Medial Compartment Osteoarthritis Knee

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Abstract

Introduction: Proximal Fibular Osteotomy (PFO) is removing 1-1.5 cm of FIBULA, 7 to 10 cm below its head, which provides symptomatic relief from pain of medial compartment Osteoarthritis (OA) knee. It is a procedure wherein we remove Proximal part of fibula to stop mechanical axis of knee going into further varus and hence putting a stop to progression of disease. The aim of the study was to observe and study the results in patients of isolated medial compartment Osteoarthritis of Knee, treated by Proximal Fibular Osteotomy.

Material and Method: The study was conducted on 36 patients amounting to 50 knee joints (male and female between the age of 50-70 years) with medial compartment OA Knee. Patients were followed up till 6 months. Medial and lateral joint space along-with visual analogue score for pain were recorded pre-operative, immediate post-operative and at final follow up.

Result: Significant improvement in mean visual analogue pain score (VAS), from 7.32 ± 0.98 preoperative to 2.72 ± 1.20 at the final follow up was observed (p-value < 0.001). Medial joint space opening from 1.17 ± 0.29 to 4.07 ± 0.69 at final follow up was observed. American knee society score was divided into 2 subsets, knee score and functional score. Both of them showed significant improvements from 39.72 ± 3.47 and 44.20 ± 8.47 (pre-operative) to 86.58 ± 10.79 and 84.60 ± 8.38 respectively, at final follow up (p-value < 0.001).

Conclusion: The objective as well as functional outcome after proximal fibular osteotomy were satisfactory. With correct patient selection and meticulous adherence to basics, Proximal fibular osteotomy offers an excellent alternative to tedious and extensive procedures like High tibial osteotomy (HTO) and Uni-compartmental Knee Arthroplasty (UKA). It is specially enthralling in country like ours where everyone cannot afford expensive surgeries and are forced to live a life of misery and morbidity.

Keywords: Medial compartment Osteoarthritis Knee, PFO, American Knee Society Score, Fibular osteotomy.

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Introduction

Knee joint is one of the largest synovial joint in human body.¹ It is a complex hinge joint which consists of 3 partially separated compartments, medial and lateral tibiofemoral compartments and a patellofemoral

compartment.¹ It is the major weight bearing joint and as a result of inherent complex anatomy, subcutaneous nature with large surface area, it is prone to get affected by various traumatic and nontraumatic disorders.² The joint is constantly exposed to loading and bending and/or rotation acting in coupled fashion.³ Primary osteoarthritis of knee is more common than that of the other joints^{4,5} The main triggering factors for development of osteoarthritis are biomechanical due to microfracture of subchondral bone or fatigue fracture of collagen fibres.

Although it is common knowledge and observation that medial compartment is the weight bearing component and it draws upon itself 60-80% of the load, none has accurately described the reason behind this non-uniformity of load sharing.⁶ The current consensus is that the weight is distributed along the mechanical axis, which due to the anatomy of the joint lies medial to the knee centre. It is evidently clear that in an osteoporotic setup, fibula delivers a lateral support to the tibia which is responsible for uneven settlement of the plateau leading to its regression⁶. This causes an axial shift of load going medially away from the medial plateau and contributes in the development of knee varus, which in turn forms a vicious cycle further accelerating the rate of progression of OA of medial compartment of knee. Taking this into consideration, fibular osteotomy alleviates the escalating load from the medial compartment and mitigate the symptoms of medial compartment OA of the knee joint.

Most of the treatment available for the disease are either too radical like joint arthroplasty or unproven like various intra-articular injections. The current gold standard TKA can reinstate anatomical alignment, provide pain relief and greatly improve functionality. But, in case of young, active patients or patients with moderate OA, it might not be taken as modality of choice. In the present study, we focused on a surgery, PROXIMAL FIBULAR OSTEOTOMY which was safe, easy to perform, was affordable and could postpone TKA in the subset of population with early OA knee. Short term efficacy of the procedure in terms of radiographic and clinical improvement was meticulously evaluated with a follow up of 6 months.

Material and Method

Institutional review board approval was obtained for this study vide number IEC-1095. All patients were informed about the benefits and complications of the

procedure. Written informed consent was obtained from all patients in study group.

The study was conducted on 36 patients amounting to 50 knee joints (male and female between the age of 50-70 years) with medial compartment OA Knee in the Department of Orthopaedics, MMIMSR from 17-Feb-2018 to 30-Aug-2019.

Patient Selection: Inclusion criteria included symptomatic isolated medial compartment OA knees, radiographically falling into Ahlback⁷ grade 1 or 2, aged between 50-70 years who consented for surgery. Exclusion criteria included Post Traumatic arthritis, patello-femoral OA, Bi or Tri Compartmental OA, Inflammatory Joint Disease, patients who had history of Previous Operations or fractures around the knee joint, patients with deformity associated with tumours around the knee and patients with comorbid conditions like deranged Hepatic or Renal Functions, uncontrolled Diabetes or Hypertension. 52 patients with medial compartment OA were identified as candidates for either unilateral or bilateral PFO. Out of these 8 were lost to follow up, 5 did not consent for surgery due to unproven nature of surgery and 3 refused for any operative intervention.

Primary and Secondary Outcomes: The primary measured outcome was difference in medial joint space, pre-operatively, immediate post-operative and at final follow up. Measurements were done on weight bearing radiograph using Indian one-rupee coin (diameter 20mm) as standardisation tool. Secondary measure outcome was pain measured by visual analogue score (VAS)⁸⁻¹⁰. Data pertaining to age, sex, height, affected side, lateral joint space and American knee society score¹¹ (2 subsets, knee and functional score) were recorded at baseline, immediate follow up and at final follow up. Intra-operative data such as use of tourniquet, requirement of blood transfusion and operative time were also recorded.

Surgical Technique: Under Spinal/Epidural anaesthesia, patient was made to lie in supine position. Tourniquet was applied in all cases but inflated according to need. The knee over the affected side was prepared with an aqueous iodine-based scrub, followed by painting the part with povidone iodine solution from middle of the thigh up to the ankle and covered with sterile drapes. Fibular head palpated and marked. Level for osteotomy was then localised 7.5-8.5 cm below the

fibular head using sterile metal scale. A hypodermic needle was placed at that point and position re-confirmed under C-arm.(Figure-1a) This over-jealous approach of correct level aided in prevention of injury to the common peroneal nerve and other post-op neurovascular complications. The level for fibular cut was decided based upon guidelines in literature¹². In patients with height less than five and half foot (165cms), cut was taken at 7.5-8cms and for those more than 165cms was taken at 8-8.5 cms. A generous 5-7 cms lateral skin incision centred over the location of hypodermic needle was given and fibula is exposed between the Peroneus and Soleus muscle. Retractors were carefully placed and gently retraced so as to avoid injury to nearby neurovascular bundle. Bone levers were avoided as they present with higher chances of neuropraxia. Multiple drill holes were done in proximal and distal margin of the segment to be resected.(Figure-1b)Osteotome used to mobilise the segment and a 1-2 cm section was removed using Kocher forceps.(Figure-1c) After resecting, open ends of the fibula were sealed off with the application of Bone Wax. Gentle thorough lavage with normal saline was done and incision was closed in layers achieving complete haemostasis. Aseptic dressing was done, followed by application of compression bandage. Patient was allowed weight bearing according to tolerance, at 1st post-op day.

Follow-up: After discharge, patients were called for follow up on post op day 12-14 for sutural removal. Then they were followed up monthly for 6 months. Data recording was done during immediate post op period (POD 2-4) and at final follow up (6 months post-op).

Statistical Analysis: Data collected was entered into Microsoft Excel worksheet and analysed statistically by using Statistical Package for Social Sciences (SPSS Inc., Chicago, IL). Mean and standard deviation was calculated for all quantitative variables for description and measures of dispersion. For normally distributed data means of two groups was compared using paired student t-test. Qualitative or Categorical variables were described as frequencies and proportions. The nonparametric test (Wilcoxon's signed rank test) was applied to analyse the VAS and KSS data.p-value less than 0.05 was considered statistically significant.

Results

The mean age of study group was 56.40. Maximum number of patients were in the age group of 50 to 60

years (72%). The study population showed a male preponderance, with males being 72% of total and females being 28%. This is against the general trend and is attributed to the subset of patients that present to the OPD, which mainly consist of daily wage workers & manual labourers. 31 patients (62%) patients were shorter than 165cms of height and 19 (38%) were taller than that. Average male height in study group was 164.6 while average female height was 152.3 cms. 22 out of 50 knees were left side (44%) and 28 were right side (56%). Tourniquet was used in 30 out of 50 patients (60%). We found no significant difference in blood loss in patients operated with or without tourniquet. Blood transfusion was not required in any of the case operated. The mean operative time for the procedure was 28.30 + 2.80 minutes (recorded from incision to closure and aseptic dressing of operative wound).

Medial joint space reduction is one of the early signs of OA before the development of osteophytes and development of deformities. The current study showed statistically significant medial joint space opening at immediate post-op as well as at the final follow up. Joint space opening at immediate post-op period was minute ($1.17 + 0.29$ pre-op to $1.78 + 0.37$ post-op), but significant (p -value < 0.001), as there were no extreme variations in the standard deviation. There was considerable medial joint space opening at the final follow up ($1.78 + 0.37$ immediate post-op to $4.07 + 0.69$ at final follow up), p -value being < 0.001 significant). Table-1 compares current study against other landmark studies, thus cementing reproducibility of results.^{6,13} It was also observed that lateral joint space reduced from $7.20 + 0.46$ pre-operatively to $5.11 + 0.64$ at final follow up. Patients reported excellent pain relief, even in the immediate post-operative period. The 10-point VAS score improved from $7.32 + 0.98$ pre-operative to $4.64 + 1.26$ immediate post-operative and $2.72 + 1.20$ at the final follow up (p -value < 0.001).Table-2 shows that comparable results were obtained in other studies conducted with similar aim.

Part-1 of American knee society score(table -3) focuses on objective scoring including pain on various activities of daily living, range of motion, stability of the joint and rest pain, if any. There was significant improvement of knee score from $39.72 + 3.47$ pre-op to $69.12 + 10.85$ immediate post-op (p -value < 0.001). Improvement continued up-to final follow up as knee score was $86.58 + 10.79$ at 6 months follow up (p -value < 0.001).Part-2 of American knee society(table -3) score

focuses on functional capabilities of the joint of patient. It includes parameters like how much is the patient able to walk without pain, whether he can climb up and down the stairs normally and functional deductions like use of crutches or walker, if any. There was improvement of functional score from 44.20 ± 8.47 pre-op to 73 ± 11.95 immediate post-op (p -value < 0.001). Improvement from immediate post-op to final follow up was also significant, 84.60 ± 8.38 (p -value < 0.001).

After the procedure, 2 patients reported increase in pain (one out of them developed a hematoma which was eventually evacuated). EHL weakness was observed in 4 out of 50 patients and all 4 of them also reported midfoot numbness. Total 6 patients reported tingling and midfoot numbness including previous 4. 1 patient developed foot drop that resolved after 3 months post-op. Neurological complications are depicted in table-4.

Table 1: Comparing improvement in medial joint space with landmark studies

	Medial Joint Space			
	Pre-Op	Post-Op	t	p-value
L Prakash	1.2 ± 0.7	4.5 ± 2.7	40.3	< 0.001
Current	1.17 ± 0.29	4.07 ± 0.69	28.766	< 0.001
	Lateral Joint Space			
	Pre-Op	Post-Op	t	p-value
Zong-You Yang et al.	12.2 ± 1.1	6.9 ± 0.7	42.633	< 0.001
L Prakash	7.2 ± 1.4	5.2 ± 1.4	42.6	< 0.001
Current	7.20 ± 0.46	5.11 ± 0.64	21.062	< 0.001

Table 2: Comparing improvement of VAS with similar studies

Series	Follow Up (Months)	Pre-Op	Final Follow Up
Zong-You Yang et al.	49.1	7.0	2.0
Xiaohu Wang et al.	13.38	8.02	2.74
L Prakash	12	6.7	2.2
Current	6	7.32	2.72

Table 3: Improvement of American knee society score

Knee Score	Mean	SD	t	p-value	Difference	
					Mean	SD
Pre-op	39.72	3.47				
6 Months	86.58	10.79	-29.790	< 0.001	-46.86	11.12
Functional Score	Mean	SD	t	p-value	Difference	
					Mean	SD
Pre-op	44.20	8.47				
6 Months	84.60	8.38	-24.088	< 0.001	-40.40	11.86

Table 4: Patients with Neurological Complications

Neurological Complications	No. of Patients	Percentage
EHL weakness + Midfoot numb	4	8%
Foot drop + Midfoot numb	1	2%
Midfoot Numbness alone	1	2%
Total patients with neurological complications	6	12%



Figure 1: a. Locating the level from fibular head, b. Multiple drill holes, c. En block resection



Figure 2: Pre-operative and post-operative radiographs, showing opening of medial joint space.

Discussion

Knee osteoarthritis is a joint disorder that is very commonly encountered with an incidence of 30% in population aged more than 60 years.¹⁴ It is reported that even in a healthy knee, medial compartment bears around 60-80% of the total load. This is why early changes of OA are encountered most commonly in this compartment. Treating the disease at the stage of uni-compartmental pathology hence saves the patient from debilitating complications that follow later on. Conservative modalities employed at early stages include intra-articular injection of steroids, PRP or hyaluronic acid. Various studies have shown that these modalities lead to an acceleration of disease pathology due to excessive joint loading after temporary pain relief is achieved and thus the harms out-weigh pain relief in long term.^{15,16} Another modality this is commonly employed at this stage are consumption of NSAIDs. PFO is a relatively cheap procedure and the economic burden is little when compared to the burden of purchasing drugs for pain relief regularly. But there is no such analysis that has

been carried out to support this claim. However, there are literature challenging cost-effectiveness of conservative non-surgical modalities that included NSAIDs, bracing and intra-articular injections.^{17,18} Operative Procedures commonly employed at this stage are HTO and UKA. Patello-femoral disturbances are commonly found in cases of HTO as it interferes with functioning of patellar tendon.¹⁹ UKA when performed in expert hands give excellent improvements, but is an extensive procedure and must not be advocated in initial stages of OA.

There have been cadaveric studies that demonstrate significant decrease in medial compartment pressure after performing proximal osteotomy of fibula.^{20,21} Our study confirms the efficacy and safety of the procedure in early OA knee involving isolated medial compartment. Proximal osteotomy of the fibula weakens the lateral fibular support and leads to subsequent shift of loading forces from the medial compartment more laterally, leading to decreased pain, opening of medial joint space and a satisfactory objective as well as functional recovery (as evident by improvement in knee society scores).

Although it is an easy procedure care must be taken to avoid neuropraxic injury to Common peroneal nerve or superficial peroneal nerve. 6 patients that had developed neurological complications in the study were managed with vitamin B12 and pregabalin supplementation. All 6-patient showed complete recovery in between 6 weeks to 3 months. It was observed that bone levers were used in all 6 of these patients. In our study, bone levers were used intra-operatively in 10 out of 50 patients. No patient developed such complications wherein we used langenback retractors. Although there is no clear evidence to suggest these two findings are related, it is our recommendation to make use of simple langenback retractors during the procedure.

Conclusion

The current study advocates PFO as a tool to decelerate the progression of the disease and hence help delay or even prevent arthroplasty. It provides excellent pain relief to the patient and improves function. It is by no means a replacement for knee arthroplasty and high tibial osteotomy which remain gold standard procedures in advanced knee OA. The key to the success of the PFO lies in correct patient selection and avoiding neurological complications.

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Source of Funding: Self

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References

1. Drake RL, Vogl AW, Mitchell AW. *Gray's Anatomy for Students*. 4th ed. Elsevier; 2019. 598–608 p.
2. Kulkarni G., Babhulkar S. *Textbook of Orthopedics And Trauma*. 3rd ed. Jaypee Publishers; 2016. 2622–2629 p.
3. Erasmus S. *White Paper: Research and Development Efforts towards the Production of the Leatt® C-Frame Carbon Knee Brace by Declaration by Independent Reviewers*. 2014;
4. Agarwal SS, Phadke SR, Phadke RV, Das SK, Singh GK, Sharma JP, et al. Handigodu disease: a radiological study. *Skeletal Radiol*. 1994 Nov 1;23(8):611–9.
5. Turek S. *The Knee. Orthopaedics: principles and their complication*. 4th ed. New Delhi: Jaypee Publishers; 1989. 1367–1371 p.
6. Yang Z-Y, Chen W, Li C-X, Wang J, Shao D-C, Hou Z-Y, et al. Medial Compartment Decompression by Fibular Osteotomy to Treat Medial Compartment Knee Osteoarthritis: A Pilot Study. *Orthopedics*. 2015;38(12):e1110–4.
7. Petersson IF, Boegård T, Saxne T, Silman AJ, Svensson B. Radiographic osteoarthritis of the knee classified by the Ahlbäck and Kellgren & Lawrence systems for the tibiofemoral joint in people aged 35-54 years with chronic knee pain. *Ann Rheum Dis*. 1997 Aug;56(8):493–6.
8. Scott J, Huskisson EC. Graphic representation of pain. *Pain [Internet]*. 1976 Jun;2(2):175–84.
9. Hawker GA, Mian S, Kendzerska T, French M. Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS) and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). *Arthritis Care Res*. 2011;
10. Streiner DL, Norman GR, Cairney J. *Health Measurement Scales*.
11. Insall JN, Dorr LD, Scott RD, Scott WN. Rationale of The Knee Society Clinical Rating System *John*. 1989;
12. Prakash L. *Proximal Fibular Osteotomy for Medial Compartment OA of Knee Joint (Book Addendum)*. 1st ed. Chennai: Institute For Special Orthopaedics; 2018. 2–5 p.
13. Wang X, Wei L, Lv Z, Zhao B, Duan Z, Wu W, et al. Proximal fibular osteotomy: a new surgery for pain relief and improvement of joint function in patients with knee osteoarthritis. *J Int Med Res*. 2017;45(1):282–9.
14. Felson DT, Naimark A, Anderson J, Kazis L, Castelli W, Meenan RF. The prevalence of knee osteoarthritis in the elderly. the framingham osteoarthritis study. *Arthritis Rheum*. 1987;30(8):914–8.
15. Henriksen M, Simonsen EB, Alkjaer T, Lund H, Graven-Nielsen T, Danneskiold-Samsøe B, et al. Increased joint loads during walking--a consequence of pain relief in knee osteoarthritis. *Knee*. 2006 Dec;13(6):445–50.

16. Briem K, Axe MJ, Snyder-Mackler L. Medial knee joint loading increases in those who respond to hyaluronan injection for medial knee osteoarthritis. *J Orthop Res.* 2009 Nov;27(11):1420–5.
17. Pinto D, Robertson MC, Hansen P, Abbott JH. Cost-effectiveness of nonpharmacologic, nonsurgical interventions for hip and/or knee osteoarthritis: systematic review. *Value Health.* 2012 Jan;15(1): 1-12.
18. Crawford DC, Miller LE, Block JE. Conservative management of symptomatic knee osteoarthritis: a flawed strategy? *Orthop Rev (Pavia).* 2013;
19. Rodrigo Peres Arruda -Rua Tavares L, Alves de Mello Junior W, Rodrigo Peres Arruda L, Muller Coluccini A, Pereira da Silva Nunes R, do Amaral Camargo Pedro M, et al. complications following medial opening wedge osteotomy of the knee: retrospective study. *Vol. 46, Rev Bras Ortop.* 2011.
20. Yazdi H, Mallakzadeh M, Mohtajeb M, Farshidfar SS, Baghery A, Givehchian B. The effect of partial fibulectomy on contact pressure of the knee: a cadaveric study. *Eur J Orthop Surg Traumatol.* 2014;24(7):1285–9.
21. Baldini T, Roberts J, Hao J, Hunt K, Dayton M, Hogan C. Medial Compartment Decompression by Proximal Fibular Osteotomy: A Biomechanical Cadaver Study. *Orthopedics.* 2018 Jul 1;41(4):- e496-501.

Effectiveness of Calf Stretching Exercises Versus Plantar Fascia Stretching Exercises in Plantar Fasciitis: An Experimental Study

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Abstract

Introduction: Plantar fasciitis or calcaneus pain syndrome is the inflammation of origin of plantar fascia and the nearby perifascial structures which is attached to the medial process of the calcaneal tuberosity. Histology suggests mainly degeneration rather than inflammation but fasciitis still remains more prominent in the literature. The windlass mechanism describes the biomechanics associated with plantar fascia.

Material and Method: This study included 60 patients who were divided into 2 randomized selected groups on the basis of arrival. 30(even) patients were made to do calf stretching exercises and 30(odd) did plantar fascia stretching exercises. The stretches mainly included 8 repetitions, 20 seconds each, 2 times a day and 3 times a week for a duration of 4 weeks. Data was collected and described by using independent t-test and Repeated Analysis of variance was also used.

Results: Maximum number of patients who had plantar fasciitis were in the age group 41-50 (36.6%). Both the stretching exercises were assessed with VAS, FFI and AOFAS at day 0 and every follow up i.e 1st week, 2nd week and at the end of 4th week which showed more improvement and better satisfactory outcome in plantar fascia stretching exercises than the calf stretching exercises. Range of motion showed more improvement with calf stretching exercises.

Conclusion: This study promotes the use of the tissue-specific plantar fascia-stretching protocol as the key exercise. Long-term benefits of the stretching includes a marked decrease in pain and high rate of satisfaction. This approach provides the health-care practitioner with an effective, non-invasive, inexpensive and straightforward treatment protocol.

Keywords: *Plantar Fasciitis, Calf Stretching Exercises, Plantar Fascia Stretching Exercises.*

Introduction

Plantar fasciitis or calcaneus pain syndrome is defined as the inflammation of origin of plantar fascia

and the nearby perifascial structures.¹ It is a condition that can be painful, debilitating and is a frequent cause of pain in the heel and in the foot.^{2,3} Plantar fasciitis is much more likely seen in obese people, prolonged standing and people with restricted flexion of their ankle.⁴

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The Clinical sign of this disease is localized pain in the heel or along the entire plantar fascia to its insertion, most noticeable with initial steps after a period of inactivity and usually lessens with increasing level of activity during the day, but will tend to worsen towards

the end of the day. Long walks or long periods on their feet can also be uncomfortable for these patients, thus disrupting the daily routine of many people.⁵⁻⁷

The etiology of PF is multi factorial, it can develop from inflammatory or degenerative factors. It is currently thought to be secondary to myxoid degeneration, microtears within the plantar fascia, collagen necrosis and angiofibroblastic hyperplasia of the plantar aponeurosis and not due to an inflammatory process.⁸ PF can also be triggered by other factors such as overload of the plantar fascia linked to intrinsic weakness in the foot, anatomical and biomechanical alterations in the plantar arch, discrepancy between the lower limbs, inappropriate footwear and alterations in the static and dynamic positioning of the Feet.⁹⁻¹²

Foot surgeons continue to debate the source and etiology of plantar heel pain, as well as the most appropriate modality of treatment.¹ According to current literature, because of the chronicity and degeneration associated with this condition it should be known as a fasciosis rather than fasciitis due to inflammation.¹³

Material and Method

This study was commenced after obtaining approval from the Institutional Ethics Committee. This experimental randomized control study was done on 60 patients who presented to the Out-Patient Door (OPD) of Department of Orthopaedics at MMIMSR, Ambala with presenting symptoms of Plantar fasciitis. Patients were diagnosed on the basis of detailed history and physical examination which mainly included the tenderness at the posteromedial aspect of the foot and the heel pad. Detailed history and local examination, basic investigations were done. Written informed consent was taken after explaining the complete procedure to the patient. Patients were informed about the disorder and about various other treatment modalities out of which the stretching exercises were mainly chosen being non-invasive and easy to perform.

This study included 60 patients who were divided into 2 randomized selected groups on the basis of arrival. 30(even) patients were made to do calf stretching exercises and 30(odd) did plantar fascia stretching exercises. The stretching exercises were done 2 times a day which included 8 repetitions 20 seconds each, 3 times a week for the duration of 4 weeks.

Procedure:

Calf Stretching Exercises: It was done by leaning forward on the wall keeping one of the knee straight & heel was kept on ground. The other leg was placed in the front, keeping the knee bent. In order to stretch calf muscles & heel cord, hips were pushed towards the wall in a balanced manner as shown in figure 2. The stretch was held for a count of 20 seconds and repeated at least 8 times in each session 2 times a day, strong pull was felt in the calf while stretching.¹⁴

Another method of calf stretching exercise in sitting position was done by applying a downward pressure at the calcaneum along with the foot in dorsiflexion. This position was maintained for the same duration.

Plantar Fascia Stretching Exercises: The patient crossed the affected leg over the contralateral leg while placing the fingers across the base of the toes, the patient pulled the toes back towards the shin until he or she felt a stretch in the arch or plantar fascia¹⁴. The plantar fascia-specific stretch was performed by dorsiflexing the toes with one hand (taking advantage of the windlass mechanism)¹⁵ and palpating the plantar fascia with the other hand to ensure the tautness as shown in figure 1. The stretch was held for a count of 20 seconds and repeated at least 8 times in each session 2 times a day. It was done especially before taking the first step in the morning and before standing following a period of prolonged sitting.

Another method involved rolling a frozen can under the foot with moderate pressure for five to ten minutes at the end of each day.

Statistical Analysis: Data were described in terms of range; mean \pm SD, median, frequencies and relative frequencies as appropriate. Comparison of quantitative variables between the study groups was done using independent t-test and Mann Whitney U test for independent samples for parametric and non-parametric data respectively. Repeated ANOVA was also used. For comparing categorical data, Chi square (χ^2) test was performed and exact test was used when the expected frequency is less than 5. A probability value (p value) less than 0.05 was considered statistically significant. All statistical calculations were done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

Results

A thorough analysis and follow up of the patients was done and the following is the summary of the results obtained. Maximum number of patients who had plantar fasciitis were in the age group 41-50 (36.6%). More number of females were affected by plantar fasciitis i.e. 42(70%). In this study exercise was performed by 35 left feet and 25 right feet. Both the stretching exercises were assessed with VAS, FFI and AOFAS at appropriate follow up intervals at day 0, 1st week, 2nd week and at the end of 4th week which showed improvement.

In the study Visual Analogue Scale (VAS) was used in both the stretching exercises which showed a decreasing trend at every follow up. p value was statistically significant in both the stretching exercises in VAS (p value < 0.000). Plantar fascia stretching exercises proved out to be clinically more satisfactory with higher mean difference in VAS than calf stretching exercises as shown in Table 1. Range of motion was also assessed at every follow up interval which showed an increasing trend more in calf stretching exercise as shown in Table 2. Range of motion had a higher mean difference in calf stretching (35.20 ± 10.23) than plantar stretching (31.67 ± 9.45) and showed a superior clinical outcome. p value (< 0.000) was significant in both the exercises in Range of Motion.

Ankle Hind Foot Scale was calculated in both the stretching exercises which had a better clinical outcome in plantar stretching exercise whereas p value (< 0.000) was significant in both. Plantar stretching exercises turned out to be clinically superior than calf stretching exercises with higher mean difference as calculated in FFI with highly significant p value (< 0.000) in both the stretching exercises.

Table 1: VAS calculated in both stretching exercises at each visit

VAS (cm)	Calf Stretching	Plantar Stretching
Day 0	6.03±0.76	7.27±0.69
1 week	4.73±0.74	5.20±0.71
2 weeks	3.63±0.55	3.80±0.55
4 weeks	2.87±0.78	2.47±0.51

Table 2: Range of motion checked at every follow up for both the exercises

Range of Motion (Degree)	Calf Stretching	Plantar Stretching
Day 0	23.20	28.30
1 Week	30.47	35.23
2 Weeks	42.03	44.40
4 Weeks	58.40	59.97

Table 3: Foot function index comparison in various studies

Foot Function Index					
Study	Type of Exercise	Mean Difference		P value	
Benedict F. et al ⁴⁴	Plantar	19.6 (8week from baseline)	36 (2yrs from baseline)	<0.0001	<0.0001
	Calf	8.3 (8weeks from baseline)	28.6 (2 yrs from baseline)	<0.0106	<0.0001
R K Jha et al ⁹⁰	Plantar	25.6 (at baseline)	14 (8 weeks from baseline)	<0.599	<0.005
	Calf	26.12 (at baseline)	16.64 (8 weeks from baseline)	<0.599	<0.005
Current study	Plantar	7.08 (at baseline)	19.86(4 weeks from baseline)	<0.000	<0.000
	Calf	6.63 (at baseline)	15.10 (4 weeks from baseline)	<0.000	<0.000

Table 4: Comparison of ankle hindfoot scale in various studies

Ankle Hindfoot Scale			
Study	Mean		p value
	At Baseline	Follow up Duration	
Hesham A. (2015) ¹³	48.79	91.33(6 months)	<0.05
Casper G. et al (2019) ⁹⁸	54.00	87.9 (3 months)	<0.01
Neena K. et al (2010) ⁹⁷	64.00	78.0 (4weeks)	<0.005
Present study	65.87 (calf)	84.67 (4weeks)	<0.131
	69.40(plantar)	89.90 (4weeks)	<0.000



Figure 1: Demonstration of tissue specific plantar fascia stretching Exercises.



Figure 2: Demonstration of calf stretching exercise

Discussion

Plantar fasciitis is a common problem in the adult population. It occurs over a wide age range and is seen in both sedentary and athletic individuals. Although its precise cause remains unclear, the most common theory is repetitive partial tearing and chronic inflammation of the plantar fascia at its insertion on the medial tubercle of the calcaneus. Non-operative treatments for plantar fasciitis vary widely and include shoe modifications, use of prefabricated and custom inserts, stretching exercises, physical therapy, non-steroidal anti-inflammatory medications, cortisone injections, night splints, application of a cast, or any combination of the foregoing modalities.

This study was designed to compare the efficacy of plantar fascia stretching versus calf stretching exercise in patients with plantar fasciitis. This experimental randomized control study was done on 60 patients who presented to the Out Patient Door (OPD) of department of orthopedics.

In our study range of motion was calculated in terms of total motion at the ankle joint. In calf stretching exercise the mean difference at the end of 4th week follow up came out to be 35.20 which showed better clinical outcome in comparison with plantar stretch exercise in which the mean difference came out to be 31.67. However at the end of the final follow up both the stretching exercises were proved to be statistically significant in which the p value was <0.000 in both the exercises. In the study conducted by David Porter et al¹⁶ the mean difference in range of dorsiflexion only came out to be 13.7 at the end of 4 month follow up and p value was <0.033 which was significant whereas in study conducted by Joel A. Radford¹⁷ the mean difference was 25.8 at the end of 2 weeks follow up and p value was 0.470 which is statistically non-significant. In study conducted by Vinod Babu K. et al¹⁸ calculated mean difference as 19.0 at the end of 2 weeks and p value <0.000.

In our study the functional outcome of the subjects was studied on the basis of Foot Function Index, the questionnaire which involves the pain sub-scale, pain scale for disability and pain scale for recreational activities. We have compared the mean difference for both plantar and calf stretching exercises at the baseline and at the end of 4th week. The mean difference for plantar stretching was 7.08 and 19.86 at baseline and follow up respectively which was significant with p value < 0.000. The mean difference for calf stretching at the baseline and at the end of 4th week follow up was 6.63 and 15.10 respectively with a significant p value of <0.000, however the clinical outcome as measured by the foot function index was more favorable for the plantar fascia stretching exercises. In other studies, conducted by Benedict F DiGiovanniet al¹⁹ had 2 groups-A (plantar fascia stretching), B (Achilles tendon stretching exercises). The mean difference for plantar stretching exercises at 8 weeks from baseline and 2 years from baseline were 19.6 and 36 respectively with significant p value of <0.0001. The mean difference for Achilles tendon stretching exercises at 8 weeks from baseline and 2 years from baseline were 8.3 and 28.6 with significant p value of <0.0106 and <0.0001 respectively. However,

the reduction in the pain and overall satisfaction was observed earlier in the group A, who followed the plantar fascia stretching exercises, but on continuing with both the exercises results were similar and equally satisfactory in both the groups after a follow up period of 2 years. R K Jha et al²⁰ conducted a study in which the mean difference at the baseline of plantar stretching exercise was 25.69, Achilles tendon stretching exercise was 26.12 with a p value of <0.599, the mean difference at 8 weeks follow up for plantar stretching exercises was 14.00, for Achilles tendon stretching exercise was 16.64 with a significant p value of <0.005 and the comparison has been showed in Table 3.

In this study, to determine the functional outcome of the patients performing plantar fascia and calf stretching exercises, Ankle Hindfoot Scale (AHS) was included. The Mean value of AHS at baseline for Calf Stretching Exercise was 65.87 and at 4week follow up were 84.67 with a significant p value of <0.000. The Mean value of AHS at baseline for Plantar Stretching Exercise was 69.40 and at 4week follow up was 89.90 with a significant p value of <0.000 and along with this the subjects also reported better and earlier relief clinically with the plantar fascia stretching exercises. In another Study conducted by Hesham A.²¹ the mean value at the baseline was 48.79 and at 6 months of follow up was 91.33 with a significant p value of <0.05. Neena K. et al²² conducted a study in which the baseline AHS mean value was 64 and at 4 weeks follow up AHS was 78 with a p value of <0.005. Casper Grin et al²³ conducted a study in which the baseline AHS mean value was 54 and 3 month follow up was 87.9 with a significant p value of <0.01 and the comparison has been shown in Table 4.

Conclusion

This study promotes the use of the tissue-specific plantar fascia-stretching protocol as the key exercise. Long-term benefits of the stretching include a marked decrease in pain and high rate of satisfaction. This approach provides the health-care practitioner with an effective, non-invasive, inexpensive and straightforward treatment protocol.

Conflict of Interest: None

Source of Funding: Self

Ethical Clearance: Ethical Clearance was obtained from the Institutional Ethics Committee (IEC), Maharishi Markandeswar (deemed to be university) Mullana, Ambala.

References

1. Schwartz EN, Su J. Plantar fasciitis: a concise review. *The Permanente Journal*. 2014;18(1): 105-107
2. Young CC, Rutherford DS, Niedfeldt MW. Treatment of plantar fasciitis. *Am Fam Physician*. 2001;63(3):467-74.
3. Riddle DL, Pulisic M, Sparrow K. Impact of demographic and impairment-related variables on disability associated with plantar fasciitis. *Foot Ankle Int*. 2004;25(5):311-7.
4. Lim AT, How CH, Tan B. Management of plantar fasciitis in the outpatient setting. *Singapore Med J* 2016;57:168–70.
5. Landorf B, Menz B. Plantar heel pain and fasciitis. *BMJ Clinical Evidence*. 2008;2008.
6. Klein SE, Dale AM, Hayes MH, Johnson JE, McCormick JJ, Racette BA. Clinical presentation and self-reported patterns of pain and function in patients with plantar heel pain. *Foot & ankle international*. 2012 Sep;33(9):693-8.
7. Tahririan MA, Motifard M, Tahmasebi MN, Siavashi B. Plantar fasciitis. *Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences*. 2012 Aug;17(8):799-804
8. Lemont H, Ammirati KM, Usen N. Plantar fasciitis: a degenerative process (fasciosis) without inflammation. *Journal of the American Podiatric Medical Association*. 2003 May;93(3):234-7.
9. Dunn JE, Link CL, Felson DT, Crincoli MG, Keysor JJ, McKinlay JB. Prevalence of foot and ankle conditions in a multiethnic community sample of older adults. *Am J epidemiol*. 2004 Mar 1;159(5):491-8.
10. Ribeiro AP, Trombini-Souza F, Tessutti V, Rodrigues Lima F, Sacco ID, João SM. Rearfoot alignment and medial longitudinal arch configurations of runners with symptoms and histories of plantar fasciitis. *Clinics*. 2011;66(6):1027-33.
11. Alshami AM, Babri AS, Souvlis T, Coppieters MW. Biomechanical evaluation of two clinical tests for plantar heel pain: the dorsiflexion-eversion test for tarsal tunnel syndrome and the windlass test for plantar fasciitis. *Foot & ankle international*. 2007 Apr;28(4):499-505.
12. Burns J, Landorf KB, Ryan MM, Crosbie J, Ouvrier

- RA. Interventions for the prevention and treatment of pes cavus. *Cochrane Database of Systematic Reviews*. 2007(4).
13. Mohamed HA. Effectiveness of Achilles tendon stretching for the treatment of chronic plantar fasciitis. *The Egyptian Orthopaedic Journal*. 2015 Oct 1;50(4):215.
 14. Page P. Current concepts in muscle stretching for exercise and rehabilitation. *International journal of sports physical therapy*. 2012 Feb;7(1):109.
 15. Fuller EA. The windlass mechanism of the foot. A mechanical model to explain pathology. *Journal of the American Podiatric Medical Association*. 2000 Jan;90(1):35-46.
 16. Porter D, Barrill E, Oneacre K, May BD. The effects of duration and frequency of Achilles tendon stretching on dorsiflexion and outcome in painful heel syndrome: a randomized, blinded, control study. *Foot & ankle international*. 2002 Jul;23(7):619-24.
 17. Radford JA, Landorf KB, Buchbinder R, Cook C. Effectiveness of calf muscle stretching for the short-term treatment of plantar heel pain: a randomised trial. *BMC musculoskeletal disorders*. 2007 Dec;8(1):36.
 18. VinodBabu. K, Lisa Michael Pereira, Sai Kumar. N, Ayyappan. V.R. Effectiveness of Instrumental Assisted Soft Tissue Mobilization Technique With Static Stretching In Subjects With Plantar Fasciitis. *Int J Physiother*. 2014; 1(3):101-111
 19. DiGiovanni BF, Nawoczenski DA, Lintal ME, Moore EA, Murray JC, Wilding GE, Baumhauer JF. Tissue-specific plantar fascia-stretching exercise enhances outcomes in patients with chronic heel pain: a prospective, randomized study. *JBJS*. 2003 Jul 1;85(7):1270-7.
 20. Jha RK, Uprety S, Shah LL. Functional outcome in patients with chronic plantar fasciitis treated with plantar fascia stretching and tendoachilles stretching exercises. *Journal of Institute of Medicine*. 2013 Oct 12;35(1):32-8.
 21. Mohamed HA. Effectiveness of Achilles tendon stretching for the treatment of chronic plantar fasciitis. *The Egyptian Orthopaedic Journal*. 2015 Oct 1;50(4):215.
 22. Sharma NK, Loudon JK. Static progressive stretch brace as a treatment of pain and functional limitations associated with plantar fasciitis: a pilot study. *Foot & ankle specialist*. 2010 Jun;3(3):117-24.
 23. Grim C, Kramer R, Engelhardt M, John SM, Hotfiel T, Hoppe MW. Effectiveness of Manual Therapy, Customised Foot Orthoses and Combined Therapy in the Management of Plantar Fasciitis—a RCT. *Sports*. 2019 Jun;7(6):128.

Efficacy of Early Decompression Surgery Versus Epidural Injection in Management of Sciatica Due to Lumbar Disc Herniation—A Randomised Control Trial

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Abstract

Introduction: Sciatica is one of the most excruciating type of pain resulting due to irritation of the sciatic nerve in the lower back. Pain radiates along the distribution of the sciatic nerve in the lower limb. Lumbar disc herniation is commonly implicated as a cause of sciatica. Treatment options include initial conservative approach with epidural injection and analgesics and in patients with no relief decompression surgery performed. The short-term efficacy of the epidural injections is well established but the long-term outcome remains controversial. Even, spinal decompression surgeries have shown significant relief of symptoms at short term but in long term remain doubtful. This study attempts to compare both these treatment options in people with disabling chronic sciatic pain.

Materials and Method: This prospective randomized controlled trial conducted on 25 patients for duration of 1 year with sciatica symptoms lasting for more than 6 weeks. Complete history and examination with imaging studies was carried out with pain assessment done by using a Roland Disability Questionnaire (RDQ) and Visual Analogue Scale (VAS). Follow up Assessment of the patient's were done at regular interval of 0, 2, 4, 12, 26, 52 weeks post intervention.

Results: Of the 25 patients 12 were assigned randomly to early surgery group and 13 to epidural injection group. Immediate post-op and follow up assessment showed significant improvement in pain and disability scores for patients randomized to early surgery group with a significant difference between areas under the curve. The short-term benefit of early surgery was no longer significant by 6 months and by the end of 1 year outcomes were similar between the two groups.

Conclusion: Early surgery achieved more rapid relief of sciatica than conservative care, but outcomes were similar by one year in patients of both groups.

Keywords: Decompression Surgery, Lumbar Disc Herniation, Sciatica, VAS.

Introduction

Sciatica is one of the most excruciating type of pain resulting due to irritation of the sciatic nerve in the lower back. Pain radiates along the distribution of the sciatic nerve in the lower limb. It is often associated with numbness and paresthesia.¹ Sciatica results in significant morbidity resulting in loss of work days. The financial burden of chronic sciatica can also have significant effect on the quality of life. Sciatica most commonly occurs

as a result of lumbar disc displacement which directly impinges on the nerve, causing irritation or inflammation of the nerve roots producing the symptoms of sciatica.² The most used test in opd basis which is routinely done is straight leg raise test or Lasegue's sign.³ Treatment options include initial conservative approach with epidural injection and analgesics and in patients with no relief decompression surgery performed. The short-term efficacy of the epidural injections is well established

but the long-term outcome remains controversial. Even, spinal decompression surgeries have shown significant relief of symptoms at short term but in long term remain doubtful. This study attempts to compare both these treatment options in people with disabling chronic sciatic pain.

Materials and Method

Study Design: Randomised Control Trial

Study Duration: 1 Year

Period of Study: June 2018 – June 2019

The study was conducted tertiary care hospital in north Indian state of Haryana.

Sciatic pain was defined by the presence of a radiating pain in the lower limbs beginning in the lumbar or gluteal region and extending below the knee, with positive straight leg raising test(3) and sciatic stress test.

Inclusion Criteria:

- Age: 18 – 70 years
- Sciatic pain for more than 6 weeks not relieved with usual care
- MRI evidence of lumbar disc herniation causing nerve root compression

Exclusion Criteria:

- Cauda equina syndrome.
- Power <3/5 in any lower limb muscle group.
- Associated with other spinal disorders like Infective Spondylodiscitis, Inflammatory Spondylodiscitis, Vertebral Fractures, tumours.
- Patients with scoliosis >15 degree
- Previous lumbar spine surgery.
- Co-morbid conditions like deranged liver or renal functions or uncontrolled diabetes or hypertension.

Patients were explained about the possible treatment options including continuing usual care or epidural injection trial and decompression surgery of the lumbar spine. Patient who had consented for further surgical intervention were included in the study.

Patients were randomly assigned for spinal decompression surgery or epidural injection with random number generating method. Even numbers

underwent lumbar decompression surgery, odd numbers were assigned for epidural injection.

Pain was assessed using a Roland Disability Questionnaire (RDQ) and Visual Analogue Scale (VAS)

Follow-up: Assessment of the patients were done at regular interval of day 1, 2, 4, 12, 26, 52 weeks post intervention. Physical Examination was done and assessment was using VAS and RDQ at each visit.

Results

During the study period total of 25 patients were included in the study and randomly divided into surgical and epidural injection management groups. Both groups were matched for age and sex distribution. The average age in surgical group was 46.1 yrs and there were 5 no of males and 7 no of females, where as the epidural group had 7 males and 6 females with an average age of 44.5 yrs. Mean duration of symptoms was 43.5 weeks for surgical groups and whereas for epidural group it was 44.2 weeks. Sensory loss was present in 6 patients(table 1) out of 12 in the surgical group and in 8 patients out of 13 in the epidural (table 1). Out of 12 patients evaluated in surgical group pre-operatively 1 patient had muscle power 3/5, 7 patients had power 4/5 and 4 patients had muscle power 5/5 whereas in the epidural group 8 patients had muscle power 4/5 and 5 patients had power 5/5 in the pre-operative period. In the Post-operative evaluation muscle power in the surgical group was 4/5 in 2 patients and 5/5 in 10 patients whereas in the epidural group 2 patients had muscle power 4/5 and 11 patients had muscle power 5/5 (table 2).

Mean VAS score pre-op in surgical group was 7 whereas in epidural group was 6.5 as compared to post-op at 52 weeks in surgical group was 0.7 and epidural was 0.8(figure 2). RDQ Score of the patient showed a general decreasing trendline with mean RDQ score pre-op in surgical group was 15.8 and epidural group was 15.7 as compared to post-op at 52 weeks in surgical group was 0.5 and in epidural group was 0.8 (figure 1). There was a significant improvement in both surgical and epidural group in subsequent follow-up from pre-op period but results showed similar trends in both the groups at 52 weeks follow-up i.e. The effect of decompression surgery in symptomatic relief was much more pronounced compared to epidural group in short term at 4 weeks ($p = <0.05$). Over a long term (52 weeks) both groups had similar symptomatic relief when assessed by both RDQ and VAS($p = >0.05$).

Table 1: Sensory Loss

Sensory Loss	Surgical Group	Epidural Group
Yes	6	8
No	6	5

Table 2: Muscle Power

Muscle Power	Surgical		Epidural	
	PreOp	PostOp	PreOp	PostOp
3	1	0	0	0
4	7	2	8	2
5	4	10	5	11

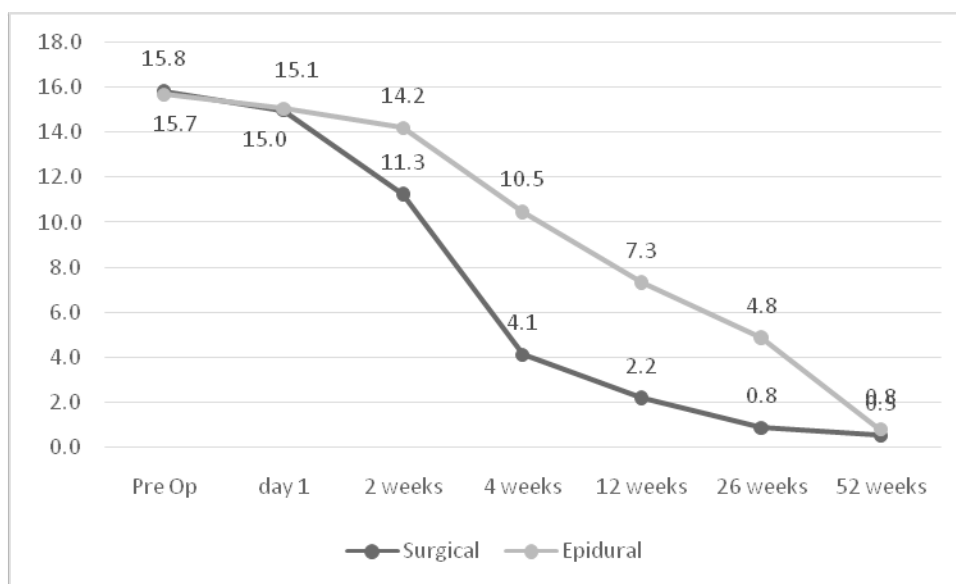


Figure 1: Mean RDQ Score in Surgical and Epidural group.

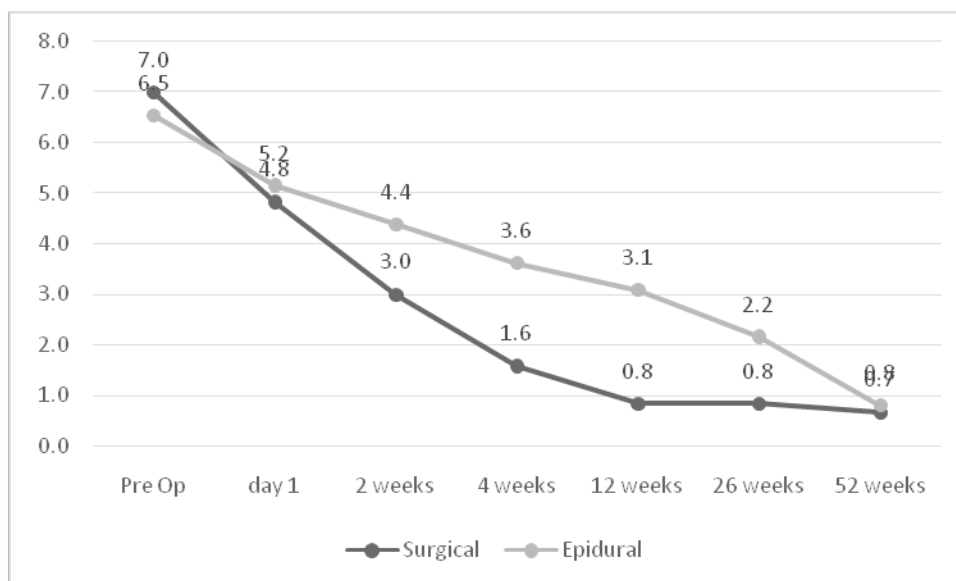


Figure 2: Mean VAS Score in Surgical and Epidural group

Discussion

Sciatic pain is said to be known to ancient Roman and Greek physicians. Hippocrates is said to be the earliest one to coin the term sciatica denoted by the greek word ischios meaning hip.⁴

20-40% of people have sciatica at some point their life commonly seen in age group of 40-60 yrs. Sciatica has high direct and indirect costs most of which are not generated by medical treatment but are attributed to loss of productivity. Range of motion, muscle power, reflexes, sensations are checked for in the patient which help to know the neurological status. Management of sciatica is divided into conservative and surgical intervention. Conservative management includes bed rest, physiotherapy, medications like NSAIDS, muscle relaxants, opioids and epidural steroid injections.⁵ This was a randomized controlled trial conducted on 30 patients in a tertiary care setup. According to our study and the results obtained, The major advantage of surgical intervention for patients with sciatica is more rapid relief of leg pain, reassurance about recovery and earlier return to normal activities. There were significant benefits at 4 weeks in the surgery group as compared to the epidural injection group, however at 1 year follow up the statistically the difference between both the treatment option groups was not significant for it to be clinically meaningful. In the study conducted by Steven J Atlas and his associates in 2001, Out of the total 402 patients, 220 patients were managed with surgical intervention and 182 who were managed with non-operative interventions. The results showed that people treated surgically reported early relief of pain lasting longer in duration than those treated non surgically.⁶ Although patients treated surgically had significantly greater improvement in symptoms, functional status and satisfaction than patients treated non-surgically, work disability outcomes and vas scores at end of follow up were almost similar for both the groups of patients.⁶ In 2006 James Weinstein published a study on surgical versus non-operative management of low back ache and radiculopathy. A randomized trial i.e. SPORT (The Spine Patient Outcomes Research Trial) was conducted on 472 patients out of which 230 were treated surgically and 242 underwent non operative treatment. Outcome of the study was that although patients in both groups reported improvement in their symptoms, the surgically treated group had better results in their symptoms but results showed that there appear to be no substantial differences between any of these method in end of

follow-up period i.e no significant statistical difference between the 2 groups of patient.⁷ In 2007 a randomized study conducted on 283 patients by Wilco C Peul and his associates who had sciatica symptoms for a minimum 6weeks. They were managed by early surgery, epidural or prolonged conservative management. Out of 283 patients 141 underwent surgery and 142 treated conservatively. The outcome of this study showed that there was significant relief from pain and faster recovery in patients who underwent early operative intervention.⁸

Our study also showed results on similar trend with greater relief of pain for patients in the surgery group as compared to epidural patients. Our results however do not imply that surgery is the only preferred treatment for all patients with sciatica caused by a herniated lumbar disc. Patients with mild symptoms did well with epidural injection also. For those with moderate or severe symptoms, surgery may hasten early recovery and result in better outcomes compared with nonsurgical treatment. However, long term follow up is needed to obtain reliable data to detect a possible difference between treatment options available.

Conclusion

In general there is evidence that early surgery in patients with sciatica provides a better relief in pain as compared to epidural injection group. No significant differences were found between surgery and epidural injection group at the end of 1 year. The therapeutic role of surgery for sciatica is restricted to faster recovery and relief of leg pain. But comparing our results epidural injection might also be one of the treatment modalities to be used for patients with sciatica as it is cost-effective.

Conflict of Interest: None

Source of Funding: Self

Ethical Clearance: Ethical Clearance was obtained from the Institutional Ethics Committee (IEC), Maharishi Markandeswar (deemed to be university) Mullana, Ambala.

References

1. Gugliotta M, da Costa BR, Dabis E, Theiler R, Jüni P, Reichenbach S, et al. Surgical versus conservative treatment for lumbar disc herniation: a prospective cohort study. *BMJ Open*. 2016;6 (12):e012938.
2. Jacobs WCH, Arts MP, van Tulder MW, Rubinstein SM, van Middelkoop M, Ostelo RW, et al. Surgical

- techniques for sciatica due to herniated disc, a systematic review. *Eur Spine J.* 2012;21(11): 2232-51.
3. Frederick M. Azar M, Professor, Engineering D of OS and B, Clinic U of T, Chief of Staff CC, Memphis T, et al. *Campbell's Operative Orthopaedics.* 13th ed.
 4. Stafford MA, Peng P, Hill DA. Sciatica: a review of history, epidemiology, pathogenesis and the role of epidural steroid injection in management. *Br J Anaesth.* 2007; 99(4):461-73.
 5. Murakibhavi VG, Khemka AG. Caudal epidural steroid injection: a randomized controlled trial. *Evid Based Spine Care J.* 2011;2(4):19-26.
 6. Atlas SJ, Keller RB, Wu YA, Deyo RA, Singer DE. Long-term outcomes of surgical and nonsurgical management of sciatica secondary to a lumbar disc herniation: 10 year results from the maine lumbar spine study. *Spine (Phila Pa 1976).* 2005; 30(8): 936-43.
 7. Weinstein JN, Tosteson TD, Lurie JD, Tosteson ANA, Hanscom B, Skinner JS, et al. Surgical vs Nonoperative Treatment for Lumbar Disk Herniation. *AMA.* 2007; 297(14):1545-6
 8. Peul WC, van Houwelingen HC, van den Hout WB, Brand R, Eekhof JAH, Tans JTJ, et al. Surgery versus Prolonged Conservative Treatment for Sciatica. *N Engl J Med* 2007;356:2245-56.

A Prospective Study to Compare the Perioperative Oral Duloxetine and Gabapentin for Postoperative Quality of Recovery in Female Patients Undergoing Lower Abdominal Gynecological Surgeries

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Abstract

Background: Continuous efforts are being taken to provide better postoperative quality of recovery especially in female patients in terms of both physical and emotional parameters after surgery and anaesthesia.

Method: The present study was carried out in 70 female patients of ASA Grade I & II between the age group of 20-50 years scheduled to undergo lower abdominal surgery. They were randomly divided into two groups of 35 patients each to receive either duloxetine 60 mg or gabapentin 900 mg orally 3 hours prior to surgery and repeated 24 hours later with the same dose.

Results: Both the groups were comparable regarding mean age and weight of the patients (Table I). There was highly significant difference in both mean and median values of quality of recovery in both the groups with better scores in the gabapentin group. The mean opioid requirement in group A was 2.83 ± 1.20 and in group B was 1.90 ± 1.04 which was also highly significant, p value 0.0009. Regarding patient satisfaction 54.28% patients in gabapentin group showed excellent satisfaction as compared to 28.50% patients in duloxetine group, p value 0.057. Side effects were observed more in Group A.

Conclusion: Gabapentin should be considered as an effective strategy for improving the postoperative quality of recovery and reducing the post-surgical narcotic consumption and related side effects.

Keywords: Duloxetine, Gabapentin, Postoperative Pain, Quality of Recovery.

Introduction

The recovery after surgery and response to general anaesthesia is different in either gender. Women's recovery after surgery is poor despite emerging faster from general anaesthesia.¹ It could be because of greater sensitivity for pain and multidrug associated side-effects.² Various pharmaceutical and regional strategies had been tested and tried to alleviate postoperative pain to improve quality of recovery.

Duloxetine is mostly used for the treatment of major depression and anxiety. It acts by inhibiting reuptake of serotonin-norepinephrine. It is also found to be useful in management of chronic pain.^{3,4} It is also effective in treating perioperative as well as acute postoperative pain and also might prevent transient emotional problems associated with pain. The combination of reduced pain and better emotional status can result in better independent state thereby improving quality of recovery after surgery. All these benefits of duloxetine are attributed to its action to augment the norepinephrine and serotonin neurotransmission in descending inhibitory pain pathways of brain and spinal cord.⁵

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Gabapentin, an antiepileptic structurally similar to γ -aminobutyric-acid was earlier used as an anticonvulsant

in late 1980s with poor results.⁶ Like duloxetine it has also showed promising results for treating chronic pain conditions and chronic neuropathic pain.^{7,8} Several meta-analysis have confirmed the efficacy of gabapentin in decreasing post-operative opioid use and pain.^{9,10} It exhibits its action by altering the peripheral and central response to painful stimulus by inhibiting the C fibre response to external painful stimulus.

Recently prevention and control of acute postoperative pain has become the primary aim of both anaesthesiologist and surgeons. Inadequate control of postsurgical pain can cause more physical and emotional trauma, longer stay at hospital, propensity to develop chronic pain leading to increased morbidity and poor quality of life. A number of pharmacological and non pharmacological method and techniques are being developed continuously in this field of utmost importance.¹¹ One such technique is use of preemptive analgesia. Here the selective drug is given to the patient hours before surgery either orally, intramuscular route or intravenously. Preemptive analgesia is thought to act by central desensitization to the painful stimulus. With this idea the present study was conducted with the objective of comparison of effect of Duloxetine with Gabapentin given orally preoperatively on quality of recovery in female patients undergoing lower abdominal gynecological surgeries.

Method

A prospective, randomized, comparative and single blinded study was carried out after ethical committee approval in 70 female patients, aged 20-50 years of ASA grade I and II undergoing elective gynecological surgery for benign diseases at a tertiary care center.

Patients were divided randomly by computer generated numbers to one of the following groups.

Group A (n=35) where patients were given table t Duloxetine 60mg orally 3 hours prior to surgery and repeated with same dose 24 hours later

Group B (n=35) where patients were given table t Gabapentin 900mg orally 3 hours prior to surgery and repeated with same dose 24 hours later

Subjects with consent refusal, ASA grade III and IV, any history of allergy to Duloxetine or Gabapentin, pregnant females, patients receiving opioids and/or antidepressants were excluded from study. A post

hoc power analysis was conducted using the software package, G Power (Faul and Erdfelder 1992). The alpha level used for this analysis was $p < 0.05$ and beta was 0.20. If the post hoc analysis reveals the statistical power of 0.40, it detects a small effect size, whereas if the power exceeds 0.80 it detects moderate to large effect size. By using the parameter Quality of recovery at 24 hours, which was the primary outcome of our study, Power of the study has been calculated to be 0.96 and with an effect size of 0.90 with 10% chance of error for total sample size 70 i.e 35 each for 2 groups.

Preoperative assessment was done a day prior to surgery. Patients were informed about the study and written informed consent was taken. Patients were nil by mouth for 6 hours. On the day of surgery in the operation theatre, all standard non invasive monitors were applied and baseline values were recorded. A large bore 18G cannula was introduced and ringer lactate was started. Under all aseptic conditions an epidural catheter was put at L₃-L₄ intervertebral space with 18G Tuohy needle of combined spinal epidural set and spinal anaesthesia was provided with 15mg of 0.5% H bupivacaine by 27G spinal needle of the same combined spinal epidural set in lateral decubitus position. After confirming the appropriate level at T₆ dermatome surgery was started. All vital parameters were monitored and maintained within 30% of baseline values.

Perioperative data recorded was the subject's age, weight and ASA physical status. The Quality of Recovery-40 questions (QOR-40) were compiled by the subjects at 24 and 48 hours after the surgery. The QOR-40 scoring system was explained to all the patients and reviewed to provide accurate understanding of all questions. The questions evaluate 5 components of patient recovery which include physical comfort, physical independence, emotional state, patient support and pain. The sum of these generates an aggregate Global QOR-40 score ranging from 40-200. Pain scale by NRS {0-10} and side effects were noted at interval of 1, 2, 4, 8, 12, 24, 36 and 48 hours. They were given epidural tramadol 100 mg diluted to 10ml with normal saline when pain was >5 NRS and postoperative nausea and vomiting (PONV) was treated with ondansetron 4mg IV stat. Number of times the analgesia by epidural route were noted. The results were collected, tabulated and statistically analysed. A p-value was used to reject type I error. A p value of <0.05 was considered statistically significant. The primary outcome of our study was the QOR-40 score at 24 hours and 48 hours. The secondary

outcomes were the postoperative opioid consumption, patient satisfaction and side effects.

Statistical Analysis: Data were described in terms of range; mean \pm standard deviation (\pm SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. Comparison of quantitative variables between the study groups was done using Student t-test and Mann Whitney U test for independent samples for parametric and non-parametric data respectively. For comparing categorical data, Chi square (χ^2) test was performed and exact test was used when the expected frequency is less than 5. A probability value (p value) less than 0.05 was considered statistically significant. All statistical calculations were done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

Observations: Both the groups were comparable regarding mean age and weight of the patients (Table I). There was highly significant difference in both

mean and median values of quality of recovery in both the groups with better scores in the gabapentin group. Total median score in the duloxetine and gabapentin group was 169 (165-173) versus 175 (171-178) at 24 hours and 187 (185-189) vs 194 (192-196) at 48 hours respectively with p value of 0.000. Opioid top-ups were required in 18 patients in Group A and 11 patients in group B. The mean opioid requirement in group A was 2.83 ± 1.20 and in group B was 1.90 ± 1.04 which was also highly significant, p value 0.0009. Regarding patient satisfaction 54.28% patients in gabapentin group showed excellent satisfaction as compared to 28.50% patients in duloxetine group, p value 0.057. Side effects were observed more in Group A in terms of nausea, vomiting, dizziness, headache and pruritis. The most common side effect observed was postoperative nausea and vomiting which was seen in 45.7% in Group A and 25.7% in Group B patients and was relieved with 4 mg intravenous administration of ondansetron. Excessive somnolence was the only side effect seen with gabapentin.

Table I: Patient characteristics

	Group A	Group B	P Value
Age	45.6 \pm 6.2	44.8 \pm 6.6	0.6029
Weight	50.2 \pm 7.4	49.2 \pm 5.5	0.5233

Table II: Mean values of quality of recovery at 24 hours and 48 hours in both the groups

At 24 Hours	Group A		Group B		p-value
	Mean	SD	Mean	SD	
Physical Comfort	51.20	2.07	55.46	2.56	0.000
Physical Independence	12.11	2.11	15.86	2.59	0.000
Pain	29.71	2.49	31.80	2.13	0.000
Emotional Status	44.31	3.36	41.26	2.13	0.000
Patient Support	31.63	2.16	30.74	1.90	0.073
At 48 Hours	Group A		Group B		p-value
	Mean	SD	Mean	SD	
Physical Comfort	57.03	1.71	60.00	0.00	0.000
Physical Independence	19.60	2.00	21.94	1.97	0.000
Pain	29.91	1.62	35.00	0.00	0.000
Emotional Status	45.00	0.00	43.14	1.63	0.000
Patient Support	35.00	0.00	33.71	1.27	0.000
At 24 Hours	Group A		Group B		p-value
	Median	IQR	Median	IQR	
Physical Comfort	52.00	49-53	56.00	54-57	0.000
Physical Independence	13.00	10-14	16.00	14-18	0.000
Pain	30.00	28-32	32.00	30-34	0.001
Emotional Status	45.00	41-47	41.00	39-43	0.000
Patient Support	32.00	30-33	30.00	29-32	0.065
Total	169	165-173	175	171-178	0.000

At 48 Hours	Group A		Group B		p-value
	Median	IQR	Median	IQR	
Physical Comfort	57.00	56-58	60.00	60-60	0.000
Physical Independence	20.00	18-21	22.00	20-24	0.000
Pain	30.00	29-31	35.00	35-35	0.000
Emotional Status	45.00	45-45	43.00	42-45	0.000
Patient Support	35.00	35-35	34.00	32-35	0.000
Total	187	185-189	194	192-196	0.000

Table III: Opioid top ups requirement in both the groups

Top Up Required	Group A, N	%	Group B, N	%	P Value
Once	3	8.50	5	14.20	
Twice	4	11.40	3	8.50	
3 times	5	14.20	2	5.70	
4 times	5	14.20	1	2.80	
> 4 times	1	2.80	0	0.00	
Mean	2.83±1.20		1.9±1.04		0.0009

Table V: Patient's satisfaction at 48 hours after surgery

Patient Satisfaction	Group A, Number	%age	Group B, Number	% Age	P Value
Excellent	10	28.50	19	54.28	0.057
Good	9	25.70	7	20	
Fair	7	7.20	7	20	
Poor	9	25.70	2	.06	
Total	35	100	35	100	

Table IV: comparison of side effects in both the groups

Side Effects	Group A Number	%	Group B Number	%	P Value
PONV	16	45.7%	9	25.7%	0.0807
Pruritis	10	37.1%	2	5.7%	0.0111
Excessive Sedation	5	14.2%	13	37.1%	0.028
Dizziness	11	31.4%	6	17%	0.164
Headache	9	25.7%	3	8.5%	0.057

Discussion

QOR-40 is evolving as a multidimensional measurement tool for assessment of recovery in patients after surgery and anaesthesia. It measures every aspects related to patient recovery in terms of physical, emotional and pain. Previously anaesthesiologists were only concerned about the adequate reversal, pain and its management. Various factors like preoperative anxiety, preoperative and postoperative pain are linked to poor quality of recovery which can be addressed by preoperative counseling and pharmacotherapy.¹² Preemptive analgesia has found to be beneficial in dealing

with preoperative as well postoperative pain. Both the drugs used in our study are effective in combating anxiety and pain. Both duloxetine and gabapentin provide better quality of recovery after hysterectomy with an edge towards gabapentin. There is statistically significant difference in the median score between duloxetine and gabapentin group. Castro-Alves LJ¹³ in his study found significant effect on quality of recovery in female patients after hysterectomy with duloxetine. Similar results of perioperative duloxetine were also documented by Koh IJ et al¹⁴ regarding better quality of recovery in centrally sensitized patients undergoing knee

arthroplasty. Effect of gabapentin on quality or recovery is not studied much. In his study Martins M et al¹⁵ found no effect on quality of recovery with gabapentin in bariatric patients. It might be due to use of single lesser dose, 75mg than required. However it has significant effect on the opioid consumption. Studies of Doha NM et al¹⁶, Arumugam S et al¹⁷, Melemeni M et al¹⁸, Khan MA¹⁹ have demonstrated the significant reduction in opioid consumption both peri and postoperatively with gabapentin when given preoperatively as preemptive analgesia. Preoperative duloxetine has also been found to be effective in reducing opioid consumption and postoperative pain when given as a part of multimodal analgesia technique or for a long period both pre and postoperatively^{20,21}. In our study gabapentin group had shown significant reduction in opioid consumption postoperatively than duloxetine group. Patients in both the groups were satisfied with their treatment with 58.28% patients in gabapentin group reported excellent satisfaction as compared to 28.50% in duloxetine group. Only two patients in gabapentin group had poor satisfaction in contrast to nine in gabapentin group. Duloxetine has been known for various side effects like nausea, vomiting, pruritis and headache etc. In our study we found significant side effects in duloxetine group where as previous studies showed no or minimal side effects^{21,22}. It could be attributed to prolonged consumption of duloxetine for 1-2 weeks preoperatively in these studies or more perception of side effects in female gender in our study. Excessive sedation was the only side effect of gabapentin as reported in previous studies. Grant MC et al²³, Achuthan S et al²⁴ studied the protective effect of gabapentin on postoperative nausea and vomiting and stressed that it should be considered for prevention of PONV.

Conclusion

To conclude preoperative gabapentin is effective in reducing postoperative pain and improves postoperative quality of recovery in female patients undergoing lower abdominal procedures without any significant side effects. Therefore gabapentin should be considered as an effective strategy for improving the postoperative quality of recovery and reducing the post-surgical narcotic consumption and related side effects.

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Conflict of Interest: Nil

Ethics Approval: Taken

References

1. Buchanann FF, Myeles PS, Ciccutini F. Effects of patient sex on general anaesthesia and recovery. *Br. J. Anaesth.* 2011;106:832-9
2. Bartley EJ, Fillingrim RB.: Sex differences in pain : a brief review of clinical and experimental findings. *Br.J.Anaesth.* 2013;111:52-8.
3. Happich M, Schneider E, Boess FG, Wilhelm S, Schacht A, Birklein F, Ziegler D. Effectiveness of duloxetine compared to pregabalin and gabapentin in diabetic peripheral neuropathic pain : Results of German Observational Study . *Clin J Pain* 2014;30:875-85.
4. Lunn MP, Hughes RA, Wiffen PJ. Duloxetine for treating painful neuropathy, chronic pain or fibromyalgia. *Cochrane Database Syst Rev* 2014;3: CD007115.
5. Bymaster FP, Lee TC, Knadler MP, Detke MJ, Iyengar S. The dual transporter inhibitor duloxetine: a review of its preclinical pharmacology, pharmacokinetic profile and clinical results in depression. *Current Pharmaceutical Design.* 2005;11:1475–93.
6. Guay DR: Update on gabapentin therapy of neuropathic pain. *Consult. Pharm.* 2003;18:158-70, 173-8.
7. Laird MA, Gidal BE: Use of gabapentin in the treatment of neuropathic pain. *Ann. Pharmacotherapy* 2000;34:802-7
8. Moulin DE, Clark AJ, Gilron I, Ware MA, Watson CP, Sessle BJ et al. Pharmacological management of chronic neuropathic pain. *Pain Res. Manag.* 2007;12:13-21.
9. Ho K Y, Gen T J, Habib A S. Gabapentin and postoperative pain, a systemic review of randomized controlled trials. *Pain* 2006,126:91-101.
10. Seib R K, Paul J E.
11. Perioperative gabapentin for postoperative analgesia *Can. J. Anaesth.* 2006, 533,461-69. Surender, Arora P, Khurana G, Sachan PK. Comparison of postoperative quality of recovery and pain relief with preoperative single-dose dexamethasone and lignocaine after laparoscopic cholecystectomy. *Anesth Essays Res* 2018;12:630-5.
12. Pogatzki-Zahn EM, Segelcke D, Schug SA. Postoperative pain – from mechanisms to treatment. *Pain Reports* 2017;9:e588

13. Castro Alves LJ, Oliveira de Medeiros ACP, Neves SP, Carneiro de Albuquerque CL, Modolo NS, De Azevedo VL et al. Perioperative Duloxetine to Improve Postoperative Recovery After Abdominal Hysterectomy: A Prospective, Randomized, Double-Blinded, Placebo-Controlled Study. *Anesthesia & Analgesia* 2016;122:98-104
14. Koh IJ, Kim MS, Sohn S, Song KY, Choi NY, In Y. Duloxetine reduces pain and improves quality of recovery following total knee arthroplasty in centrally sensitized patients: A prospective, randomized controlled study. *J Bone Joint Surg Am.* 2019;101:64-73
15. Martins MJ, Martins CPMO, Castro-Alves LJ, Nascimento Jesus G, Campos GO, Barbosa Cerqueira SB et al. Pregabalin to improve postoperative recovery in bariatric surgery: a parallel, randomized, doubleblinded, placebo-controlled study *journal of pain research*; 2018;11: 2407—15
16. Doha NM, Rady, El Azab SR. Preoperative use of gabapentin decreases the anesthetic and analgesic requirements in patients undergoing radical mastectomy. *Egyptian Journal of Anaesthesia* 2010; 26, 287–291
17. Arumugam S, Lau CSM, Chamberlain RS. Use of preoperative gabapentin significantly reduces postoperative opioid consumption: a meta-analysis. *Journal of Pain Research* 2016;9 631–640.
18. Melemenis A, Staikou C, Fassoulaki A. Gabapentin for acute and chronic post-surgical pain. *Signa Vitae* 2007; 2: 42 – 51
19. Khan MA, Siddiqi KJ, Aqeel M. Effect of gabapentin on opioid requirements in patients undergoing total abdominal hysterectomy. *Anaesth Pain & Intensive Care* 2013;17:131-135
20. Attia JZ and Mansour HS. Perioperative Duloxetine and Etoricoxib to improve postoperative pain after lumbar Laminectomy: a randomized, double-blind, controlled study. *BMC Anesthesiology* 2017 17:162
21. Koh IJ, Kim MS, Sohn S, Song KY, Choi NY, In Y. Duloxetine reduces pain and improves quality of recovery following total knee arthroplasty in centrally sensitized patients. *J Bone Joint Surg Am.* 2019;101:64-73
22. Saoud A, Elkabarity R. Effect of Perioperative Duloxetine on Postoperative pain relief following Anterior Cervical Microdiscectomy and fusion. A Pilot Study. *WScJ* 2013;4: 57-66.
23. Grant MC, Lee H Page AJ, Hobson D, Wick E, Wu CL. The effect of preoperative gabapentin on postoperative nausea and vomiting : a meta-analysis. *Anaesthesia and Analgesia* 2016;122;976-985
24. Achuthan S, I Singh I, Varthya SB, Srinivasan A, Chakrabarti A, Hota D : Gabapentin prophylaxis for the postoperative nausea and vomiting in abdominal surgeries: a quantitative analysis of evidence from randomized, controlled clinical trials. *Br. J. Anaesth.* 2015;114,588-89.

A Comparative Study of the Proseal Laryngeal Mask Airway (PLMA) Insertion by Three Different Technique I.E. Introducer, Digital and Stylet

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Abstract

Background: Supraglottic airway devices have been widely used as an alternative to tracheal intubation during general anesthesia. Proseal Laryngeal Mask Airway (PLMA) is an effective alternative to ETT with inflatable cuff forming pressure seal around laryngeal inlet and permitting ventilation. In view of this, the present study was undertaken to compare the different insertion techniques to insert PLMA in adult patients undergoing elective surgeries.

Methodology: Ninety patients scheduled for elective surgical procedures under general anesthesia belonging to ASA grade I and II were included in the study and were randomly divided into three groups with 30 patients in each group. In Group I (n=30), PLMA was inserted using introducer, in Group II (n=30) PLMA was inserted using digit and in group III (n=30) PLMA was inserted using stylet. Groups were compared in relation to number of attempts, insertion time, ease of insertion, orogastric tube insertion and, hemodynamic changes.

Results: The success first attempt rate for placement of PLMA was highest with introducer as compared to digit or stylet and the results were statistically significant ($p=0.029$). The mean time of insertion for PLMA using introducer was 27.03 ± 4.08 seconds which was shortest whereas with digit it was highest 35.27 ± 4.97 ($p=0.000$) and by using stylet 31.33 ± 3.12 seconds. There was no change in hemodynamic after the insertion of PLMA with either technique.

Conclusion: To conclude introducer technique of PLMA insertion was best as compared to digit and stylet technique.

Keywords: Proseal Laryngeal Mask Airway; Supraglottic Airway Device.

Introduction

Supraglottic airway devices (SAD) have become a popular fixture filling gap between intubation and face mask. These devices cover larynx, sit in hypopharynx and provide an effective airway without intubating the trachea. The classic laryngeal mask airway (cLMA) was

the first SAD invented by Dr. Archie Brain in 1981. Brain's goal was to develop device that could rapidly overcome an obstructed airway and yet be simple and atraumatic to insert. It forms a seal around larynx and permits both spontaneous and controlled ventilation.¹

PLMA, a reusable device, which has a specially designed cuff to provide a better and more effective seal than classic LMA along with the presence of gastric drainage port which can be considered as a potential protection against aspiration.^{2,3}

The drainage tube of Proseal LMA enhances seal and serves to evacuate gastric contents and decompress the stomach; thus, reducing the chances of aspiration.⁴

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There are advantages of PLMA as compare to ETT such as reduce anesthetic requirement for airway tolerance, ease of insertion by inexperienced person, improved hemodynamic stability at induction and during emergence, minimal increase in intraocular pressure following insertion.

So, the present study was undertaken in Department of Anaesthesia, Maharishi Markandeshwar Institute of Medical Sciences and Research Deemed to be University to compare the method of PLMA insertion by three different techniques i.e. introducer, digital & stylet.

Material and Method

The present study was conducted in Department of Anesthesiology, Maharishi Markandeshwar Institute of Medical Sciences And Research, Mullana Deemed to be University. After approval of protocol from the Institutional Ethics Committee, 90 healthy adult patients were included in the study as per following inclusion criteria

Exclusion Criteria:

- Cardiac, Hepatic and Renal diseases
- Upper respiratory tract infection
- Anticipated difficult airway (MP III and IV)
- Known uncontrolled hypertension
- Known diabetic and epileptic
- Pregnant patients
- Emergency surgeries
- Mouth opening < 2.5 cm
- Patients with increased risk of aspiration
- Obese patient (BMI>25kg/m²)
- Cervical spinal disease
- Head and neck surgical procedures

Study Design: Randomized, prospective comparative study.

In the study, patients were randomly divided into three groups with 30 patients in each group, for insertion of PLMA by different techniques (introducer, digit, stylet) using coded sealed envelope method.

Group I (n=30): Insertion of PLMA by introducer tool. Group II (n=30): Insertion of PLMA by index finger.

Group III (n=30): Insertion of PLMA by stylet tool.

A thorough pre-anesthetic evaluation was done prior to the surgery and all the necessary routine investigations were carried out. A written informed consent was taken from every patient.

All patients were asked to fast overnight. They were pre medicated with table t alprazolam 0.25mg and table t ranitidine 150mg orally at bed time the previous night before surgery and again 2 hours prior to surgery with 1-2 sips of water.

An IV line was secured with 18G cannula and 0.9% normal saline was started. Inj. glycopyrrolate 0.2mg, Inj. midazolam 0.03mg/kg and Inj. fentanyl 1-2 mcg/kg were administered intravenously. Baseline parameters- peripheral oxygen saturation, heart rate, systolic, diastolic and mean blood pressure were noted.

Anesthesia was induced with Propofol 2.5mg/kg i/v, titrated to loss of response to verbal commands. Oxygen and Nitrous oxide (1:1) were provided via face mask and adequacy of mask ventilation was confirmed. Thereafter neuromuscular blockade was achieved with Inj. vecuronium 0.1mg/kg i/v. The patient's lungs were ventilated with a face mask for 90 seconds to allow for full relaxation of the jaw before placing the device. Appropriate size of PLMA was chosen as per group allocation of the patient. The cuff of PLMA was fully deflated prior to insertion. A clear water based jelly (KY jelly) was used for lubricating the posterior aspect of the cuff. For PLMA insertion by introducer, stylet & index finger technique and in all three group standard recommended insertion technique was followed.

For males size 4 was used, in females size 3 was used

After placement, in case of PLMA, cuff was inflated. The PLMA was then connected to the circle system of anesthesia machine and manual ventilation was started. The position of the device was confirmed by square wave capnograph trace, bilateral chest movements on gentle manual ventilation and auscultation of epigastrium and larynx.

The time interval between removing of face mask and obtaining an effective airway by square capnograph was recorded as Insertion Time. The device was fixed by taping the tube over chin according to the manufacturer's instructions. Manual ventilation was started. In presence

of partial or complete airway obstruction or a significant air leak, the device was removed and reinsertion attempted. A maximum of three insertion attempts were allowed before the device was considered as failure. An alternative device such as endotracheal tube (ETT) was used in such a situation. Number of Attempts to secure the airway was noted. The Ease of Insertion was graded as easy and difficult. If the device was placed without resistance or if any one maneuver (head hyperextension, mask rotation, finger manipulation) was required, it was graded as 'easy'. When there was resistance to insertion or more than one maneuver was required, it was graded as 'difficult'. Orogastric tube insertion was performed to confirm correct position of the distal end of the drain tube at the proximal end of oesophagus. Correct placement was decided by suction of fluid or detection of injected air by epigastric auscultation. It was graded as easy= if placed in one attempt, difficult = if placed in two attempts .

The ventilation of lung was done with tidal volume of 8ml/kg, the respiratory rate was adjusted to maintain EtCO₂ of 35-40 mm of Hg with inspiratory: expiratory ratio of 1:2. Anesthesia was maintained by nitrous oxide: oxygen mixture (60:40), isoflurane (0.5-0.8%) and intermittent boluses of vecuronium (0.01mg/kg) administered i/v.

After the completion of procedure, anesthesia was discontinued and residual neuromuscular blockade was antagonized with neostigmine methyl sulphate (0.05mg/kg) and glycopyrrolate (0.01mg/kg). 100% oxygen was provided on emergence and device was removed once the patient was fully awake.

The following parameters were observed:

- Number of attempts at PLMA insertion by all three different techniques.
- Insertion time

- Ease of insertion of the supraglottic device (easy, difficult & failure).
- Heart rate, non invasive blood pressure, arterial oxygen saturation, end tidal CO₂ level, before insertion and after insertion of PLMA by three different technique.
- Orogastric tube insertion (easy, difficult & failed).

Result

There was no statistical significant difference with respect to the demographic profile, ASA grading and mallampati class. (Table 1-3).The insertion of PLMA by introducer in first attempt was more successful as compare to stylet and digit (p< 0.00029).

The time taken for placement of PLMA in introducer was least (27.3+/-4.08) as compared to the digit and stylet. (p 0.000).The ease of insertion of PLMA was highest with introducer technique (group I) and least with group digit (group II). There was no significant statistical difference between three groups (p 0.044). (Table 4,5). Regarding the number of attempt of gastric tube there was no significant statistical difference between three groups (p 0.585).The ease of gastric tube insertion there was no statistically significant difference between three groups. (Table 6.) Hemodynamic response in three groups were comparable in terms of heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, EtCO₂ and arterial saturation before and after insertion of PLMA.

Table 1: Age and Weight Distribution

Group	I	II	III	P Value
	Mean	Mean	Mean	
Age	40.90	41.70	17.17	0.504
Wt.(kg)	57.27	58.90	61.27	0.480

Table 2: Gender Distribution

Group	I	II	III	Total	Chi-square Value	P-value
F	21	21	16	58		
M	9	9	14	32	2.425	0.298
Total	30	30	30	90		

Table 3: ASA Grade

ASA	Group						Total	Chi-square value	p-value
	I		II		III				
I	28	93.3%	23	76.7%	23	76.7%	74	3.801	0.150
II	2	6.7%	7	23.3%	7	23.3%	16		
Total	30	100.0%	30	100.0%	30	100.0%	90		

Table 4. No. of attempt, Insertion time and Ease of insertion by PLMA

PLMA	Group I (Introducer)	Group II (Digit)	Group III (Stylet)	p-value
Number of Attempt				
1 st	28(93.3%)	20(66.6%)	25(83.3%)	000.0029
2 nd	2(6.6%)	10(33.3%)	05(16.6%)	
Insertion Time (SEC.)	27.3+/-4.08	35.2+/-4.97	31.33+/-3.12	0.000
Ease of Insertion				
Difficulty	2(6.6%)	9(30.0%)	4(14.4%)	0.044
Ease	28(93.3%)	21(70.0%)	26(86.7%)	

Table 5. Comparison between three groups in no. of attempts and time of insertion

Variables	I VS II	I VS III	II VS III
	p-value	p-value	p-value
No. of attempt	0.008	0.314	0.095
Insertion time	0.000	0.000	0.000

Table 6. No. of attempt, Insertion time and Ease of insertion of Gastric tube

Gastric Tube	Group I (Introducer)	Group II (Digit)	Group III (Stylet)	P value
Number of Attempt				
1 st	28(93.3%)	29(96.7%)	27(90.0%)	0.585
2 nd	2(6.7%)	1(3.3%)	03(10.0%)	
Ease of Insertion				
Difficulty	2(6.7%)	4(13.3%)	3(10.0%)	0.690
Ease	28(93.3%)	26(86.7%)	27(90.0%)	

Discussion

PLMA is considered a type of 'double mask', separates respiratory and gastric tracts, physically 'plugging' inside the upper esophageal sphincter (UES) and being the first SAD to offer a dedicated channel access to the gastric content.

In our study, insertion of PLMA by introducer was successful in first attempt in 93.3% cases as compared to 66.7% cases by using digits and 83.3% by using stylet. Second attempt was required in 6.7% cases in group I, 33.3% cases in group II and in 16.7% cases in group III to insert PLMA. On comparing, introducer group with digit group there was statistically significant difference

($p=0.08$). There was no statistically significant difference when introducer group was compared with stylet group and when digit was compared with stylet. Similarly Chen M⁵ et al, concluded that the stylet and introducer groups were comparable. In contrast to our study Myatra S et al⁶ study concluded that PLMA insertion with a stylet tool has a higher first attempt insertion success and superior placement than conventional introducer tool. In their study in stylet group, the stylet was introduced up to the tip of drain tube so that PLMA cuff could not fold on itself. The stylet shapes and stiffens the cuff of the PLMA which may have prevented failed pharyngeal placement and positioning. In introducer group there were failed insertions due to failed pharyngeal placement of PLMA.

Das B et al⁷ found that combined IT and stylet technique is better than the digital or IT technique and no significant difference between digital or IT technique in pediatric patients without cervical spine motion.

In our study the mean time required to insert the PLMA by using introducer, digits, stylet was 27.03 ± 4.08 ; 35.27 ± 4.97 ; 31.33 ± 3.12 seconds respectively. Statistically, this result was highly significant ($p < 0.000$). Chen M et al⁵ concluded that introducer is best technique as it required less time as compared to stylet ($p < 0.001$). Singh C et al⁵ 2017, showed significant difference in insertion time. The insertion of PLMA by introducer took less time as compare to digit ($p < 0.02$). In contrast with our results Myatra S et al⁶ the insertion of PLMA by using introducer required more time as compare to stylet

In our study, the ease of insertion of PLMA was highest with introducer technique (group I) and least with group digit (group II). There was no significant statistical difference between three groups ($p = 0.044$).

In our study the ease of gastric tube insertion was statistically non significant (p value 0.585). In group I 93.3% had easy insertion of gastric tube while 6.7% had difficult insertion. In group II 96.7% had easy insertion of gastric tube while 3.3% had difficult insertion. In group III 90.0% had easy insertion of gastric tube while 10.0% had difficult insertion. Singh C⁷ et al study was concurrent with our study showed that orogastric tube insertion success in introducer group was 100% in first attempt and in digit group the first attempt rate was 90%. Similarly study conducted by Saini S et al⁸ was concurrent with our study and showed that orogastric tube insertion was 100% in introducer group while 88% success rate by using digital technique. Myatra S et al⁶ in their study concluded that there were failure of insertion of gastric tube was more in introducer technique as compare to stylet group. In introducer group the PLMA tip was folded on itself where as in stylet group the stylet was inserted till the drain tube, so the PLMA cuff could not be folded.

In our study, the basal heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, was comparable in all three groups. There was no significant difference in change between group I, group II and group III after the insertion of PLMA by introducer, digits and stylet respectively.

The attempt rate of introducer technique was more

successful and higher as compared to digital technique for insertion of PLMA because introducer use less area and provides adequate curvature and stiffness to PLMA. Moreover it directs the cuff over the oropharyngeal inlet and facilitates good depth of insertion. The stylet technique can provide the curvature and stiffness to the PLMA. Thus makes it insertion easy. Hence there was no significant difference regarding number of attempt as compare to introducer technique.

The digital technique requires more skill. At many times, depth of insertion of finger in the patient's mouth may not be sufficient to place the device hence number of attempts required to insert PLMA by digits was high.

Conclusion

In conclusion insertion of PLMA by introducer technique is the best technique as compared to digit and stylet techniques in terms of least number of attempts, lesser insertion time, easy to insert, successful placement of orogastric tube and no hemodynamic changes.

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References

1. Venkateshwarlu G. Randomized controlled study comparing two supraglottic airway devices: the I-Gel and the conventional laryngeal mask airway in anaesthetized patients. *J Evid Based Med Health* 2015; 2(57):8898-102.
2. Samir E, Saker A.S. The Air Q as conduit for fiberoptic aide tracheal intubation in adult patient undergoing cervical spine fixation; A prospective randomized study. *Egyptian J Anaesth.* 2012; 28:133-7.
3. Steet E, Rajeev S, Firoz T, Yousuf F, Chug F, Wong J, Wong D. Safety efficacy of LMA Supreme vs. LMA P; A randomized controlled trial. *European Journal of Anaesth* 2010;27(7):602-7.
4. Cook TM, Lee G, Nolan JP. The Pro Seal laryngeal mask Airway: a review of the literature. *CanJ Anaesthesiology* 2005;52(7):739-60.
5. Chen M, Hsu H, Lu I, Shih C, Shen Y, Tseng K, et al. Techniques for the insertion of the Proseal laryngeal mask airway: comparison of the foley airway stylet tool with the introducer tool in a

- prospective, randomized study. *BMC Anesthesiol.* 2014; 14:105.
6. Myatra S, Khandale V, Gupta S, Solanki S, Divatia J. A novel technique for insertion of Pro Seal laryngeal mask airway: comparison of the stylet tool
 7. Das B, Mitra S, Samanta A, Samal R. A comparative study of three methods of ProSeal laryngeal mask airway insertion in children with simulated difficult laryngoscopy using a rigid neck collar. *Acta Anaesthesiologica* 2014;52:110-3.
 7. Singh C, Jain P, Bharadwaj A. PLMA A clinical evaluation and comparison of three techniques of insertion using introducer; index finger & thumb. *Indian Journal of Research.* 2017;9(6);116-9.
 8. Saini S. Comparison of Pro Seal laryngeal mask airway placement techniques using digital, introducer tool and gum elastic bougie in anaesthetized paralyzed patients 2015;(3):3703-7.
 9. Myatra S, Khandale V, Gupta S, Solanki S, Divatia J. A novel technique for insertion of Pro Seal laryngeal mask airway: comparison of the stylet tool with the introducer tool in a prospective, randomized study. *Can J Anaesth.* 2017;61(6):475-81.

Study of Drug Utilisation and Prescribing Pattern in the Department of Dermatology

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Abstract

Skin diseases seriously impact the quality of life of an individual. It affects all age groups and its chronic nature disturbs the financial status of the sufferer and family. Periodic audit of prescription in the form of drug utilisation study is a way to improve the quality of prescription and reduces the irrational prescribing and use of drugs. The present study was done to assess the drug prescribing patterns in dermatology outpatient department.

Keywords: Drug utilisation, Dermatology, Irrational.

Introduction

Drug utilisation studies facilitate us to understand the pattern of prescribing drugs and their usage in a scientific manner.¹ Rational prescribing is the most desired component in the drug supply-use chain that is required to ensure the rational use of drugs and a cost-effective medical care. However, irrational prescribing and use of drugs has been reported as a global problem² in terms of depletion of available therapeutic resources, higher cost of treatment, worsening of existing disease condition, ineffective and unsafe treatment, iatrogenic illness and increasing resistance to antimicrobials.³ Therefore, an effort was started in 1985 in the form of a global conference of experts at Nairobi to promote rational use of drugs.⁴

World Health Organization developed prescribing indicators and that are used globally for documentation of most important problems associated with prescribing such as poly-pharmacy, preference of prescribers for branded products, deviation from essential medicines

list and overuse of costlier medicines i.e. antibiotics and injections.^{5,6}

In India there is a practice of prescribing irrational combination of drugs, over use of antibiotics, multivitamins and irrational drugs. . This behavior of irrational prescribing drugs by the clinicians was due to lack of knowledge about drugs, unethical drug promotion, academic literatures, professional colleagues, commercial publicity and government regulations.^{7,8} Skin disorders have strong detrimental effect on quality life of the individuals in terms of physical, social, psychological as well as financially.⁹ Dermatologists prescribed antibiotic range was almost 5% worldwide and most of the disease conditions require prolonged treatment.¹⁰

Method

This was a prescription based prospective cross sectional study under taken in department of pharmacology in collaboration with department of dermatology at MMIMSR, Ambala from 27th October 2017 to 30th April 2019. After getting approval from institutional ethics committee a total of twelve hundred prescriptions of patients attending department of dermatology were considered for the study. The inclusion criteria for the study included patients of all age group and both gender, first time visitors at the department of dermatology (outdoor and indoor) and

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subjects who have given informed consent to access their prescription. Subjects who are not willing to give consent and patients coming on subsequent visits and for follow up were excluded from the study. The prescriptions were collected from outpatient department slip or prescription in case of outpatients, case sheets or record in case of indoor patients and from hospital medical record in case where prescriptions cannot be collected due to some unavoidable reason. The data was analyzed for demographic profile of the patient, disease pattern, average number of drugs prescribed, common class of drugs prescribed, drug dosage form and their route of administration.

Statistical Analysis: The collected data was entered in to SPSS version 24 for analysis. The descriptive analysis of categorical variables was calculated as absolute (n) and relative (%) frequencies.

Results

A total of 1200 patients attending the department of dermatology with their prescriptions were included in the study after meeting inclusion criteria. Table 1 presents the demographic data of the patients. All the study participants were in the range of age group 1 to 90 years. More than 71% of our patients were in the age group of 13-40 years. Majority of them belongs to 21-30 years. In this study, number of male patients was 697(58.1%) and number of female patients was 503 (41.9%). The male to female ratio was 1:0.39. Majority of them were married (63.8%). In the study, majority (29.4%) of the patients were housewives followed by students (29.9%), farmers (15.9%), labourers (7.3%), shopkeepers (6.8%) and least 0.1% were accountant and zamindar in each respectively.

Table 1: Demographic data of the patients.

Variable	Number (N)	Percentage (%)
Age Group in Years		
≤12	53	4.4
13-20	246	20.5
21-30	358	29.8
31-40	245	20.4
41-50	147	12.2
51-60	93	7.8
>61	58	4.8
Sex		
Male	697	58.1
Female	503	41.9

Variable	Number (N)	Percentage (%)
Marital Status		
Married	765	63.8
Unmarried	435	36.2
Occupation		
Accountant	1	0.1
Army	2	0.2
Businessman	14	1.2
Carpenter	5	0.4
Employee	25	2.1
Farmer	191	15.9
Housewife	353	29.4
Labourer	87	7.3
Not applicable	31	2.6
Retired	7	.6
Shopkeeper	81	6.8
Student	347	28.9
Teacher	26	2.2
Worker	29	2.4
Zamindar	1	0.1

As shown in Figure 1, dermatophytosis (52.3%) was the most common skin disease noticed in the patients followed by scabies (12.8%), eczema (5%), urticaria (4.7%) and acne (4.5%). Very small percentage of patients had psoriasis (1.4%), folliculitis (0.8%), dermatitis (0.5%), eczema (0.5%) and others but these were relatively uncommon.

Table 2 shows the analysis of number of drugs prescribed per prescription. A total of 3915 drugs were prescribed. The average number of drugs prescribed per prescription was 3.26. Analysis of polypharmacy showed maximum 6 and minimum 1 drug was prescribed. Majority of study participants 672 (56.0%) received 4 drugs followed by 3 drugs in 255 (21.3%) participants.

Table 2: Analysis of the number of drugs prescribed per prescription (n=3915).

Number of Drugs/ Prescription	Number (N)	Percentage (%)
One	13	1.1
Two	211	17.6
Three	255	21.3
Four	672	56.0
Five	45	3.8
Six	4	0.3

In our study, total of 3915 drugs were prescribed in 5 different dosage forms. The most common dosage

form, prescribed was a table t (63.7%) followed by cream (21.1%) and lotion (12.7%) and other dosage forms like capsule (2.3%) and syrup (0.1%) were very less in the prescribed drugs.

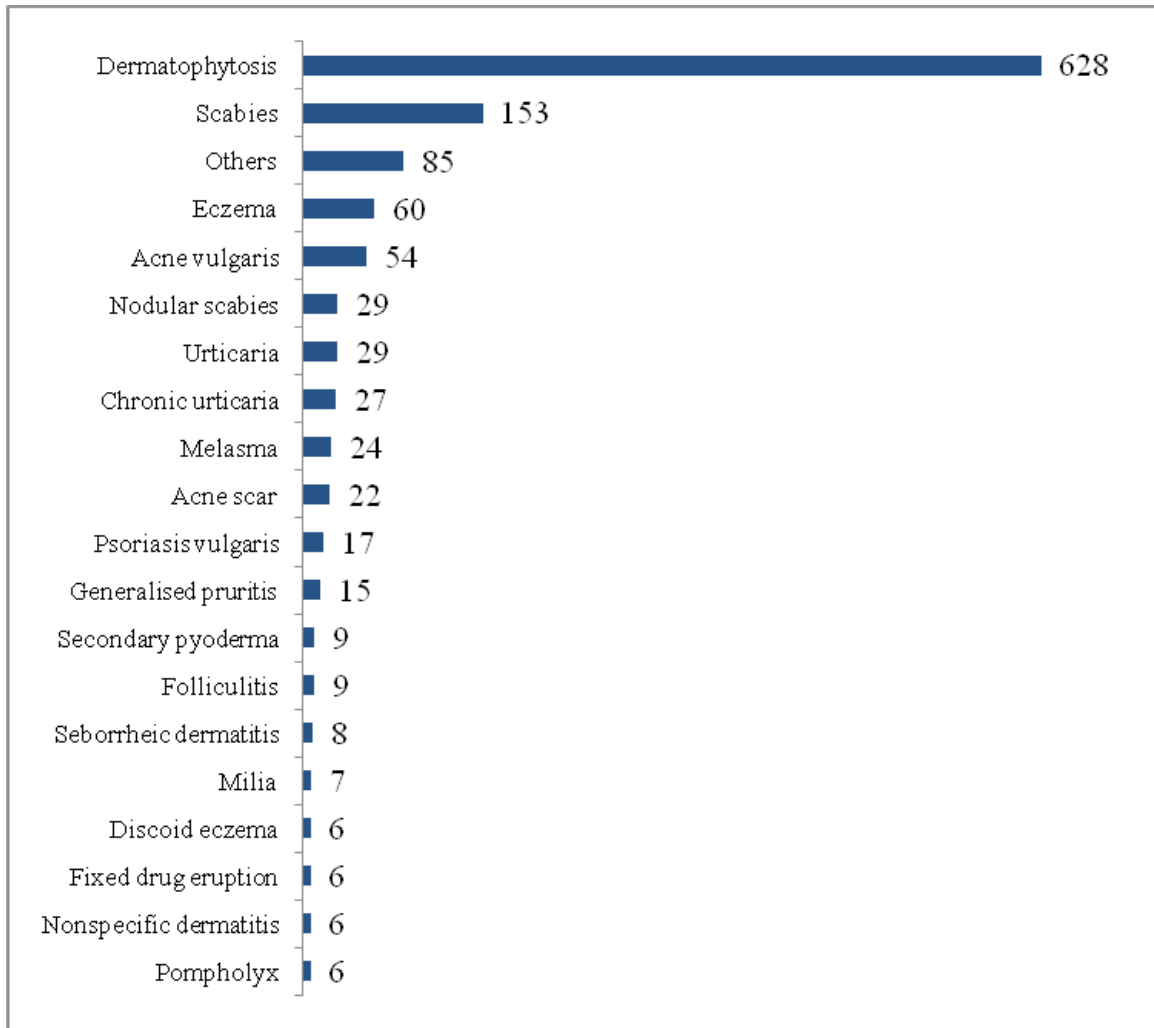


Figure 1: Distribution of patients as per the disease condition.

Table 3: Analysis of various dosage forms in the prescribed drugs (n=3915).

Dosage form	Number (N)	Percentage (%)
Tablets	2496	63.7
Capsule	90	2.3
Syrup	5	0.1
Creams	826	21.1
Lotions	498	12.7

As shown in Table 4, antihistaminics(39.8%)were the most common drugs prescribed (39.8%). Among antihistaminics, hydroxyzine (49.3%) was common followed by cetirizine (45.3%), Ebastine (4.5%), bepotastine (0.7%) and levocetirizine was less commonly used (0.2%).

Antifungals (31.2%) were the second most commonly used drug. Among oral antifungals terbinafine is the commonly prescribed drug (89.5%) followed by itraconazole (9.8%) and among topical agents luliconazole (75.5%), miconazole (12.2%) and ciclopirox (4.5%) were used in the form of creams and ketoconazole (4.7%) in form of lotion.

Fixed drug combinations (9.1%) were used in both oral and topical route. Among oral route montelukast and levocetirizine was the most prescribed combination (96%) and through topical route clobetasol and gentamycin cream (48.9%) was the commonly prescribed medication.

Antibiotics (3.5%) were used in both oral and

topical route. Topical corticosteroids were prescribed more frequently compared to oral drugs. Among antihelmintics, oral Ivermectin was the drug prescribed in few cases (n=40). Antivirals and antifibrinolytics were given in each 0.2% cases. Immunosuppressants were

prescribed in 0.3% cases. Other miscellaneous drugs in the form of topical agents were prescribed in 11.1% cases. Other drugs used are multivitamins (2.7%) and injectable antineoplastics were prescribed in one case.

Table 4: Distribution of various drug groups and their routes of administration.

Drug Groups	Oral N (%)	Topical N (%)	Injectable N (%)	Total
Antihistamines	1558 (99.9)	2 (0.1)	-	1560 (39.8)
Antifungals	585(47.7)	641(52.3)	-	1226 (31.2)
Miscellaneous	-	435 (100.0)	-	435 (11.1)
Fixed Drugs Combinations	226 (65.7)	131 (10.0)	-	357 (9.1)
Antibiotics	70 (50.4)	69 (49.6)	-	139 (3.5)
Multivitamins	102 (95.3)	-	5 (4.7)	107 (2.7)
Anthelmintics	40 (100.0)	-	-	40 (1.0)
Corticosteroids	9 (34.6)	14 (53.8)	3 (11.5)	26 (0.7)
Immunosuppressants	6 (50.0)	6 (50.0)	-	12 (0.3)
NSAIDS	5 (62.5)	3 (37.5)	-	8 (0.2)
Antivirals	6 (100.0)	-	-	6 (0.2)
Antifibrinolytics	3 (42.9)	4 (57.1)	-	7 (0.2)
Antineoplastic	-	-	1 (100.0)	1 (0.0)
Total	2610 (66.5)	1305 (33.3)	9 (0.2)	3924 (100.0)

Discussion

A prescription is a valuable source of data to analyse the attitude and knowledge of the prescribers in treating a disease condition rationally using pharmaco-therapeutic approach bearing in mind the patient's physical and financial conditions.¹¹ In our study, the total number of patients attending OPD dermatology was 1200 including only new patients with one visit. In the present study, the percentage of male patients (58.1%) visiting the dermatology department was higher when compared to female patients (41.9%). This was comparable to previous studies by Gambre et al, Jena et al and Bhagawati et al, where the percentage of male (58.7%; 56.6%; and 52.27%) outnumbered the percentage of female patients (41.34%, 43.3% and 47.73%) of total 600, 719, 449 and 238 prescriptions respectively. One of the possible reasons could be that most of the female in our study (29.4%) and in India were housewives, who are financially dependent.¹²⁻¹⁴

Majority of the patients in our study belonged to the age group 13-40 years (>71%) and the maximum number of patients (29.8%) belonged to age group 21-30 years. This was in line with the study by Sajith et

al.¹⁵ According to his study, out of 320 prescriptions, a maximum number of patients (38.8%) belonged to the age group 20-30 years of age.

Majority of the patients in our study group were married (63.8%) and the findings were similar to Bandyopadhyay findings.¹⁶ Also, the majority were housewives (29.4%) followed by students (28.9%) and farmers (15.9%). Since, the study was conducted in one of the best medical university, located in Mullana, a village in Ambala district, most of the participants were housewives, followed by students and farmers.

Out of 58 types of dermatologic disease noticed in our study, most of the patients visited the dermatology department for complaints of dermatophytosis, (52.3%) and scabies which is increasingly prevalent in India due to climatic condition, poor hygienic conditions, occupation type, family history, poor economic background over-crowdedness etc. Our findings were consistent with the study by Gambre et al, where the most common dermatological disorder encountered among 600 OPD prescriptions from a dermatology department of a tertiary care hospital in Mumbai, India was dermatophytosis (33.2%).¹² But study by Sajith et al

reported acne vulgaris, a common skin disorder among adolescents and young adults.¹⁵

For many years, transdermal route of medicinal administration has been preferred in dermatology due to sustained drug delivery, ease of administration, controlled dosage of antibiotics, low risk of side effects or drug interactions, better patient's compliance and to overcome the disadvantages of oral route such as rapid metabolism of medicines, poor bioavailability and chances of intolerance.¹⁷ In our study, we concluded that the most preferred route of drug administration was oral (66.5%), in dosage forms such as tablets (63.7%), capsules (2.3%) or syrups (0.1%) when compared to topical (33.3%). Our findings were comparable to Pathak et al but different from Bhagawatiet al where the most preferred route was topical (49.22%).^{11,14}

Prescription assessment according to WHO prescribing indices (world health organisation, 1993) reveal that the average number of drugs prescribed per prescription, was 3.26 (3915 drugs per 1200 prescriptions), with a maximum of 6 drugs and a minimum of 1 drug per prescription. This was much lesser than those reported by Kumar et al, where, the average number of drugs per prescription was 4.76.² However, current study findings were in line with studies by Patil et al which assessed drug utilisation pattern in OPD of dermatology wing at a tertiary hospitals in Mumbai, North-East India, Puducherry and Luthiana, where the average number of drugs per prescription was 3.27.¹⁸

The most commonly prescribed class of drug was antihistamine which was mostly prescribed orally followed by antifungals. Our findings were in consistent with previous studies by Patil et al which reported the most commonly prescribed class of drugs as Antihistamines followed by Antifungals with oral dosage form being the most commonly prescribed form.¹⁸ Also our findings of the most commonly prescribed class of drug and its route of dosage were in line with studies by Bhagawatiet al, Tikoo et al and Krishna et al.^{14,19,20} Out of different anti-histamines, most commonly prescribed oral H1 Anti-histamines were, Hydroxyzine and Cetirizine and similar findings were reported by Afzal Khan et al.²¹

Total percentage of oral antibiotics prescribed from the entire study group was 2.7%, which was much lesser than studies Pathak et al, assessing prescription pattern of antibiotics in Dermatology OPD in India.¹¹

When compared to the WHO standards of less than 40% by Suhaina et al, our study shows a lower percentage of antibiotics prescription.²² While topical route of administration was preferred in our study, similar findings was reported by Pathak et al.¹¹ Most common orally administered antibiotics was azithromycin which was consistent with the study by Kumar et al.²

Conclusion

The findings of the study conclude that the common skin diseases encountered in the study population was dermatophytosis and scabies which are increasingly widespread in India. These observations suggest the prescribers to consider age, economic status, occupation and family history before writing any prescription. The study also suggests the prescribers to consider factors of polypharmacy. It should be noted that comorbid condition like diabetes and hypertension should be taken into consideration while practicing polypharmacy as it not only increase financial burden, but can also cause adverse reactions, especially among elderly population

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Source of Funding: Self

Ethical approval and Informed consent: The study protocol was reviewed by the Ethical Committee of Hospital and was granted ethical clearance. After explaining the purpose and details of the study, a written informed consent was obtained from the participants

References

1. Bhagawati I, Pathak P. A Study on Drug Utilisation Pattern in Dermatology Outpatient Department in a Tertiary Care Teaching Hospital of North East India. *JMSCR*. 2016;4(8):11857-61.
2. Kumar J, Chandra S, Sinha HK. Utilisation pattern of drugs among dermatological outpatients in a tertiary care hospital of eastern India. *IJPR*. 2016;6(09):297.
3. De Vries TP, Henning RH, Hogerzeil HV, Fresle DA, Policy M, World Health Organization. *Guide to good prescribing: a practical manual*. Geneva: World Health Organization; 1994.
4. *The Rational Use of Drugs*. Report of the conference of experts, Nairobi, 25-29 November 1985. WHO Geneva: 1987: 78-85.

5. Sjoqvist F, Birkett D. Introduction to Drug Utilisation Research (WHO Booklet). Drug utilisation. In: Bramley DW, editor. New York: WHO Office of Publication; 2003: 76–79.
6. Sweileh WM. Audit of prescribing practices of topical corticosteroids in outpatient dermatology clinics in north Palestine. *Eastern Mediterr Health J*. 2006;12(1/2):161–9.
7. Soumerai S. Factors influencing prescribing. *Aust J Hosp Pharm*. 1988;18:9–16.
8. Hogerzeil HV. Promoting rational prescribing: an international perspective. *Br J ClinPharmacol*. 1995;39:1–6.
9. Joel JJ, Jose N, Shastry CS. Patterns of Skin Disease and Prescribing Trends in Rural India. *SchAcad J Pharm*. 2013;2(4):304–9.
10. Divyashanthi CM, Nandhini A, Kumar SA. Study on drug utilisation pattern of antibiotics among dermatology in-patients of a tertiary care teaching hospital, Karaikal, Puducherry. *Int J Basic ClinPharmacol*. 2014;3(6):1072–7.
11. Pathak AK, Kumar S, Kumar M, Mohan L, Dikshit H. Study of Drug Utilisation Pattern for Skin Diseases in Dermatology OPD of an Indian Tertiary Care Hospital - A Prescription Survey. *J ClinDiagn Res*. 2016;10(2):F1-5.
12. Gambre R, Khobragade A, Jalikar K, Patel S .Analysis of Prescribing Pattern of Drugs Among Patients Attending Dermatology Outpatient Department of A Tertiary Care Hospital. *European Journal of Pharmaceutical and Medical Research*. 2018;5(3):259-73.
13. Jena M, Panda M, Patro N, Mishra S. Pattern of utilisation of corticosteroids in department of dermatology at a tertiary care teaching hospital. *J Chem Pharm Res*. 2014;6(8):86-91.
14. Bhagawati I, Pathak P .A Study on Drug Utilisation Pattern in Dermatology Outpatient Department in a Tertiary Care Teaching Hospital of North East India. *JMSCR*. 2016;4(08):11857-61
15. Sajith M, Lokhande KD, Padma S, Pawar AP. Prevalance of various skin disorders and prescribing pattern of antihistamines in tertiary care hospital, Pune. *IJPSR*. 2014;5(3):73-7.
16. Bandyopadhyay D. A study of prescription auditing in a tertiary care teaching hospital of Eastern India. *Journal of Drug Delivery and Therapeutics*. 2014;4(1):140-9.
17. Leite-Silva VR, De Almeida MM, Fradin A, Grice JE, Roberts MS, Hadgraft, Grice, Magnusson, Anissimov, Higuchi, Mitragotri. Delivery of drugs applied topically to the skin. *Expert Rev Dermatol*. 2012;7(4):383-97.
18. Patil A, Dighe D, Kolte S, Pradeep R, Deshmukh YA. Drug utilisation pattern in dermatology outpatient department at a tertiary care hospital in Navi Mumbai. *Int J Basic ClinPharmacol*. 2017;6(3):559-62
19. Tikoo D, Chopra SC, Kaushal S, Dogra A. Evaluation of drug use pattern in dermatology as a tool to promote rational prescribing. *JK science*. 201;13(3):128.
20. Krishna J, Singh A, Goel S, Roy A, Singh AK, Yadav KP. Clinical pharmacological study of prescribing pattern of dermatological drugs from a tertiary care teaching hospital. *Indian J Sci Res*. 2015;6(2):41.
21. Afzal Khan AK, Mirshad PV, Mohammed Muneersha TK, Fasalurahaman OM, Abdulla NH. Evaluation of H1-Antihistamine usage among dermatology inpatients at a teaching hospital in Southern India. *Der Pharmacia Lettre*. 2013;5(6):115-8.
22. Suhaina AS, Reneega G. Drug Prescribing Pattern with Cost Analysis and Monitoring of Adverse Drug Reactions in Dermatology. *IJSS*. 2018;6(8):146-50.
23. Mohamed Saleem TK, Dilip C, Nishad VK. Assessment of Drug Prescribing Patterns in Dermatology Outpatient Department in a Tertiary Care Hospital, Malabar, Kerala. *IJPP*. 2012;5(3):62-8.

Fibromyalgia: Latest Drugs for the Treatment

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Abstract

Fibromyalgia is a chronic condition with unknown aetiology. Fibromyalgia is characterized by chronic widespread pain and several additional symptoms such as fatigue, cognitive dysfunction, depressive episodes and anxiety. The underlying pathophysiology of fibromyalgia is still poorly understood and treatment is often unsatisfactory. Current treatments include drugs that target serotonin and noradrenaline levels within the central nervous system, e.g., tricyclic antidepressants, serotonin noradrenaline reuptake inhibitors and voltage-gated calcium channel subunit ligands, e.g., gabapentin and pregabalin. Investigation of a range of novel targets, such as melatonergic, cannabinoid, dopamine, NMDA, angiotensin, orexin and opioid receptors and ion channels, in addition revisiting bioamine modulation and subunits has provided efficacy outcomes that improve the health status of patients with FM. Nevertheless, modest and limited efficacy is often observed reflecting the heterogeneity of FM with existence of subpopulations of patients, the contribution of peripheral and central components to the pathophysiology and the extensive range of accompanying co-morbidities. The complexity and multidimensional nature of FM is emphasized by the diversity of pharmacological targets gaining interest. Clues to underlying mechanisms which offer themselves as novel and potential targets for new medications are being provided by advances in the understanding of the pathophysiology of FM.

Keywords: *Fibromyalgia, chronic pain, fatigue, NMDA receptors, melatonin receptors, gabapentanoids.*

Introduction

The biggest health burden at global level is chronic pain. As such chronic pain being a grave public health concern, which is affecting 14%-16% of the adult population in western countries.¹⁻³ The percentage of people suffering on account of chronic pain at global level is between 30%-40%.⁴ According to a survey it was found that number of adults suffering from chronic pain in India are between 18%-20%.⁵ Irrespective of huge advancements in the management of chronic pain conditions, there is a section of these individuals for which pain management still remains a gruesome problem. A large number of data suggests that dysfunctions arising

from spinal cord and brain are the most common causes of the failure to the treatment of chronic pain.^{6,7} One of the most commonly affecting chronic pain condition at global level being fibromyalgia.^{8,9} Fibromyalgia (FM) is a chronic wide spread musculoskeletal pain and tenderness, along with neuropsychological symptoms like – anxiety, sleep disturbance, generalised fatigue, stiffness, impaired cognition and depression. FM is more common among female as compared to males with a ratio of 9:1.¹⁰ In this paper we will review current and upcoming treatment strategies for the treatment of fibromyalgia.

Current Treatment Strategies: The treatment of FM can be divided into two therapeutic approaches—pharmacological and non-pharmacological but this article emphasises on the pharmacological bases for the treatment of fibromyalgia. As fibromyalgia has a strong association with various neuropsychological symptoms therefore suppression of excitatory neurotransmitters release makes it a noticeable pharmacological property for the treatment of fibromyalgia. Various classes of

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drugs currently being used for the management of fibromyalgia are— anti-depressants like amitriptyline and cyclobenzaprine; serotonin noradrenaline reuptake inhibitors like milnacipran, duloxetine; selective serotonin reuptake inhibitors like fluoxetine, paroxetine; voltage-gated calcium channel subunit ligands like gabapentin and pregabalin and weak opioid and

serotonin-noradrenaline reuptake inhibitor.¹¹⁻¹³ All these drugs focused on reducing pain, anxiety and fatigue and improving sleep in patients with fibromyalgia. The main limitation of the efficacy of current treatment is worsened by the increasing incidence of adverse effects leading many patients to discontinue the therapy.

Novel drugs undergoing clinical trials or completed trials for potential treatment of fibromyalgia:

Drugs	Mechanism of Action	Domains
ASP0819 ¹⁴	Calcium-activated potassium channel openers	Pain
NYX-2925 ¹⁵	NMDA receptor modulator	Pain
Dextromethorphan ¹⁶	Uncompetitive NMDA Receptor Antagonist and Sigma-1 Receptor Agonist	Pain
Milnacipran ¹⁷	SNRI	Pain, cognition
ASP8062 ¹⁸	GABA _B receptor agonist	Pain, sleep disturbance and fatigue
EMA401 ¹⁹	Angiotensin 2 receptor antagonist	Pain
Suvorexant ²⁰	Orexin receptor antagonist	Sleep, insomnia, pain

Conclusion

The goal of this review was to provide an overview of the recent updates in the treatment of fibromyalgia. Fibromyalgia is a complex chronic pain condition where current and emerging pharmacological therapies suppress the central hyper-excitability associated with the pathophysiology. A diversity of pharmacological targets and mechanisms such as bioamine modulation, subunits, NMDA receptors, melatonin receptors and cannabinoid receptors, has been identified at which drugs act to demonstrate effectiveness in the management of the symptoms of FM. Although efficacy has been demonstrated by many of the drug treatments discussed leading to improved health status in patients with FM, outcomes related to individual mechanisms of action were not always consistent and not all symptoms were controlled by a single drug. The modest and limited efficacy often observed may reflect the heterogeneity of FM with existence of subpopulations of patients, the contribution of peripheral and central components to the pathophysiology and the extensive range of accompanying co-morbidities. Although the optimal treatment approach would be drug monotherapy, the complexity and multidimensional nature of FM emphasizes the need for a pharmacology targeting multiple molecular mechanisms. In addition to biological variables psychological and social factors have been identified to contribute to the complexity

of FM supporting consideration of a biopsychosocial model. Nevertheless, clues to underlying mechanisms as novel and potential targets for new medications are being provided by advances in the understanding of the pathophysiology of FM.

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Ethical Clearance: Review article

References

1. Manchikanti L, Singh V, Datta S, Cohen SP, Hirsch JA. Comprehensive review of epidemiology, scope and impact of spinal pain. *Pain Physician*. 2009; 12(4):E35-70.
2. Harker J, Reid KJ, Bekkering GE, Kellen E, Bala MM, Riemsma R, Worthy G, Misso K, Kleijnen J. Epidemiology of chronic pain in denmark and sweden. *Pain Res Treat*. 2012;2012:371248.
3. Blyth FM, March LM, Brnabic AJM, Jorm LR, Williamson M, Cousins MJ. Chronic pain in Australia: A prevalence study. *Pain*. 2001; 89(2-3):127-34.
4. Dahlhamer J, Lucas J, Zelaya, C, et al. Prevalence of Chronic Pain and High-Impact Chronic Pain among Adults—United States, 2016. *MMWR Morb Mortal Wkly Rep*. 2018;67(36):1001-6.

5. Saxena AK, Jain PN, Bhatnagar S. The prevalence of chronic pain among adults in India. *Indian J Palliat Care*. 2018;24(4):472-77.
6. Clauw DJ. Fibromyalgia: A clinical review. *JAMA- J Am Med Assoc*. 2014;311(15):1547-55.
7. Brummett CM, Urquhart AG, Hassett AL, et al. Characteristics of fibromyalgia independently predict poorer long-term analgesic outcomes following total knee and hip arthroplasty. *Arthritis Rheum*. 2015;67(5):1386-94.
8. Wolfe F, Ross K, Anderson J, Russell IJ, Hebert L. The prevalence and characteristics of fibromyalgia in the general population. *Arthritis Rheum*. 1995; 38(1):19-28.
9. Assumpção A, Cavalcante AB, Capela CE, Sauer JF, Chalot SD, Pereira CA, Marques AP. Prevalence of fibromyalgia in a low socioeconomic status population. *BMC Musculoskelet Disord*. 2009; 10:64.
10. Bartels EM, Dreyer L, Jacobsen S, Jespersen A, Bliddal H, Danneskiold-Samsøe B. [Fibromyalgia, diagnosis and prevalence. Are gender differences explainable?]. *Ugeskr Laeger*. 2009;-171(49):3588-92.
11. Macfarlane GJ, Kronisch C, Dean LE, et al. EULAR revised recommendations for the management of fibromyalgia. *Ann Rheum Dis*. 2017;76(2):318-28.
12. Ablin J, Fitzcharles MA, Buskila D, Shir Y, Sommer C, Häuser W. Treatment of fibromyalgia syndrome: Recommendations of recent evidence-based interdisciplinary guidelines with special emphasis on complementary and alternative therapies. *Evidence-based Complement Altern Med*. 2013;2013.
13. Hauser W, Arnold B, Eich W, Felde E, Flügge C, Henningsen P, Herrmann M, Köllner V, Kühn E, Nutzinger D, Offenbächer M, Schiltenswolf M, Sommer C, Thieme K, Kopp I. Management of fibromyalgia syndrome--an interdisciplinary evidence-based guideline. *Ger Med Sci*. 2008;6:Doc14.
14. A Study to Assess the Analgesic Efficacy and Safety of ASP0819 in Patients With Fibromyalgia - Tabular View - ClinicalTrials.gov. <https://clinicaltrials.gov/ct2/show/record/NCT03056690?cond=fibromyalgia & draw=5 & rank=18>. Accessed November 8, 2019.
15. Aptinyx Announces Results of Phase 2 Fibromyalgia Study of NYX-2925 Have Been Selected for Late-Breaking Presentation at the American College of Rheumatology Annual Meeting Nasdaq: APTX. <http://www.globenewswire.com/newsrelease/2019/10/28/1936144/0/en/Aptinyx-Announces-Results-of-Phase-2-Fibromyalgia-Study-of-NYX-2925-Have-Been-Selected-for-Late-Breaking-Presentation-at-the-American-College-of-Rheumatology-Annual-Meeting.html>. Accessed November 8, 2019.
16. Dextromethorphan in Fibromyalgia - Full Text View - ClinicalTrials.gov. <https://clinicaltrials.gov/ct2/show/NCT03538054?cond=fibromyalgia & draw=6 & rank=1>. Accessed November 8, 2019.
17. Effect of Milnacipran on Pain in Fibromyalgia - Full Text View - ClinicalTrials.gov. <https://clinicaltrials.gov/ct2/show/NCT01288807?cond=fibromyalgia & draw=13 & rank=73>. Accessed November 8, 2019.
18. A Study to Assess the Analgesic Efficacy and Safety of ASP8062 in Subjects With Fibromyalgia - Full Text View - ClinicalTrials.gov. <https://clinicaltrials.gov/ct2/show/NCT03092726?cond=fibromyalgia & draw=5 & rank=17>. Accessed November 8, 2019.
19. Smith MT, Muralidharan A. Targeting angiotensin II type 2 receptor pathways to treat neuropathic pain and inflammatory pain. *Expert Opin Ther Targets*. 2015;19(1):25-35.
20. Koshorek G, Verkler J, Withrow D, Roth T, Roehrs T. 0373 Effects of Suvorexant on Sleep in Fibromyalgia. *Sleep*. 2019;42 (Supplement_1):A152-A152.

A Study on Delay in Giving the Early Morning Sample and Barriers in Accessing Sputum Smear Microscopy Services at Tertiary Care Hospital

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Abstract

Sputum examination is the most widely used test for diagnosis of TB. Under RNTCP two samples of sputum are required for examinations which are preferably 1st spot and early morning sample or two spot samples collected on the same day. Patients usually come from far off places at the tertiary care centre and frequent visits are usually not possible. Giving an early morning sample is usually defaulted by the patient due to various reasons. The present study was aimed at studying the delay in giving the early morning sample and barriers in accessing the sputum smear microscopy services at a tertiary care hospital. In this study 300 presumptive TB patients were studied. Patients were asked to give a 1st spot sample for sputum smear examination and asked to bring early morning sputum sample. Patients who refused to give early morning sample were asked to give 2nd spot sample and the reason for not coming early morning were noted. The patients who did not come despite agreeing to come were noted. If they came after a delay of few days, then also the reason of delay were noted. It was found that nearly one third (31%) of the patients agreed and came on the next day to give early morning sample. A large number of patients (16%) did not come at all to give the early morning sample.

Keywords: Pulmonary tuberculosis, presumptive TB patient, sputum microscopy, spot sample, early morning sample, RNTCP.

Introduction

On world TB day on 24th March 2014, WHO has urged the countries to find, treat and cure the 'missing' million 1 million patients who are not getting the TB services, so that the progress towards 'Zero' TB mortality, infection, sufferings and stigma is accelerated^{1,2}.

A presumptive Pulmonary Tuberculosis patient may have any of the symptoms like fever of more than 2 weeks, cough of more than 2 weeks, loss of appetite, loss

of weight, haemoptysis or any abnormality in the chest X-Ray or HIV patient and contact of sputum positive patients cases having cough of any duration. Sputum smear microscopy is the most commonly used method for diagnosis of TB^{3,4}. In RNTCP two methods are currently used; one is by ZN staining based microscopy using a regular microscope and secondly is LED based fluorescent microscopy (LED FM)⁵. Under RNTCP the medical officers of the health care facilities should find out all the presumptive TB patients from those attending the health care facilities and refer them for examination to the designated microscopy centre. In medical colleges and other hospitals too the patients should be referred by the treating physician using the RNTCP laboratory request form⁶.

Earlier there was a provision of testing three samples of sputum. Several studies have shown that screening of tuberculosis using two samples for testing

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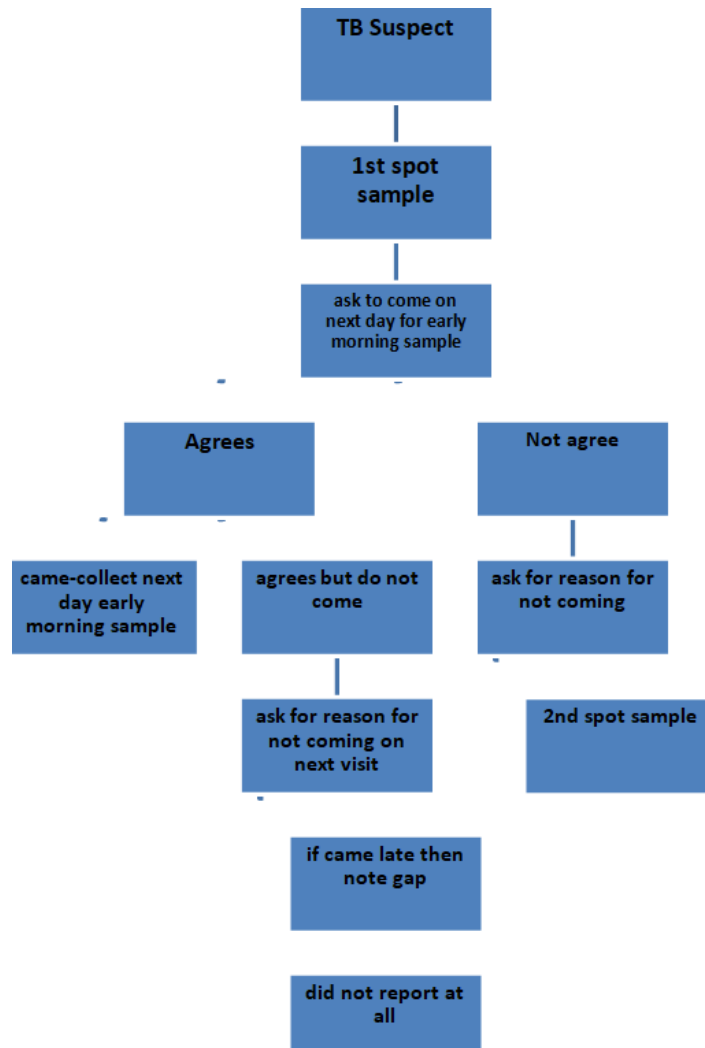
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is as effective as testing three samples^{7,8,9,10,11}. Under RNTCP for sputum smear microscopy two samples are collected within a day or two consecutive days. One spot sample is collected on the spot under the supervision while other sample is collected early in the morning¹². Patient is asked to come back with the early morning specimen on the next day. If patient refuses to come next day to give the early morning sample then there is the provision to give a second spot sample on the same day. Some patients do not report back for early morning sputum specimen examination due to various reasons. So in this present study we planned to study the delay in collection of the sputum smear various reasons given by the patients for the delay.

Material and Method

This study was conducted in the department of Respiratory Medicine. The presumptive TB patients coming to OPD of respiratory department of MMIMSR, MM(D)U Mullana during one year were taken up for

study after taking informed consent. A total of 300 cases were studied. A detailed history was taken followed by clinical examination. Relevant blood and radiological investigations were also advised. Subsequently they were advised to collect two sputum samples for microbiological examination. Patients were asked to give the 1st spot sample and were asked to come the next day to give early morning sample. Patient who refused to come the next day were offered 2nd spot sputum examination and reasons for refusal to come next day were noted. A note was also made of patients who did not come on the next day to give the early morning sputum specimen despite agreeing to come and the reason for not coming were recorded. If the patient came late with early morning sample despite agreeing to come on the next day, then the number of days in gap were noted along with their reason for coming late. Note was also made of the patients who did not come at all after a duration of one month.



Findings:**Table 1. Distribution of cases as per Age group**

Distribution of Cases as per Age group		
Age Group	N	%
< 20 years	21	7%
21-30 Years	68	22.7%
31-40 years	53	17.7%
41-50 years	59	19.7%
51-60 years	55	18.3%
61-70 years	37	12.3%
>70 years	7	2.3%
Total	300	100%
Mean \pm SD	43.05 \pm 15.96 Years	

Table 2. Distribution of cases according to schedule of early morning sample

Distribution of cases according to schedule of early morning sample		
	N	%
Refused to come	95	31.6%
Came Next Day	93	31%
Came after Gap of some days	64	21.3%
Did not Come despite agreeing at all	48	16%

Table 3. Distribution of cases according to reason for refusal to come for early morning sample

Reasons for refusal to come next day to give early morning sample		
	N	%
Lack of money	7	7.4%
Loss of wages	4	4.2%
Distance from hospital	19	20%
Lack of time	21	22.1%
Lack of transport	9	9.5%
No one to accompany	18	18.9%
No leave from employer	4	4.2%
Social function	4	4.2%
Other	9	9.5%
Total	95	100%

Table 4. Reasons for not coming next day or coming late to give early morning sample despite agreeing to come

Reasons for not coming on next day/coming late despite agreeing to come		
	N	%
Lack of money	2	3.1%
Loss of wages	12	18.7%
Distance from hospital	18	28.1%
Lack of time	7	10.9%
Lack of transport	5	7.8%
No one to accompany	9	14.0%
No leave from employer	2	3.1%
Social function	2	3.1%
Other	7	10.9%
Total	64	100%

Table 5. Distribution of cases according to number of days lapsed for follow up

Number of Days	No of Patients
Next Day	93
1	12
2	8
3	7
4	5
5	4
6	1
7	5
8	5
9	1
10	2
11	3
12	3
13	1
14	3
15	1
16	1
20	1
22	1
Total	157

Out of total 300 patients 184(61.3%) patients were males while 116 (38.7%) patients were females. Mean age of the study population was 43.05 years. The highest proportion of population was in 21-30 years (22.7%) age group. 95 (31.3%) patients refused to come next day to give early morning sample. 93 (31%) patients came next day while 64 (21.3%) came after a period of few days.

48 (16%) patients never came despite agreeing to come. Approximately 2/3rd amongst the patients did not report the next day. Only 31% of total patients came on the next day.

The top three reasons for refusal to come on next day for early morning sample was lack of time (22.1%). Second most common reason was distance from hospital (20%) and the third most common reason was that no one was available to accompany the patient (18.9%). The top three most common reasons given by patient for not coming on the next day and coming late despite previously agreeing to come was the distance from hospital (28.1%) followed by loss of wages (18.7%) and third common reason was no one to accompany (14.0%).

Although 93 patients came on the next day 64 patients came after a gap ranging from 1 day to 22 days (although patient was followed up till 30 days before labelling as did not come at all). 27 out of 64 patients came back with the early morning sputum sample within 3 days, while 42 patients came within a week.

Discussion

Tertiary care hospitals and medical colleges are playing a very important role in diagnosis and management of tuberculosis. 23 percent of the new smear positive cases are being detected at the medical colleges¹³. Smear positive pulmonary tuberculosis is the most common and infectious form of tuberculosis. Each case of untreated pulmonary tuberculosis can spread infection to 5-15 persons per year¹⁴. Thus, it is of prime

importance to rapidly detect such patients to curb the menace of tuberculosis.

Out of the study population of 300, 95 patients refused to come next day so a second spot sample was taken. Those who agreed to come (205), were asked to get an early morning sample. 93 came next day with a sample while 64 of these did not come next day but came after a gap of few days. 48 patients did not come at all despite agreeing to come. Only 31% of cases came on the next day.

The reasons for not coming were several. Among these were lack of money, loss of wages, distance from hospital, lack of time, lack of transport, no one to accompany, no leave from employer, social function etc. Among all of these, the most common reason for refusal to come as well as for coming later than next day was distance from hospital in both case and control groups. In present study, this reason may be because the institute is located in a rural area and most of the population it caters to comes from surrounding district of Saharanpur, Yamunanagar and Kurukshetra. These areas constitute a vast geographical region. Frequent visits can be difficult, time consuming and heavy on the pocket of the patient. Other common reasons were lack of time, no one able to accompany the patient. Patient may also lose wages and employer doesn't allow leave for frequent visits to hospital. This in addition to the cost of investigation and treatment is usually difficult for the patient and their family to bear. Patients of extremes of age group and women usually require someone to accompany them for the hospital visit as the tertiary care centres are situated at far off places. Frequent visits to give sample or collect reports become difficult as they do not have someone to accompany them. Sometimes patient or family members have some prior commitments or any social function which prevents them from coming for follow up to the tertiary care hospitals. Because of these reasons patients despite agreeing are unable to give early morning sample on the next day and bring the sample after a gap of few days. Patient may not receive their reports on the same day too. This causes the delay in the diagnosis. These factors also lead to increase in the cost of the treatment of tuberculosis¹⁵. Few new studies are thus focussing on assessing the feasibility of diagnosing pulmonary TB by examining two spot samples in one day¹⁶.

Conclusion

Although early diagnosis of pulmonary TB patients

is important to prevent the transmission to others, there are various barriers while accessing the microscopy services at tertiary care centre. The distance from the hospital is a main reason for difficulty in giving early morning samples. Patients are asked to bring early morning sample as advised by RNTCP, but many patients refuse to give the early morning sample. For such patients there is a provision to give a second spot sample. But adequate counselling can prevent early default of the patients. Efforts should be made to reduce the number of the visits to the tertiary care hospital. Frequent visits by a TB patients may also lead to spread of the infection while they are using public transport to commute. Fast tracking of TB patients may be helpful. Alternate strategies for single day diagnosis of TB should be sought for.

Conflict of Interest: None

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Ethical Clearance: Ethical Clearance was obtained from the Institutional Ethics Committee (IEC), Maharishi Markandeshwar (Deemed to be) University, Mullana, Ambala.

References

1. WHO Regional Office for South East Asia. WHO urges to reach 1million missing TB cases. New Delhi(IN): SEARO; 2014 Mar 24. Available from <http://www.searo.who.int/mediacentre/releases/2014/pr1568/en/>
2. Uplekar M, Weil D, Lonroth K, Jaramillo E, Lienhardt C, Dias HM, et al. WHO's new end TB strategy. *Lancet*. 2015;385(9979):1799–801.
3. Wilkision D, Sturm AW. Diagnosis of TB in resource poor setting: The value of sputum concentration. *Trans R Soc Trop Med Hyg* 1997;9:420-1.
4. ? Toman K. Tuberculosis case finding and chemotherapy: Questions and answers. WHO Geneva. Available from: <https://www.who.int/tb/publications/toman/en/> [Last accessed on 2014 Aug 6].
5. Reza LW, Satyanarayna S, Enarson DA, Kumar AMV, Sagili K, et al. (2013) LED-Fluorescence Microscopy for Diagnosis of Pulmonary Tuberculosis under Programmatic Conditions in India. *PLoS ONE* 8(10): e75566. doi:10.1371/journal.pone.0075566
6. Technical and operational guidelines for tuberculosis

- control, Revised National Tuberculosis Control Programme, New Delhi(IN): Central Tuberculosis Division, Directorate General of Health Services, Ministry of health and family welfare Government of India; 2016:15
7. A. D. Harries, N. B. Mphasa, C. Mundy, A. Banerjee, J. H. Kwanjana and F. M. L. Salaniponi, "Screening tuberculosis suspects using two sputum smears," *International Journal of Tuberculosis and Lung Disease*, vol. 4, no. 1, pp. 36–40, 2000.
 8. Gopi PG, Subramani R, Selvakumar N, Santha T, EusuffSI, Narayanan PR. Smear examination of two samples for diagnosis of pulmonary tuberculosis in Tiruvallur district, South India. *Int J Tuberc Lung Dis* 2004;8:824-8
 9. Thomas A, Chandrasekaran V, Joseph P, Rao VB, Patil AB, Jain DK, et al. Increased yield of smear positive pulmonary TB cases by screening patients with ≥ 2 weeks cough, compared to ≥ 3 weeks and adequacy of 2 sputum smear examinations for diagnosis. *Indian J Tuberc* 2008;55:77-83.
 10. Sarin R, Mukerjee S, Singla N, Sharma PP. Diagnosis of tuberculosis under RNTCP: Examination of two or three sputum specimens. *Indian J Tuberc* 2001;48:13-16.
 11. Hamid S, Hussain SA, Imtiyaz A. Screening tuberculosis suspects: How many sputum specimens are adequate?. *Ann Trop Med Public Health* 2012;5:317-20
 12. Changes in RNTCP policy on diagnosis of smear positive pulmonary TB: TB INDIA 2009 RNTCP status report. p. 73. Available from: <http://tbcindia.nic.in/showfile.php?lid=2921>. [Cited on 2015 Dec 15].
 13. Sharma SK, Mohan A, Chauhan LS, Narain JP, Behera D, Kumar A, et al. Contribution of medical colleges to tuberculosis control in India under the Revised National Tuberculosis Control Programme (RNTCP): Lessons learnt and challenges ahead. *Indian J Med Res* 2013;137:283-94
 14. World Health Organisation [Internet]. Geneva: Tuberculosis Key facts; 17 October 2019. Available from: <https://www.who.int/news-room/fact-sheets/detail/tuberculosis>
 15. Prasanna T, Jeyashree K, Chinnakali P, Bahurupi Y, Vasudevan K, Das M. Catastrophic costs of tuberculosis care: a mixed method study from Puducherry, India. *Glob Health Action*. 2018;11(1):1477493. doi: 10.1080/16549716.2018.1477493. PMID: 29902134; PMCID: PMC6008578
 16. Pradhan G, Pattnaik M, Sethy H M, Patnaik J, Mohanty T, Giri P K. Diagnosis and treatment of pulmonary tuberculosis in one day: Way forward for END TB STRATEGY 2015. *J Family Med Prim Care*, 2019 Jan;8(1): 184-8. doi: 10.4103/jfmpe.jfmpe_358_16.

An Unusual Presentation of Achalasia Cardia: Mediastinal Widening

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Abstract

Cough as symptom to diagnose achalasia cardia. Achalasia typically presents with dysphagia and regurgitation of undigested food. Diagnosis is usually performed with esophageal manometry, barium swallow before macroscopic anatomical changes appear. But sometime cough as a symptom can diagnose. We present a 45-year old women whose diagnosis was suspected with chest-x-ray showing enlargement of right mediastinum. Diagnosis was then confirmed with upper endoscopy and barium swallow.

Keywords: Cough, Dyspnoe Achalasia; Dysphagia; Barium swallow; Heller myotomy; Pneumatic dilatation.

Introduction

Achalasia cardia is a rare primary neuromuscular motility disorder of the esophagus due to a reduction in ganglion cells of the myenteric plexus of the lower esophagus.¹ Achalasia cardia was first described by Sir Thomas Williams in 1672. In 1929, Hurt and Rake described the disease which is due to failure of relaxation of the lower esophageal sphincter (LES) and they coined the term achalasia, means failure to relax.² It has an incidence of 1.6 cases/lakh population and the prevalence of 10 cases/lakh individuals. However, the incidence of achalasia cardia in India is not known due to underreporting of the cases. It affects both genders equally and can affect any age group, more commonly seen between 25 and 60 years of age group individuals.³ The autoimmune etiology is being proposed in majority of the cases that usually follows the viral infection.⁴ Since achalasia cardia is a rare disease, therefore, we report a case of primary achalasia cardia in an adult.

Case Report: A 45 years old female presented to our department with complaints of cough and dyspnoe from last 1 month. Cough without any expectoration increase while lying down supine, no diurnal variation, dyspnoe mild grade (mmrc 2) no positional variation, no history fever or haemoptysis.



Figure 1: Plain X-ray showing mediastinal widening with retrocardiac mass and absent gastric air bubble

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Chest x-ray suggestive of mediastinal widening right side [Figure 1]. CT chest done which suggestive of grossly distended dilated oesophagus in entire course with thickening of lower oesophagus and GE junction likely involving adjacent cardia of stomach

with narrowing of GE junction. Which is suggestive of achalasia cardia and possibility of GE junction malignancy and lymphoma. [Figure 2].

After this we go for barium swallow and endoscopy and finally diagnosis of achalasia cardia and treated with balloon dilation. [Figure 3].

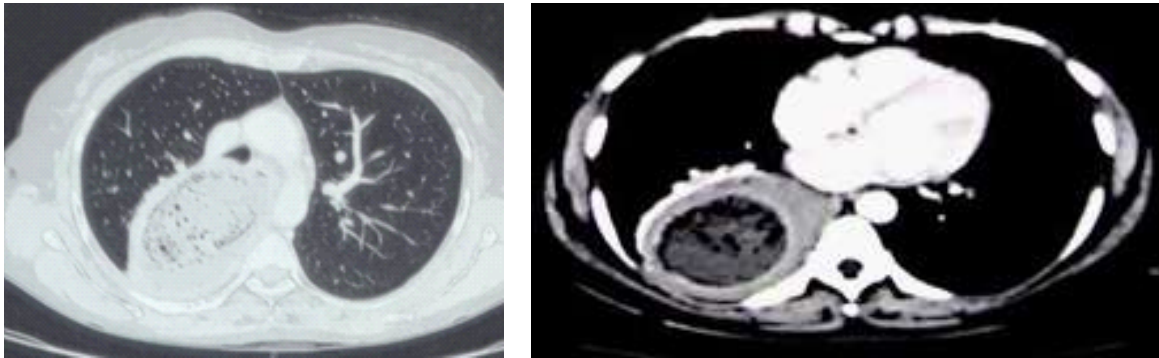


Figure 2: Computed Tomography showing dilated oesophagus without secondary involvement



Figure 3: Barium meal showing narrowing of lower end of oesophagus and dilation of the upper part, suggestive of achalasia cardia

Discussion

In a significant number of patients, the respiratory symptoms bring them to the doctor. Chronic pulmonary inflammatory conditions like aspiration pneumonitis, bronchiectasis and pulmonary fibrosis are common in these patients due to aspiration in the recumbent position.

Common causes of mediastinal widening mentioned are

Traumatic Aortic Injury

Vascular Anomalies:

- unfolded aorta
- double SVC
- aberrant right subclavian artery
- azygos continuation of the IVC
- pneumomediastinum

Lung:

- atelectasis

- pulmonary masses abutting the mediastinum
- mediastinal lymphadenopathy
- enlarged pulmonary arteries
- mediastinal lipomatosis

Masses:

- anterior mediastinal masses
- middle mediastinal masses
- posterior mediastinal masses

Thymus

Diaphragmatic hernia

Technical factors (on chest x-ray):

- rotation
- poor inspiration
- supine position
- lordotic position

As achalasia cardia not commonly presented among causes of mediastinal widening here we draw attention that symptoms of respiratory system can also leads to diagnosis of achalasia cardia and apart from thinking of malignancy as cause for cough while seeing chest xray one of rare differential should be kept in mind.

Achalasia is characterized by insufficient LES relaxation and loss of peristalsis. It is shown in less than 0.2% of all upper endoscopies. The mean age at diagnosis is usually over 50 years. Esophageal manometry is key to diagnosis.⁵ Treatment options are multiple, but randomized controlled trials are few, so decisions are based on local expertise, patient performance status and patient and physician preferences.^{5,6} In those patients who fit and willing to undergo surgery either a pneumatic dilation protocol or a laparoscopic surgical myotomy with a partial fundoplication as the first treatment are recommended. These techniques should be performed in high-volume centres of excellence. Laparoscopic Heller myotomy presents serious complications in There are two other alternative treatments. Botulinum toxin injection, which is recommended in patients who are not good candidates for pneumatic dilation or surgery, is a safe procedure, but over 50% relapse after 6 months, requiring multiple injections. Pharmacological treatments (calcium channel blockers, phosphodiesterase-5-inhibitor, anticholinergic agents) are the last alternative and is employed when

dilation or surgery cannot be performed and when botulinum injection has failed.⁶⁻⁹ Although an excess risk of carcinoma (standardized incidence ratio: 10.5, 95% CI 7.0-15.9) has been observed in operated and nonoperated patients, making upper endoscopy a first line investigation in symptomatic relapse, guidelines do not support surveillance.⁶

Conclusion

In a significant number of patients, the respiratory symptoms bring them to the doctor. Chronic pulmonary inflammatory conditions like aspiration pneumonitis, bronchiectasis and pulmonary fibrosis are common in these patients due to aspiration in the recumbent position.

A plain chest X-ray shows mediastinal widening, an air-fluid level at the arch of the aorta and a paramediastinal double stripe. The height of the air-fluid column above the cardia indicates the fluid column the LES can support. Pneumonitis or lung abscess may be seen. On barium swallow, there is absence of peristalsis, gross oesophageal dilation and failure of LES to relax. Achalasia cardia among one of rare differential diagnosis of mediastinal widening.

Conflict of Interest: None

Source of Funding: Self

Ethical Clearance: Ethical Clearance was obtained from the Institutional Ethics Committee (IEC), Maharishi Markandeshwar (deemed to be) University, Mullana, Ambala

References

1. Islam MB, Rahman MK, Sarker AK. Achalasia cardia – Case report. *J Teach Assoc* 2001;14:85-7
2. Sarumpaet F, Dairi L. A case report of achalasia. *IOP Conf Ser Earth Environ Sci* 2018;125:012209.
3. Spechler SJ. Achalasia: Pathogenesis, clinical manifestations and diagnosis. *UpToDate*. Waltham, MA: 2019.
4. Furuzawa-Carballeda J, Torres-Landa S, Valdovinos MÁ, Coss-Adame E, Martín Del Campo LA, Torres-Villalobos G, et al. New insights into the pathophysiology of achalasia and implications for future treatment. *World J Gastroenterol* 2016;22:7892-907.
5. Vaezi MF, Pandolfino JE, Vela MF. ACG clinical guideline: diagnosis and management of achalasia. *Am J Gastroenterol*. 2013; 108: 1238-49.

5. Lake JM, Wong RK. Review article: the management of achalasia - a comparison of different treatment modalities. *Aliment Pharmacol Ther.* 2006; 24: 909-18.
6. Campos GM, Vittinghoff E, Rabl C, Takata M, Gadenstatter M, et al. Endoscopic and surgical treatments for achalasia: a systematic review and meta-analysis. *Ann Surg* 2009; 249:45-57.
7. Rebecchi F, Giaccone C, Farinella E, Campaci R, Morino M. Randomized controlled trial of laparoscopic Heller myotomy plus Dor fundoplication versus Nissen fundoplication for achalasia: long-term results. *Ann Surg.* 2008; 248: 1023-30.
8. Andersen, H. A., Holman, C. B. and Olsen, A. M.: Pulmonary complications of cardiospasm. *J. Amer. Med. Assoc.* 1953; 151: 608-12.
9. Rickham, P. P. and Boeckman, C. R.: Achalasia of the oesophagus -n young children. *Clin. Pediatr. (Phila.).* 1963; 2: 676-80.

Determine the Various Risk Factors and Co-Morbidities in the Patient's Admitted with Acute Exacerbation of Chronic Obstructive Pulmonary Disease: A Cross Sectional Study

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Abstract

Aim: study the prevalence of various risk factors and co-morbidities in patients with acute exacerbation of chronic obstructive pulmonary disease.

Material and Method: 73 patients admitted with AE-COPD data on body mass index (BMI), smoking, symptoms, co-morbidities course of the disease, spirometry management were obtained.

Results: Eighty-eight percent of the admitted patients had current or past smoking habit of 'Bidi' and 9% were cigarette smokers. of admitted patients, 46% had at least one co-morbid condition. Mean FEV1 was 42.5%.

Conclusion: Study concluded that the hospitalized patient with AE-COPD suggests spirometric impairments because majority of the patients had current or past smoking habits. Diabetes and cardiovascular diseases were found to be the major co-morbidities.

Keywords: AE-COD, Co-morbidities, FEV1.

Introduction

Chronic respiratory diseases which include asthma and chronic obstructive pulmonary diseases, it is responsible for an estimated burden of more than 100 million people in India.¹ Chronic obstructive pulmonary disease progresses over many decades and tends to present in advanced stages, thus most treated patients are middle aged or elderly. Chronic obstructive pulmonary disease is the fourth leading cause of death worldwide resulting in more than 2.7 million deaths in 2000.²

Hospitalisations due to exacerbations of COPD account for major economic costs in addition to causing

disease progression.³ The available studies^{4,5} have mostly focused on risk factors for admission of stable COPD patients, external factors (e.g., air pollution) and admission⁶, or prognostic factors for hospital mortality.⁷⁻⁹ Spirometry is essential to make a clinical diagnosis of COPD. The presence of FEV1/FVC less than 0.70 (post - bronchodilator) confirms the presence of persistent airflow limitation and help in making diagnosis as COPD.¹⁰

Observational studies with various designs have evaluated risk factors for hospitalization due to COPD. But due to paucity of the data in the present population this study was conceived to determine the various risk factors and co-morbidities in the patient's admitted with Acute Exacerbation of Chronic Obstructive Pulmonary Disease

Materials and Method

Study Design, Study Duration, Study Population and Study area

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A cross-sectional study was carried out among patients admitted over a period of one year with AE-COPD in a tertiary care hospital in Ambala, India.

Inclusion Criteria: Patients with COPD were diagnosed as per the criteria of World Health Organization-Government of India (WHO-GOI) guidelines-2003 for the management COPD.¹¹

Methodology

Baseline data relating to demographics, respiratory disease history, frequency of admissions to hospital for COPD in the past one year, current respiratory medications and co morbidities was collected. Data on BMI, smoking, symptoms, disease course, other investigations, management and outcome during the hospitalization were obtained from the patient and in-patient records. Records of previous hospitalizations were also obtained. If a patient was admitted number of times during the study period, the parameters recorded during most recent admission were considered for analysis.

Statistical Analysis: The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2010) and then exported to data editor page of SPSS version 19 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics included computation of percentages and mean.

Results

We collected data of 81 admitted patients over one year duration. 77 patients met the inclusion criteria for the study. Our sample comprised of 72.7% males. The demographic baseline characteristics of the patients are shown as;

Table 1: 63.8% of the admitted patients had smoking habit. of admitted patients, 46% had at least one co-morbid condition. Mean FEV1 was 41.2%. The medication histories during showed 34 (44.2%) patients were using inhaled and oral corticosteroids, respectively before admission. There were 59 (77.6%) patients on inhaled β2-agonists, out of which 18 (23.4%) were on short-acting and 41 (53.2%) were on long acting β2-agonist, respectively.

Table 2: Patients were admitted with different types of co-morbidities but 19 (24.7%) diabetes, 11 (14.3%) cardiovascular disease and 8 (10.4%) hypertension were found more common and often co-existed.

Table 1: Distribution of demographic and characteristics of the study population

Variables	
Age	59.34±4.1
Male/Female	56:21
FEV1%	41.21±6.71
Smoking habit (n=77)	49 (63.4%)
Inhaled short acting β2 -agonists	18 (23.4%)
Inhaled long acting inhaled β2 -agonists	41(53.2%)
Inhaled and oral corticosteroids	34 (44.2%)

Tables 2: Distribution of different co-morbidities in the study population

Co-morbidities	Number (N)	Percentage (%)
No co-morbidity	31	40.3
Diabetes	19	24.7
Coronary artery diseases	11	14.3
Hypertension	8	10.4
Diabetes and Hypertension	6	7.8
Tuberculosis	4	5.2
Others	2	2.6
Total	77	100.0

Discussion

This study was carried out to determine the factors associated with hospital admission among adults who were admitted with exacerbations of COPD. Our findings revealed that hospitalizations due to AECOPD were impairment of FEV1. The consistent and important association of decreased FEV1 during frequent exacerbations is well known. A low FEV1 is also a pre-eminent risk factor for mortality from COPD in most epidemiological studies.^{12,13}

We believe this is the first study from northern India to gather information about associated risk factors for hospitalization due to AE-COPD. In addition, this study was done in reference to recommendation of current WHO-GOI guidelines.¹¹ We found various associated risk factors for exacerbations which may be useful clinically and may be considered in formulating further guidelines.

Nearly half of the patients in our study had one or more co-morbidities. Fifteen percent patients had cardiovascular related problems and 11% of patients had at least two co-morbidities. Our results also suggest that co-morbidity is a risk factor for frequent exacerbations. This was found in agreement with the study conducted

by Ball et al.¹⁴ found that co-existent cardiopulmonary disease was a risk factor for hospitalization. Among these, diabetes may be an important risk factor for exacerbations requiring longer periods of hospitalization associated with aggressive bacterial infection.¹⁵

With the growing prevalence of COPD and exacerbations, there is a need for closer follow-up and precise therapeutic and preventive measures to avoid hospital admissions. The risks factors observed in the present study might find a role in decision making in the clinical management of AE-COPD and may reduce frequency of hospitalization.

Conclusion

Present study concluded that the hospitalized patient with AE-COPD suggests spirometric impairments because majority of the patients had current or past smoking habits. Diabetes and cardiovascular diseases were found to be the major co-morbidities.

Conflict of Interest: None

Source of Funding: Self

Ethical approval and Informed consent: The study protocol was reviewed by the Ethical Committee of Hospital and was granted ethical clearance. After explaining the purpose and details of the study, a written informed consent was obtained from the patients who participated in the study. It was emphasized that strict confidentiality would be maintained at all times and the patients could withdraw at any time without being penalized.

References

- Vijayan VK. Chronic obstructive pulmonary disease. *Indian J Med Res* 2013;137:251-69.
- Decramer M, Wim Janssens, Marc Miravittles. Chronic Obstructive Pulmonary Disease, *Lancet* 2012; 379: 1341–51 Published Online February 6, 2012.
- Gudmundsson G, Gislason T, Janson C, Lindberg E, Hallin R, Ulrik CS, et al. Risk factors for rehospitalisation in COPD: role of health status, anxiety and depression. *Eur Respir J* 2005;26:414-9.
- Garcia-Aymerich J, Monso E, Marrades RM, Escarabill J, F elz MA, Sunyer J, et al. Risk factors for hospitalization for a chronic obstructive pulmonary disease exacerbation. EFRAM study. *Am J Respir Crit Care Med* 2001;164:1002-7.
- Kessler R, Faller M, Fourgaut G, Menecier B, Weitzenblum E. Predictive factors of hospitalization for acute exacerbation in a series of 64 patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1999;159:158-4.
- Anderson HR, Spix C, Medina S, Schouten JP, Castellsague J, Rossi G, et al. Air pollution and daily admissions for chronic obstructive pulmonary disease in 6 European cities: results from the APHEA project. *Eur Respir J* 1997;10:1064-71.
- Almagro P, Calbo E, Ochoa de Echaguen A, Barreiro B, Quintana S, Heredia JL, et al. Mortality after hospitalization for COPD. *Chest* 2002;121:1441-8.
- Connors AF Jr, Dawson NV, Thomas C, Harrell FE Jr, Desbiens N, Fulkerson WJ, et al. Outcomes following acute exacerbation of severe chronic obstructive lung disease. The SUPPORT investigators (Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments). *Am J Respir Crit Care Med* 1996;154:959-67.
- Fuso L, Incalzi RA, Pistelli R, Muzzolon R, Valente S, Pagliari G, et al. Predicting mortality of patients hospitalized for acutely exacerbated chronic obstructive pulmonary disease. *Am J Med* 1995;98:272-7.
- Miravittles M, Guerrero T, Mayordomo C, Sanchez Agudo L, Nicolau F, Segu JL. Factors associated with increased risk of exacerbation and hospital admission in a cohort of ambulatory COPD patients: a multiple logistic regression analysis: The EOLO Study Group. *Respiration* 2000;67:495-501.
- Jindal SK, Gupta D, Aggarwal AN. Guidelines for management of chronic obstructive pulmonary disease (COPD) in India: a guide for physicians (2003). *Indian J Chest Dis Allied Sci* 2004; 46:137-53.
- Vilkman S, Keistinen T, Tuuponen T, Kivela SL. Survival and cause of death among elderly chronic obstructive pulmonary disease patients after first admission to hospital. *Respiration* 1997;64:281-4.
- Burrows B, Bloom JW, Traver GA, Cline MG. The course and prognosis of different forms of chronic airways obstruction in a sample from the general population. *N Engl J Med* 1987;317:1309-14.

14. Ball P, Harris JM, Lawson D, Tillotson G, Wilson R. Acute infective exacerbations of chronic bronchitis. *Q J Med* 1995;88:61-8.
15. Osman IM, Godden DJ, Friend JA, Legge JS, Douglas JG. Quality of life and hospital re-admission in patients with chronic obstructive pulmonary disease. *Thorax* 1997;52:67-71.

Outcome of Trabeculectomy in Early Primary Open Angle Glaucoma in Respect of Retinal Nerve Fiber Layer Thickness and Optic Nerve Head Parameters

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Abstract

Introduction: Glaucoma is the group of acute and chronic multifactorial condition where lowering IOP is the mainstay of the treatment in the patients, but despite of all effort progression of disease is inevitable. The prevalence of primary open angle glaucoma (POAG) in India is 1.62% and increasing with age, where 98.5% were not even aware of the disease. In our study, we assessed the outcome of trabeculectomy using retinal nerve fiber layer (RNFL) thickness measurements and clinical parameters.

Material and Method: Twenty seven patients of primary open angle glaucoma undergoing trabeculectomy were included. Ophthalmological examinations including best corrected visual acuity, pupils and anterior segment evaluation, intraocular pressure, fundus and optic disc examination, perimetry and optic coherence tomography were performed preoperatively and 1 week, 1 month and 3 months postoperatively in each and every subject.

Results: With mean age of 57.9 years, total of 18 male and 9 female patients were recruited. IOP was decreased by 43.85% from baseline but best corrected visual acuity was increased marginally after 3 months postoperatively. Optic nerve head parameters were improved significantly. Visual Field analysis showed that mean sensitivity and mean deviation were improved from 8.73 ± 4.5493 and 19.044 ± 4.6111 preoperatively to 9.859 ± 5.5606 and 17.926 ± 5.4928 dB postoperatively, respectively.

Conclusion: Our data suggested that in early POAG, trabeculectomy provides good IOP control and clinical outcome with little complication rate under experienced hands.

Keywords: Optic nerve head parameters, Primary open angle glaucoma, Retinal nerve fiber layer thickness, Trabeculectomy.

Introduction

Glaucoma is the group of acute and chronic multifactorial optic neuropathies affecting retinal

ganglion cell (RGC) axons leading to optic atrophy and demonstrable visual field defects. Being the second most common cause of blindness in the world, glaucoma affected 64.3 million adults (aged 40–80 years) in 2013.^{1,2} The prevalence of primary open angle glaucoma (POAG) in India is 1.62% and increasing with age, where 98.5% were not even aware of the disease.²

Out of the multiple factors, increased intraocular pressure (IOP) is the most important and only preventable factor for decreasing vision in glaucoma³. Decreasing IOP is the aim in the treatment and associated with decrease rate of disease progression in POAG.⁴ As a

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surgical option in treatment, trabeculectomy is the well-known and preferred technique of filtering surgery for POAG to decrease IOP.³

Increased IOP decreases axonal outflow in RGC by mechanical pressure and cause ischemic injury to RGC. This RGC loss can be measured with retinal nerve fiber layer (RNFL) thickness and optic nerve head (ONH) parameter by optical coherence tomography (OCT). OCT can be used to measure same parameters to check treatment effectiveness and disease progression.⁵

Here, our project aimed to study RNFL and ONH parameter using OCT and automated visual field analysis before and after trabeculectomy in POAG and effectiveness of the surgery at our center.

Material and Method

Study Population: Patients diagnosed with POAG undergoing Trabeculectomy were included in the study. If both eyes require surgery then the eye with greater IOP and glaucoma progression was included in the study. Patients with optic neuropathy due to other causes than POAG, previous eye surgery, other ocular diseases, advanced stage of glaucoma, inconclusive OCT and unable to undergo surgery were excluded from the study. The study was ethically cleared by Institutional ethics committee of our institute.

Initial Assessment: Ophthalmological examinations including best corrected visual acuity (BCVA), pupils and anterior segment evaluation, IOP, fundus and optic disc examination, perimetry and optical coherence tomography were performed in each and every subject.

Surgical procedure and postoperative care: Trabeculectomy was performed under local anaesthesia in accordance with standard procedures. Postoperative assessment included all preoperative parameters, slit lamp biomicroscopy and post-operative bleb examination. OCT scans, perimetry and disc photography were repeated at 1 week, 1 month and 3 months. The results were recorded and analysed.

Statistical Analysis: All statistical analyses were performed using GraphPad Prism version 7.03. Continuous variables were expressed as mean \pm SD. The data collected from the study was analysed by using repeated measure ANNOVA with Bonferroni correction. P-value of <0.05 was considered significant.

Results

Age and gender distribution: A total of 27 patients were recruited in this study. The age distribution of patients in various groups. The mean age of patients was found to be 57.9 years. A total of 18 male and 9 female patients were recruited in this study. The distribution of patients on the basis of gender is depicted in Table 1.

Clinical parameter evaluation and their association: Various clinical parameters were recorded pre and post-operatively and the mean of the clinical parameters in different observational periods were used to check the association of the particular clinical parameter in different durations of observational period.

- 1. Visual Acuity Test:** The visual acuity test values were found to be slightly increase post-operatively in different observation periods but the difference was not found to be statistically significant as shown in Table 2.
- 2. Intra-Ocular Pressure (IOP):** The IOP values were found to be randomly decreased after 1 week of surgery and then there was a slight increase in the values after 1 month and 3 months post-operatively. The difference of IOP in the different observational periods was found to be statistically significant as shown in Table 3.
- 3. Optic Nerve Head Parameters:** Various optic nerve parameters have been evaluated have been evaluated pre and post-operatively. The disc area was found to be increased upto 1 month post-operatively and then decreased and the difference was not statistically significant. The rim area showed to be marginally increased post-operatively and the difference was found to be statistically significant. The rim volume was found to be increased post-operatively upto 1 month and then showed to remain static and the difference was found to be statistically significant. The cup area showed fluctuating values. The cup volume was found to be decreased post-operatively after 1 month and the difference was statistically significant. The cup volume and cup/disc ratio values were found to be marginally decreasing post-operatively and the difference was found to be statistically significant as shown in Table 4.
- 4. Peripapillary RNFL Thickness (μm):** The peripapillary RNFL thickness was measured and recorded. The peripapillary RNFL thickness was measured pre and post-operatively but there was no

statistically significant association with any of the measured parameters as shown in Table 5.

- Automated Visual Field Analysis:** The mean value of mean sensitivity was found to be increased from 1 month to 3 months post-operatively and this difference was found to be statistically significant. The mean values of mean deviation were found to be decreased post-operatively and this difference was statistically significant. The mean values of square root loss of variance were found to be decreased post-operatively but this difference was not statistically significant as shown in Table 6.

Table 1: Age Distribution

Age Group (in Years)	Number of Patients	Percentage (%)
41-50	7	25.9
51-60	9	33.33
61-70	9	33.33
71-80	2	7.40
Gender		
Male	18	66.7
Female	9	33.3

Table 2: Visual Acuity Test

Observation Period	Mean	Standard Deviation	p-Value
Pre-Op	11.93	±2.868	
Post-Op 1 week	12.15	±2.641	1
Post-Op 1 month	13.07	±2.286	0.13
Post-Op 3 months	14.07	±2.129	0

Table 3: Intra-Ocular Pressure (mm Hg)

Observation Period	Mean	Standard Deviation	p-Value
Pre-Op	26.93	±2.786	
Post-Op 1 week	9.07	±3.430	<0.05
Post-Op 1 month	11.41	±4.254	<0.05
Post-Op 3 months	11.81	±3.552	<0.05

Table 4: Optic Nerve Parameter Head Parameters

Parameter	Observation Period	Mean	Standard Deviation	p-Value
Disc area (mm ²)	Pre-Op	2.5493	±0.345	
	Post-Op 1 week	2.6181	±0.399	1
	Post-Op 1 month	2.7281	±0.456	0.26
	Post-Op 3 months	2.6307	±0.603	1
Rim area (mm ²)	Pre-Op	0.5037	±0.276	
	Post-Op 1 week	0.5870	±0.262	0.12
	Post-Op 1 month	0.6452	±0.259	0.04
	Post-Op 3 months	0.6707	±0.293	0.008
Rim volume (mm ³)	Pre-Op	0.0463	±0.019	
	Post-Op 1 week	0.0541	±0.024	0.04
	Post-Op 1 month	0.0630	±0.023	0
	Post-Op 3 months	0.0630	±0.033	0.04
Cup area (mm ²)	Pre-Op	2.0640	±0.504	
	Post-Op 1 week	1.9960	±0.508	0.95
	Post-Op 1 month	2.0290	±0.534	1
	Post-Op 3 months	1.9393	±0.586	0.02

Parameter	Observation Period	Mean	Standard Deviation	p-Value
Cup volume (mm ³)	Pre-Op	0.6981	±0.339	
	Post-Op 1 week	0.6515	±0.324	0.003
	Post-Op 1 month	0.6170	±0.315	0.001
	Post-Op 3 months	0.5933	±0.313	0
Cup/Disc ratio	Pre-Op	0.7896	±0.700	
	Post-Op 1 week	0.7563	±0.133	0.02
	Post-Op 1 month	0.7300	±0.132	0.02
	Post-Op 3 months	0.7004	±0.180	0

Table 5: Peripapillary RNFL Thickness parameters (µm)

Parameter	Observation Period	Mean	Standard Deviation	p-Value
Inferior Quadrant	Pre-Op	63.30	±8.978	
	Post-Op 1 week	69.48	±9.002	0
	Post-Op 1 month	68.93	±11.19	0.97
	Post-Op 3 months	66.67	±9.919	0.14
Superior Quadrant	Pre-Op	67.52	±12.801	
	Post-Op 1 week	69.81	±13.270	1
	Post-Op 1 month	69.37	±12.122	0.88
	Post-Op 3 months	67.85	±13.640	1
Nasal Quadrant	Pre-Op	62.63	±8.317	
	Post-Op 1 week	65.33	±8.256	0.85
	Post-Op 1 month	64.22	±9.316	1
	Post-Op 3 months	63.22	±9.112	1
Temporal Quadrant	Pre-Op	50.81	±9.915	
	Post-Op 1 week	50.52	±9.345	1
	Post-Op 1 month	51.48	±9.267	1
	Post-Op 3 months	51.85	±10.117	1

Table 6: Automated Visual Field analysis parameters

Parameter	Observation Period	Mean	Standard Deviation	p-Value
Mean Sensitivity (dB)	Pre-Op	8.730	±4.5493	
	Post-Op 1 month	9.267	±4.9947	0.09
	Post-Op 3 months	9.859	±5.5606	0.04
Mean Deviation (dB)	Pre-Op	19.044	±4.6111	
	Post-Op 1 month	18.260	±5.1640	0.003
	Post-Op 3 months	17.926	±5.4928	0.01
Square Root Loss of Variance (dB)	Pre-Op	7.822	±2.1344	
	Post-Op 1 month	7.533	±2.1378	0.53
	Post-Op 3 months	7.530	±2.1380	0.85

Discussion

Glaucoma is the heterogenous condition where lowering IOP is the mainstay of the treatment in the patients, but despite of all effort progression of disease is inevitable.⁶ With increasing age, risk of POAG is increasing and in our study mean age is 57.9 years which

is matching with other Indian and foreign studies.⁷⁻⁹ Sex distribution M:F is 2:1 in our study which coinciding with other studies^{7,8} but one south Indian cohort study reported 1:1.⁹

Different studies mentioned decrease in IOP by 38 to 56% from preoperative baseline IOP after 3

months postoperative.^{5,10-12} In our study, IOP decreased by 43.85% from baseline after 3 months, which is comparative with other international studies.^{5,10-12}

Hong et al suggested better visual acuity after triple procedure than trabeculectomy in POAG¹⁰, while 3 months postoperative BCVA improvement was fair in our study but data was not statistically significant. Change in ONH parameters as depicted in Table 4 were matching with available literature.^{5,10-12}

RNFL thickness was increased initially postoperative period but at 3 months postoperatively started decreasing. Increase in RNFL thickness was not significant and not correlating with clinical improvement or change in ONH parameters. Berkowska et al stated similar changes in RNKL thickness but it also mentioned that rate of change in RNFL thickness was correlating with rate of change in lamina cribrosa depth.⁵

No patients in our study was prescribed oral medications for IOP control. There was no endophthalmitis, hyphema, bleb leak or any other serious complications reported, except only one patient had hypotony postoperatively which was managed conservatively. Although our study had some limitations i.e short postoperative follow up, small number of subjects, review of literature suggested very few Indian studies providing such data.

In conclusion, our data suggested that in early POAG, trabeculectomy provides good IOP control and clinical outcome with little complication rate under experienced hands.

Conflict of Interest: None

Source of Funding: Self

Ethical Clearance: Ethical Clearance was obtained from the Institutional Ethics Committee (IEC), Maharishi Markandeshwar (Deemed to be) University, Mullana, Ambala.

References

1. Tham Y, Li X, Wong T, Quigley H, Aung T, Cheng C. Global Prevalence of Glaucoma and Projections of Glaucoma Burden through 2040. *Ophthalmology*. 2014;121(11):2081-90.
2. Vijaya L, George R, Paul P, Baskaran M, Arvind H, Raju P et al. Prevalence of Open-Angle Glaucoma in a Rural South Indian Population. *Investigative Ophthalmology & Visual Science*. 2005;46(12):4461.
3. Shields M. Trabeculectomy vs full-thickness filtering operation for control of glaucoma. *Ophthalmic Surg*. 1980;11:498-505.
4. Konstas A, Kahook M, Araie M, Katsanos A, Quaranta L, Rossetti L et al. Diurnal and 24-h Intraocular Pressures in Glaucoma: Monitoring Strategies and Impact on Prognosis and Treatment. *Advances in Therapy*. 2018;35(11):1775-1804.
5. Krzyżanowska-Berkowska P, Czajor K, Helemejko I, Iskander D. Relationship between the rate of change in lamina cribrosa depth and the rate of retinal nerve fiber layer thinning following glaucoma surgery. *PLOS ONE*. 2018;13(11):e0206040.
6. Loskutova E, O'Brien C, Loskutov I, Loughman J. Nutritional supplementation in the treatment of glaucoma: A systematic review. *Survey of Ophthalmology*. 2019;64(2):195-216.
7. Chiam N, Baskaran M, Li Z, Perera S, Goh D, Husain R et al. Social, health and ocular factors associated with primary open-angle glaucoma amongst Chinese Singaporeans. *Clinical & Experimental Ophthalmology*. 2017;46(1):25-34.
8. Angmo D, Wadhvani M, Upadhyay A, Temkar S, Dada T. Outcomes of Trabeculectomy Augmented With Subconjunctival and Subscleral Ologen Implantation in Primary Advanced Glaucoma. *Journal of Glaucoma*. 2017;26(1):8-14.
9. Vijaya L, Rashima A, Panday M, Choudhari N, Ramesh S, Lokapavani V et al. Predictors for Incidence of Primary Open-Angle Glaucoma in a South Indian Population. *Ophthalmology*. 2014;121(7):1370-1376.
10. Hong S, Park K, Ha S, Yeom H, Seong G, Hong Y. Long-Term Intraocular Pressure Control of Trabeculectomy and Triple Procedure in Primary Open Angle Glaucoma and Chronic Primary Angle Closure Glaucoma. *Ophthalmologica*. 2007; 221(6):395-401.
11. Kim J, Kim T, Lee E, Girard M, Mari J. Microvascular Changes in Peripapillary and Optic Nerve Head Tissues After Trabeculectomy in Primary Open-Angle Glaucoma. *Investigative Ophthalmology & Visual Science*. 2018;59(11):4614.
12. Rayees Ahmad Sofi, Shah Nawaz Shafi, Waseem Qureshi, Sehrish Ashraf. Merits of trabeculectomy in advanced and end-stage glaucoma. *International Journal of Health Sciences*. 2018;12(2):57-60.

Axenfeld-Rieger Syndrome—A Rare Phenomenon

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Abstract

Purpose: Axenfeld-Rieger syndrome is an ocular anterior segment dysgenesis, autosomal dominantly inherited, commonly associated with glaucoma and systemic anomalies. This study presents various clinical manifestations of Axenfeld-Rieger syndrome within one family.

Material and Method: Three members of the family: patient 1--father (54 years old), patient 2--son (12 years old) and patient 3--daughter (8 years old), underwent complete ophthalmic examination, including standard glaucoma diagnostics. It was impossible to perform complete eye examination in one case (patient 1) because of severity of ocular changes.

Results: All family members described had iris abnormalities (hypoplastic iris stroma) and advanced glaucoma, however severity of symptoms were different in each case. The most advanced disease was recognized in patient 1. Other findings included: posterior embryotoxon (patients 2 and 3), iridocorneal angle abnormalities (patients 2 and 3), stretch holes and extraocular features (patient 2): dental anomalies (microdontia and hypodontia), maxillary hypoplasia and periumbilical skin fold. All of these symptoms supported the diagnosis of Axenfeld-Rieger syndrome. In addition, we also diagnosed high myopia & strabismus (patient 2) and corneal scar in (patient 1).

Conclusion: Reported cases of Axenfeld-Rieger syndrome demonstrate phenotypic variability of the disease among family members, which is characteristic for this disorder and can cause diagnostic problem.

Keywords: Axenfeld-Rieger syndrome, Glaucoma, Corectopia, Iris Stretch holes, Maxillary hypoplasia, dental abnormalities.

Introduction

In 1920, Axenfeld characterized the anomaly which bears his name when he described posterior embryotoxon and iris strands adherent to the anteriorly displaced Schwalbe's line.¹ Rieger described patients with congenital iris abnormalities including iris hypoplasia,

correctopia and polycoria, now referred to as Rieger anomaly, in 1935.²

Axenfeld-Rieger syndrome is autosomal dominant in most cases, but it can also occur sporadically. It has complete penetrance with variable expressivity and is associated with a 50% risk of glaucoma. ARS is a genetically heterogeneous group of abnormalities as a result of mutations in at least 4 different gene loci. Mutations in PITX2 on ch 4q25, FOXC1 on 6p25, PAX6 on 11p13 and FOXO1A on 13q14 have been associated with formation of ARS.³ Developmental anomalies of anterior angle cause increase of outflow resistance and ocular hypertension in nearly 50% of the cases.⁴ The characteristic craniofacial signs like maxillary hypoplasia, dental features including

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hypodontia, oligodontia and microdontia and umbilical anomalies were also reported in ARS patients.⁵

Materials and Method

We present the clinical features & findings of a family with Axenfeld-Riegers syndrome.

Case 1-Father: A 35 year's old male was brought to us by a social activist for PKP in the month of August with corneal opacity Right eye (and phthisis left eye). The patient had a history of glaucoma since 16 years and had undergone a Trabeculectomy 2 times since then. IOP was still not controlled and patient eventually developed corneal opacity secondary to corneal decompensation. Left eye was lost in childhood due to infective keratitis. The visual acuity was PL, PR -ve. The patient underwent keratoplasty procedure. Graft clarity: Pristine clear graft I.O.P : Controlled with single Medication. VISION: F.C 2mtrs, Pt. is mobile & is now self dependent to a large extent.

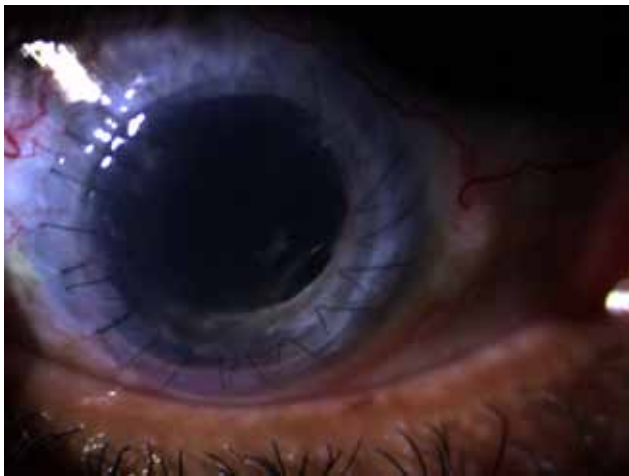


Fig 1: Keratoplasty with pristine clear graft

Case 2-Son: 12 year-old male Best visual acuity equal to 6/18 (R/E) and 6/18 (L/E).

Slit lamp evaluation revealed: Bilateral posterior embryotoxon, Iris atrophy, Corectopia, Stretch holes.

- The IOP
 - R/E 51mm hg
 - L/E 12 mmHg.
- On Fundus examination
 - C:D ratio

R/E 0.9

L/E 0.3.

He was on medical management, we preferred surgical intervention and performed trabeculectomy. And IOP is controlled without any medication now Pt is on regular follow up with us.



Fig 2: Corectopia with stretch hole in iris with posterior embryotoxn



Fig 3: Iris stretch holes



Fig 4: Maxillary hypoplasia with dental abnormalities



Fig 6:

Discussion

Case 3- Daughter: An 8 year-old female with visual acuity equal to 6/12 (R/E) and 6/9 (L/E). IOP was 17 mm Hg in both the eyes. Slit lamp examination revealed :Pseudopolycoria, iris atrophy, Embryotoxon.

General physical examination revealed:

- Maxillary hypoplasia
- Microdontia
- Diastema
- Fundus examination revealed the healthy disc with C:D ratio 0.3 in both the eyes.

This is a remarkable case series in which a family, including two generations presented with Axenfeld-Rieger anomaly. The trait appeared to be autosomal dominant with high penetrance (100% in this case), considering that both siblings inherited the abnormalities of the father. The mechanism of the ocular development has been widely studied and discussed. Often the factors that result in disturbance of neural crest may act at more than one phase of this process, producing anomalies that involve more than one tissue derived from neural crest. Espana et al.⁶ and Parikh et al.⁷ reported 2 cases with unusual presentation of detached Schwalbe line suspended in anterior chambers, respectively. The anterior segment structure Schwalbe line has its genesis from neural crest cells, the impaired development of which is related to the pathogenesis of ARS may explain such clinical manifestation.⁴ Hypoplasia of extraocular muscles derived from mesodermal complex also appeared in ARS. Bhate and Martin⁸ reported a 6-year-old boy with hypoplasia of right inferior rectus muscle presenting exotropia; while Park et al.⁹ reported another 4-year-old girl with more posteriorly insertion of superior oblique presenting exotropia and dissociated vertical deviation (DVD). Since around 50% of ARS patients will develop glaucoma, conventional glaucoma surgeries like trabeculectomy and trabeculotomy are still required. With a 20-year followup, Mandal and Peheré confirmed



Fig 5: Pseudopolycoria, Iris Atrophy, Embryotoxon

the safety and effectiveness of the combination of trabeculotomy and trabeculectomy for ARS children with early-onset of glaucoma.¹⁰ Mitomycin C(MMC) or the newly developed Ologen Collagen matrixreducing subconjunctival fibrosis may effectively lower IOP in long-term.¹¹⁻¹² As to the maxillary hypoplasia and dental anomalies of ARS, specialized oral and maxillofacial surgery, special dental care and application of orthodontic unit may be helpful.¹³

Conclusion

Two different inherited genes appearing together in an entire family may suggest a single molecular and genetic etiology, but additional studies are necessary to explain the relationship among these overlapping phenotypes and their inheritance. All three family members described had iris abnormalities (hypoplastic iris stroma) and advanced glaucoma, however severity of symptoms were different in each case. The most advanced disease was recognized in Case 1.

Other findings included: Posterior embryotoxon (Case 2 and 3) Iridocorneal angle abnormalities (case 2 and 3). Stretch holes and extraocular features (Case 2): Dental anomalies (microdontia and hypodontia), maxillary hypoplasia and periumbilical skin fold. All of these symptoms supported the diagnosis of Axenfeld-Rieger syndrome. In addition, we also diagnosed high myopia & strabismus (Case 2) and corneal scar in Case 1.

Perhaps, in future, it would be possible to develop alternative therapeutic tools for the treatment of glaucoma, based on the knowledge of their etiology.

Conflict of Interest: None

Source of Funding: Self

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References

1. Axenfeld TH. Embryotoxon cornea posterius. *Klin Monatsbl Augenheilkd.* 1920;65:381-2.
2. Rieger H. Beitrage zur Kenntnisseltener Missbildungen der Iris, II: uber Hypoplasie des Irisvorderblattes mit Verlagerung und Entrundung der Pupille. *Albrecht von Graefes Arch Klin Exp Ophthalmol.* 1935;133:602-5.
3. Glaser T, Walton DS, Maas RL. Genomic structure, evolutionary conservation and aniridia mutations in the human PAX6 gene. *Nat Genet.* 1992;2(3):232-9
4. Shields MB, Buckley E, Klintworth GK, et al. Axenfeld-Rieger syndrome. A spectrum of developmental disorders. *Surv Ophthalmol* 1985; 29:387-409.
5. Childers NK, Wright JT. Dental and craniofacial anomalies of Axenfeld-Rieger syndrome. *J Oral Pathol* 1986;15:534-9.
6. Espana EM, Mora R, Liebmann J, et al. Bilateral prominent schwalbe ring in the anterior chamber in a patient with axenfeld-rieger syndrome and megalocornea. *Cornea* 2007;26:379-81.
7. Parikh RS, Parikh SR, Debashish B, et al. Unusual presentation in Axenfeld-Rieger syndrome. *Indian J Ophthalmol* 2011;59:312-4
8. Bhate M, Martin FJ. Unilateral inferior rectus hypoplasia in a child with Axenfeld-Rieger syndrome. *J AAPOS* 2012;16:304-6.
9. Park SW, Kim HG, Heo H, et al. Anomalous scleral insertion of superior oblique in Axenfeld-Rieger syndrome. *Korean J Ophthalmol* 2009;23:62-4.
10. Mandal AK, Pehera N. Early-onset glaucoma in Axenfeld-Rieger anomaly: long-term surgical results and visual outcome. *Eye (Lond)* 2016; 30:936-42.
11. Radhakrishnan OK, Pahuja K, Patel K, et al. OLOGEN ((R)) implant in the management of glaucoma in an unusual case of Axenfeld-Rieger syndrome. *Oman J Ophthalmol* 2014;7:90-2.
12. Mandal AK, Prasad K, Naduvilath TJ. Surgical results and complications of mitomycin C-augmented trabeculectomy in refractory developmental glaucoma. *Ophthalmic Surg Lasers* 1999; 30:473-80.
13. Bender CA, Koudstaal MJ, van Elswijk JF, et al. Two cases of axenfeldrieger syndrome, report of the complex pathology and treatment. *Cleft Palate Craniofac J* 2014;51:354-60.

Study of Correlation of Hyperuricemia with Knee Osteoarthritis

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Abstract

The present study was conducted to identify the link between increased uric acid and osteoarthritis and to find out the prevalence of hyperuricemia in population suffering from osteoarthritis of knee.

Material and Method: The study was conducted on 100 patients (male and female between the age of 40-70 years) with knee pain for more than 6 weeks to establish a correlation between knee osteoarthritis and hyperuricemia.

Result: In the current study female preponderance was seen. Mean age of the patients was 50.10 years and maximum patients were in the age group of 40-50 years. KOA patients had higher values of uric acid as compared to patients without KOA however no statistically significant relation was found between increasing uric acid levels and severity of KOA with p-value .668 being insignificant. The mean BMI of patients with KOA was higher than the patients without KOA but no statistical significant relation was found between increased incidence of KOA in females as compared to males with increasing BMI p-value 0.777 being insignificant. There was no statistically significant correlation between hyperuricemia and either gender with p-value being $>.05$ (0.119). VAS and WOMAC scoring was done at 0 and 16 weeks however no significant improvement was seen except for the pain component which improved in KOA patients.

Conclusion: In this present study we observed increased prevalence of OA knee in females and in patients with hyperuricemia and also with patients with higher BMI. Serum levels of CRP and ESR also show positive prevalence in patients with KOA in this study. However, no statistically significant correlation was observed between levels of hyperuricemia and severity of KOA. Hence in conclusion our study points towards positive correlation between hyperuricemia and KOA. Limitations of our study included inability to homogenise groups in terms of BMI, age, activity level, smoking, alcohol etc.

Keywords: Knee osteoarthritis, Hyperuricemia, WOMAC Score.

Introduction

Osteoarthritis is a disease of biomechanics. Although the increased mechanical forces initiate the cartilage damage its progression depends on cellular and biochemical factors, including chondrocyte activation

and the secretion of inflammatory mediators.^{1,2} A strong association has been found and well recognised for joint affected by gout, especially first metatarsophalangeal joint.³ Uric acid (UA) is constitutively present in normal cells is found in increased concentration with cell injury or death³. The sole presence of hyperuricemia might eventually lead to increase pericellular urate levels leading local formation of crystals at the microscopic level. Thus, asymptomatic hyperuricemia might affect cartilage damage even in the absence of frank gout.⁴ Unfortunately, few studies have addressed this potentially important issue and the results have been mixed. Increase

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in uric acid beyond its limit of solubility can lead to MSU crystal formation, which can stimulate the NLRP3 inflammasome and promote IL-1 β production which may lead to acute and sometimes chronic inflammation. MSU crystal aggregates can also directly damage the cartilage. Age and obesity can predispose to both osteoarthritis⁵ and gout and hence confound the association between both conditions.^{6,7} Whether serum UA may serve as a biomarker to convey or predict OA risk is not known. The present study was conducted to identify the possible link between increased uric acid and osteoarthritis and to find out the prevalence of hyperuricemia in population suffering from osteoarthritis of knee.

Materials and Method

This study was commenced after obtaining approval from the Institutional Ethics Committee vide IEC number - 1098. Study was done on 100 patients who presented to the Out-Patient Door (OPD) of tertiary care center with presenting symptoms of insidious onset of knee pain for more than 6 weeks. Patients with history of gout, rheumatoid conditions, history of previous trauma in same knee were excluded from the study. Upon presentation, patients were subjected to detailed history, relevant investigations including serum uric acid levels, ESR and CRP. Thorough general examination and knee examination with bilateral knee x-rays was done in weight bearing anteroposterior view and lateral view. The clinical severity was studied by Western Ontario Mac Master University (WOMAC) scores and the radiological severity by Kellgren & Lawrence (KL) grading of the disease. In the study serum uric acid levels were divided in to 3 groups <6, 6-8 and >8.

Statistical Analysis: Data collected was entered into Microsoft Excel worksheet and analyzed statistically by using Statistical Package for Social Sciences (SPSS Inc., Chicago, IL). Mean and standard deviation was calculated for all quantitative variables for description and measures of dispersion. For normally distributed data means of two groups was compared using paired student t-test. Qualitative or Categorical variables were described as frequencies and proportions. p value less than 0.05 was considered statistically significant.

Results

The mean age of the cohort was 50.10 years (range 40-70 years) and majority of the study population were between 40 to 55 years. Study had more preponderance of females with knee pain as compared to males (59%

and 41% respectively). All the patients with Knee osteoarthritis (KOA) were graded according to severity based upon radiological finding according to Kellgren Lawrence (KL) grade, total patients in KL grade 2 were 35%. of the total, in KL-3 were 39%. and KL-4 were 26%.

Out of 100 patients, 42 patients had hyperuricemia and 58 patients had no hyperuricemia. Out of 100 patients 31 patients had hyperuricemia with knee osteoarthritis (KOA), 11 patients just had hyperuricemia with no KOA, 26 patients had KOA without hyperuricemia and 32 patients had no KOA or hyperuricemia. The study showed a significant relation between hyperuricemia and knee osteoarthritis with p-value <0.05 being significant as seen in Table 1. Increasing severity of KOA was compared to increasing uric acid levels however there was no statistically significant relationship found (p-value 0.668) as shown in Table 2.

Total number of patients with hyperuricemia in the study were 42 from which males and females were 21 each. Out of 21 female patients 18 had hyperuricemia with KOA and only 13 males had hyperuricemia with KOA implying there was increase incidence of hyperuricemia in females with KOA as observed in this study but the overall comparison was statistically insignificant (p<0.05) (Table 3).

In the study at time of presentation BMI, ESR, CRP levels of patients were taken in to account and it was seen that mean BMI in knee osteoarthritis patient was comparatively higher being 26.54 and in patients with no radiological signs of KOA was 23.10 so signifying that patients with high BMI values were more prone to develop KOA (p-value= 0.043). However, there was no statistically significant gender predilection seen towards increasing BMI.

It was seen in the study that patients with Knee OA had mean CRP of 5.56 and mean ESR 20.84 respectively. While patients without Knee OA had mean CRP level 3.67 and mean ESR levels 15.10 respectively. The p-value-0.001 for CRP and p-value 0.002 for ESR respectively showed that the results were statistically significant and the patients with KOA had raised levels of CRP and ESR as compared to patients with no KOA.

The overall mean WOMAC score in the study was 40.6 \pm 12.5 (range 21 to 69). On sub analysis patients with Knee osteoarthritis (n=57) had a mean WOMAC score of 58.2 \pm 8.4 (range 42 to 68) while those without OA knee (n=43) had a mean WOMAC score of 29.7 \pm 6 (range

21 to 44) (p value =0.0043). The mean WOMAC score for males with OA knee and hyperuricemia (n=13) was 53±11.8 (range 47 to 65) and that for females (n=18) was 61.2±9.6 (range 54.4 to 69) (p value =0.682). It was seen that WOMAC score was higher in patients with

KOA and hyperuricemia as compared to patients with KOA without hyperuricemia and increased uric acid had positive correlation with grading of knee osteoarthritis (r=0.568) (Fig 1).

Table 1: Correlation of Osteoarthritis (OA) and Hyperuricemia

		Group				Total	Chi-square value	p-value
		OA		Non-OA				
Hyperuricemia	Absent	26	46%	32	74%	58	8.348	0.004*
	Present	31	54%	11	26%	42		
Total		57	100%	43	100%	100		

Table 2: Correlation of Uric acid levels and grading of severity of KOA (Kellgren lawrance grading).

Radiographic Grade	KL-2	KL-3	KL-4	Total	Chi-square value	p-value	
Uric acid levels	<6	9	11	6	26	2.371	0.668
	6-8.0	7	6	3	16		
	>8	4	5	6	15		
Total	20	22	15	57			

Table 3: Incidence of Hyperuricemia with knee osteoarthritis in both genders.

Hyperuricemia			Group				Total	Chi-square value	p-value
			Osteoarthritis		Non-Osteoarthritis				
Absent	SEX	F	21	55%	17	45%	38	4.852	0.051
		M	5	25%	15	75%			
	Total	26	45%	32	55%	58			
Present	SEX	F	18	86%	3	14%	21	3.079	0.079
		M	13	62%	8	38%			
	Total	31	74%	11	26%	42			

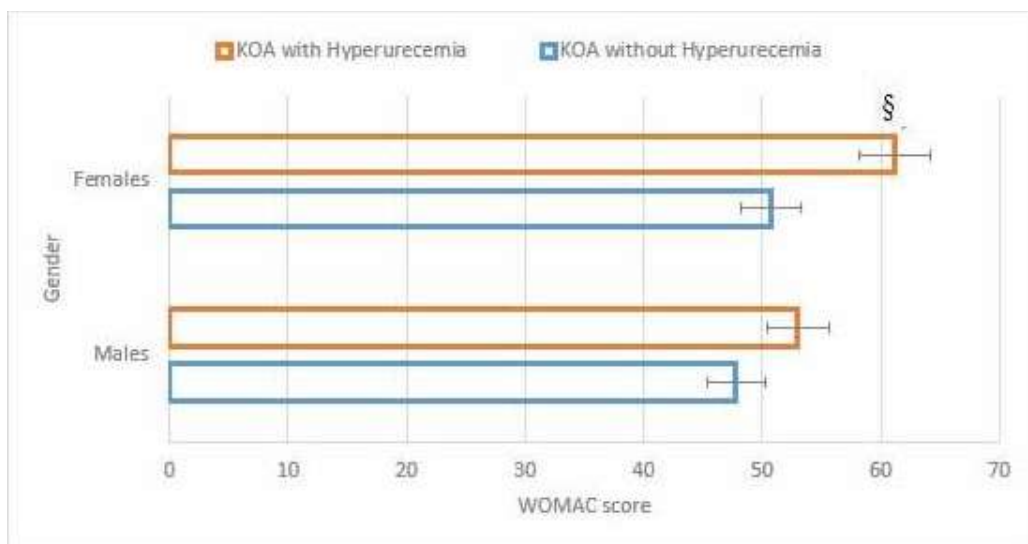


Fig. 1: WOMAC score with KOA (Knee Osteoarthritis) with and without hyperuricemia in males and females. Although differences in WOMAC score with and without hyperuricemia was seen in both males and females, Statistical significance is seen in females. • Mean statistical significance (p=0.029)

Discussion

The beginning and progression of knee osteoarthritis is determined by the surrounding environmental factors, mechanical forces, structural alteration and genetic factors.⁸ Aetiology of OA still remain unclear but various factors contribute to risk and progression which include obesity, joint malalignment, trauma, age and female gender.⁹ Shared pathophysiological features have been identified between crystal induced inflammation and OA recently, however the data from various studies regarding the relation between uric acid and OA still remains controversial.¹⁰⁻¹⁵ One cross sectional study that used the New Haven 1960 Census identified an association between uric acid and whole body OA.¹⁰ However, subsequent retrospective studies, including the Health and Nutrition Examination Survey, Framingham Heart Study Cohort and Chingford Study, demonstrated no association between knee OA and the serum uric acid level.¹⁶⁻¹⁸ Results from different cohort studies that found that uric acid was associated with the severity or susceptibility of OA lost statistical significance after adjusting for covariates including age, BMI, or gender.^{14,15} Recently, different groups have suggested that the highest tertile of uric acid level is associated with generalized OA or osteophytes in knee OA.^{11,19}

The study population showed a female preponderance in the present study. Other studies had more of male preponderance. Jain et al.²⁰ had a study group comprising of 66.2% males and 33.8% females. Ding x et al¹⁹ had a study group which had 52.3% males and 33.8% females. Challa et al.²¹ conducted a study which comprised of 67.6% males and 32.4% females, While the study by Kim et al.²² showed a female preponderance similar to current study with 42.7% male and 57.3% females. The current study population had 59% females and males were 41%.

Study by Ding et al.¹⁹ demonstrated out of 775 patients with hyperuricemia 72.4% were males and 27.6% were females. In the study by Sujit Jos et al.²³ out of 154 patients with hyperuricemia 78% were males while 28% were females, therefore both the studies showed male preponderance towards hyperuricemia however the current study had equal no of males (50%) and females (50%) with hyperuricemia implying insignificant correlation between hyperuricemia and either gender.

In this study there was female preponderance towards developing KOA. Study by Kim et al.²² had total no of 669 patients with OA out of which 112(16.7%) were males and 557(83.3%) were females. Challa et al.²¹ carried a study in which total number of KOA patients were 187 out of which 134 (71.6%) and 53 (28.3%) were females. In the study by Sujit jos et al.²³ out of 183 total KOA patients 131(71.6%) were males and 52 (28.4%) were females. All the studies showed male preponderance towards developing KOA but in the current study we found statistically significant distribution of gender in developing OA knee. Fifty-seven patients had OA knee out of which 39 (69.4%) were females and 18 (31.6%) were males, showing statistically significant correlation of female gender to develop KOA when compared to males ($p=0.016$).

In our present study, we have observed positive correlation of presence of hyperuricemia with knee osteoarthritis. There was no statistically significant correlation between the level of hyperuricemia and the severity of osteoarthritis among the subjects. The positive correlation was also observed as high ESR and higher levels of CRP among subjects with OA knee in our study. Possible explanation of observation of positive incidence of hyperuricemia with KOA but statistical variations observed may be due to confounding factors like age distribution, BMI, menopause in female. In our study we found higher WOMAC scores in subjects with Osteoarthritis and Hyperuricemia as compared to patients without hyperuricemia. Women had higher WOMAC score for the same grade of OA as compared to male counterpart. The increase in both hyperuricemia and OA in women after menopause may point to hormonal mechanisms. Despite this limitation our study successfully points towards positive association of hyperuricemia with knee osteoarthritis warranting further evaluation.

Conclusion

We conclude that the presence of hyperuricemia, is associated with increased knee OA prevalence and severity especially in women. Measurement of serum uric acid levels is an inexpensive utility which can serve as a biomarker for osteoarthritis progression. The potential help of uric acid lowering drugs to limit OA progression requires further investigations.

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References

1. Kapoor M, Martel-Pelletier J, Lajeunesse D, et al. Role of proinflammatory cytokines in the pathophysiology of osteoarthritis. *Nat Rev Rheumatol*. 2011;7(1):33–42.
2. Sellam J, Berenbaum F. The role of synovitis in pathophysiology and clinical symptoms of osteoarthritis. *Nat Rev Rheumatol* 2010; 6: 625–35
3. Simkin PA. The pathogenesis of podagra. *Ann Intern Med* 1977;86:230–3
4. Denoble AE, Huffman KM, Stable r TV, et al. Uric acid is a danger signal of increasing risk for osteoarthritis through inflammasome activation. *Proc Natl Acad Sci U S A*. 2011;108(5):2088–93
5. Blagojevic M, Jinks C, Jeffery A, Jordan KP. Risk factors for onset of osteoarthritis of the knee in older adults: a systematic review and meta-analysis. *Osteoarthritis Cartilage* (2010) 18(1):24–33.10.1016/j.joca.2009.08.010
6. Ma CA, Leung YY. Exploring the link between uric acid and osteoarthritis. Vol. 4, *Frontiers in Medicine*. Frontiers Media S.A.; 2017.
7. Leung YY, Allen JC, Jr, Noviani M, Ang LW, Wang R, Yuan JM, et al. Association between body mass index and risk of total knee replacement, the Singapore Chinese Health Study. *Osteoarthritis Cartilage*. 2015;23(1):41–7.
8. Vincent KR, Conrad BP, Fregly BJ, Vincent HK. The pathophysiology of osteoarthritis: a mechanical perspective on the knee joint. *PM & R*. 2012;4(5):S3-9.
9. Saag KG, Choi H. Epidemiology, risk factors and lifestyle modifications for gout. *Arthritis research & therapy*. 2006;8(1):S2.
10. Acheson RM, Collart AB. New Haven survey of joint diseases. XVII. Relationship between some systemic characteristics and osteoarthrosis in a general population. *Annals of the Rheumatic Diseases*. 1975;34(5):379-87.
11. Sun Y, Brenner H, Sauerland S, Günther KP, Puhl W, Stürmer T. Serum uric acid and patterns of radiographic osteoarthritis—the Ulm Osteoarthritis Study. *Scandinavian journal of rheumatology*. 2000;29(6):380-6.
12. Krasnokutsky S, Oshinsky C, Attur M, Ma S, Zhou H, Zheng F, et al. Serum Urate Levels Predict Joint Space Narrowing in Non-Gout Patients With Medial Knee Osteoarthritis. *Arthritis Rheumatol*. 2017;69(6):1213–20.
13. Roddy E, Doherty M. Gout and osteoarthritis: a pathogenetic link? *Joint Bone Spine* (2012) 79(5):425–7.
14. Bagge E, Bjelle A, Eden S, Svanborg A. Factors associated with radiographic osteoarthritis: results from the population study 70-year-old people in Göteborg. *The Journal of rheumatology*. 1991; 18(8):1218-22.
15. Schouten JSAG, Van Den Ouweland FA, Valkenburg HA. A 12 year follow up study in the general population on prognostic factors of cartilage loss in osteoarthritis of the knee. *Ann Rheum Dis*. 1992;51(8):932–7.
16. Felson DT, Anderson JJ, Naimark A, Walker AM, Meenan RF. Obesity and knee osteoarthritis. The Framingham Study. *Ann Intern Med*. 1988;109(1):18–24.
17. Anderson JJ, Felson DT. Factors associated with osteoarthritis of the knee in the first national Health and Nutrition Examination Survey (HANES I) evidence for an association with overweight, race and physical demands of work. *American journal of epidemiology*. 1988;128(1):179-89.
18. Hart DJ, Doyle DV, Spector TD. Association between metabolic factors and knee osteoarthritis in women: the Chingford Study. *The Journal of rheumatology*. 1995;22(6):1118-23.
19. Ding X, Zeng C, Wei J, Li H, Yang T, Zhang Y, et al. The associations of serum uric acid level and hyperuricemia with knee osteoarthritis. *Rheumatol Int*. 2016;36(4):567–73.
20. Jain S, Jain M. A prospective study on association of serum uric acid level with knee osteoarthritis. *Int J Med Res Rev*. 2016;4(3):289–93.
21. Supradeeptha C, Shandilya SM, Naresh A, Satyaprasad J. Association of hyperuricemia and osteoarthritis knee in costal indian population. *International Journal of Recent Trends in Science And Technology*. 2013;7(3):129-31.
23. Jos S, Anand R, Nazar N, Jose R. A study of the association between hyperuricemia and knee osteoarthritis in the coastal Indian population. *Int J Res Med Sci*. 2018;6(9):3076.

How Efficacious is Esmolol in Suppressing the Stress Response to Laryngoscopy and Intubation in ENT Surgeries

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Abstract

Introduction: Attenuation of stress response during laryngoscopy and intubation has been one of the major concerns of the anaesthetist. Various techniques have been used to suppress this response like deepening the level of anaesthesia and various drugs like β blockers, local anaesthetic etc. In this study Esmolol was used to suppress the stress response.

Material and Method: 60 patients undergoing elective ENT surgery under general anaesthesia of ASA grade I and II were randomly divided into two groups of 30 each. Group I (n=30)-Control –no drug was given. Group II (n=30)-patients received pretreatment with Injection Esmolol 0.5mg/kg.

Results: The results were tabulated and statistically analyzed with student t-test and Chi square test using ANOVA (analysis of variance).

Conclusion: Esmolol attenuates the stress response to laryngoscopy and intubation in the form of increase in pulse rate and blood pressure and that esmolol given 3 minutes before induction provides stable cardiovascular conditions as compared to the control group and attenuates the pressor response but does not obliterate it completely.

Keywords: *Esmolol, Stress Response, Laryngoscopy, Intubation.*

Introduction

Induction of anaesthesia, laryngoscopy and intubation are associated with various stress responses. Increase in blood pressure and heart rate occurs most commonly from sympathetic discharge due to laryngotracheal stimulation, which leads to increased plasma nor epinephrine concentrations.¹ The circulatory perturbations consist of elevations in heart rate and systemic^{2,3} and pulmonary artery pressures⁴ which occasionally lead to myocardial ischaemia, heart failure

and cerebrovascular catastrophies.^{5,6} These changes start within seconds of laryngoscopy, peak within 1-2 minutes and return to control level within 5 minutes. Various techniques and drugs have been used to attenuate these cardiovascular responses like deepening the anaesthesia, pretreatment with ganglion blockers, β blockers, calcium channel blockers and vasodilators. Also prior administration of local anaesthetics, topical anaesthesia of upper respiratory passages and use of narcotic analgesics. β blockers like esmolol minimize the increase in heart rate and myocardial contractility by attenuating the positive chronotropic and inotropic effects of increased adrenergic activity. Esmolol is an ultra short acting β 1 adrenoceptor antagonist with rapid onset and a plasma half life of approximately 9 minutes.⁷ The primary objective of our study was to study the efficacy of esmolol in blunting the haemodynamic response to laryngoscopy and intubation

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Material and Methodology

The prospective randomized study was done on 60 patients of ASA I and II grade, aged 20-60 years, of either sex undergoing elective ENT surgery under general anesthesia at a tertiary care centre after approval by the institute ethical committee. The following patients were excluded from the study, those with coronary artery disease, heart failure, IInd and IIIrd degree heart block, ASA grade III/IV, Mallampati grade III and IV. A written informed consent was taken from all the patients. All the patients were kept nil per oral for at least 8 hours. Patients were randomly divided into two groups. In Group I (n=30)-Control Group -no drug was given and in Group II (n=30) patients received pretreatment with injection Esmolol 0.5mg/kg. In the operation theatre, routine monitors like ECG, pulseoximetry and NIBP were attached. Premedication was done with injection Midazolam 1mg and injection Fentanyl 2µg/kg in both the groups. After stabilization time of 5 minutes, pulse rate, blood pressure and ECG were recorded (baseline =T0) Patients were pre-oxygenated with 100% oxygen for 3 minutes. For control group, T1 measurement was taken just before anaesthetic induction. In group II, injection esmolol 0.5mg/kg was given and pulse rate and blood pressure recording was done 3 minutes after pretreatment(T1). Induction was done Injection Propofol 2mg/kg followed by Injection Suxamethonium 2mg/kg I/V. Following successful intubation, anaesthesia was maintained by nitrous oxide and oxygen mixture and isoflurane 1-1.5% and injection vecuronium bromide as musclerelaxant. After the surgery anaesthesia was reversed with injection neostigmine 0.05mg/kg and injection glycopyrrolate 0.01mg/kg. Blood pressure and pulse rate were recorded as follows. T0-Preinduction baseline, T1-3 minutes after giving the study drug, T2-after giving the induction agent propfol, T3-1 minute after intubation, T4-3 minute after intubation, T5-5 minute after intubation.

Statistical Analysis: Data was analyzed using Statistical Package for Social Sciences (SSPS) version 17 for windows. Categorical data like gender was presented as numbers. Age, weight, heart rate and blood pressure were presented as Mean±SD. Intra group comparison of mean heart rate was done using ANOVA. The p value ≤0.05 was considered significant.

Results

The mean age of group I was 35.87±11.97 and of group II was 38.17±11.70 and difference between both

the groups was statistically non significant. (p>0.05). The mean weight of group I was 50.03±7.31 and of group II was 55.33±11.56 and the difference between them was statistically non significant (p>0.05). There were 36% males and 64% females in group I and 30% males and 70% females in group II. (Table 1)

The mean baseline heart rate (T0) of group I was 82±6.659 and of group II was 85.37±11.156. At 1 minute after intubation (T3) the mean pulse rate of group I was 122.07±7.799 and in group II was 100.47±12.011 beats per minute and the difference between both the groups was highly significant. At 3 minute after intubation (T4) the mean pulse rate of group I was 117.60±7.990 and of group II was 97.20±15.992 and the difference between both the groups was highly significant. At 5 minute after intubation (T5), the mean heart rate of group I was 114.67±8.470 and of group II was 90.50±10.382 and the difference between both the groups was highly significant. (Table 2)

The mean baseline systolic blood pressure (SBP) (T0) of group I was 123.30±6.176 and of group II was 124.33±7.858 mm Hg. At 1 minute after intubation (T3) the mean SBP of group I was 169.03±8.471 and in group II was 138.57±12.519 and the difference between both the groups was highly significant. At 3 minute after intubation (T4) the mean SBP of group I was 155.07±7.692 and in group II was 129.27±9.490 and the difference between both the groups was highly significant. At 5 minute after intubation (T5), the mean SBP in group I was 152.67±9.018 and in group II was 120.40±7.885 and the difference between both the groups was highly significant. (Table 3)

The mean baseline diastolic blood pressure (DBP) (T0) of group I was 79.53±3.627 and of group II was 81.20±4.390 mm Hg. At 1 minute after intubation (T3) the mean DBP of group I was 107.27±6.443 and of group II was 89.27±11.537 and the difference between both the groups was highly significant. At 3 minute after intubation (T4) the mean DBP of group I was 100.20±5.44 and in group II was 86.27±7.894 and the difference between both the groups was highly significant. At 5 minute after intubation (T5), the mean DBP in group I was 99.00±6.057 and in group II was 80.10±7.625 and the difference between both the groups was significant. (Table 4).

The mean arterial pressure MAP (T0) in group I was 92±5.02 and in group II was 89.17±7.03 mm Hg. At 1 minute after intubation (T3) the mean arterial pressure of

group I was 115.08 ± 4.72 and in group II was 102.32 ± 8.79 and the difference between both the groups was highly significant. At 3 minute after intubation (T4) the mean arterial pressure of group I was 112.10 ± 4.92 and in group II was 93.71 ± 7.32 and the difference between

both the groups was highly significant. At 5 minute after intubation (T5), the mean arterial pressure in group I was 105.50 ± 3.40 and in group II was 94.80 ± 4.46 and the difference between both the groups was significant. (Table 5).

Table 1: Comparison of Demographic variables of patients in both the groups

Variables	Group I (n=30)	Group II (n=30)	p value	Statistical Significance
Age (Years)	35.87 ± 11.91	38.17 ± 11.70	>0.05	NS
Gender (Male/Female)	11/19	9/21	>0.05	NS
Weight (Kg)	50.33 ± 7.31	55.33 ± 11.56	>0.05	NS

Table 2: Comparison of Heart rate between both the groups

Time	Group I (n=30)	GroupII (n=30)	T value	P value	Statistical Significance
T0	82 ± 6.659	85.37 ± 11.156	1.419	>0.05	NS
T1	78.40 ± 6.667	79.20 ± 11.149	0.337	>0.05	NS
T2	78.40 ± 6.667	79.07 ± 11.546	0.274	>0.05	NS
T3	122.07 ± 7.799	97.47 ± 16.389	7.424	<0.001	S
T4	117.60 ± 7.990	97.20 ± 15.992	6.250	<0.001	S
T5	114.67 ± 8.470	90.50 ± 10.382	9.879	<0.001	S

Table 3: Comparison of Systolic blood pressure (SBP) between both the groups.

Time	Group I (n=30)	GroupII (n=30)	T value	P value	Statistical Significance
T0	123.30 ± 6.176	124.33 ± 7.858	0.446	>0.05	NS
T1	116.67 ± 5.523	111.80 ± 8.083	0.069	>0.05	NS
T2	134.13 ± 9.240	111.30 ± 8.470	0.802	>0.05	NS
T3	169.03 ± 8.471	138.57 ± 12.519	0.217	<0.001	S
T4	155.07 ± 7.692	129.27 ± 9.490	0.285	<0.001	S
T5	152.67 ± 9.018	120.40 ± 7.885	1.871	<0.001	S

Table 4: Comparison of Diastolic blood pressure between both the groups.

Time	Group I (n=30)	GroupII (n=30)	T value	P value	Statistical Significance
T0	79.53 ± 3.627	81.20 ± 4.390	1.603	>0.05	NS
T1	77.07 ± 6.883	71.60 ± 8.211	2.795	>0.05	NS
T2	75.97 ± 8.219	70.30 ± 7.760	2.746	>0.05	NS
T3	94.27 ± 6.443	89.27 ± 11.537	2.072	<0.05	S
T4	90.20 ± 5.448	86.27 ± 7.894	1.846	<0.05	S
T5	88.00 ± 6.057	80.10 ± 7.265	7.470	<0.05	S

Table 5: Comparison of Mean blood pressure between both the groups.

Time	Group I (n=30)	GroupII (n=30)	P value	Statistical Significance
T0	92.47 ± 5.02	89.17 ± 7.03	>0.05	NS
T1	89.53 ± 6.07	84.133 ± 7.36	>0.05	NS
T2	87.55 ± 36.22	96.94 ± 8.87	>0.05	NS
T3	115.08 ± 4.72	102.32 ± 8.79	<0.05	S
T4	112.10 ± 4.92	93.71 ± 7.32	<0.05	S
T5	105.50 ± 3.40	94.80 ± 4.66	<0.05	S

Discussion

The noxious stimuli of laryngoscopy and intubation produce marked sympathetic responses manifesting as tachycardia and hypertension. Anaesthetics use a wide variety of techniques and drugs to obtund these responses. Esmolol a cardioselective β adrenergic blocking agent is used to blunt the stress response due to its short duration of action as it is metabolized by plasma esterases.

Patients in both the groups did not differ significantly with respect to the demographic data ie age weight and sex.

In our study in group I there was a 32% increase in the pulse rate with an average increase of 40.07 beats/min as compared to the baseline value at 1 minute interval after intubation, whereas in group II after the administration of esmolol hydrochloride there was an increase of 12.1 beats/min (12%). Helfman et al. (1991) studied the effects of esmolol in a dose of 150mg post laryngoscopy and intubation and observed that there was a significant fall in heart rate from 98 beats per minute to 78 beats per minute with a mean change of 15%.⁸

In the present study the average increase in SBP was 27% in the control group at 1min interval after intubation. There was a 10.2% increase in SBP at 1minute interval after intubation in the esmolol group which came near to baseline value 5 minute after intubation. Kumar et al. (2003) observed that there was an average rise in SBP (19.6%) immediately after intubation in the control group. Esmolol group showed significantly less rise in SBP (6%) after intubation.⁹

In our study in group I there was no significant change in DBP at 3min interval and following induction. At 1 minute interval after intubation there was a rise in DBP by 27.74 mmHg (25.8%) and a rise in DBP by 19.47 mmHg at 5minute interval after intubation. Where as in group II at 1 minute interval after intubation there was rise in DBP by 11 mmHg (11.9%) which was statistically significant. At 3and 5 minute interval after intubation, the mean DBP returned to the baseline value. Taneja et al. (2003) in their study showed that a highly significant rise in DBP was observed in control as well as the esmolol group after following laryngoscopy and intubation which returned to baseline values at 4 minute after intubation in the control group and 2 minute after intubation in the esmolol group.¹⁰

In our study in group I there was no significant

change in MAP at 3min interval and following induction. At 1 minute interval after intubation there was a rise in MAP by 22.61 mmHg (19.64%) and a rise in MAP by 13.03 mmHg at 5 minute interval after intubation. Where as in group II at 1 minute interval after intubation there was rise in DBP by 13.15mmHg (12.5%) which was statistically significant. At 5 minute interval after intubation, the mean MAP returned to the baseline value. Lui et al. (1986) in their study observed that the rise in MAP was 19mmHg (18.4%) after intubation in the esmolol group as compared to 30 mmHg (31.25%) in the control group which was statically highly($p < 0.001$).¹¹ Also Ebert et al. (1989) compared the effects of placebo, fentanyl and esmolol in circulatory response to laryngoscopy and found that the mean change in MAP in the esmolol group was 16.2mmHg(13.3%) after intubation as compared to 32.3mmHg (24%) in the control group. The rise in MAP was statistically highly significant in both the groups at 1minute after intubation and returned to the baseline value in the esmolol group at 5 minute after intubation which was statistically non significant ($p > 0.05$).¹²

Conclusion

Laryngoscopy and endotracheal intubation does produce pressor response in form of increase in pulse rate and blood pressure and that esmolol given 3 minutes before induction provides stable cardiovascular conditions as compared to the control group and attenuates the pressor response but does not obliterate it completely.

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References

1. Sheppard S, EagleCJ, Strunin L. A bolus dose of esmolol attenuates tachycardia and hypertension after tracheal intubation. *Can J Anaesth* 1990;37:202-5.
2. Stoelting RK. Blood pressure and heart rate changes during short duration laryngoscopy for tracheal intubation: influence of viscous or intravenous lidocaine. *Anaesth Anal* 1978;57:197-9.

3. Prys-Roberts C, Greene LT, Meloche R, Fox P. Studies of anaesthesia in relation to hypertension II: Haemodynamic consequences of induction and endotracheal intubation. *Br J Anaesth* 1971;43:531-46.
4. Sorenson MB, Jacobsen E. Pulmonary haemodynamics during induction anaesthesia. *Anaesthesiology* 1977;46:246-51.
5. Roy WL, Edelist G, Gilbert B. Myocardial ischemia during non cardiac surgical procedures in patients with coronary artery disease. *Anaesthesiology* 1979; 51:393-7.
6. Fox EJ, Sklar GS, Hill CH, Villanueva R, King BD. Complications related to the pressor response to endotracheal intubation. *Anaesthesiology* 1977; 47:524-5.
7. Garzynski RJ, Shaffer JE, Lee RJ. Pharmacology of ASL-8052, a novel β adrenergic receptor antagonist with an ultrashort duration of action. *J. Cardiovasc. Pharmacol* 1983;5668-77.
8. Helfman SM, GoldMartin, DeLisser E, Herrington CA. Which drug prevents tachycardia and hypertension associated with tracheal intubation; Lidocaine, Fentanyl or Esmolol? *Anesth Analg* 1991;72:482-6.
9. Kumar S, Mishra MN, Mishra LS. Comparative study of the efficacy of i.v. esmolol, diltiazem and magnesium sulphate in attenuating hemodynamic response to laryngoscopy and tracheal intubation. *Indian J Anaesth* 2003;47:41-4.
10. Taneja B, Dali JS, Dua CK. Lignocaine Hcl versus Esmolol-influence on cardiovascular responses to laryngoscopy and tracheal intubation. *Anaesth Clin Pharmacol* 2003;19:53-7.
11. Lui PL, Gatt S, Gugino LD, Mallampati SR, Covino BG. Esmolol for control of increases in heart rate and blood pressure during endotracheal intubation after thiopentone and succinylcholine. *Canadian Anaesth Soc Jour.* 1986;33(5):556.
12. Ebert JP, Pearson JD, Gelman S, Harris C, Bradley EL. Circulatory response to laryngoscopy: the comparative effects of placebo, fentanyl and esmolol. *Canadian Journal of Anaesthesia* 1989;36(1.1):301-6.

A Prospective Observational Study Comparing Three Different Techniques of Intubation Using C-Mac Video Laryngoscope

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Abstract

Aim: To compare three different techniques of endotracheal intubation using C-MAC video laryngoscope.

Methodology: A prospective, randomized clinical study. A total 60 patients of ASA physical status I and II, aged 18 – 60 years were randomly divided into three groups of 20 each. In Group NS patients were intubated using ETT alone, Group S – stylet was used and Group B – bougie was used. Comparison was done in terms of time for intubation, procedure time and success rate.

Results: All the patients in B group were intubated in first attempt whereas maximum number of attempts was required in NS group followed by S group. Mean intubation time was least for S group followed by B group and maximum for NS group with significant p value between NS vs S and S vs B. Mean procedure time taken was least for S group followed by NS group and maximum for B with significant p-value between NS vs S group and S vs B.

Conclusion: Use of bougie as an aid to endotracheal intubation performed best as compared to stylet or no stylet when used with conventional C-MAC blade.

Keywords: Conventional C-MAC, no-stylet, stylet, bougie.

Introduction

Airway management is the prime goal in anaesthesia. Orotracheal intubation is the most common way to secure airway.¹The best view for intubation can be achieved by flexion at the cervical spine and extension at the atlanto-occipital joint also known as sniffing position.²Despite continuous efforts of improvements in airway devices, the most common obstacles in anaesthesia, critical care and emergency is unexpected difficult airway.³ Video laryngoscopy provides improved glottic view in comparison to classical Macintosh blade laryngoscopes and attenuated response to hemodynamic instability.⁴

The C-MAC is a video laryngoscope similar to Macintosh blade, with a micro camera at the distal third of the blade, coloured images are transmitted from a distal camera to a display monitor. The video unit displays a magnified colour image from the distal camera.⁵

Studies have been done comparing C-MAC video laryngoscope blade to Macintosh laryngoscope blade in emergency, ICU, predicted difficult intubation, restricted neck movements and found to be superior in terms of higher success rate of first attempt, improved glottic view and decreased esophageal intubations. Therefore, in our studies we compared different techniques of endotracheal tube placement using stylet, bougie or endotracheal tube alone through C MAC laryngoscope.

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Materials and Method

A prospective, randomized study was conducted after ethical committee clearance in 60 patients at Department of Anaesthesiology, Maharishi Markendeshwar Institute

of Medical Sciences and Research, Mullana, Ambala over a period of 2 years. Informed consent was taken from the patients.

Patients aged between 18 – 60 years, ASA I and II and undergoing elective surgery under general anesthesia were taken. Patients excluded from the study were ASA III, IV or V, patients with anticipated difficult intubations, pregnant patients, any contradiction to use muscle relaxant.

Study Design:

Patients was randomized in one of the three groups by a computer generated randomization:

Group NS – No stylet used. Endotracheal tube alone was used for intubation.

Group S – With stylet. Stylet was used along with tube.

Group B – With bougie. Bougie was placed first and then tube is passed over it.

Anaesthetic Technique: Standard NPO guidelines was followed and patients were kept fasted overnight. Tab. Alprazolam 0.25mg and Tab Ranitidine 150mg was given on previous night and on the coming morning of surgery as pre medication.

Inside the operation theatre (OT) availability of C-MAC videolaryngoscope was checked, charging status and proper functioning of equipment was ensured. The usual baseline heart rate (HR), non-invasive blood pressure (NIBP) and oxygen saturation (SpO₂) of the patient was recorded.

After securing intravenous access in the OT patient was pre oxygenated by manual ventilation for three minutes. In the meantime, appropriate sized endotracheal tube was selected. Induction was achieved with fentanyl 12mcg/kg, etomidate 0.3mg/kg followed by rocuronium 0.9mg/kg after confirming mask ventilation. Maintenance of anaesthesia was done with isoflurane, 40% oxygen, nitrous oxide and vecuronium 0.1mg/kg.

With the use of C-MAC videolaryngoscope Macintosh blade was inserted through midline up to

the valleculum, tongue was shifted and depressed along with lifting of epiglottis with the tip of the blade. After visualization of the vocal cords endotracheal intubation was done according to the group in which the patient belonged (i.e. group NS, S, B). Once successful intubation was done, laryngoscope blade was removed and ETT was connected to a closed circuit, ventilated with 100% oxygen. ETT was secured in place after confirming equal bilateral air entry.

During procedure, if saturation falls below 90%, patient was taken on manual ventilation with 100% oxygen. If failure of intubation occurs, mask ventilation was resumed to achieve SpO₂ of 97%-100%. Next attempt was done using other technique. If intubation was not successful by all three method, then intubation was done with conventional laryngoscope using Macintosh blade.

In our study, the primary outcome was to evaluate time for intubation, time for procedure and number of attempts to intubate. Secondary outcomes were recorded as failed intubations and complications such as desaturation and bradycardia (heart rate less than 20% of baseline).

Parameters to be Recorded:

- 1. Time for Intubation:** Time taken from insertion of the blade between the teeth until the tracheal tube was seen passing through the vocal cords.
- 2. Time for Procedure:** Time for intubation plus etCO₂ trace seen on monitor.
- 3. Success Rate:** No of attempts taken to successfully intubate.

Observation and Result

This prospective randomized study was carried out on 60 patients of age 18 – 60 years and ASA I or II scheduled for elective surgery under general anesthesia.

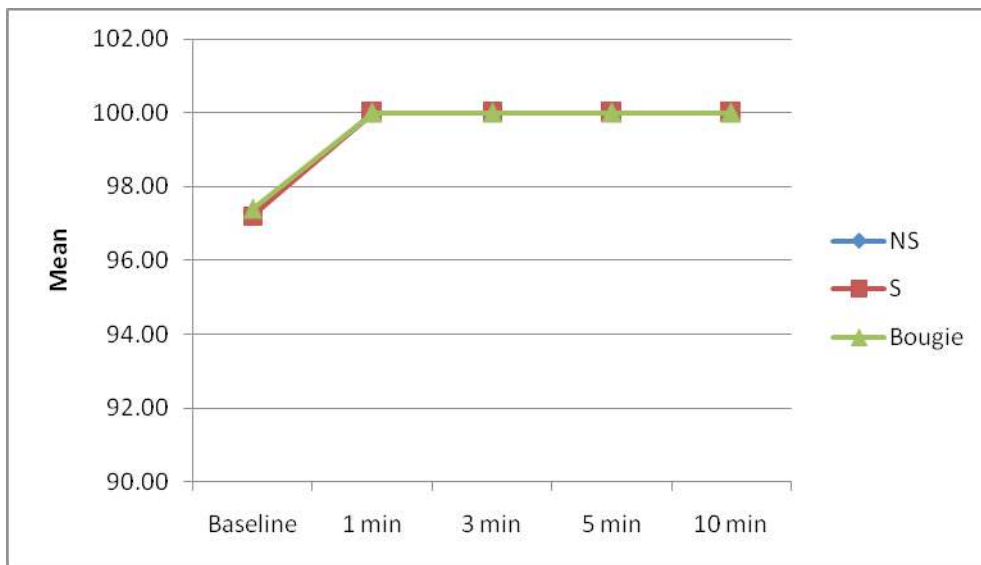
All the patients were comparable in terms of demographic data including age, sex, ASA grade, MP grade.

Table 1: Demographic characteristics

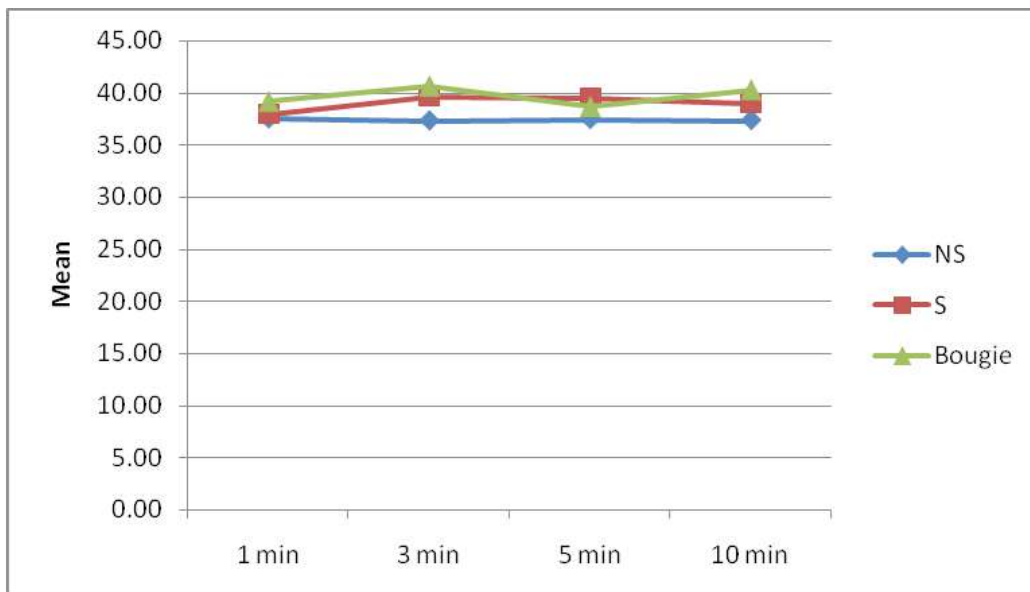
	NS	S	B	p-value
Age (Years) Mean ± SD	31.05 ± 8.68	32.65 ± 9.94	34.05 ± 9.89	0.611
Sex (M/F)	9/11	9/11	15/5	0.089
ASA (I/II)	7/13	10/10	7/13	0.535
MP (I/II)	8/12	8/12	8/12	1.000
Mouth Opening (cms) Mean ± SD	6.44 ± 0.55	6.40 ± 0.52	6.43 ± 0.51	0.971

Table 2: Comparing insertion parameters between three groups

	NS	S	B	p-value
Number of attempts (I/II)	8/12	16/4	20/0	0.000
Intubation time (seconds) Mean ± SD	47.60 ± 10.19	20.10 ± 10.47	47.15 ± 3.77	0.000
Procedure time (seconds) Mean ± SD	72.50 ± 11.59	40.45 ± 12.76	73.50 ± 7.25	0.000



Graph 1: Comparison of SPO2 in Different Time Intervals between the Groups



Graph 2: Comparison of EtCO2 in Different Time Intervals between the Groups

Discussion

Intubation is a lifesaving procedure. Up until the development of video laryngoscopes, classic Macintosh and Miller blade remained unequaled. With development of video laryngoscopes, they are now considered as a vital part in managing airway today. Many studies have now proved that video laryngoscopes provide better view of glottis and improves the operator view during laryngoscopy. They are also used in managing difficult airway and emergency situations.⁶⁻⁸

In our study we evaluated three different techniques of intubation using C-MAC video laryngoscope. Thus after approval from Institutional Ethical committee we conducted a prospective randomized study for a period of two years in which patients were allocated into three groups of twenty each. Informed consent was taken from all patients.

All the study groups were comparable in relation to distribution of age, gender and ASA grading, Mallampati grading and mouth opening.

Number of Attempts for Intubation: Comparing the number of attempts in our study among NS group, 40% of intubations were successful in single attempt while other 60% took two attempts, among S group 80% of intubations were successful in single attempt while 20% took two attempts and among B group 100% of intubations were successful in single attempt. No patient required more than 2 attempts in any group. The p values for NS vs S was 0.022, S vs B was 0.035 and NS vs B was 0.000 which was significant.

Brian E Driver et al conducted a study in which first attempt intubation success rate using C-MAC in Stylet group was 321/366 (88%) as compared to 356/362 (98%) in Bougie group with significant p-value of 0.001 which is in accordance with our study where on comparison between S and B group significant p-value of 0.035 was obtained. So better intubation success in first attempt was seen with B group in our study as well as in Brian E Driver's study.⁹

Bisanth Batuwitige et al. conducted a study in which they were able to intubate all patients successfully in first attempt using bougie which coincides with our study.¹⁰

Dilek Omur et al. compared number of attempts in different groups i.e. no stylet, hockey sticks, d blade

type and, copilot stylet, gum elastic bougie and found significantly higher number of attempts with no stylet in comparison to hockey stick stylet with significant p-value < 0.05 which is in accordance to our study.³

Time for Intubation: In our study the mean intubation time taken by NS, S and B group was 47.60±10.19, 20.10±10.47 and 47.15±3.77 seconds respectively. Hence least time was required by S group and longest duration was taken by NS group. The p-values on comparing NS with S group were 0.000, S group with B was 0.000 which were significant and NS vs B were 0.871 which was non-significant.

Our study is similar to Bisanth Batuwitige et al. study where significant p-value of <0.05 was observed among Stylet and Bougie groups for intubation time.¹⁰

Our study is also in accordance with Renu Sinha et al. who found that time for intubation in non - stylet group was 19.5 seconds and in stylet group was 13.0 seconds with significant p-value of 0.03.¹¹

Study conducted by Dilek et al. stated that time to intubation in non - stylet group was 41.8±18.7 seconds, for stylet group was 17.3±9.8 seconds while for bougie it was 38.6±20.6 seconds with significant difference between non stylet and stylet group as well as stylet and gum elastic bougie group which is similar to our study.³

Pulak Tosh et al. found mean intubation time with Stylet group was 16.97±7.91 and in Bougie group was 77.43±35.55 seconds with statistical significantly (p-value <0.001) lower time required for intubation in stylet group which is in accordance to our study.¹²

Nidhi Gupta et al conducted a study in which mean time for intubation in NS group was 52 seconds whereas for S group it was 27 seconds with significant p value of 0.006 supporting the results of our study.¹³

Procedure Time: In our study the mean procedure time taken by NS, S and B group was 72.50±11.59, 40.45±12.76 and 73.50±7.25 seconds respectively. Hence least time was required by S group and longest duration was taken by B group. The p values on comparing NS with S group was 0.000, S group with B was 0.000 which were significant and NS vs B was 0.771 which was non – significant.

Our study is consistent with studies conducted by D. Omur et al.³ and Renu Sinha et al.¹¹

D.Omur et al. concluded that procedure time for Non-Stylet, Stylet group and Bougie was 55.0±19.3, 30.8±7.9 and 3.9±18.3 seconds with statistically significant p-value of 0.009.³

Renu Sinha et al. noted that time for procedure in Non-Stylet group was 30.5 seconds while for Stylet group it was 24.5 seconds and the p value was 0.02 which was significant.¹¹

Conclusion

The intubation attempts were seen least with bougie group but intubation and procedure time was prolonged. The use of bougie as an aid to intubation is best as compared to stylet or no stylet when used with conventional C – MAC blade.

Conflict of Interest: None

Source of Funding: Self

Ethical Clearance: Ethical Clearance was obtained from the Institutional Ethics Committee (IEC), Maharishi Markandeswar (deemed to be university) Mullana, Ambala.

References

1. Kulkarni AP, Tirmanwar AS. Comparison of glottis visualization and ease of intubation with different laryngoscope blades. *Indian J Anaesth.* 2013;57(2):170-4.
2. Lewis SR, Butler AR, Parker J. Videolaryngoscopy versus direct laryngoscopy for adult patients requiring tracheal intubation. *Cochrane Database of Systematic Reviews.* 2016;11(11):CD011136.
3. Omur D, Bayram B, Kuvaki B. Comparison of different stylets used for intubation with the C-MAC D-Blade videolaryngoscope: a randomized controlled study. *Rev Bras Anesthesiol.* 2017;67(5):450-6.
4. Xue FS, Li HX, Liu YY. Current evidence for the use of C-MAC videolaryngoscope in adult airway management: a review of literature. *Therapeutics and Clinical Risk Management. Ther Clin Risk Manag.* 2017;13:831-41.
5. McElwain J, Malik MA, Harte BH. Determination of the optimal stylet strategy for the C-MAC videolaryngoscope. *Anaesthesia.* 2010;65(4):369-78.
6. Kılıçaslan A, Topal A, Erol A, Uzun ST. Comparison of the C-MAC D-Blade, Conventional C-MAC and Macintosh Laryngoscopes in Simulated Easy and Difficult Airways. *Turk J Anaesthesiol Reanim.* 2014;42(4):182–9.
7. Serocki G, Neumann T, Scharf E, et al. Indirect videolaryngoscopy with C-MAC D-Blade and Glide Scope: a randomized, controlled comparison in patients with suspected difficult airways. *Minerva Anesthesiol.* 2013;79(2):121-9.
8. Serocki G, Neumann T, Scharf E, et al. Indirect videolaryngoscopy with C-MAC D-Blade and Glide Scope: a randomized, controlled comparison in patients with suspected difficult airways. *Minerva Anesthesiol.* 2013;79(2):121-9.
9. Buhari FS, Selvaraj V. Randomized controlled study comparing the hemodynamic response to laryngoscopy and endotracheal intubation with McCoy, Macintosh and C-MAC laryngoscopes in adult patients. *J Anaesthesiol Clin Pharmacol.* 2016;32(4):505–9.
10. Sinha R, Sharma A, Ray BR. Comparison of the success of two techniques for the endotracheal intubation with C-MAC video laryngoscope Miller blade in children: a prospective randomized study. *Anaesthesiology Research and Practice.* 2016;2016:4196813.
11. Goksu E, Kilic T, Yildiz G. Comparison of the C-MAC video laryngoscope to the Macintosh laryngoscope for intubation of blunt trauma patients in the ED. *Turk J Emerg Med.* 2016;16(2):53-6.
12. Cavus E, Neumann T, Doerges V, et al. First clinical evaluation of the C-MAC D-Blade videolaryngoscope during routine and difficult intubation. *Anesth Analg.* 2011;112(2):382-5.
13. Howard-Quijano KJ, Huang YM, Matevosian R, Kaplan MB, Steadman RH. Video-assisted instruction improves the success rate for tracheal intubation by novices. *Br J Anaesth.* 2008;101(4):568–72.

Evaluation of Ambu Aura Gain and Plma in Short Surgical Procedures: A Prospective Randomised Study

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Abstract

Background and Aim: The importance of supraglottic airway devices is soaring high as an aid to intubation and a means to ventilation. Proseal is a modification of classic LMA while Ambu auragain is a newer perilaryngeal sealer. The aim of the study was to evaluate the efficacy of the devices in view of insertion parameters.

Methodology: Study Design: A prospective, randomised study. A total 100 patients of ASA grade I or II, aged 18-65 years, were randomly allocated into two groups of 50 each. In group I (n=50) ambu aura gain was used and in group II (n= 50) PLMA was used. Both the devices were compared in relation to insertion parameters, haemodynamic changes and complications.

Observations and Results: Ambu aura gain was easier to insert (p-0.019), requiring less time for insertion (11.6 versus 13.4 seconds) with p-0.008. Ease of insertion of nasogastric tube was easier with group I (p-0.014). Other parameters and post op complications were comparable.

Conclusion: Ambu aura gain aids easy and rapid insertion along with easy insertion of nasogastric tube as compared with PLMA.

Keywords: Ambu aura gain, PLMA, ease of insertion, efficacy.

Introduction

The placement of second generation SAD is an asset to the difficult airway armamentarium owing to gastric access port and an increased seal pressure.¹ PLMA improves laryngeal seal without increasing mucosal pressure and provides high airway seal pressure with positive pressure ventilation.² Ambu aura gain (AAG) is a new second generation perilaryngeal sealer introduced in 2014.³

The present study, aims to evaluate the efficiency of AAG and PLMA with respect to ease of insertion of device, number of attempts, mean difference in insertion time between both groups, ease of insertion of nasogastric tube (NG), quality of initial airway and confirmation of correct placement by fiberoptic laryngoscopes as a primary outcome measure. Haemodynamic changes and complications that occurred were observed as a secondary outcome measure.

Material and Method

The present study was conducted in the department of Anaesthesiology, Maharishi Markandeshwar Institute of Medical Sciences and Research, (Deemed to be University), Mullana during february 2017-july 2019. After approval of protocol from the Institutional Ethics Committee, 100 adult patients were included in the study as per following inclusion criteria.

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Patients aged between 18- 65 years of either gender, ASA grade I and II with written informed consent were included in the study. Patients excluded from the study were obese patients (BMI >30), with anticipated difficult airway (Mallampati III and IV), patients with a history of difficult intubation, pregnant patients, patients with complaints of sore throat and an oral or laryngeal pathology, patients with cervical spine disease and neck pathology along with non-fasting patients.

Allocation of Groups:

Study Design: Prospective, randomised study.

The study population was randomly divided into two groups with 50 patients in each group. The patients were randomly allocated to either AAG or PLMA group using coded sealed envelope method.

Group 1 (n=50): Insertion of AAG

Group 2 (n=50): Insertion of PLMA

Methodology

A thorough preanaesthetic evaluation was done a day prior to the surgery and all the necessary routine investigations were carried out.

All patients were kept fasting overnight. They were given tab alprazolam 0.25 mg and tab ranitidine 150 mg by mouth on the night before operation and again on the day of surgery at 6.00 am with a sip of water.

In the operation theatre (OT), baseline parameters-oxygen saturation (SpO₂), heart rate (HR), systolic (SBP), diastolic (DBP) and mean blood pressure (MBP) were noted. An intravenous (IV) line was secured with 18G cannula and ringer lactate (RL) 500 ml was started. Patients were premedicated with IV glycopyrrolate (0.005mg/kg), IV midazolam (0.05mg/kg) and IV fentanyl (1µg/kg).

After three minutes of pre oxygenation, anaesthesia was induced with IV propofol (2.5mg/kg) and IV suxamethonium (1mg/kg). Appropriate size of PLMA or AAG was selected according to the weight of the patient and the group allocation.

Following parameters were noted while inserting SAD:

1. Number of attempts: maximum two attempts were allowed for insertion.

2. Insertion time was recorded as the time gap between taking up of the supraglottic device and securing an efficient airway. Maximum of two insertion attempts were allowed considering device as a failure. Alternative device such as an ETT was used in such a situation. Numbers of attempts taken to secure the airway were noted.

3. Ease of insertion was graded as very easy/easy/difficult.
 - Very easy - If the device had placed without resistance and no manoeuvre was required

- Easy - If the device was placed with aid of a single manoeuvre (head hyperextension, mask rotation, finger manipulation)

- Difficult - If resistance present on introduction

- If requirement of manoeuvre was more than one time

4. Ease of insertion of NG was graded as easy and difficult.

5. Assessment of the quality of the initial airway during manual ventilation was judged and graded as

- Excellent- if there was no audible leak;

- Good- if there was an audible leak with sufficient ventilation and EtCO₂ of 40mm Hg or less;

- Poor- if sufficient ventilation required again to position and to place the device.

6. Fiberoptic grading of the airway tube position was carried out for both the groups. The fiberoptic positions were graded as

- grade 1 if vocal cords were visible,

- grade 2 if vocal cords and posterior epiglottis were visible,

- grade 3 if vocal cords and anterior epiglottis were visible and

- grade 4 if vocal cords were not visible.

Fibreoptic grade 1 and 2 was considered as good anatomical placement of device.

Anaesthesia was maintained by N₂O:O₂ mixture (50:50), isoflurane (0.5-0.8%) on spontaneous ventilation. Adequacy of ventilation was observed by SpO₂ and EtCO₂.

The following perioperative complications were observed:

- Gastric insufflation,

- Regurgitation/Aspiration,
- Bronchospasm and Laryngospasm.
- Trauma, sore throat, hoarseness, post-operative nausea and vomiting.

The haemodynamic parameters were monitored at stipulated time intervals.

Statistical analysis: SPSS version20 p-value<0.05 was considered significant. For qualitative data Chi Square test, Fisher Exact Test and for quantitative data student t-test was used.

Observations and Results

The study was conducted on 100 healthy adult patients of ASA grade I and II of either sex, aged 18-65 years, scheduled for elective surgery under general anaesthesia.

The demographic profile including age, gender, BMI, ASA grade, MP grade were comparable in both the groups.

Table 1: Demographic characteristics expressed as mean ± SD

	AAG (n=50)	PLMA (n=50)	p-value
Age (Years) Mean ±SD	38.0±15.7	40.4±14.6	0.231
Gender (M/F)	28/22	19/31	0.071
BMI (kg/m ²) Mean ±SD	23.9±1.6	23.4±1.3	0.134
ASA (I/II)	28/22	26/24	0.688
MP (I/II)	27/23	28/22	0.841

Table 2: SAD insertion related parameters

	AAG (n=50)	PLMA (n=50)	p-value
Ease of insertion (Veryeasy/easy/difficult)	36/13/1	23/21/6	0.019*
Time to insertion (minute)	11.6	13.4	0.008*
Ease of insertion of NG (Easy/difficult)	48/2	40/10	0.014*
No. of attempts (1/2/3)	36/13/1	37/11/2	0.860
Quality of initial airway (Excellent/good/poor)	35/15/0	36/12/2	0.412
Fibreoptic grading (1/2/3)	24/23/3	25/23/2	1.00

* Statistically significant

Table 3: Haemodynamic parameters

	AAG (n=50)	PLMA (n=50)	p-value
Heart Rate (per minute)			
T ₀	83.4±10.2	80.6±11.0	0.198
T ₁	89.8±10.7	89.7±10.8	0.948
T ₂	85.9±8.5	87.5±10.3	0.423
T ₃	79.9±7.8	81.3±9.5	0.435
T ₄	75.3±7.7	76.1±8.3	0.636
MAP (mmHg)			
T ₀	94.7±8.0	92.4±7.7	0.154
T ₁	100.5±7.5	101.4±6.5	0.535
T ₂	95.1±7.9	97.2±6.3	0.157
T ₃	90.2±4.9	91.9±5.5	0.095
T ₄	86.0±5.1	87.6±5.1	0.126

Table4: Side effects among both the groups

Side Effect	AAG (n=50)	PLMA (n=50)	p-value
Sore Throat	4	4	1.00
Hoarseness	4	4	1.00
Cough	3	3	1.00
Any Other	0	0	-

Haemodynamic parameters (HR, SBP, DBP, MAP, SpO₂, EtCO₂) and side effects (intra and post-operative complications) were comparable in both the groups.

Discussion

The anaesthesiologist must ensure a patent airway and adequate ventilation. Till date the cuffed tracheal tube was considered as ideal for providing a safe glottis seal under general anaesthesia.⁴

The laryngeal mask airway (LMA) was introduced in 1982 to simplify airway management. It can often be used instead of tracheal intubation,⁵ therefore avoiding complications specifically associated with it.⁶ Positioning of the first generation LMAs was often found to be difficult.⁷ Their use was also limited by the potential risks of aspiration and instability following insertion.⁸ Several modifications were introduced to

reduce these problems. The second generation of LMAs also allow passage of a tube for gastric decompression.⁹

The PLMA is one of such devices. It is a modification of classic LMA.¹⁰ The cuff of the PLMA is specially designed with an aim to provide a more effective seal around the glottis than CLMA and the drain tube provides a bypass channel for regurgitated gastric contents.¹¹

AAG is a new second generation perilaryngeal sealer introduced in 2014.¹² It is a single use, disposable, cuffed laryngeal mask airway.¹³

Group 1 comprised of 50 patients in whom AAG was used while group II consisted of 50 patients in whom PLMA was used.

In our study, patients in both the groups were comparable with respect to age, gender, BMI, ASA and MP grade and the results were similar with other studies.

Table 5: Comparison of insertion parameters between present study and other studies

Study Author & Year	Ease of Insertion of Device Very Easy/Easy/Difficult			Insertion Time (Seconds)			Ease of Insertion of NG Easy/ Difficult		
	AAG	PLMA	p-value	AAG	PLMA	p-value	AAG	PLMA	p-value
Present study	36/13/1	23/21/6	0.019*	11.6	13.4	0.008*	48/2	40/10	0.0143*
Singh K et al 2017 ¹³	0/18/12	0/22/8	0.273	13.57	11.60	0.001*	21/9	0/30	0.001*
Joshi R et al 2018 ¹⁴	34/11/2	38/8/1	0.3	12	20	<0.001*	46/1	39/8	0.01*

*Statistically significant

As shown in table no. 5: AAG is easier to insert than PLMA as in AAG group insertion of device was very easy in 72% patients, easy in 13% patients and was difficult in only 1% patients while in PLMA insertion of device was very easy in 46% patients, easy in 42% patients and difficult in 6% patients with p-value of 0.019 which was statistically significant.

While in the study done by Singh K et al¹³ and Joshi R et al¹⁴, showed the statistically non-significant results which was non-consistent with our present study.

In our study the mean time required to insert the AAG and PLMA was 11.6 and 13.4 seconds respectively. Statistically the result was significant (p- value=0.008) and was consistent with Joshi R et al¹⁴, study while in the study conducted by Singh K et al¹³, showed more time was required for AAG insertion as compared to PLMA. In his study insertion time for AAG and PLMA was 13.57 and 11.60 seconds respectively. The result was statistically significant (p- value=0.001).

Also the ease of insertion of NG was studied. It

was easy in 96% cases in AAG and 80% in PLMA while it was difficult in 4% cases in AAG and 20% in PLMA group. The result was statistically significant (p -value=0.014) and consistent with the other two studies.

Number of attempts taken to insert the device, quality of initial airway and fibreoptic grade were comparable in both the groups and consistent with other studies.

Haemodynamic parameters[HR (per minute), SBP (mmHg), DBP (mmHg), MAP (mmHg), SPO₂ (%) and EtCO₂ (mmHg)] were compared in both the groups at various time periods as, T0 before the insertion of device, T1 at the insertion of device, T2 at two minutes after the device insertion, T3 at five minutes after the device insertion and T4 after the removal of the device. All the parameters were compared among both the groups at T0, T1, T2, T3 and T4 time interval and the result was comparable among both the groups and was statistically non-significant at all-time intervals. In other studies also similar results were observed.

Side effects such as sore throat, hoarseness of voice, cough and any other side effect were compared in both the groups after the removal of the device and it was found that the results were comparable in both the groups and were statistically non-significant and consistent with other studies.

Limitations of the Study: Because of the smaller study group, the results cannot be extrapolated to a larger population and further studies are required to prove its efficacy as a conduit for endotracheal intubation.

Conclusion

The present study concluded that AAG and PLMA, can be used effectively as an alternative to endotracheal intubation in short surgical procedures. AAG aids easy and rapid insertion as a supraglottic airway device, requiring less time for insertion as compared with PLMA. Also insertion of nasogastric tube was easier with AAG than PLMA. Patients exhibited stable haemodynamic parameters throughout the surgery without any complications hence can be used in clinical practice as a new emerging alternative to endotracheal intubation.

Conflict of Interest: None

Source of Funding: Self

Ethical Clearance: Ethical Clearance was

obtained from the Institutional Ethics Committee (IEC), Maharishi Markandeswar (deemed to be university) Mullana, Ambala.

References

1. Suhitharan T, Teoh WHL. Use of extraglottic airways in patients undergoing ambulatory laparoscopic surgery without the need for tracheal intubation. *Saudi J Anaesth*. 2013 Oct;7(4):436–41.
2. Patel MG, Swadia V, Bansal G. Prospective randomized comparative study of use of PLMA and ET tube for airway management in children under general anaesthesia. *Indian J Anaesth*. 2010 Jan;54(2):109–15.
3. Miller M, Ronald D. *Miller's Anesthesia*. 8 Edition. Saunders; 2014.
4. Lalwani J, Prasad Dubey K, Swaroop Sahu B, Jain Shah Jaya Lalwani P, Jain Shah P. ProSeal laryngeal mask airway: An alternative to ProSeal laryngeal mask airway: An alternative to endotracheal intubation in paediatric patients for endotracheal intubation in paediatric patients for short duration surgical procedures short duration surgical procedures. *Indian J Anaesth* | [Internet]. [cited 2019 Sep 19];54. Available from: <http://www.ijaweb.org/>
5. Ramaiah R, Das D, Bhananker S, Joffe A. Extraglottic airway devices: A review. *Int J Crit Illn Inj Sci*. 2014;4(1):77.
6. Maltby JR, Beriault MT, Watson NC, Liepert D, Fick GH. The LMA-ProSeal is an effective alternative to tracheal intubation for laparoscopic cholecystectomy. *Can J Anaesth* [Internet]. 2002 Oct [cited 2019 Sep 16];49(8):857–62. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/12374716>
7. Lardner DRR, Cox RG, Ewen A, Dickinson D. [Comparison of laryngeal mask airway (LMA)-Proseal and the LMA-Classic in ventilated children receiving neuromuscular blockade]. *Can J Anaesth* [Internet]. 2008 Jan [cited 2019 Sep 19];55(1):29–35. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/18166745>
8. Keller C, Brimacombe J, Kleinsasser A, Loeckinger A. Does the ProSeal laryngeal mask airway prevent aspiration of regurgitated fluid? *Anesth Analg*. 2000;91(4):1017–20.
9. Brimacombe J, Keller C. Laryngeal mask airway

- size selection in males and females: Ease of insertion, oropharyngeal leak pressure, pharyngeal mucosal pressures and anatomical position. *Br J Anaesth.* 1999;82(5):703–7.
10. Qamarul Hoda M, Samad K, Ullah H. ProSeal versus Classic laryngeal mask airway (LMA) for positive pressure ventilation in adults undergoing elective surgery. *Cochrane database Syst Rev* [Internet]. 2017 [cited 2019 Sep 19];7:CD009026. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/28727896>
 11. Brimacombe J, Keller C. The ProSeal laryngeal mask airway: A randomized, crossover study with the standard laryngeal mask airway in paralyzed, anesthetized patients. *Anesthesiology* [Internet]. 2000 Jul [cited 2019 Sep 17];93(1):104–9. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/10861152>
 12. Jagannathan N, Hajduk J, Sohn L, Huang A, Sawardekar A, Gebhardt ER, et al. A randomised comparison of the Ambu® AuraGain™ and the LMA® supreme in infants and children. *Anaesthesia.* 2016;71(2):205–12.
 13. Singh K, Gurha P. Comparative evaluation of Ambu AuraGain™ with ProSeal™ laryngeal mask airway in patients undergoing laparoscopic cholecystectomy. *Indian J Anaesth.* 2017 Jun 1;61(6):469–74.
 14. Joshi R, Rudingwa P, Kundra P, Panneerselvam S, Mishra SK. Comparison of ambu auragain™ and LMA® proseal in children under controlled ventilation. *Indian J Anaesth.* 2018 Jun 1; 62(6):455-60.

Association between CO in Blood and Lung Physique of Toll Road Officers

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Abstract

Introduction: Carbon monoxide (CO) is an odorless and colorless gas produced by incomplete combustion of carbons, its characteristic is easily bonded to hemoglobin rather than oxygen. Short-term immediate visible effect on respiratory tract after inhalation of toxic gas exposure is an inflammatory reaction, whereas restriction and obstruction abnormalities will appear as long-term effects of toxic gas exposure. Therefore, it is necessary to check lung physique to detect pulmonary abnormalities early before clinical complaints found.

Objective: To analyze the association between CO in blood and lung physique of toll road officers.

Method: The samples were male and female, aged 37 - 55 years and had a minimum of 20 years working hours. Samples were collected by random sampling and statistically analyzed using SPSS (SPSS, Inc., Chicago, IL).

Result: The level of CO in blood of toll road officers are higher than CO levels in the air. It was obtained restriction and obstruction abnormalities. There was no significant association between blood levels of CO and FEV1, FEV1/FVC, and PEFr but there was a significant relationship between blood CO concentration and FVC.

Conclusion The exposure of CO to toll road officers caused decreased ventricular lung function. There were obstructive and restrictive abnormalities of the lung. The level of CO in the blood did not correlate with most of pulmonary physiological parameters.

Keywords: *Blood levels of Carbon Monoxide, Lung Physiological Examination, Toll Road Officers, Carbon Monoxide Exposure.*

Introduction

Rapid economic progress drives an increasing transportation needs, on the other hand the natural environment that supports human needs is increasingly threatened by quality, thus the negative effects of air pollution on human life are increasingly growing ⁽¹⁾.

Short-term immediate visible effect on respiratory tract after inhalation of toxic gas exposure is an inflammatory reaction, whereas restriction and obstruction abnormalities are long-term effects after toxic gas exposure, but few researchers have investigated the long-term effects of exposure inhalation of toxic gas ⁽²⁾. One of these toxic gases is carbon monoxide (CO). CO is an odorless, colorless gas produced by incomplete combustion of carbon, its nature is easily bonded to hemoglobin rather than oxygen, thus oxygen supposedly bound to hemoglobin is replaced by CO resulting in tissue cyanosis ⁽³⁾.

Some previous studies suggested that CO has a negative effect on the body. Previous research examined

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the acute and chronic respiratory complaints of toll gate workers and administrative workers in Taiwan (4). The results found significant differences for acute respiratory tract complaints on toll gate workers compared to administrative workers, while for chronic complaints there was no significant difference. Another study of the acute effects of cardiorespiratory system on smokers using pipes reported that after 2 hours, there was an increase in HbCO, blood pressure, and transient pulse, decrease FVC, PEFr and decrease percentage of eosinophil in the blood. Another study of in and out of town workers due to air pollution caused by various types of vehicles in Nigeria showed the highest impact for motorcycle users and smokers with FVC <80% and FEV1/FVC <70% (5).

Examination to measure respiratory function is pulmonary physiological examination. Lung physique is parameter used to assess any changes or anatomical abnormalities of the lung influencing lung function (6). A pulmonary physiological examination can detect early pulmonary abnormalities before clinical complaints. The Central Bureau of Statistics states that the use motor vehicles since 1987-2012 increased significantly. In 2012, the growth of motor vehicles was 94,373,324 units. The decline of air quality occurred over the last few years indicates that it is important to promote emissions reduction efforts by socializing industrialists and communities or by conducting research for the application of emission reduction technologies (7).

PT Jasa Marga (Persero) Tbk is a State-Owned Enterprise engaged with toll road service providers. High vehicle sales growth and better regulatory authority policy will make Jasa Marga's position stronger in toll road industry in Indonesia. The officers have a high risk of CO exposure that can interfere health, especially respiratory function. In addition, studies about relationship between CO gas and lungs in Indonesia are still limited.

Method

The subjects of this research were employees of PT. Jasa Marga who worked on the gate and administration of Waru - Sidoarjo Toll road that met the criteria of inclusion and exclusion. Inclusion criteria were ≥10 year working time, having the same shift, aged 30-55 years, able and cooperatively underwent CO testing in the blood and lung physique (FVC, FEV1, FEV1/FVC and PEFr). Exclusion criteria were having lung disease

history based on existing medical record data, which might affect the lung function (6).

This research was conducted at toll road of waru-sidoarjo owned by PT. Jasa Marga Tbk. The data collection was done based on: reading and recording medical record data, filling questionnaire and physical examination, subject demography factor (sex, age, education, place of work, duration of work), and result of CO examination in blood and lung physique (8). The method of analyzing CO in the blood was releasing CO with H2SO4 dilute solution. This free CO was reacted with excess PdCl2 solution, CO would oxidize to CO2 while Pd2+ would be reduced to Pd metal. The residual Pd2+ was reacted with KI dilute solution resulting I2 and Pd. The color of I2 solution (in KI, due to excessive KI) was measured its intensity with the spectrophotometer. By using standard solution, it could be known the concentration of I2 equivalent to PdCl2 which is equivalent to CO. The spectrophotometer worked in double beam spectrophotometer method based on Lamber-Beer (Beer-Lambert-Bouguer) law. While examination of lung physique performed at the time agreed using a portable spirometer device of Koko Legend model 314000.

It was analysed the impact of CO exposure on lung physique using observational analytic statistic of association between lung physiology change and the working hours and habit of using self-protection tool (mask) which functioned to describe the influence of CO exposure on lung abnormalities. The test used is Pearson correlation test with significant value of p <0.05 using the SPSS program (9).

Result

Table 1: Subject Frequency Distribution

Characteristic		N (%)
Sex	Male	24 (63.2%)
	Female	14 (36.8%)
Age	<41 years	3 (7.9%)
	41 – 45 years	7 (18.4%)
	46 – 50 years	22 (57.9%)
	>50 years	6 (15.8%)
Education	Elementary	1 (2.6%)
	Junior High School	1 (2.6%)
	Senior High School	28 (73.7%)
	College	8 (21.1%)
Work place	Indoor (non-counter)	15 (39.5%)
	Outdoor (counter)	23 (60.5%)

Characteristic		N (%)
Working hours	11 – 20 years	10 (26.3%)
	21 – 30 years	26 (68.4%)
	>30 years	2 (5.3%)
Pulmonary restriction	Mild	15 (39.5%)
	Normal	23 (60.5%)
Pulmonary obstruction	Moderate	7 (18.4%)
	Mild	11 (28.9%)
	Normal	20 (52.6%)

*pulmonary physical abnormalities criteria based on Pneumobile Project Indonesia

Distribution of subject’s characteristics can be seen in Table 1. Most of them were male as many as 24 (63.2%), aged 46-50 years as many as 22 (57.9%), high school educated as many as 28 (73.7%), work at counters as many as 23 (60.5%), having work period of 21-30 years as many as 26 (68.4%). Subjects who had restriction lung abnormalities in the normal category was 23 (60.5%) and obstruction in the normal category was 20 (52.6%).

Table 2: Subject’s characteristics based on restriction and obstruction

Characteristic		Restriction		Obstruction		
		Mild	Normal	Moderate	Mild	Normal
Workplace	Outdoor	13 (56.5%)	10 (43.5%)	5 (21.7%)	8 (34.8%)	10 (43.5%)
	Indoor	2 (13.3%)	13 (86.7%)	2 (13.3%)	3 (20.0%)	10 (66.7%)
Smoking status	Smoker	9 (52.9%)	8 (47.1%)	3 (17.6%)	7 (41.2%)	7 (41.2%)
	former smoker	3 (75.0%)	1 (25.0%)	1 (25.0%)	2 (50.0%)	1 (25.0%)
	non-smoker	3 (17.6%)	14 (82.4%)	3 (17.6%)	2 (11.8%)	12 (70.6%)
Mask using	Never	6 (46.2%)	7 (53.8%)	4 (30.8%)	3 (23.1%)	6 (46.2%)
	Sometimes	6 (30.0%)	14 (70.0%)	1 (5.0%)	7 (75.0%)	12 (60.0%)
	Always	3 (60.0%)	2 (40.0%)	2 (40.0%)	1 (20.0%)	2 (40.0%)

It was found that the toll officers who worked at both counter and non-counter had a restriction disorder. Lifestyle of smokers, former smokers and non-smokers also provided different restriction abnormalities. Similarly, the use of masks also obtained different restriction abnormalities, in the case of different mask type used. It was found that toll officers who worked at both counter and non-counter had moderate and mild abnormalities obstruction although some were normal. Smokers, former smokers and non-smokers also provided both abnormal and normal. Similarly, the use of masks obtained different abnormalities of obstruction, where the type of mask used was not the same⁽¹⁰⁾.

Table 3: Distribution of CO in blood based on smoking status and mask using

	Total	Average ±SD (µg/Nm ³)	p
Smoking Status			
Smoker	17	15.85±2.43	0.053
Former Smoker	4	16.34±2.95	
Non-Smoker	17	14.33±2.48	
Mask Using			
Never	13	16.50±2.24	0.482
Sometimes	20	15.37±2.47	
Always	5	14.18±3.39	

The comparative analysis of CO gas in smoking subject was p = 0.053 and using mask subject was p = 0.482. The highest abnormalities is found on subject with outdoor job.

Table 4: Level of CO in blood and lung physique

	Kadar gas CO (µg/Nm ³)	FVC (ltr)	FEV1 (ltr/dtk)	FEV1/FCV (%)	PEFR (ltr/sc)
Total (N)	38	38	38	38	38
Average±SD	15.21 ± 2.56	2.53 ± 0.29	1.66 ± 0.25	0.65 ± 0.07	6.85 ± 1.29

The results showed a minimum value of 10.19 µg/Nm³ and maximum of 18.06 µg/Nm³, with average of 15.2192 µg/Nm³. While CO examination in air East

Java Province Environmental Unit showed the value of 12,549.7 µg/Nm³.

Table 5: Association of CO in blood and lung physique

Variable		FVC	FEV1	FEV1/FCV	PEFR
CO level	r	-0.598	-0.309	0.216	0.274
	p	0.000	0.059	0.193	0.096

There was a significant relationship between CO and FVC levels at the 0.598 with negative prognostic value. This meant that the higher the CO in the blood, the lower the FVC value. While the CO in the blood did not have a relationship with the value of FEV1, FEV1/FVC and PEFR.

Discussion

In this study, the data shows restriction abnormalities by a significant inverse relationship between CO and FVC indicated by negative values that had moderate strength at the level of 0.598 whereas for FEV1, the ratio of FEV1/FVC and the Peak Expiration Flow (PEFR) had no association with CO in the blood. Researchers suspected that abnormalities could be caused by smoking, masks and workplace location. In addition, the effect of nutritional status, location of residence and type of transportation used might also cause deterioration of lung function (4).

Previous research mentioned that non-smokers would experience an average decrease of FEV1 at a rate of 30 ml/year, whereas in smokers there would be an average decline of twice faster, which was about 60 ml/year. It also mentioned that the cessation of smoking would restore the rate of decrease in FEV1 to non-smokers rate. Nevertheless, the inflammatory process would remain in the former smokers, which would lead to narrowing of respiratory tract (11).

Increased HbCO levels could decrease lung volume including vital pulmonary capacity. The relatively stronger and more stable HbCO bond caused decreased oxygen in the lung. Therefore, the ability of Hb in binding oxygen would decrease, resulting in a decrease in diffusion capacity due to carbon monoxide (DLCO) (12). If this happened for a long time it would cause abnormalities of the pulmonary parenchyma structure thus the pulmonary physiological measurement would

obtain decrease value of vital capacity (VC) and total lung capacity (TLC). This finding was consistent with previous studies conducted on 944 tunnel and bridge workers over 3 years of decrease in FVC and FEV1 as well as an increase in HbCO (13). The different results in FEV1 might be influenced by the length of research observation. The results obtained in this study were similar to a study of 510 Taiwan toll-road workers for 1 year that obtained no difference in the prevalence of chronic lung disease. Restriction abnormalities could be expected if a decrease of VC and FEV1/FVC ratio was normal or increased (5).

Overall, there was no significant relationship between blood CO concentration and lung function according to FEV1, FEV1/FVC, PEFR parameters, because only FVC parameter obtained significant relationship. This meant that the lung physique considered homogeneous and the results could be ignored (14). This conclusion might be influenced by several factors such as the existence of a workplace exchange policy where every half hour was switching the counter, in addition to the use of personal protective equipment in the form of masks that were still used by the officers in different type and frequency (15). Another factor was the number of vehicles to be handled by each officer that was not always the same.

Conclusion

It was found a significant relationship of CO in the blood and the decrease of FVC value (p <0.05), which was shown by negative prognostic value with moderate strength at 0.598 level. This meant that the higher the CO gas in the blood, the lower the FVC.

Ethical Clearance: This research involves participants in the process using a questionnaire that was accordant with the ethical research principle based on the regulation of research ethic regulation. The present study was carried out in accordance with the research

principles. This study implemented the basic principle ethics of respect, beneficence, non-maleficence, and justice.

Conflict of Interest: The authors have not found any conflict of interest related to this research so far.

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References

1. Sukoco BM, Suprayogi N, Hidayati NA. The Effects of Market Orientation on Environmental Social Responsibility Programmes: The Moderating Effects of Institutional Pressures. *Pertanika J Soc Sci Humanit.* 2018;
2. Gobel IA, Mukono J, Sukmono RE. Effect of Limestone Dust Exposure on Lung Physiology Decline and Increase of Interleukin6 Level of Blood Serum of Limestone Processing Workers in Kesamben Village, Plumpang Sub-district of Tuban Regency. *Res J Pharm Biol Chem Sci.* 2015;6(4):530–8.
3. Pimpin L, Retat L, Fecht D, de Preux L, Sassi F, Gulliver J, et al. Estimating the costs of air pollution to the National Health Service and social care: An assessment and forecast up to 2035. *PLoS Med.* 2018;15(7):e1002602.
4. Tualeka AR, Kalamillah H, Meidikayanti W. Association between Duration Working with Lung Disruption Condition using Pulmonary Vital Capacity (PVC) Test on Lathe Worker at Yogyakarta, Indonesia. *Indian J Forensic Med Toxicol.* 2019;13(2).
5. Cipolla M, Sorgenti M, Gentile C, Bishara MM. Air Pollution and Lung Diseases. In: *Clinical Handbook of Air Pollution-Related Diseases.* Springer; 2018. p. 327–39.
6. Sentana IWB, Jawas N, Asri SA, Wardani AE. Hybrid CPU and GPU Computation to Detect Lung Nodule in Computed Tomography Images. *Int J Electr Eng Informatics.* 2018;10(3):466–78.
7. Rizki RR, Natalia K, Lepong DRU, Hermawaty T, Wibowo A. An Analysis of Law No. 17 Of 2014 on National Parliamentary Assembly, House of Representative, Regional House Council, and Regional House Representative: Viewed From The Principles of Good Governance. In: *IOP Conference Series: Earth and Environmental Science.* IOP Publishing; 2018. p. 12127.
8. Fahmi MZ, Haris A, Permana AJ, Wibowo DLN, Purwanto B, Nikmah YL, et al. Bamboo leaf-based carbon dots for efficient tumor imaging and therapy. *RSC Adv.* 2018;8(67):38376–83.
9. Zhu Z-Q, Chen L-S, Wang H, Liu F-M, Luan Y, Wu L-L, et al. Carotid stiffness and atherosclerotic risk: non-invasive quantification with ultrafast ultrasound pulse wave velocity. *Eur Radiol.* 2019;29(3):1507–17.
10. Hansell A, Dorion D, de Hoogh K, Probst-Hensch N, Fortier I, Cai Y, et al. Air pollution, lung function and COPD: results from the population-based UK Biobank study. 2019;
11. Choi J, Oh JY, Lee YS, Min KH, Hur GY, Lee SY, et al. Harmful impact of air pollution on severe acute exacerbation of chronic obstructive pulmonary disease: particulate matter is hazardous. *Int J Chron Obstruct Pulmon Dis.* 2018;13:1053.
12. Caravaggio N, Caravella S, Ishizaka A, Resce G. Beyond CO₂: A multi-criteria analysis of air pollution in Europe. *J Clean Prod.* 2019;219:576–86.
13. Dasgupta S, Hamilton K, Pandey KD, Wheeler D. Air pollution during growth: accounting for governance and vulnerability. 2004;
14. Lee AG, Kaali S, Quinn A, Delimini R, Burkart K, Opoku-Mensah J, et al. Prenatal Household Air Pollution Is Associated with Impaired Infant Lung Function with Sex-Specific Effects. Evidence from GRAPHS, a Cluster Randomized Cookstove Intervention Trial. *Am J Respir Crit Care Med.* 2019;199(6):738–46.
15. Gu H, Cao Y, Elahi E, Jha SK. Human health damages related to air pollution in China. *Environ Sci Pollut Res.* 2019;1–11.

Assess the Genetic Variant's Linkage with T2DM in Several Pathways of Pathophysiology of Type-2 Diabetes Mellitus

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Abstract

Type two diabetes mellitus (T2DM) is utmost shared form of diabetes described by the raised plasma glucose levels and instigated because of the both insulin action and secretion's impairment. This is actually turning prevalent while leading to numerous complications. Furthermore, its occurrence and prevalence are surging at a distressing degree in few countries such as Iraq while increasing a main concern of health. Mutually, the environmental and genetic features play an essential role to manifest such composite genetic ailment. The purpose of this research was the recognition of the genomic regions' relatedness.

The few current years showed an outbreak of molecular genetics inspection while comprising the whole genome scans. This was utilized to assess the genetic variant's linkage with T2DM in several pathways of pathophysiology.

Numerous candidate genes are recognized as related to the T2DM, although, merely few of them demonstrates the stability in relationship to various ethnic group and population. Comparatively, because of greater T2DM risk in Iraq as well as the constituent substructure residents and enormous genetic heterogeneity, the number of researches is smaller enough to distinguish the illnesses' genetic base in Iraq.

Keywords: *Genome-wide Association scan (GWAS), Insulin deficiency Candidate genes, Ethnic variability Indian scenario.*

Introduction

The current intense advancement in several affected individuals specifies the lifestyle features associated to the development and inactive professions might be mostly significant in initiating the genetic elements responsible for this diabetes type. Thus, being authoritative to specifically inaugurate the essential environmental & genetic factors after such intricate genetic syndrome in order to initiate the preventive measures^[1].

Our attempt of reviewing the already directed research regarding molecular genetics universally, regarding T2DM and also the ethnic, environmental & epidemiological factors involved in the T2DM expression.

Obesity is the utmost prevailing non-infectious ailment of 21st century which is related to the dispositioning of the triglycerides in hepatocytes moving towards the non-alcoholic NAFLD (fatty liver disease).

Nowadays, NAFLD is about a 3rd of the world population. The epidemiological researches have determined that cultural background is significant factor in complexities and treatment of the disease^[2].

Background: Adjusting for the population stratification's probable impacts which is a substantial concern for the intricate traits of genome wide association studies (GWAS)^[3].

Genetic structure's principal component analysis

(PCA) of population in study having successive integration of initial numerous principal components (PCs) in GWAS regression [4].

In livestock, residual inconsistency has been considered as a background due to the concerns of improving the uniform production. Numerous researches have delivered the indications related to the residual alteration is partly under the control of genetics. Though, some of the examinations have illuminated the genes that control them.

Background and Objectives

Polycystic ovary syndrome (PCOS) is the women's utmost communal disorder of reproductive endocrine with perimenopause. About the specified phenotypic overlap amongst type 2 diabetes mellitus (T2DM) & PCOS, the investigation was done to acknowledge regarding the T2DM implicated genes' association to the vulnerability of PCOS amongst women of city Baghdad.

Introduction

Diabetes mellitus (DM) is a complex heterogeneous group of disorders characterized by persistent hyperglycemia and caused by an absolute or relative deficiency of insulin, which is an anabolic hormone, produced by the beta cells of the islets of Langerhans located in the pancreas. While the World Health Organization (W.H.O) [5, 6] describes DM as a metabolic disorder of multiple etiologies characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, action or both, the American Diabetic Association (ADA) [7-8] defines DM as a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. The different types of Diabetes mellitus include Type1 & 2 and rare forms of MODY and Gestational diabetes

Method

A total of 248 women with PCOS and 210 healthy women as controls were genotyped, in the teaching hospitals in Baghdad governorate. For a panel of 15 single nucleotide polymorphisms (SNPs) from the nine T2DM genes, such as IGF2BP2, TCF7L2, SLC30A8, CDKAL1, HHEX, CDKN2A, IRS1, CAPN10 and PPARG, on SequenomMassARRAY platform [9].

Numerous related researches have deliberated

the significance of illuminating the association amongst the type 2 diabetes development and genetic polymorphism [10].

The pursuit of candidate genes primarily relied on the gene encoding proteins unswervingly incorporated in the T2DM pathophysiology, associated encoders such as development of pancreas, secretion, production and insulin's inactivity [11].

Progressively, several developing investigations recommended the involvement of different other factors in T2DM development, for instance, other molecules & pro-inflammatory cytokines' expression perform in the process of inflammation which also play a crucial role in DM's chronic complications' development [12].

Numerous studies indicate that the impact of several polymorphisms on the cytokines pro-inflammatory genes are a risk for developing the metabolic syndrome, diabetes and obesity [13].

Results

None of the 15 SNPs were observed to be substantially related to PCOS after Bonferroni correction for multiple testing, either in the univariate or multivariate context.

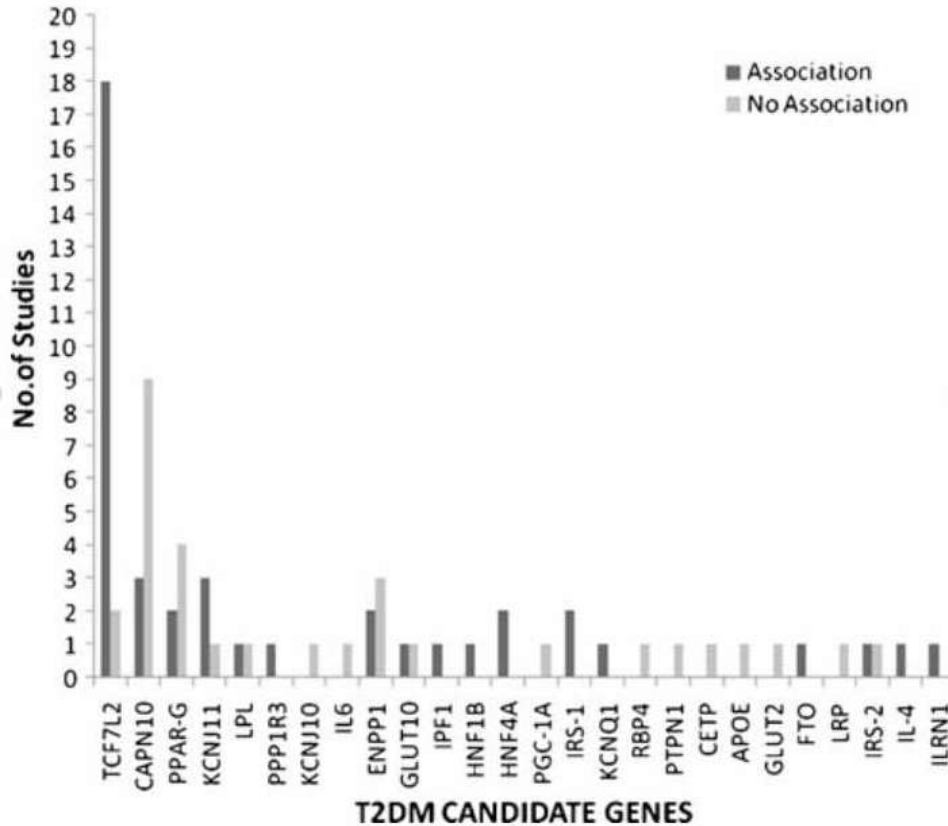
The cumulative effect of risk alleles observed with reference to T2DM was also not seen with reference to PCOS. Interpretation & The latest review of article (18) demonstrated the T2DM genetic base context. The candidate genes list incorporated in the T2DM etiology with particular location of chromosome & genomic regions having specified roles. While, various population's T2DM candidate gene research with their study design and variants are organized. Moreover, Fig.1. Signifies the bar diagram presenting numerous studies with or without several candidate gene & T2DM linkage [8].

Genetic foundations of T2DM is finely demonstrated in the latest article review [14]. Moreover, the candidate genes list incorporated in the T2DM etiology along with relevant locations of chromosomes & region of genome as well as their functions.

Furthermore, the candidate genes of T2DM in several populations with the alterations & study design.

The Fig. (1) Indicate a bar diagram presenting several researches with or without a relationship amongst various candidate genes & T2DM.

T2DM CANDIDATE GENE ASSOCIATION STUDIES



In Caucasians, the GWAS (Genome-wide association studies) have acknowledged the 14 index single nucleotide polymorphism (iSNPs) which stimulates the risk of colorectal cancer (CRC). An estimation about the function of 11 iSNPs or sSNPs (surrogate SNPs) in greater linkage disequilibrium (LD, $r(2) \geq 0.8$) was done inside the 100kb iSNPs' locality in 2000 age & gender matched Singapore Chinese cases (SCH) & controls.

Merely sSNPs, rs7226855, rs2059254, rs11986063, rs3087967, & rs6695584 at 18q21.1, 16q22.1, 8q23.3, 11q23.1, & 1q41, and iSNP rs6983267 at 8q24.21 corresponding lydisclosedindication of linkage with the risk of CRC having odd ratios (OR) in a range from 1.13 to 1.40. Further, the sSNP rs827401 at 10p14 was related to the risk of rectal cancer (OR = 0.74, 95% CI 0.63-0.88) nonetheless the prognosis of illness (OR = 0.91, 95% CI 0.69-1.20).

Amusingly, the sSNP rs3087967 at 11q23.1 was linked to the male CRC risk such as (OR = 1.34, 95% CI 1.14-1.58) in comparison to the women (OR = 1.07, 95% CI: 0.88-1.29), thus, proposing a specified gender function.

The half of the variants recognized for Caucasians, comprising finely mapped loci of BMP pathway i.e. BMP2, GREM1, LAMA 5 and BMP4 did not indicated any confirmation for the relation of CRC in SCH (OR ~1; p-value > 0.1).

Associating these outcomes of research with Hong Kong & Northern Chinese indicated the variants at 10p14, 18q21.1, 11q23.1 & 8q24.21 chromosomes.

Complementary outcomes amongst the Chinese and Caucasians can be because of various genetic heterogeneity, LD patterns and allelic frequencies.

The investigation of intricate genetics for autoimmune diseases has proceeded at an inconceivable speed over former four years. This is due to the thorough conclusions of massive advantages prepared by the GWAS (genome wide association studies). However, new genetic discoveries are unceasingly being testified with the speedy genetic technological growth, huge collection of samples and refined statistical analysis. This is pretty clear now that the multiple genes participate in various complicated genetic ailments while comprising RA (rheumatoid arthritis). There are also several

communal risk factors related to genetics that cause the spectrum autoimmune illnesses [15].

The particulars of recent genetic setting of RA explains about capability of GWAS regarding shared autoimmune risk loci, missing heritability, presence of genetic heterogeneity and subsets of disease.

Moreover, separation of mechanism related to the genes directly encouraging the RA cause will give us a clue about considerate acknowledgement of this sickness. Further it will provide a direct clinical impression and also notifying the improvements of novel therapies used for RA treatment.

The conclusions indicate that extra communal alternates causing the CRC predisposition are still needed to be recognized.

Genome-wide association studies (GWAS) for the colorectal cancer (CRC) acknowledged the 5 regions nearby the genes related to the transforming growth factor β -genes such as GREM1, RPHN2, CDH1, SMAD7 and BMP4.

Accurate risk alleles are still needed to be recognized in such regions as well as their function in non-European population for CRC risks are still required to be studied. Our former research described substantial genetic heterogeneity for GWAS acknowledged single nucleotide polymorphisms (SNPs) amongst the European Americans (EAs) & African American (AAs) [16].

It was hypothesized that associations might not be replicated in AAs because of its independent or differential genetic structure.

Examining this hypothesis, about 1352 controls such as 367 EAs and 985 AAs as well as about 195 tagging SNPs through five regions of genes in 1194 cases of CRC i.e. 795AAs & 399 EAs were genotyped. Further, imputation was done to test the relation among the imputed & genotyped SNPs comprised of covariates, e.g. sex, ancestry and age.

Two out of 5 genes were initially connected to the CRC and indication of such association was observed in AAs containing rs1862748 in CDH1 (ORAdd = 0.82, P = 0.02) as well as in GERM1 SNPs rs10318 (ORRec = 60.1, P = 0.01), rs12902616 (OR Rec = 1.28, P = 0.005) and rs11632715 (ORRec = 2.36; P = 0.004) and finally, linkage disequilibrium with SNP rs4779584 that had

been formerly recognized [17].

Analyzing such associations more generally in the AAs gene regions, we analyzed 3 substantial statistical association peaks in RHPN2 and GERM1 and these were not acknowledge in EAs. It was concluded that several CRC risk alleles were common among the AAs, EAs and other certain populations [18].

DM (Diabetes mellitus) is deliberated as a universal epidemic illness and its form of type 2 includes > 95% of all incidences. Moreover, TNF- α (Tumor necrosis factor-alpha) is considered as a pro-inflammatory cytokine whose dysregulation has been connected to a diverse human illnesses such as T2DM (type 2 diabetes mellitus).

This cytokine's controlled expressions are related to the resistance of insulin that have a resilient genetic impact. This relationship can be considerate through the literature of entire case researches from 2000 to present date.

Further, the frequencies of genotype exhibited in 10 publications of diverse ethnicities were paralleled. The relationship among the T2DM developing risk and TNFA promotor genotypes remained scandalous because of several inconsistencies in various available researches.

The alterations in ethnicity might play a role in such contradictory outcomes from the dispersal of TNFA promoters' polymorphism which is distinct amongst the persons having unrelated racial basis.

Though, the association among the T2DM occurrence & existence of polymorphism at TNFA gene's position 308 is not completely known, therefore, the outcomes of these studies recommended the necessity for additional inquiry [19].

The characterization of diabetes as being a metabolic disorder of numerous etiologies which is categorized by chronic hyperglycemia due to the instabilities of protein, carbohydrates and fats' metabolisms causing from the insulin action or secretion flaws.

Being an anabolic hormone, insulin which is synthesized by pancreas β - cells which endorses the glucose conversion to glycogen in skeletal muscles Insulin through exciting the uptake of glucose and triggering glycogen synthase with the assistance of insulin signaling pathway.

Conclusion

The resistance of insulin plays a substantial function in PCOS & T2DM's intricate traits' pathophysiology.

The nine genes considered in our study were reported to play a prominent role in the manifestation of T2DM among populations of different ethnic backgrounds 17, including in the population of Hyderabad 20.

These genes are known to be implicated in different pathways such as insulin secretion and action, pancreatic beta-cell function & homeostasis of glucose, and the cross-talk between these pathways is, in turn, linked to insulin signaling cascade.

T2DM 9 genes deliberated in this investigative research might not be a PCOS' chief liability factor amongst the women of India. Our outcome complement the lack of indication of the relationship of the T2DM genes having PCOS amongst Caucasians & Chinese while mentioning the potential pattern's possibility. Precisely intended inclusive studies that include women with T2DM and PCOS are required to explore the precise role of the diabetes genes.

Lastly, this study states the primary challenges confronted during the translation of genetic discoveries into influential biological mechanisms which participate into the phenotype & genotype association.

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Ethical Clearance: Not required

Conflict of Interest: None

References

1. Sharma A, Chavali S., Tabassum R, Tandon N, Bharadwaj D. Gene prioritization in type 2 diabetes using domain interactions and network analysis. *BMC Genomics*. 2010;11:84.
2. Salonen J.T., Uimari P, Aalto JM, Pirskanen M, Kaikkonen J, Todorova B, et al. Type 2 diabetes whole-genome association study in four populations: the diagen consortium. *Am J Hum Genet*. 2007;81:338–45.
3. Dehwah MAS, Shuang Z, Hua WZ, Min W, Qing-Yang H. Type2 diabetes: genetic advance and aetiology. *J Appl Sci*. 2009;9:3407–23.
4. Radha V, Vimalaswaran KS, Deepa R, Mohan V. Review article: the genetics of diabetes mellitus. *Indian J Med Res*. 2003;117:225–38.
5. Das SK. Genetic epidemiology of adult onset type 2 diabetes in Asian Indian population: past, present and future. *Int J Hum Genet*. 2006;6:1–13.
6. Zeggini E. A new era for type 2 diabetes genetics. *Diabet Med*. 2007;24:1181–6.
7. Ridderstrale M, Groop L. Genetic dissection of type 2 diabetes. *Mol Cell Endocrinol*. 2009;297:10–7.
8. Grant SF, Thorleifsson G, Reynisdottir I, Benediktsson R, Manolescu A, Sainz J, et al. Variant of transcription factor 7-like 2 (TCF7L2) gene confers risk of type 2 diabetes. *Nat Genet*. 2006;38:320–3.
9. Scott LJ, Bonnycastle LL, Willer CJ, Sprau AG, Jackson AU, Narisu N, et al. Association of transcription factor 7-like 2 (TCF7L2) variants with type 2 diabetes in a Finnish sample. *Diabetes*. 2006;55(9):2649–53.
10. Melzer D, Murray A, Hurst AJ, Weedon MN, Bandinelli S, Corsi AM, et al. Effects of the diabetes linked TCF7L2 polymorphism in a representative older population. *BMC Med*. 2006;4:34.
11. Munoz J, Lok KH, Gower BA, Fernandez JR, Hunter GR, Lara-Castro C, et al. Polymorphism in the transcription factor 7-like 2 (TCF7L2) gene is associated with reduced insulin secretion in non diabetic women. *Diabetes*. 2006;55:3630–4
12. Ramachandran A, Snehalatha C, Viswanathan V. Burden of type 2 diabetes and its complications. The Indian scenario. *Curr Sci*. 2002;83:1471–6.
13. Cox NJ. Challenges in identifying genetic variation affecting susceptibility to type 2 diabetes: examples from studies of the Calpain 10 gene. *Hum Mol Genet*. 2001;10:2301–5.
14. American Diabetes Association (ADA). Type 2 diabetes in children and adolescents. *Diabetes Care*. 2000;23(3):381–9.
15. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995–2025: Prevalence, numerical estimates, and projections. *Diabetes Care*. 1998;21:1414–31.
16. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care*. 2004;27:1047–53.
17. Roglic G, King H. Diabetes mellitus in Asia. *Hong Kong Med J*. 2000;6:10–1. PubMedGoogle Scholar

18. Malecki MT, Moczulski DK, Klupa T, Wanic K, Cyganek K, Frey J, et al. Homozygous combination of calpain 10 gene haplotypes is associated with type 2 diabetes mellitus in a Polish population. *Eur J Endocrinol.* 2002;146:695–9.
19. Elbein SC. The genetics of human noninsulin-dependent (type 2) diabetes mellitus. *J Nutr.* 1997;127:1891S–6. mellitus in a Mexican ethnic group. *Ann Génét.* 2004;47:339–48.

Aerodigestive Tract of Foreign Body in 12 Indonesian Academic Hospital

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Abstract

Objective: To explore the profile of patients with aerodigestive tract of foreign bodies, who had performed bronchoscopy and esophagoscopy in 12 Otorhinolaryngology centers

Method: A descriptive research with a retrospective approach. Data samples were obtained from the recapitulation of medical services in the Broncho-Esophagology Division at 12 centers of Otorhinolaryngology education throughout Indonesia. All the extraction was carried out in the operating room of the emergency room at each education center.

Results: We obtained 487 cases of the laryngo-tracheo-bronchial foreign body, and 1499 of esophageal, then 1177 patients male and 809 female as subjects. The number of patients with aerodigestive foreign body was dominated by male n=1177 (59%) than female by n=809 (41%). The highest percentage of organic object was found in peanuts by n=84 (74%) and inorganic objects was needle n=180 (48%). The highest number of organic objects was meat n=271 (51%), and inorganic objects was coins n=481 (49%).

Conclusion: There was no significant difference in sex in male and female. The highest foreign body in the feeding process was a coin, while in the airway flow was a needle. The types of unknown objects can be related to educational background, cultural culture, and dietary in every country.

Keywords: *Aerodigestive, foreign body, bronchoscopy, esophagoscopy, academic hospital.*

Introduction

Foreign body of the aerodigestive tract are all objects either in the form of food boluses, or other hard objects that are ingested intentionally, or not so that they can cause blockages and injury in the aerodigestive tract. The foreign body aspiration process occurs when there is an object in the laryngotracheobronchial tract. The ingestion of foreign body occurs when the object

enters through the esophagus.¹ Aspiration and ingestion of foreign body is still a cause of significant morbidity and mortality.¹⁻³

The main symptoms that appear in an foreign body aspirations can mainly be shortness of breath and stridor.² In cases of ingestion, the symptoms that appear can be a permanent sensation that is persistent or arises when swallowing.³ Mental retardation and disorders in children generally come with complaints of choking feeling, unwillingness to eat, vomiting, excessive salivation and saliva mixed with blood.¹ Along with the development of bronchoscopy and esophagoscopy technique has reduced morbidity and mortality due to complications from the act of expulsion of foreign bodies in the aerodigestive tract.⁴

Research in India shows at least 25.000 cases of aerodigestive foreign bodies have been handled by local government hospitals. 5 Cases of aerodigestive

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foreign bodies can occur in adults and children. Types of foreign bodies that are ingested in children and adults are different. In adults, the most ingested species are cuts of meat, bones, and dentures.¹ In children, generally small toys and coins.^{2,3} References from India suggest that most foreign bodies, especially those aged 1-10 years with percentages by 44.98% of the total cases.⁶ Predisposing factors are include not growing molar teeth that able to chew and swallow well, coordinating the process of swallowing and imperfect laryngeal inlet in the age group 6 months to 1 year, mental retardation, growth disorders, and other neurological diseases.^{6,7, 8}

Rigid bronchoscopy and esophagoscopy are the main choices for foreign body extraction in the aerodigestive tract, while they can be used to diagnose cases of suspicion.^{1-3,9} A study in Tunisia reported that in less than 10 years at least 333 (53.2%) foreign bodies extraction with esophagoscopy and 215 (34.3%) extraction with bronchoscopy.^{7, 8} Other studies taken at third-level health facilities in India stated, in the past 7 years 1.125 cases of aerodigestive foreign body. The most cases in esophagus were located at cricopharyngeal (78.92%). Most foreign airway objects were found in the right-sided main bronchus (61.94%).⁵

The aim of this study was to explore the profile of patients with aerodigestive tract of foreign bodies, who had performed bronchoscopy and esophagoscopy in 12 Otorhinolaryngology centers throughout Indonesia during the period 2011 to 2015.

Materials and Method

Types of Research: The type of research was descriptive with a retrospective approach.

Sample, Place and Time of Research: Data samples were obtained from the recapitulation of medical services in the Broncho-Esophagology Division at 12 centers of Otorhinolaryngology education throughout Indonesia. The 12 education centers are Universitas Brawijaya (UB), Universitas Gajah Mada (UGM), Universitas Indonesia (UI), Universitas Airlangga (UNAIR), Universitas Andalas (UNAND), Universitas Diponegoro (UNDIP), Universitas Hasanuddin (UNHAS), Universitas Padjajaran (UNPAD), Universitas Sebelas Maret (UNS), Universitas Udayana (UNUD), Universitas Sriwijaya (UNSRI) and Universitas Sumatera Utara (USU). All the extraction was carried out in the operating room of the emergency room at each education center. The data were taken from 2011 to 2015.

Research and Analyze Data: The data of foreign body of the aerodigestive tract consists of laryngo-trachea-bronchial, and esophageal foreign body. Each data was divided into organic and inorganic group. The sample in this study included patients who had carried out foreign body extraction procedures by using rigid bronchoscopy and esophagoscopy at the emergency department at each education center. The samples that were not successfully extracted the foreign body and had incomplete data were not included in the calculation. Furthermore, the sample was processed using the Microsoft Excel 2013 program.

Results

Demographic Characteristics: In the period from January 2011 to December 2015, there were 1986 cases of aerodigestive foreign body which were successfully extracted with complete data. There were 487 cases of the laryngo-tracheo-bronchial foreign body, and 1499 of esophageal, then 1177 patients male and 809 female as subjects. (Table 1)

The highest number of laringotracheobronchial foreign body was in the Universitas Padjajaran by n=164 (34%), while the lowest case was in the Universitas Sebelas Maret by n=15 (13%). The highest number of esophageal foreign body was in the Universitas Airlangga by n=241 (16%), while the lowest case was found in the Universitas Sriwijaya by n=54 (4%).

Characteristics of Subject: The number of patients with aerodigestive foreign body was dominated by male n=1177 (59%) than female by n=809 (41%). The dominance of the esophageal in male was n=944, while the dominance of laryngo-tracheo-bronchial in female was n = 254 and has the highest in the 0-10 year age group by n=827 (42%). Then, the number of patients decreased in the next decade n=280 (14%). While the number of patients with the oldest aerodigestive in the age group >90 years was n=1 (0%). The highest number of patients of laryngo-tracheo-bronchial in the first decade age group was n=259, then decreased in the next decade by n=199. (Table 2).

The highest percentage of organic object was found in peanuts by n=84 (74%), while the lowest was cinnamon by n=1 (1%). The highest number of inorganic objects was needle n=180 (48%), followed by whistle n=92 (25%), and then corrosive battery by n=6 (2%). (Table 3).

The highest number of organic objects was meat n=271 (51%), followed by bone n=184 (35%), and meatballs by n=24 (5%). The highest number of inorganic objects was coins n=481 (49%). Followed by teeth n=295 (30%) and the last battery by n=14 (1%). (Table 4).

Table 1. Recapitulation of laryngo-tracheo-bronchial and esophageal foreign body.

University	Laryngotracheobronchial				Esophagus			
	Orga-nic	Inorga-nic	Total	Percents (%)	Orga-nic	Inorga-nic	Total	Percents (%)
Universitas Brawijaya	5	12	17	3	61	56	117	8
Universitas Gajah Mada	3	18	21	4	57	72	129	9
Universitas Indonesia	7	49	56	11	17	82	99	7
Universitas Airlangga	27	60	87	18	90	151	241	16
Universitas Andalas	13	22	35	7	16	65	81	5
Universitas Diponegoro	1	16	17	3	58	89	147	10
Universitas Hasanudin	10	23	33	7	13	113	126	8
Universitas Padjajaran	30	134	164	34	68	134	202	13
Universitas Sebelas Maret	11	4	15	3	69	49	118	8
Universitas Udayana	8	12	20	4	62	36	98	7
Universitas Sriwijaya	2	20	22	5	9	55	64	4
Universitas Sumatera Utara	2	15	17	3	7	70	77	5
Total	114	373	487	100	527	972	1499	100

Table 2. Sex of the patient

	Laryngo-tracheo-bronchial	Esophagus	Total	Percents (%)
Sex				
• Male	233	944	1177	59
• Female	254	555	809	41
Age (yr)				
• 0-10	259	568	827	42
• >10-20	199	81	280	14
• >20-30	6	85	91	5
• >30 – 40	5	98	103	5
• >40 – 50	8	194	202	10
• >50 – 60	6	216	222	11
• >60 – 70	3	148	151	8
• >70 – 80	1	94	95	5
• >80 – 90	0	14	14	1
• >90	0	1	1	0

Table 3. Organic and Inorganic objects in laryngo-tricho-bronchial

	Total	Percents (%)
Organic		
• Peanuts	84	74
• Fruit Seeds	14	12
• Bones	6	5
• Cake	6	5
• Fruit	3	3
• Cinnamon	1	1
Inorganic		
• Needle	180	48
• Whistle	92	25
• Elastic Toy	23	6
• Pin	19	5
• Spake	10	3
• Sequins	10	3
• Teeth	7	2
• Pen	6	2
• Battery	6	2
• Other	20	5

Table 4. Organic and inorganic object of esophagus foreign body

	Total	Percents (%)
Organic		
• Meat	271	51
• Bones	184	35
• Meat Ball	24	5
• Rujak	16	3
• Fruits Seed	10	2
• Union	7	1
• Casava	3	1
• Squid	2	0
• Peanuts	2	0
• Other	8	2
Inorganic		
• Coin	481	49
• Teeth	295	30
• Needle	36	4
• Toys	27	3
• Earring	19	2
• Batre	14	1
• Pin	11	1
• Blister	8	1
• Whistle	8	1
• Other	73	8

Discussion

The revolutionary management of patients with foreign body in the aerodigestive tract using rigid bronchoscopy and esophagoscopy was pioneered by Chevalier Jackson in 1904. This management reduced mortality from 20% to 2%.¹⁰ Rigid bronchoscopy and esophagoscopy are options for the diagnosis and extraction of foreign body in the aerodigestive tract. The use of rigid esophagoscopy is more advantageous for extraction because the flow airway is more patent. The use of extractor instruments such as forceps and telescopes can be entered in large sizes object.⁹ Selection of rigid bronchoscopy is also the main choice in cases of laryngo-tricho-bronchial foreign body because it is easier to control the flow of oxygen, carry out secret extraction and ease of extraction.¹¹

Based on the results study, there were 487 cases of laryno-tracheo-bronchial and 1499 esophageal foreign body. These results were consistent with studies at tertiary health facilities in India that there were 878 foreign body in the digestive tract and 247 cases in the respiratory tract.⁶ Based on the results of the study, foreign body in the laryno-tracheo-bronchial were found consisting of 114 organics and 373 inorganic objects. This result different from the study in India which showed respiratory organic object (n=189, 527 cases) was higher than inorganic (n=58, 927 cases).⁶ This result was opposite from the study in Nepal which stated that 72.22% of cases were organic and 27.77% inorganic.¹² Quoted from Rajashekhar T, the type of unknown object can be related to educational background, culture, and dietary in every country.¹³ Sex distribution of patient obtained by male (n = 1177) was higher than female (n = 809). This was in consistent with other studies that showed a non-significant comparison between male (n = 137) and female (n = 110).⁶ Other studies also showed that there were no significant differences in sex distribution.^{13,14} The results of the comparison were insignificant that caused by the number of sample cases that were still lacking.

The results was found that the highest cases were in the 0-10 year age group (n = 259). This was in accordance with several other studies which stated the highest average age in the group was 0-10 years.^{5,6} Predisposing factors in children are congenital anomalies, not yet growing molar teeth, coordination of swallowing processes, imperfect laryngeal sphincter in the 6 months to a year, mental retardation, growth disorders, and

underlying neurological diseases. Predisposing factors in adults are the use of dentures accompanied by loss of palpable sensation, neural disorders, and psychosis.⁹

Based on the results of the study, the highest number of organic object was obtained n=84 (74%), and the lowest was cinnamon by n=1 (1%). While the highest number of inorganic objects was needle n=180 (48%), followed by whistle n=92 (25%). This result is similar to that of Showkat et al., which stated that the highest unknown organic objects were peanuts (18.51%). The high incidence of needles can be caused by the habit of biting it by patients when wearing clothes.

The highest number of unknown organic esophageal object was meat n=271 (51%), followed by bones n=184 (35%). The highest number of inorganic objects was coins n=481 (49%), followed by teeth n=295 (30%). These results are in accordance with research by Shawat, where bone, coins, meat, and teeth are the highest 4 large unknown object in the digestive tract.⁶ The results of the study also found corrosive objects, namely batteries by 2% on airway flow and 1% on the esophageal tract. Batteries are dangerous materials and must be immediately evacuated and treated as life-threatening unknown objects. The electrochemical composition has the potential to damage the surrounding mucosal area extensively.¹⁵ Quoted by Thabet et al, the consequences of damage to the mucous area depend on the position of the battery, the duration, size, power and mechanism of absorption of heavy metals by the body.¹⁵

Conclusion

An foreign body in the highest aerodigestive tract occurs at less than 10 years. This case depends on predisposing factors, such as congenital anomalies, the absence of molar teeth that to be able to swallow properly, coordination of the process of swallowing and laryngeal sphincter that was not perfect, mental retardation, growth disorders, and underlying neurological diseases. Predisposing factors in adults were dentures who have lost sensation from the palate, neural disorders, and psychosis. There was no significant difference in sex in male and female. The highest foreign body in the feeding process was a coin, while in the airway flow was a needle. The types of unknown objects can be related to educational background, cultural culture, and dietary in every country.

Conflict of Interest: The authors report no conflict of interest related to this manuscript

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References

1. Friedman EM, Yunker WK. Ingestion injuries and foreign bodies in the aerodigestive tract. Lippincott-Raven 2015.
2. Marshall ES, Mark RE. Ballenger's Otorhinolaryngology Head and Neck Surgery. Philadelphia: B.C. Dekker; 2009.
3. Gregory N, Melanie W, Catherine J. Ballenger's Otorhinolaryngology Head and Neck Surgery. London: BC Decker; 2009.
4. Revadi G, Philip R, Gurdeep S. Removal of foreign-bodies under general anaesthesia. A review of rigid endoscopy for foreign-bodies of the hypopharynx and oesophagus. The Medical journal of Malaysia 2010;652:143-5.
5. Rajeswari PSR, Sudha B, Nageswara RB, Surya PRS, Ramachandra RB. Retrospective Study on Foreign Bodies in Aerodigestive Tract in Government ENT Hospital. Journal of Evolution of Medical and Dental Sciences 2015;439:6793-6.
6. Showkat, al. e. Aerodigestive tract foreign bodies. Aerodigestive tract foreign bodies: an experience at a tertiary-care hospital 2015.
7. Hariga I, Khamassi K, Zribi S, Amor MB, Gamra OB, Mbarek C, et al. Management of foreign bodies in the aerodigestive tract. Indian journal of otolaryngology and head and neck surgery : official publication of the Association of Otolaryngologists of India 2014;66Suppl 1:220-4.
8. Yang YH, Zhang XG, Zhang JL, Zhang YB, Kou CP. Risk factors for preoperative respiratory complications in children with tracheobronchial foreign bodies. The Journal of international medical research 2016;442:338-45.
9. Kavitt RT, Vaezi MF. Disease of the esophagus. In: Flint PW, Haughoy BH, Lund VJ, al e, editors. Cummings otolaryngology Head and Neck Surgery. Philadelphia: Elsevier Saunders; 2015. p. 993.
10. Kamath P, Bhojwani KM, Prasannaraj T, Abhijith K. Foreign bodies in the aerodigestive tract-a clinical study of cases in the coastal belt of South India. American journal of otolaryngology 2006;276:373-7.

11. Bain A, Barthos A, Hoffstein V, Batt J. Foreign-body aspiration in the adult: presentation and management. *Canadian respiratory journal* 2013;206:e98-9.
12. Ramesh P. Foreign Bodies in the Ear, Nose and Throat: An Experience in a Tertiary Care Hospital in Central Nepal. Bharatpur, Chitwan: Nepal Int Arch Otorhinolaryngol Chitwan Medical College Teaching Hospital; 2015.
13. Rajashekhar TP, Advait P. Foreign bodies in aerodigestive tract in children: spectrum of presentation and management. 2017.
14. Panduranga K, Kiran M, Thomas P, Abhijith. Foreign bodies in the aerodigestive tract—a clinical study of cases in the coastal belt of South India. Mangalore, Karnataka State, India: Kasturba Medical College; 2006.
15. Thabet MH, Basha WM, Askar S. Button Battery Foreign Bodies in Children: Hazards, Management, and Recommendations. 2013.

The Relationship between the Cochlear Roughness, the Stimulus Level 30dB and the Otoacoustic Emissions

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Abstract

The hearing mechanism is influenced by a number of factors, whether sound or physiology. These factors include the stimulus level of sound and cochlear roughness.

In this work, the otoacoustic emissions was studied with the stimulus level of sound 30 dB different cases. In each case the cochlear roughness was changed to study the otoacoustic emission. Cochlear roughness changes for each case and it is noted that the hearing mechanism is affected by cochlear roughness. The most important conclusion of this work is that cochlear roughness is very important to hearing efficiency. It is clear that the stimulus level gave good results regarding the hearing mechanism.

Keywords: *Hear process, frequency map, ear, stimulus level, distribution.*

Introduction

External acoustic emissions OAEs are a physiological byproduct Mammal Cochlear Activity Probst Et al, (1991)¹. OAE generation and backward transfer. It is effectively prescribed by a cochlear transmission line models which including resonant cross-resonance, for example, Talmadge et al. (1998)². These conditions must also model for the mechanism of mediated active reactions outer hair cells OHCs, which are responsible for excellent threshold sensitivity and frequency resolution of Mammals hearing system.

In 1895, Helmholtz introduced the roughness as the term for the first time to describe cruel, clatter Phonological sensation or noisy³. Hearing roughness is an aspect of the bell associated with frequent and rapid fluctuations. Amplitude or frequency, is often described by referring to qualities such as cruelty, Lightness, hoarseness. Used as a measure of sound quality assessment in industrial applications, such as the automotive industry, for example, Gonzales et al., (2003)⁴, and clinical evaluation of sound quality, for example, Webb et al.,(2004)⁵.

Different roughness models have been developed in the past, the detection of frequency components in the spectrum of the sound and map it onto a psychoacoustical

curve of roughness is called curve mapping model. The type of the roughness model was designed by Vassilakis (2000)^{6,7}.

Roughness is important in musical contexts as well. Perceived tension provisions. The ropes show a great positive relationship with the roughness of the estimated ropes Values of Bigand et al., (1996)⁸. Roughness assumes amplitude modulation tones due to inability. The auditory system to solve the stimulation components, ie carrier and two lateral bands, either spectrally or temporarily Zwicker and Fastl, (1990)⁹.

Based on earlier work before Terhardt et al., Zwicker and Fastl(1990)¹⁰ suggested that the roughness be limited by frequency resolution at low carrier frequencies and time resolution at higher carrier frequencies.

For carriers less than 2000 Hz, the modulation rate at which the peak of roughness occurs is high the peak, the rate of formation at which the roughness disappears, all grow with the increase of the carrier repeat. This is due to the amplitude of the audio channels as the carrier frequency.

Increases, allowing the interaction between stimulation components more spaced. In the carrier frequencies above 2000 Hz, Zwicker and Fastl 1990(9)

reported that roughness up to peak at modulation rates of about 70-80 Hz and disappear at about 250 Hz,

Regardless of the carrier frequency, which indicates that time accuracy is the limiting factor.

Method

The calculations were done by the non-linear model, the stimulus level 30 dB was studied for six different cochlear roughness.

Results and Discussion

One of the auditory tests is otoacoustic emission. In this work the otoacoustic emission of low stimulus levels is studied and the stimulus level 30 dB is used. Cochlear roughness is an important factor for hearing. In this work, the relationship between roughness and intensity level 30 dB is studied. The study is in the form of stages to study the relationship between the stimulus level 30

dB and roughness and the impact of this relationship on the hearing mechanism.

The results are in the form of different cases in each case roughness varies and the value of cochlear roughness for the first case is the lowest value for the rest of the cases and is considered the lowest, the cases are as follows:

The first case: In this case, the transient evoked otoacoustic emission is studied with the stimulus level 30 dB, which is considered to be one of the lowest stimulus levels so that the roughness of the cochlea is weaker in comparison with the following cases.

Figure 1 shows the energy distribution of the transient evoked otoacoustic emissions of the first case. It is very clear that the otoacoustic emission through energy distribution is weak and this reflects hearing loss and the reason that the coarseness of the cochlea is very weak.

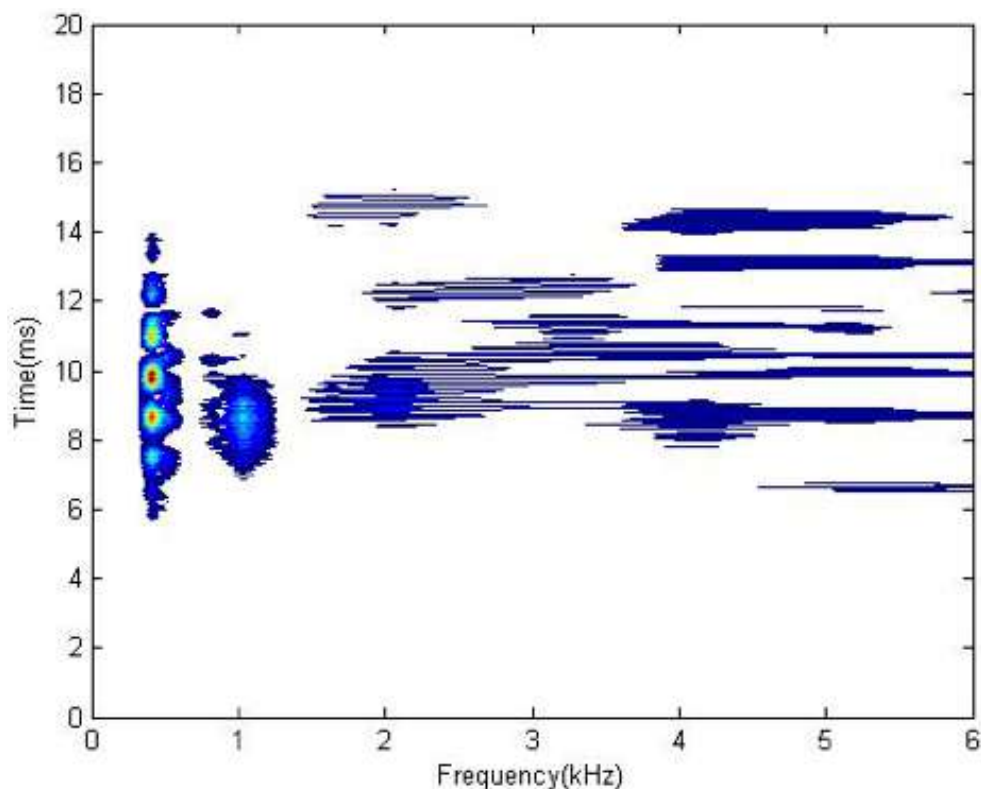


Figure 1: The otoacoustic emission (30 dB) for the first case.

The second case: In the second case, the study mechanism for otoacoustic emission is continued using the same stimulus level 30 dB, but with different cochlear

roughness. In this case, roughness is greater than in the previous case.

Figure 2 shows the transient evoked otoacoustic emission of the second case, shows that otoacoustic emission status is better than the second case compared to Fig. 1, which represents the first case, and because

the roughness in the second case is greater than the second case, the reason for the improvement of auditory emission is the change in cochlear roughness.

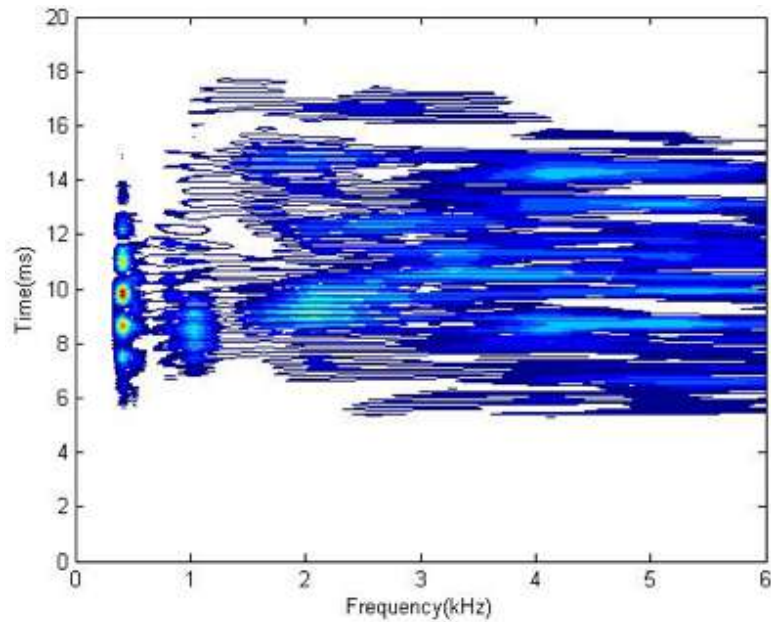


Figure 2: The otoacoustic emission (30 dB) for the second case

The third case: In the third case, the process of changing the roughness continues to be different from the previous cases. The otoacoustic emission of the stimulus level 30 dB is obtained using a different roughness condition than the previous ones.

Figure 3 shows the otoacoustic emission of the stimulus level 30 dB for another different cochlear roughness condition.

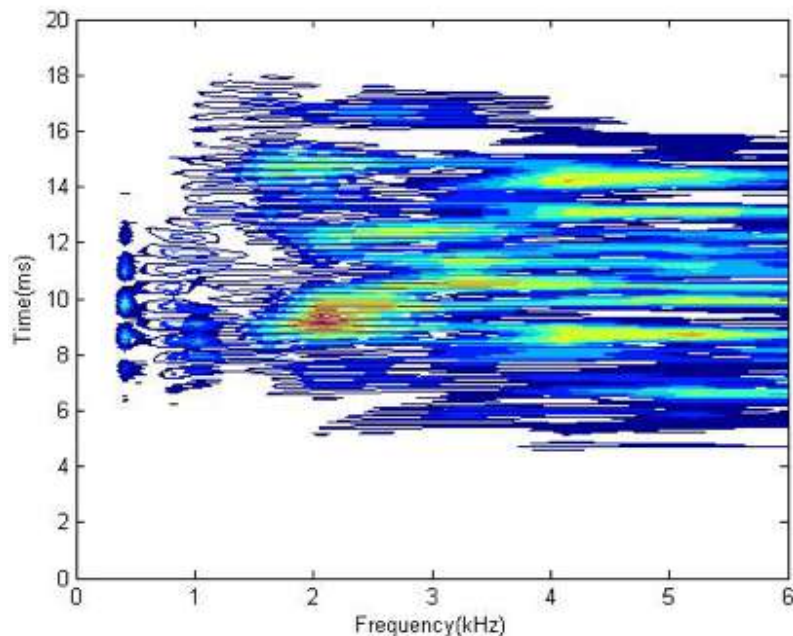


Figure 3: The otoacoustic emission (30 dB) for the third case

The fourth case: In the fourth case, the process of changing the roughness continues to be different from the previous cases. The otoacoustic emission of the stimulus level 30 dB is obtained using a different roughness condition than the previous cases.

Figure 4 shows the otoacoustic emission of the stimulus level 30 dB for another different cochlear roughness condition.

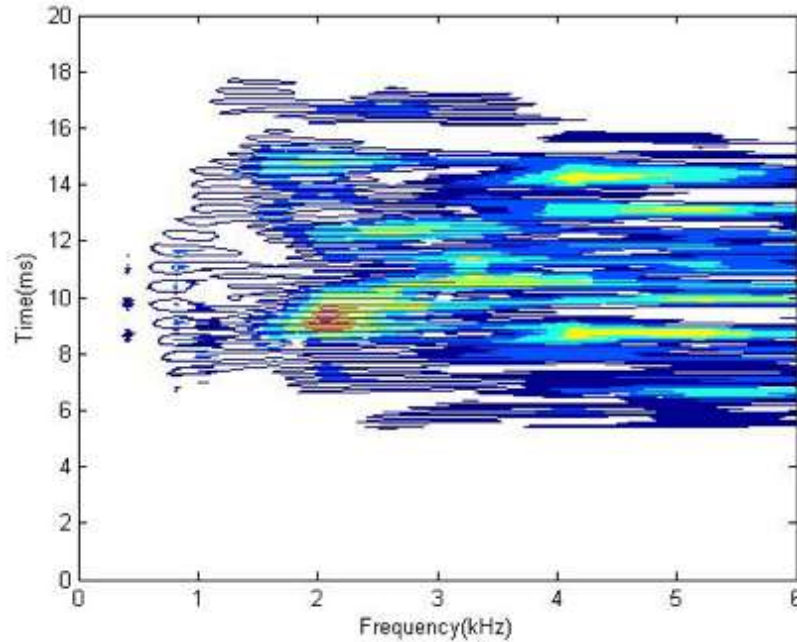


Figure 4: The otoacoustic emission (30 dB) for the fourth case.

The fifth case: In the fifth case, the otoacoustic emission of the stimulus level 30 dB is obtained using a new cochlear roughness condition different from all previous cases.

Figure 5 shows the otoacoustic emission of the stimulus level 30dB using different roughness from all previous cases.

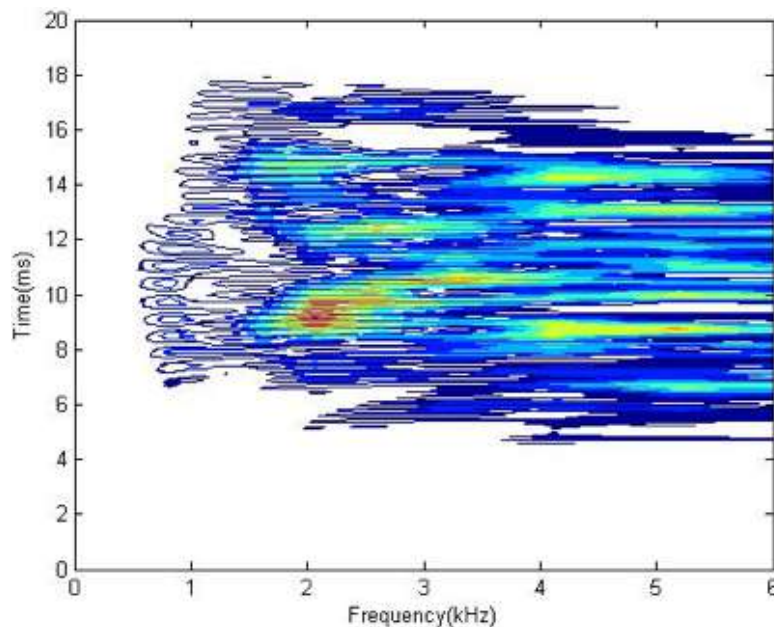


Figure 5: The otoacoustic emission (30 dB) for the fifth case.

The sixth case: The sixth and final case where a different cochlear roughness condition is used to obtain the otoacoustic emission of the stimulus level 30 dB.

Figure 6 shows the otoacoustic emission of the last case using roughness in a different case than all previous cases of the stimulus level 30dB.

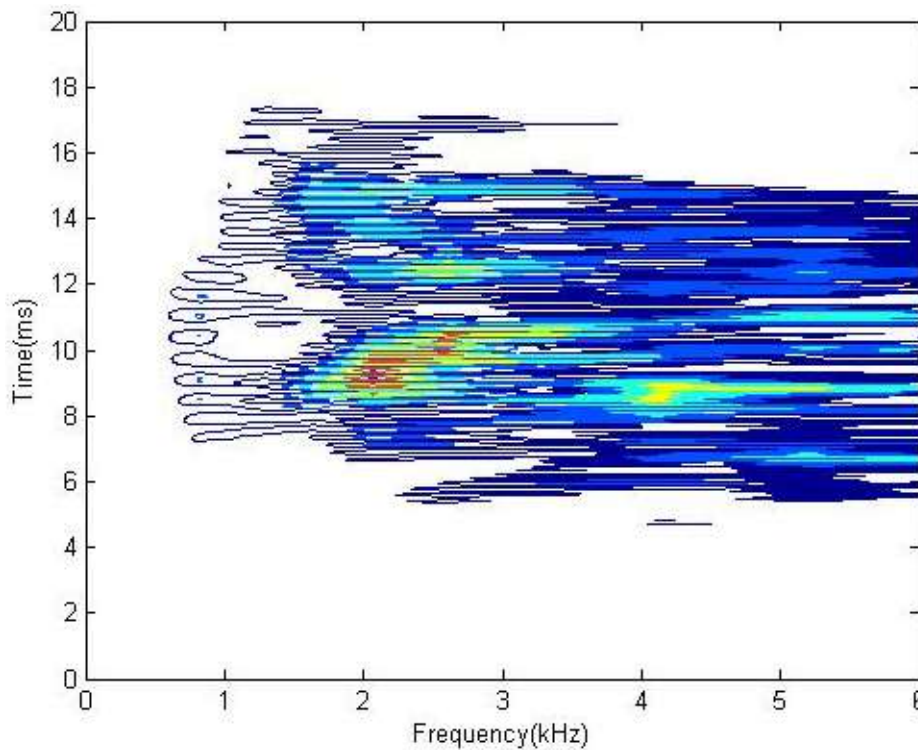


Figure 6: The otoacoustic emission (30 dB) for the sixth case.

The six cases in this work represent the study of hearing through the most important auditory tests, which is the otoacoustic emission for the purpose of studying the relationship between the stimulus level 30 dB, the roughness and hearing.

The calculations were made using a non-linear model, where six different roughness conditions were used with one stimulus level of 30 dB.

By studying Figures 1, 2, 3, 4, 5, and 6, it is noted that otoacoustic emission is different for all cases and the cause of variation is roughness.

Figure 1 shows a state of the otoacoustic emission in poor condition and Figure 2, although better than Fig. 1, but also in poor condition, cochlear roughness condition is the cause of the poor state of otoacoustic emission.

For the other four cases, the third, the fourth, the fifth, and the sixth, the resulting of the otoacoustic emission is better than the first and the second.

In general, the last four cases 3, 4, 5 and 6 give different but acceptable results. This is because the roughness of the four cases is better than cases 1 and 2.

At the same time, cases 3 and 4 almost gave similar results, and cases 5 and 6 also gave similar results, but cases 5 and 6 gave better results than cases 3 and 4.

The reason for the different otoacoustic emission status of the six cases is the different roughness condition used for each case.

According to the results of the work obtained, both in terms of the cochlear roughness or the stimulus level. The results of the work are in agreement with previous studies^{11,12}.

Conclusion

In analyzing the results of the work, the otoacoustic emission reflects the auditory state. The results of the six cases were different. In the first and second cases,

the otoacoustic emission was not good and reflected an unusual state of hearing.

We conclude from this that the cochlear roughness is the cause of the difference in the results, where the roughness condition is not good so the first and second case that gave a poor auditory emission.

Because the roughness of the other four cases was different but good, it gave good and acceptable auditory resurgence.

We conclude that roughness plays an important role in the auditory process and the role of roughness can be described as total and partial.

The stimulus level 30 dB, which is classified as low stimulus level, gave acceptable results for otoacoustic emission and according to the role of roughness and the stimulus level 30 dB reflected a consistent good condition as the stimulus level. It is concluded that the hearing mechanism depends directly and importantly on the relationship between coarseness and coarseness level. According to the results obtained in this work, the results were good, acceptable and compatible with previous studies.

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References

- 1- Probst, R., Lonsbury-Martin, B. L., and Martin, G. K. "A review of otoacoustic emissions," *J. Acoust. Soc. Am.* (1991). 89, 2027–2067.
- 2- Talmadge, C. L., Tubis, A., Long, G. R., and Piskorski, P. "Modeling otoacoustic emission and hearing threshold fine structures," *J. Acoust. Soc. Am.* (1998). 104, 1517–1543.
- 3- Helmholtz H.L.F. von, *Sensation of tone as a physiological basis for the theory of music*, 3rd Ed., Longmans, Green, and Co., (1895) London, New York.
- 4- Gonzalez, A., Ferrer, M., de Diego, M., Pinero, G., and Garcia-Bonito, J. "Sound quality of lowfrequency and car engine noises after active noise control," *J. Sound Vib.* (2003). 265, 663–679.
- 5- Webb, A., Carding, P., Deary, I., MacKenzie, K., Steen, N., and Wilson, J. "The reliability of three perceptual evaluation scales for dysphonia," *Eur. Arch. Otorhinolaryngol.* (2004). 261, 429–434.
- 6- Vassilakis P.N., *Perceptual and physical properties of amplitude fluctuation and their musical significance*, (2001), Ph.D. Thesis, University of California.
- 7- Leman M. Visualization and calculation of the roughness of acoustical musical signals using the syn-chronization index model (SIM), *Proceedings of the COST G-6 Conference on Digital Audi Effects* (2000), (DAFX-00), pp. DAFX 1–DAFX 6, Verona.
- 8- Bigand, E., Parncutt, R., and Lerdahl, F. "Perception of musical tension in short chord sequences: The influence of harmonic function, sensory dissonance, horizontal motion, and musical training," *Percept. Psychophys.* (1996). 58, 125–141.
- 9- Zwicker, E., and Fastl, H. *Psychoacoustics: Facts and Models* _Springer-Verlag, NewYork_, (1990). pp. 231–236.
- 10- Terhardt, E. "Pitch, consonance, and harmony," *J. Acoust. Soc. Am.* (1974). 55, 1061–1069.
- 11- AL-Maamury A., Al-Rawi F., Al-Rubaiee A. "The Effect of Basilar Membrane Roughness on the Otoacoustic Emissions", *Indian Journal of Public Health Research and Development*, 2019, 10(5): 652--656.
- 12- Al-Maamury M. A., Dhifaf A. " Effect of some factors and variables on the frequency - time distribution of the optoacoustic emissions", *Indian Journal of Public Health Research and Development*, 2019, 10(10): 685--691.

Circuit Training to Increase Cardiorespiratory Endurance in Male Basketball Players

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Abstract

In playing basketball, body fitness is important. It is closely related to biomotor abilities which consist of several components, one of which is endurance. An attack movement in a basketball game would require good cardiorespiratory endurance. Aerobic endurance is related to oxygen intake. This study aims to determine the improvement of cardiorespiratory endurance in male students who took basketball as a preferred extracurricular activity gained through circuit training. This is experimental research with one-group pretest-posttest design. The sample of this research consisted of 15 male students. Circuit training was carried out three times a week for four weeks at an exercise intensity of 65%–90% of maximum heart rate. From hypothesis testing with a paired t-test, it was found out that $P = 0.000$ ($0.000 < 0.05$), suggesting that there was a meaningful difference. This result shows that circuit training improved cardiorespiratory endurance.

Keywords: *circuit training, cardiorespiratory endurance, male basketball players*

Introduction

Basketball games are considered to be one of the most dynamic and flexible sports which require high levels of physical fitness^[1]. Physical relations are associated with biomotor abilities because biomotor abilities are the abilities to measure human performance^[2]. One of these biomotor components greatly affects a person's endurance, namely resilience. Resilience is the ability of the heart, lung, and blood vessels to work optimally when carrying out activities for a long time without experiencing interference^[3]. Resilience can be grouped into anaerobic resistance and aerobic resistance^{[4],[5]}. The training session applied by the coach was directed

more to technical training and games. This affected the physical strength of poorly trained players^{[1],[6]}.

Cardiorespiratory endurance can be increased by a variety of training techniques, one of which is circuit training^{[1],[7]}. Circuit training is a combination of several types of exercises carried out in several training posts^[2]. At each training post, an athlete will perform a predetermined type of exercise^[8]. One circuit training set is said to be complete if an athlete has completed training in all training posts according to the prescribed dose. The movements included in this circuit training are as follows: push-ups, sit-ups, vertical jumps, abdominal curls, back extensions, astride jumping over benches, pull-ups, bench stepping, burpe, shuttle run, thrust squats, side bend, skipping, and running on the spot^[9].

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Material and Method

Participants: The population in this study was all male students who took extracurricular activities at a middle school in Denpasar, Bali. The sample in

this study was male students who took basketball as a preferred extracurricular activity. The sample used had to meet the following criteria: the participants were male middle school students who took basketball as an extracurricular activity, were aged 13–14 years, had low cardiorespiratory endurance of < 35 (poor), and did not take part in any cardiorespiratory resistance training program other than circuit training during the study. After each of these posts the students were given a break period of 15 to 20 seconds before proceeding to the next post. After completing one circuit, the students were also given a break period of 15 to 20 seconds.

Circuit training measures: In this study, some interviews and observations were carried out, and information related to age and some complaints experienced was generated. This would affect the daily physical activity and the training process and would let the researchers know whether the respondents observed were not too large. Several circuit training posts consisting of running on the spot, shuttle run, skipping, squats, push-ups, sit-ups for each set were established.

This exercise was performed in 2 repetitions (sets) with a break time of 15–20 seconds between stages and between circuits.

- a. Stage 1: Running on the spot. This training post lasted for 20 seconds.
- b. Stage 2: Shuttle run. This training post lasted for 30 seconds (the students run back and forth and touched the predetermined boundary line).
- c. Stage 3: Skipping or jumping rope. This training post lasted for 30 seconds (the students made a leap using the rope provided).
- d. Stage 4: Squat. This training post lasted for 30 seconds (the students stood then bent both knees to a half squatting position and repeated continuously for a specified time period).
- e. Stage 5: Push-up. This training post lasted for 30 seconds.
- f. Stage 6: Sit-up. This training post lasted for 30 seconds.

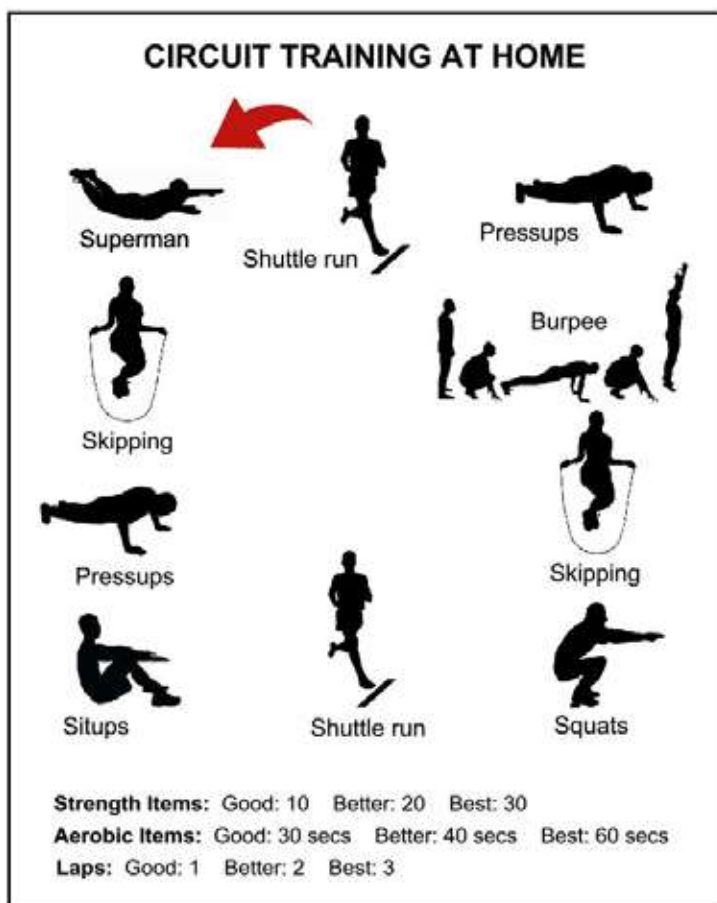


Fig. 1. Circuit training^[9]

Statistical Analyses: This study used an experimental method with one-group pretest-post design. The data in the study were analyzed using SPSS. The analysis was conducted to describe the results of the research in the field without having to manipulate the facts. The data from the group were subjected to a Shapiro-Wilk test at a significance level of 0.05. It was used to examine the average chest expansion before and after treatment in each group.

Finding and Results

Table 1 shows the number of respondents based on age: 10 respondents (66.7%) were 13 years old, and the remaining 5 respondents (33.3%) were 14 years old.

Table 1: Age distribution of respondents

No	Age	Frequency	Percentage (%)
1	13	10	66,7
2	14	5	33,3
Total		15	100%

Table 2 shows the number of respondents based on the VO_{2max} values obtained from the Balke test before the circuit training was performed: 5 respondents (33.3%) obtained values of < 35 and fell into the very poor category, 8 respondents (53.3%) obtained values of 35–37 and fell into the poor category, and 2 other respondents (13.3%) obtained values of 38–44 and fell into the fair category.

Table 2: Distribution of VO2 max values through Balke Test before being given Circuit Training

The VO2 max value in the balke test	Total		
	Category	F	Percentage (%)
< 35	Very poor	5	33,3
35 – 37	Poor	8	53,3
38 – 44	Fair	2	13,3
Total		15	100%

Table 3 shows the number of respondents based on the VO_{2max} values from the Balke test after the circuit training was performed: 1 respondent (6.7%) obtained a value of < 35 and fell into the very poor category, 6 respondents (40.0%) obtained values of 35–37 and fell into the poor category, and 8 respondents (53.3%) obtained values of 38–44 and fell into the fair category.

Table 3: Distribution of VO2 max values through Balke Test after being given Circuit Training

VO2 max value	Total		
	Category	F	(%)
< 35	Very poor	1	6,7
35 – 37	Poor	6	40,0
38 – 44	Fair	8	53,3
Total		15	100%

Table 4 shows that the average VO_{2max} value obtained by a sample of 15 from the Balke test before the circuit training was performed was 35.68, the median was 36.2, the lowest value was 31.60, and the highest value was 39.60. Meanwhile, from the Balke test after the circuit training was performed to the same sample, the average VO_{2max} value was 38, the median was 38.5, the lowest value was 33.30, and the highest value was 44.

Table 4: Results of Measurement The average VO2 max value through the balke pre-test and post-test.

Variable		Mean	Median	Min	Max	%
Balke test	Pre-test	35,68	36,20	31,60	39,60	6,5%
	Post-test	38,00	38,50	33,30	44,00	

Table 5 shows the results of the normality test using the Shapiro-Wilk test. The pre-test VO_{2max} was 0.980. Because 0.980 > 0.05, the pre-test data were normally distributed. Meanwhile, the post-test VO_{2max} was 0.848. Because 0.848 > 0.05, the post-test data were normally distributed.

Table 5: Data Normality Test Results Measurement of VO2 max values through the balke test

Variable		Statistics	Sig,	Interpretation
Balke test	Pre-Test	0,982	0,980	Normal
	Post-Test	0,969	0,848	Normal

Table 6 shows that the paired t-test comparing the pre-test and post-test VO_{2max} values obtained from the Balke tests conducted on the sample yielded a significant result of 0.000 (0.000 < 0.05), indicating that there was a change in cardiorespiratory endurance after circuit training was performed.

Table 6: Results of paired t-test analysis

Results		Df	Sig	Information
Balke test	Pre-Test	14	0,000	There are significant differences
	Post-Test			

Discussion

Cardiorespiratory endurance in males aged 13–14 (adolescents) can increase if training is applied in accordance with a stipulated dosage or training load^{[10], [11]}. Age affects all components of physical fitness, and VO_{2max} plays an important role in respiratory fitness. VO_{2max} of children aged 8–16 years shows a progressive and linear increase in peak aerobic ability. Thus, it can be increased by applying active sports such as circuit training^{[12], [13], [14]}. However, circuit training produces different levels of VO_{2max} , causing non-optimal VO_{2max} achievement^{[6], [15]}. Circuit training is designed to develop cardiorespiratory fitness, cardiovascular endurance, flexibility, strength, and muscle endurance^[16]. This exercise has a number of advantages: it can be performed in a short time period; it can be applied to one person or a group of persons; and it does not require any complicated equipment^[2]. Circuit training is designed to stimulate the cardiorespiratory organs, and, as a result, the resistance aspect is emphasized^[17].

Some research studies reveal that male basketball players aged 10–12 years saw an increase of VO_{2max} after carrying out circuit training exercises for 6 weeks as well as average initial score and average final score by 7.68 ml/kg BW/minute (20.68%)^{[18], [3]}. According to the American College of Sports Medicine in 2006, the target heart rate range one should achieve when conducting a circuit training exercise to experience cardiorespiratory benefits is 65%–90% of the maximum heart rate^{[15], [21]}. This is in accordance with the results of the research conducted—that is, the dose used should be based on the size of the maximum heart rate to achieve changes in the cardiorespiratory aspect^[19]. Recent studies related to exercises that have an effect on cardiorespiratory function have shown that breathing exercises are able to increase the amount of O_2 intake, for instance, chest expansion, with a p value of <0.05 ^{[20], [22]}. Thus, the exercise also has an impact on the aerobic capacity of both sick patients and healthy people.

The results of this study show an increase in the cardiorespiratory endurance of male students taking basketball as an extracurricular activity based on the VO_{2max} values obtained from a Balke test ($p=0.000$). The students were given circuit training 3 times a week for 4 weeks of meetings with a training load of 65%–90% of the maximum heart rate. Each circuit training treatment consisted of 2 sets of exercises, each of which consisted of 6 types of exercises that had to be

carried out in each training post provided. Based on the VO_{2max} values before the circuit training was given to the sample, 20% of the respondents fell into the very poor category, 66.7% to the poor category, and 13.3% to the fair category. The 6 types of exercises were running on the spot, shuttle run, skipping, squats, push-ups, and sit-ups. This study's results are supported by previous research that was conducted on middle school students, which reveals that 6-week circuit training exercises on leg muscle strength could increase VO_{2max} ^{[18], [23], [8]}.

The main limitation of our study is that we have yet to find any other types of training comparative to circuit training for increasing the cardiorespiratory fitness of middle-school basketball players, thus we are in need of literature related to other types of aerobic training. Therefore, more precisely, we recommend exercise to overcome the decline in cardiorespiratory fitness, for example, a decrease in the functional aerobic capacity.

Conclusions

From the observations conducted three times a week for four weeks, it was found that the provision of circuit training could increase the cardiorespiratory endurance of male students who took basketball as an extracurricular activity. However, in order to gain further insights regarding the improvement of cardiorespiratory fitness of long-term male basketball players, the sample size should be greater because the fitness level of each man may vary.

Conflict of Interest: The authors declare that there is no conflict of interest related to this study.

Source of Funding: The authors declare that there is no source of funding from anyone.

Ethical Clearance: The experiment was approved taken from by the Research Ethics Committee of Medical Faculty of Udayana University/Sanglah Hospital.

References

1. Vasconcelos T, Hall A, Viana R. The influence of inspiratory muscle training on lung function in female basketball players - a randomized controlled trial. *Porto Biomed J* [Internet]. PBJ-Associação Porto Biomedical/Porto Biomedical Society; 2017;(xx):10–3. Available from: <http://dx.doi.org/10.1016/j.pbj.2016.12.003>

2. Berner Y, Barer Y, Shefer G, Stern N. Circuit resistance training is an effective means to enhance muscle strength in older adults A Systematic Review and Meta-analysis. *Ageing Res Rev* [Internet]. Elsevier B.V.; 2017; Available from: <http://dx.doi.org/10.1016/j.arr.2017.04.003>
3. Siahkouhian M, Khodadadi D, Shahmoradi K. Effects of high-intensity interval training on aerobic and anaerobic indices: Comparison of physically active and inactive men. *Sci Sport* [Internet]. Elsevier Masson SAS; 2013;28(5). Available from: <http://dx.doi.org/10.1016/j.scispo.2012.11.006>
4. Meseguer Zafra M, García-Cantó E, Rodríguez García PL, Pérez-Soto JJ, Tárraga López PJ, Rosa Guillamón A, et al. Influence of a physical exercise program on VO₂max in adults with cardiovascular risk factors. *Clin E Investig En Arterioscler Publ of La Soc Esp Arterioscler* [Internet]. Sociedad Española de Arteriosclerosis; 2018;(xx). Available from: <https://ezproxy.southern.edu/login?url=http%3A%2F%2Fsearch.ebscohost.com%2Flogin.aspx%3Fdirect%3Dtrue%26db%3DCmedm%26AN%3D29395495%26site%3DDehost-live%26scope%3Dsite>
5. Getty AK, Wisdo TR, Chavis LN, Derella CC, McLaughlin KC, Perez AN, et al. Effects of circuit exercise training on vascular health and blood pressure. *Prev Med Reports* [Internet]. Elsevier; 2018;10(February):106–12. Available from: <https://doi.org/10.1016/j.pmedr.2018.02.010>
6. Broch K, Urheim S, Massey R, Stueflotten W, Fosså K, Hopp E, et al. Exercise capacity and peak oxygen consumption in asymptomatic patients with chronic aortic regurgitation. *Int J Cardiol*. 2016;223:688–92.
7. Ouergui I, Marzouki H, Houcine N, Franchini E, Gmada N, Bouhleb E. Relative and absolute reliability of specific kickboxing circuit training protocol in male kickboxers Reproductibilité relative et absolue d'un protocole de circuit. *Sci Sport* [Internet]. Elsevier Masson SAS; 2016;1–8. Available from: <http://dx.doi.org/10.1016/j.scispo.2016.01.004>
8. Bhambhani Y, Rowland G, Farag M. Effects of Circuit Training on Body Composition and Peak Cardiorespiratory Responses in Patients With Moderate to. 2005;86(February):268–76.
9. Sousa M De, Zouita A, Abderrahmane A Ben. Progressive circuit resistance training improves inflammatory biomarkers and insulin resistance in obese men. *Physiol Behav* [Internet]. Elsevier Inc; 2018;#pagerange#. Available from: <https://doi.org/10.1016/j.physbeh.2018.11.033>
10. Gontarev S, Kalac R. Association between high blood pressure, physical fitness, and fatness in adolescents. *J Phys Educ Sport*. 2016;16(2):1040–5.
11. Wu W, Yang Y, Chu I, Hsu H, Tsai F. Research in Developmental Disabilities Effectiveness of a cross-circuit exercise training program in improving the fitness of overweight or obese adolescents with intellectual disability enrolled in special education schools. *Res Dev Disabil* [Internet]. Elsevier Ltd; 2017;60:83–95. Available from: <http://dx.doi.org/10.1016/j.ridd.2016.11.005>
12. Randers MB, Hagman M, Brix J, Christensen JF, Pedersen MT, Nielsen JJ, et al. Effects of 3 months of full-court and half-court street basketball training on health profile in untrained men. *J Sport Heal Sci* [Internet]. Elsevier B.V.; 2018;7(2):132–8. Available from: <https://doi.org/10.1016/j.jshs.2017.09.004>
13. Sirbu E. The effects of moderate aerobic training on cardiorespiratory parameters in healthy elderly subjects. *J Phys Educ Sport*. 2012;12(4):560–3.
14. Kato Y, Suzuki S, Uejima T, Semba H, Nagayama O, Hayama E, et al. The relationship between resting heart rate and peak VO₂: A comparison of atrial fibrillation and sinus rhythm. *Eur J Prev Cardiol* [Internet]. American College of Cardiology Foundation; 2016;23(13):1429–36. Available from: <http://journals.sagepub.com/doi/10.1177/2047487316633885>
15. Gmiat A, Micielska K, Koz M, Flis DJ, Smaruj M, Kujach S, et al. Physiology & Behavior The impact of a single bout of high intensity circuit training on myokines' concentrations and cognitive functions in women of different age. 2017;179(January):290–7.
16. Romero-arenas S, Blazeovich AJ, Martínez-pascual M, Pérez-gómez J, Luque AJ, López-román FJ, et al. Effects of high-resistance circuit training in an elderly population. *EXG* [Internet]. Elsevier Inc.; 2013;48(3):334–40. Available from: <http://dx.doi.org/10.1016/j.exger.2013.01.007>
17. Lehnert M, Stastny P, Sigmund M, Xaverova Z, Hubnerova B, Kostrzewa M. The effect of combined

- machine and body weight circuit training for women on muscle strength and body composition. *J Phys Educ Sport*. 2015;15(3):561–8.
18. Plevková L, Peráčková J, Pačesová P, Kukurová K. The effects of a 6-week strength and endurance circuit training intervention on body image in Slovak primary school girls. 2018;(1):459–64.
 19. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. 2016;37(27):2129–2200m.
 20. Permadi AW. Comparison of respiratory training method for chest wall expansion in patients with chronic obstructive pulmonary disease. *J Phys Educ Sport*. 2018;18(4):2235–9.
 21. Galazoulas C. Effects of static stretching duration on isokinetic peak torque in basketball players in semi-professional male basketball players. *J Phys Educ Sport*. 2016;16(2):1058–63.
 22. Ocak Y, Savas S, Isik O, Ersoz Y. The Effect of Eight-week Workout Specific to Basketball on some Physical and Physiological Parameters. *Procedia - Soc Behav Sci* [Internet]. Elsevier B.V.; 2014;152:1288–92. Available from: <http://linkinghub.elsevier.com/retrieve/pii/S1877042814054317>
 23. Sansone P, Tessitore A, Palauskas H, Lukonaitiene I, Tschan H, Pliauga V, et al. Physical and physiological demands and hormonal responses in basketball small-sided games with different tactical tasks and training regimes. *J Sci Med Sport* [Internet]. Sports Medicine Australia; 2018;11–5. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1440244018304638>

Relationship between Self-Care for Fluid Limitation and Interdialytic Weight Gain among Patients with Hemodialysis at Ratu Zalecha Hospital, Martapura

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Abstract

Chronic kidney failure is progressive and irreversible which caused metabolism disorder as well as electrolyte imbalance. This condition makes the patients to conduct hemodialysis. Patients with hemodialysis must have the ability to do self-care for fluid limitation management. Self-care deficit in managing fluids can cause interdialytic weight gain. The aim of this study was to measure the correlation between self-care for fluid limitation and interdialytic weight gain among chronic kidney disease patients with hemodialysis in Ratu Zalecha hospital Martapura. This study used cross-sectional study, total sampling and the final sample was 50 respondents. Data were collected in 2018. We used Spearman Rank Correlation to analyze the data. The result showed that there was a correlation of self-care for fluid limitation and interdialytic weight gain among patients with hemodialysis in Ratu Zalecha Hospital Martapura (p -value < 0,000; r = 0,589). The capability of self-care for fluid limitation and increase self-confidence among patient with hemodialysis to prevent interdialytic weight gain is needed.

Keywords: *Self-care, Fluid limitation, Interdialytic weight gain, hemodialysis.*

Introduction

Kidney has an important role in the human body to maintain fluid volume and distribution ⁽¹⁾. Kidney failure requirements long treatment ⁽¹⁾. More than 500 million people had Chronic kidney failure ⁽²⁾ and only 0.1% of kidney failure was detected ⁽³⁾. 2,622,000 people with kidney failure conducted end-stage renal disease (ESRD), and 77% undergo hemodialysis treatment ⁽³⁾. *National Center For Chronic Disease Prevention and Health Promotion* (2014) noted that the prevalence of chronic kidney failure was increased ⁽⁴⁾.

Chronic kidney failure is progressive and irreversible. The urea creatinine will increase as the body inability to maintenance metabolism and keep fluid and electrolyte balance ⁽⁵⁾. Additionally, kidney failure caused endocrine disorder and metabolic disorder, so it needs hemodialysis or kidney transplantation ⁽⁵⁾. Hemodialysis is needed to remove metabolic residual from the blood such as water, sodium, potassium, hydrogen, urea,

creatinine, uric acid, and others substance through semi-permeable membranes ⁽⁶⁾. Hemodialysis also assists to maintain fluid balance, but the patients have to control their fluid regularly.

Patients with hemodialysis need to be trained to calculate fluid balance within 24 hours so they can control the fluid based on their needs. The fluid restriction will prevent fluid excess, because fluid excess can cause disruption of function in other organs, such as lung and cardio ⁽⁷⁾. Another consequence is interdialytic weight gain, edema, wet rheumatism in the pulmonary, swollen eyelids and shortness of breath ⁽⁵⁾.

Patient with hemodialysis is required to do self-care independently, it refers to self-care. Self-care is an individual effort to fulfill their needs by optimizing intellectual abilities, behavior and utilizing the environment ⁽⁸⁾. Self-care can be achieved by applying Dorothea E. Orem's nursing self-care theory. According to Orem's theory, every individual with a certain age

and condition has the ability to treat, protect, control, minimize and maintain the body to get healthy and well-being as well as optimal life both healthy and sick, or recovering from illness⁽⁵⁾.

Self-care deficit in managing fluids can cause an increase in body weight between two dialysis times due to increased body fluid volume, it refers to interdialytic weight gain⁽⁹⁾. Interdialytic weight gain is one of the complications in patients with chronic renal failure who undergo hemodialysis caused by the inability of the renal excretion function. Increasing the value of the interdialytic weight gain will cause a negative effect such as hypotension, muscle cramps, hypertension, shortness of breath, nausea vomiting⁽¹⁰⁾, also cause hypertension, peripheral edema, pulmonary edema, and increase the risk of dilatation and cardiac hypertrophy⁽⁷⁾. The problem in this study was to measure the relationship between self-care of fluid limitation and interdialytic weight gain among patients with chronic renal failure and hemodialysis in Ratu Zalecha Hospital Martapura.

Method

Participants and Settings: All of the procedures of this study got permission from Institutional review board in one of University in Indonesia. This study used cross-sectional design to analyze the correlation between self-care for fluid limitation and Interdialytic Weight Gain. The Dependent variable was self-care for fluid limitation and the independent variable was Interdialytic Weight Gain.

Data were collected from patient with hemodialysis in Ratu Zalecha Hospital Martapura, South Kalimantan, Indonesia, and used total sampling. We collected the data from Januari until February 2018. Total patients with hemodialysis in this hospital were 81. It produced 60% respond rate, so the final sample was 50 respondents.

Instruments: We used self-report questionnaires to collect the data.

Self-care for fluid limitation: We developed this questionnaire based on self-care concept from Orem theory (11, 12). It had 3 dimensions self-care maintenance, self-care management, and self-care confidence with total of 20 items. Self-care maintenance refers to knowledge regarding decision-making with true-false question (7 items), self-care management refers to behavior regarding health maintenance (7 items), with Likert scale (always-never), and self-

care confidence regarding self-efficacy (6 items) with Likert scale (strongly disagree-strongly agree). The score between 51-80 means high score in self-care, and score between 20-50 means low score in self-care. This questionnaire had good convergent validity ($r > 0.2$) and adequate internal consistency with cronbach alpha= 0.839.

Interdialytic weight gain (IDWG): This is an observational instrument and measure body weight before hemodialysis, body weight after hemodialysis. We used Nerbass theory to determine the different bodyweight as well as the percentage of body weight (13). If the percentage of bodyweight $< 5\%$ refer to normal.

Statistical analysis: We used SPSS for windows to analyze the data (p value of < 0.05 are considered to describe statistically significant differences). Descriptive statistics (frequency and percentage) were used to calculate all variables. A spearman correlation was used to explore the relationship between self-care for fluid limitation and Interdialytic Weight Gain. Regarding response rate we used the recommendation from the previous study, that was 60% response rate⁽¹⁴⁾.

Findings:

Characteristic of Respondents:

Table 1 shows the characteristic of participants, included in this study: age, gender, and length of hemodialysis. Regarding age, 34% of participants were 45-55 and 56 -65 years old, the proportion of male was 54% and female was 46%. Length of hemodialysis showed that 54% of participants undergo hemodialysis around 12-24 months and 40% of participants undergo hemodialysis > 24 months.

Table 1. Demographic characteristic of participants

Characteristic	N	%
Total = 50		
Age (years)		
18-40	3	6
41-45	8	16
46-55	17	34
56-65	17	34
>65	5	10
Gender		
Male	27	54
Female	23	46

Characteristic	N	%
Length of Hemodialysis		
<12 months	3	6
12 – 24 months	27	54
>24months	20	40

Descriptive statistics among variables: Table 2 shows 58% participants had good self-care for fluid limitation and 42% had low self-care for fluid limitation. In term of Interdialytic Weight Gain, 58% participants had normal Interdialytic Weight Gain and 42% participants had abnormal Interdialytic Weight Gain.

Table 2. Statistical Description of variables

Variables	N	%
Total = 50		
Self-care for fluid limitation		
High	29	58
Low	21	42
Interdialytic Weight Gain		
Normal	29	58
Abnormal	21	42

Correlation among study variables: Table 3 shows significant correlation between self-care for fluid limit and Interdialytic Weight Gain with moderate relationship ($r = 0.589$, p value < 0.01)

Table 3. Relationship between self-care for fluid limit and Interdialytic Weight Gain

	Interdialytic Weight Gain
Self-care for fluid limit	0.589**

** p value < 0.01

Discussion

Self-care for fluid limitation among patients with hemodialysis in Ratu Zalecha Hospital Martapura

Patients with hemodialysis generally have complex problems and require to fulfill their needs. One of their needs was related with ability to care themselves. Patients with hemodialysis must have ability to maintain their fluid intake to achieve optimum quality of life. Self-care in this study used Orem theory^(11, 12, 15). Based on this study, 58% of respondents had good self-care for fluid limitation (table 2). Most respondents showed higher self-care maintenance (knowledge) followed by self-care confidence (self-esteem) and self-care management (behavior). Previous study noted that quality of life

could be achieved by increasing self-care⁽³⁾.

This study also showed most of the respondents had low self-care management to manage the fluid intake. The patients did not calculate the fluid intake and urine output a day. They consume 2-3 glasses of water in a day, with urine output 500 ml/24 hours and also manage thirst by brush their teeth and gargling. However, they did not know that they must restrict salty food that induces thirstily. Previous study mentioned about the obstacle of self-care management among patients with hemodialysis was internal and external factors. Internal factors were low of motivation to diet and fluid restriction during activity. External factor was cost of hemodialysis⁽¹⁶⁾. Fluid restriction is needed to give comfort to patients before and after conducting hemodialysis⁽⁵⁾.

Interdialytic weight gain among patients with hemodialysis in Ratu Zalecha Hospital Martapura:

Interdialytic weight gain is related to the patient’s fluid restriction. Fluid restriction is one of the treatments for end-stage renal disease (ESRD) to prevent worse conditions. The amount of fluid was determined for a day, and it depends on kidney function, the patient’s edema and urine output⁽¹⁷⁾. This study showed that 58% participants increased of body weight and it was normal range. 42% of participants were an abnormal range (table 2). Fluid intake among patients with chronic renal failure related to Interdialytic weight gain. This study was similar to previous study⁽¹⁷⁾. We assumed that Interdialytic weight gain due to thirsty condition among participants, it was similar to Black and Hawks theory⁽¹⁸⁾.

Increased interdialytic weight gain exceeding 5% of dry weight can cause several of complications such as hypertension, interdialytic hypotension, left heart failure, ascites, pleural effusion, congestive heart failure, and also can lead to mortality. Many factors contribute to interdialytic weight gain, such as internal factors (thirst, stress, and self-efficacy) also external factors such as family support and fluid intake⁽¹⁹⁾.

Relationship between self-care for fluid limitation and Interdialytic weight gain among patients with hemodialysis in RSU Ratu ZalechaMartapura

In this study showed 82.8% respondents had high self-care for fluid restriction experienced an increase in normal interdialytic weight gain and the remain was respondents with low self-care for fluid restriction experienced an increase in abnormal interdialytic weight

gain. This study also showed that self-care for fluid restriction was statistically significant with interdialytic weight gain (table 3) with moderate correlation ($r=0.589$). This study was similar previous study about significant relationship between fluid intake and interdialytic weight gain⁽¹⁷⁾.

Limitation: This study had some limitation. This study used cross-sectional study and relatively small sample size. Therefore, the results may be generalized carefully. Further study is needed to increase self-care for fluid limitation among patients with hemodialysis to prevent Interdialytic weight gain.

Conclusion

Besides the limitations, this study produced enough response rate. We are confident that self-care for fluid limitation related to interdialytic weight gain. This study suggests evidence to increase self-care for fluid limitation to prevent Interdialytic weight gain.

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References

1. Arif M, Kumala S. Buku Ajar Asuhan Keperawatan Gangguan Sistem Perkemihan (Nursing Care Book of Urinary System Disorders). Jakarta: Salemba Medika. 2011.
2. Rostanti A, Bawotong J, Onibala F. Faktor Faktor Yang Berhubungan Dengan Kepatuhan Menjalani Terapi Hemodialisa Pada Penyakit Ginjal Kronik Di Ruangan Dahlia Dan Melati Rsup Prof. Dr. R. D Kandou Manado (Factors Associated with Compliance among Chronic Kidney Patients with Hemodialysis Therapy in the Dahlia Room and Jasmine Rsup Prof. Dr. R. D Kandou Manado). JURNAL KEPERAWATAN. 2016;4(2).
3. Nurcahyati S, Karim D. Implementasi self care model dalam upaya meningkatkan kualitas hidup penderita gagal ginjal kronik (Self Care Model to Increase Quality of Life among Patients with Chronic Kidney Disease). Jurnal Keperawatan Sriwijaya. 2016;3(2):25-32.
4. Promotion NCFCDPaH. Indicator Definitions - Chronic Kidney Disease USA2015 [cited 2019 28 May]. Available from: <https://www.cdc.gov/cdi/definitions/chronic-kidney.html>.
5. Fahmi FY, Hidayati T. Gambaran self care status cairan pada pasien hemodialisa (literatur review) (Description of self care fluid status among hemodialysis patients (literature review)). Care: Jurnal Ilmiah Ilmu Kesehatan. 2016;4(2):53-63.
6. Brunner S, Suddarth D. Buku ajar keperawatan medikal bedah (Adult health nursing). Jakarta: EGC. 2002.
7. Rahman A. Optimalisasi Pembatasan Cairan Pada Pasien Gagal Ginjal Kronik Yang Mendapatkan Hemodialisa di RSUPN dr (Optimization of Fluid Restrictions among Chronic Kidney Failure Patients with Hemodialysis at RSUPN Dr.). Cipto Mangunkusumo Jakarta Depok: Fakultas Ilmu Keperawatan Depok. 2014.
8. Sulistyaningsih DR. Penerapan Teori Model Self Care (Orem) Pada Gangguan Sistem Perkemihan (Studi Kasus Di Rumah Sakit Cipto Dan RSPAD Jakarta) (Application Self Care theory among Patients with Urinary system Disorder (Case study at Cipto Hospital and RSPAD Jakarta)). 2014.
9. Umayah E. Hubungan Tingkat Pendidikan, Pengetahuan dan Dukungan Keluarga Dengan Kepatuhan Dalam Pembatasan Asupan Cairan Pada Pasien Gagal Ginjal Kronik yang Mejalanii Hemodialisa Rawat Jalan di RSUD Sukoharjo (Relationship between Education Level, Knowledge, and Family Support and Compliance in Fluid Restriction among Outpatients with Chronic Kidney Failure at Sukoharjo Hospital): Universitas Muhammadiyah Surakarta; 2016.
10. Smeltzer SC, Bare BG. Buku Ajar Keperawatan Medikal Bedah Brunner dan Suddarth (Adult Health Nursing Brunner and Suddarth). Alih bahasa oleh Agung Waluyo...(dkk), EGC, Jakarta. 2002.
11. Alligood MR. Nursing Theorists and Their Work-E-Book: Elsevier Health Sciences; 2017.
12. Nursalam S. Metodologi Penelitian Ilmu Keperawatan Pendekatan Praktis (Research Method Nursing Science). Jakarta: Salemba Medika. 2015.
13. Nerbass FB, Morais JG, Santos RGd, Krüger TS, Koene TT, Luz Filho HAd. Factors related to

- interdialytic weight gain in hemodialysis patients. *Brazilian Journal of Nephrology*. 2011;33(3):300-3005.
14. Dong Y, Peng C-YJ. Principled missing data method for researchers. SpringerPlus. 2013;2(1):222.
 15. Asmadi N, Kep S, editors. *Konsep dasar keperawatan (Fundamental Nursing)2008*: EGC.
 16. Arova FN. *Gambaran self-care management pasien gagal ginjal kronis dengan hemodialisis di wilayah Tangerang Selatan tahun 2013 (Description of self-care management among patients with chronic kidney failure with hemodialysis in the South Tangerang area 2013)*. 2013.
 17. Istanti YP. Hubungan antara Masukan Cairan dengan Interdialytic Weight Gains (IDWG) pada Pasien Chronic Kidney Diseases di Unit Hemodialisis RS PKU Muhammadiyah Yogyakarta (Relationship between Fluid Intake and Interdialytic Weight Gains (IDWG) among Chronic Kidney Diseases Patients in Hemodialysis Unit PKU Muhammadiyah Hospital Yogyakarta). *Profesi (Profesional Islam): Media Publikasi Penelitian*. 2013;10(01).
 18. Riyanto W. Hubungan antara Penambahan Berat Badan di Antara Dua Waktu Hemodialisa (Interdialysis Weight Gain= IDWG) terhadap Kualitas Hidup Pasien Penyakit Ginjal Kronik yang Menjalani Terapi Hemodialisa di Unit Hemodialisa IP2K RSUD Fatmawati Jakarta (The Relationship between Weight Gain in Two Hemodialysis Time (Interdialysis Weight Gain = IDWG) and the Quality of Life of Chronic Kidney Disease Patients with Hemodialysis Therapy in IP2K Hemodialysis Unit, Fatmawati Regional Hospital, Jakarta). Depok: Universitas Indonesia. 2011.
 19. Cahyaningsih ND. *Hemodialisis (hemodialysis)*. Jogjakarta: Mitra Cendikia; 2008.

Relation between Human Epididymis Protein 4 and Endometrial Pathology in Women with Postmenopausal Bleeding

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Abstract

Objective: To evaluate the value of human epididymis protein 4 (HE4) in predicting endometrial pathology in women with postmenopausal bleeding (PMB).

Method: A cohort study included 100 women with PMB. Women with endometrial thickness (ET) >5mm were subjected to hysteroscopic guided fractional curettage (FC) followed by total abdominal hysterectomy and bilateral salpingo-oophorectomy with or without pelvic lymphadenectomy.

After exclusion of 10 patients, the value of serum HE4 was tested in 90 patients for the ability to predict endometrial pathology based on hysterectomy specimen.

Results: Level of HE4 showed a significant difference among women with different endometrial pathologies. HE4 showed a significant positive correlation with the severity of the endometrial lesion, with mean values of 38.33±27 pmol/L for atrophic endometrium (11 cases), 51.26±28.59 pmol/L for simple endometrial hyperplasia (SEH, 51 cases), 148.4 ±67.34 pmol/L for atypical endometrial hyperplasia (AEH, 16 cases) and 390.9±351.72 pmol/L for endometrial carcinoma (EC, 12 cases) Using the cut-off value of 69.5 pmol/L for preoperative HE4 yielded a sensitivity of 75% and a specificity of 88.5% in prediction of EC.

Conclusion: HE4 can predict endometrial pathology in women with PMB with a high specificity and a fair sensitivity.

Keywords: Human epididymis protein 4 (HE4); postmenopausal bleeding; endometrial carcinoma; endometrial pathology.

Introduction

Endometrial carcinoma accounts for 20% to 30% of malignant tumors in the female reproductive system.

As a consequence to increased obesity, hypertension, diabetes, and prolonged life expectancy, the incidence and mortality of endometrial carcinoma have risen lately, with a tendency for onset at a younger age¹. The prognosis is closely related to the disease stage. If the diagnosis is during stage I, then the survival rate is about 90%².

There are no specific tumor markers for endometrial carcinoma. CA-125 was detected in 1983 by Bast et al.³ as the epithelial ovarian carcinoma antigen. However, CA-125 is less effective in the diagnosis of EC compared with the diagnosis of other gynecological carcinomas.

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CA-125 can only produce obvious effect in diagnosing some common tumors in advanced stage⁴.

HE4 biomarker has been recently studied. It was identified in the epithelium of the distal epididymis and was predicted to be a protease inhibitor involved in sperm maturation⁵. In 2003, HE4 was approved by the FDA as a serum tumor marker for ovarian carcinoma and attracted great attention⁶. Recent studies indicate that HE4 is highly expressed in ovarian and endometrial carcinoma tissues with increased serum level in these patients as well⁷.

Materials and Method

This prospective cohort study included 100 women with PMB who were recruited from Kasr Al Aini Hospital, Cairo University, Egypt between June 2014 and August 2016. An informed written consent was obtained from all participants prior to inclusion.

All patients included in the study had single or multiple episodes of PMB with an ET of more than 5mm. Exclusion criteria were having history of other malignancies, history of intake of chemotherapy or radiotherapy, the use of hormone replacement therapy, and being unfit for surgical intervention.

Full history was taken (including the duration of menopause, the number of episodes of PMB, and previous investigations and current medications), general examination was performed (including blood pressure measurement, calculation of body mass index ($BMI = \text{weight (kg)} / [\text{height (m)}]^2$), and the presence of any signs of systemic diseases), and local examination was performed for all patients.

Transvaginal ultrasound (TVS) done by the same observer to nullify the effect of interobserver variability.

For the level of HE4: 5 ml of venous blood were withdrawn from all patients. The samples were left to clot. The separated sera were stored at -20° until all samples were obtained. Frozen samples were allowed to reach room temperature prior to use. Samples were then mixed thoroughly by gently inverting multiple times before analysis. HE4 was quantitatively assayed using the enzyme immunoassay (EIA) method (Fujirebio Diagnostics, Inc. Göteborg, Sweden). The functional sensitivity of the HE4 EIA is $\leq 25\text{pM}$. The analytical specificity is $100 \pm 15\%$.

All patients were then submitted to hysteroscopy

under general anesthesia and guided endometrial biopsy.

Definitive management was later performed in the form of total abdominal hysterectomy, bilateral salpingo-oophorectomy, with or without pelvic lymph nodal dissection and histopathological examination.

Results

Women with malignancy had significantly older age, lower parity, higher BMI and longer duration of menopause when compared to those with non-malignant lesion (table 1).

ET of the malignant group was significantly higher than that of the non-malignant group (20.33 ± 7.4 versus $12.68 \pm 4.22\text{mm}$, $p: <0.001$), level of preoperative serum HE4 was significantly higher in the malignant group as compared to the non-malignant group (390.92 ± 351.72 versus $61.25 \pm 31.65\text{pmol/L}$, $p: <0.001$) (table 1).

The level of HE4 in different endometrial pathologies of the cases group is presented in (table 2).

A scale was proposed in which the endometrial pathologies were arranged in a descending manner according to the severity of the lesion, where malignancy was the severest, followed by AEH, then SEH, and atrophic endometrium being the least severe form. Hence, correlation between the preoperative HE4 level and the severity of the endometrial lesion could be evaluated. This study showed that there was a significant strong positive correlation between the preoperative level of HE4 and the severity of the endometrial pathology ($r=0.735$, $p: <0.001$).

ROC curve was generated to evaluate the performance of the preoperative level of HE4 in distinguishing malignant from non-malignant endometrium (figure 1).

Using the cut-off value of 69.5 pmol/L for preoperative HE4 yielded a sensitivity of 75%, a specificity of 88.5% and an AUC-ROC of 0.933 (table 3).

All malignant cases (12 cases) were of the endometrioid type, 5 were stage Ia, 5 were stage Ib, and 2 were stage II. All were operable and a total abdominal hysterectomy and bilateral salpingo-oophorectomy with pelvic lymphadenectomy was performed for all.

For the degree of differentiation, 2 cases were grade 1 (G1), 8 cases were grade 2 (G2), and 2 cases were grade 3 (G3).

Multivariate stepwise linear regression for factors with significant differences between malignant and non malignant cases as age, parity, and duration of menopause are shown in table 4.

The level of HE4 in the malignant cases according to the tumor stage, grade and lymph node involvement is described in table 5.

Discussion

In this study, we focused on examining the role of HE4 in distinguishing malignant from non-malignant lesions of the thickened endometrium in women with PMB through histopathological examination of hysteroscopic directed endometrial curettage followed by hysterectomy, and to correlate HE4 level with the endometrial lesion.

The prevalence of EC in the present study was 13.3%. This is similar to that reported in previous studies⁸.

HE4 is a new detection index. Being highly expressed in ovarian and endometrial carcinoma cells⁷.

In this study, the preoperative level of HE4 was significantly higher in the endometrial carcinoma cases than its level in the non-malignant cases.

HE4 actually exists in normal tissues e.g. male vas deferens, mammary gland epithelium, female genital tract including the endometrium⁹. So its level is suspected to increase with increased endometrial thickness. As suspected its level is increased in cancers arising from these tissues¹⁰.

The National comprehensive cancer network in 2012 signified the value of HE4 as a tumour marker for epithelial ovarian tumors and as both the uterus and the ovary share a common embryological origin so HE4 can be used as a marker for endometrial tumors¹¹.

In the present study, upon examining the diagnostic performance of HE4 in predicting the presence of EC among patients with PMB, using the cut-off value of 69.5 pmol/L for preoperative HE4 yielded a sensitivity of 75% and a specificity of 88.5%, and an AUC-ROC of 0.933, Having more serious consequences separating AEH and EC patients from SEH and atrophic endometrium cases, HE4 was significantly higher in the former group 218.14 ± 273.46 versus 54.2 ± 22.45 , $p < 0.001$ with a new cut off value calculated to help differentiation of AEH and

EC cases, HE4 value of 62.5 pmol/L yielded a sensitivity of 85.9% and specificity of 62.9% with AUC of 0.832 .

Similar to our findings, previous study on 2015 reported the sensitivity and specificity of HE4 in distinguishing EC patients from healthy females were 62.2% and 95% respectively, with an AUC of 0.996 . Another one on the same year reported a sensitivity of 72.4% and a specificity of 75.4% for the cut-off 76.5 pmol/L¹⁵. Also, Capriglione et al in 2015¹⁶ reported sensitivity and specificity that are near to ours in detecting EC patients 83.3% and 96% respectively.

An earlier study on 2013 has reported that the sensitivity of HE4 in detecting malignant cases was 75% and the specificity was 65.5%, and that the sensitivity was improved after combining HE4 with other markers (CA-125, CEA, and serum amyloid –A) to be 84%¹³.

Another publication in the same year revealed that the sensitivity of HE4 in detecting malignant endometrium was 59.4% with 100% specificity for the cut-off value of 70pmol/L. After adding CA-125, the sensitivity was elevated to be 60.4%. The authors concluded that HE4 at cutoff of 70 pmol/L yields the best sensitivity and specificity¹². The lower sensitivity of the marker in their study compared to ours might be due to that they took into consideration other types of EC while all our cases were of the endometrioid type.

Previous study on 2016 have reported that HE4 was significantly higher in grade 3 (G3) carcinomas compared with grade 1 (G1) and 2 (G2), and that patients who needed lymphadenectomy had significantly higher HE4 level than those who had no indications for this procedure¹⁴.

A recent study on 2017 stated that preoperative serum HE4 is significantly correlated with primary tumor diameter and depth of myometrial invasion, but not with tumor grade or cervical involvement and lymphovascular infiltration and that serum HE4 levels could be useful in identifying EC patients at high risk of lymphatic spread who would benefit from lymphadenectomy¹⁷.

A meta-analysis done in 2014 reported that HE4 is the most accurate and sensitive EC marker identified to date. In particular, this new marker seems to have a good performance in diagnosis. The best cut-off of HE4 in diagnosis ranges between 50 and 70 pmol/L, resulting at least in 78.8% of sensitivity and 100% of specificity in all stages. Another important aspect to consider is HE4

capacity in predicting the stage of disease and myometrial involvement, which can help scheduling the appropriate timing of imaging and surgery in a more individualized fashion and as indicator of patient prognosis¹⁸.

Our study confirmed the known fact that malignancy is suspected to be found in women with postmenopausal bleeding when they are older, lower parity, higher BMI and have longer interval between menopause and presentation.

ACOG confirmed these findings by stating that the clinically identified risks for carcinoma endometrium include age and high body fat¹⁹.

The present study is strengthened by its prospective

nature, and that it depended on hysterectomy specimen for diagnosis of different endometrial pathologies as well as malignancy, beside the analysis of positive results of lymphadenectomy.

The main limitation of the study is the small sample size included which resulted in a limited number of malignancy cases with the resultant limited variations in malignancy stages and pathological subtypes. Larger number of participants would have better detected the value of the studied marker (HE4) in diagnosis and prognosis of endometrial malignancies. Nevertheless, the study highlighted the presence of this new marker and pointed to its possible value in diagnosis of the disease and the prediction of its occurrence at certain cut-off value with the reported sensitivity and specificity.

Table (1): Characteristics of the studied population

	Malignant group (n=12)	Non-malignant group (n= 78)	P value
Age (Years)	63.5 ± 6.86	55.97 ± 5.68	<0.001
Parity	2.67 ± 1.49	4.71 ± 2.15	0.002
BMI (Kg/m ²)	37.19 ± 5.58	32.95 ± 6.49	0.034
Duration of menopause (Years)	11.67 ± 5.41	4.83 ± 4.26	<0.001
Endometrial thickness (mm)	20.33 ± 7.4	12.68 ± 4.22	<0.001
Preoperative HE4 (pmol/L)	390.92 ± 351.72	61.25 ± 31.65	<0.001

Data are presented as mean± SD

Table (2): Level of HE4 in different endometrial pathologies

	EC (n= 12)	AEH (n= 16)	SEH (n= 51)	Atrophic endometrium (n= 11)	P value
HE4 (pmol/L)	390.92 ± 351.72	148.44 ± 67.34	51.26 ± 28.59	38.33 ± 27	<0.001

Data are presented as mean± SD

Table (3): Tests of diagnostic accuracy of preoperative HE4 level in distinguishing malignant from non-malignant endometrium

		Cut-off value	Sensitivity (%)	Specificity (%)	AUC-ROC	PPV	NPV	Accuracy
HE4 level (pmol/L)	Malignant versus non- malignant cases	69.5	75	88.5	0.933	50	95.8	86.7

Table (4): Multivariate stepwise linear regression for age, parity, and duration of menopause

	Beta Coefficient Adjusted	S.E.	Wald	p value	OR	95% CI for OR	
						Lower	Upper
Age	0.259	0.294	0.779	0.377	1.296	0.729	2.304
Parity	-1.064	0.492	4.676	0.031	0.345	0.132	0.905
Duration of Menopause	0.189	0.253	0.557	0.455	1.208	0.735	1.985

Table (5): The level of HE4 in the malignant cases according to the tumor stage, grade and lymph node involvement

	No. Patients	HE4 Level	P Value
Figo stage			
I	10	322.56±182.66	Ia vs Ib =0.012 Ib vs IIa=0.241 I vs II=0.001
Ia	5	262.32±319.51	
Ib	5	435.4±293.59	
IIa	2	501.72±423.74	
Grade			
G1	2	82.16±55.23	<0.001
G2	8	308.89±275.85	
G3	2	920.54±166.17	
Lymph nodes			
Positive	3	635.42±426.88	<0.001
Negative	9	167.84±112.43	

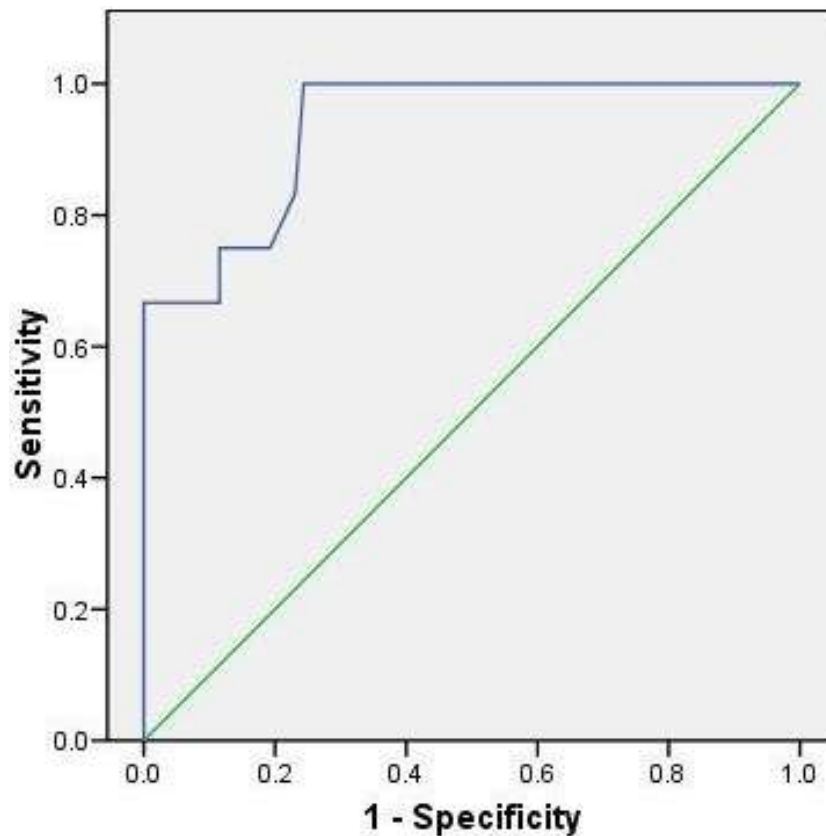


Figure 1: ROC curve

Conclusion

HE4 can predict endometrial pathology in women with PMB with a high specificity and a fair sensitivity.

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Clinical Trial Registry No.: NCT03558321

References

1. Brennan DJ, Hackethal A, Metcalf AM. Serum HE4 as a prognostic marker in endometrial carcinoma:

- a population based study. *Gynecologic Oncology* 2014; 132(1): 159–165.
2. Bie Y, Zhang Z. Diagnostic value of serum HE4 in endometrial carcinoma: A meta-analysis. *World J Surg Oncol.* 2014; 12:169.
 3. Bast RC, Klug TL, St John E, et al. A radioimmunoassay using a monoclonal antibody to monitor the course of epithelial ovarian carcinoma. *N Engl J Med* 1983; 309: 883–887.
 4. Liu X, Zhao F, Hu L, et al. Value of detection of serum human epididymis secretory protein 4 and carbohydrate antigen 125 in diagnosis of early endometrial carcinoma of different pathological subtypes. *Onco Targets Ther.* 2015 May 26; 8:1239-1243.
 5. Kirchhoff C. Molecular characterization of epididymal proteins. *Rev Reprod* 1998, 3: 86–95.
 6. Helstrom I, Raycraft J, Hayden-Ledbetter M. The HE4 (WFDC2) protein is a biomarker for ovarian carcinoma, *Cancer Research* 2003; 63 (13): 3695–3700.
 7. Xia C, Ping Z, Xiaoyan L. Relationship between the serum human epididymis secretory protein 4 and clinical pathological features in patients with epithelial ovarian cancer. *Labeled Immunoassays Clin Med.* 2010; 17(6):365–367.
 8. Damle RP, Dravid NV, Suryawanshi KH, et al. Clinicopathological Spectrum of Endometrial Changes in Peri-menopausal and Post-menopausal Abnormal Uterine Bleeding: A 2 Years Study. *J Clin Diagn Res.* 2013 Dec; 7(12):2774-2776.
 9. Mehri Jafari-Shobeiri, MarzyeJangi, Ali Dastranj Tabrizi, Manizheh Sayyah-Melli, Parvin Mostafa-Gharabaghi, Elaheh Ouladsahebmadarek, Esmail Neginfar, Yasmin Pouraliakbar. Diagnostic Value of Novel Biomarker Human Epididymis Protein 4 (HE4) in Detecting Endometrial Cancer. *International Journal of Women's Health and Reproduction Sciences* Vol. 4, No. 1, January 2016, 29-33
 10. Simmons AR, Baggerly K, Bast RC Jr. The emerging role of HE4 in the evaluation of epithelial ovarian and endometrial carcinomas. *Oncology (Williston Park)* 2013;27:548-556.
 11. Xiao Li, Yiping Gao, Mingzi Tan, et al., “Expression of HE4 in Endometrial Cancer and Its Clinical Significance,” *BioMed Research International*, vol. 2015, Article ID 437468, 8 pages, 2015. <https://doi.org/10.1155/2015/437468>
 12. Angioli R, Plotti F, Capriglione S, et al. The role of novel biomarker HE4 in endometrial cancer: a case control prospective study. *Tumour Biol.* 2013; 34:571–576.
 13. Omer B, Genc S, Takmaz O, et al. The diagnostic role of human epididymis protein 4 and serum amyloid-A in early-stage endometrial cancer patients. *Tumour Biol.* 2013 Oct; 34(5):2645-50.
 14. Gąsiorowska E, Magnowska M, Iżycka N, et al. The role of HE4 in differentiating benign and malignant endometrial pathology. *Ginekol Pol.* 2016; 87(4):260-264.
 15. Minář L, Klabenešová I, Jandáková E. The importance of HE4 in differential diagnosis of endometrial cancer. *CeskaGynekol.* 2015 Aug; 80(4):256-63.
 16. Capriglione S, Plotti F, Miranda A, et al. Utility of tumor marker HE4 as prognostic factor in endometrial cancer: a single-center controlled study. *Tumour Biol.* 2015 Jun; 36(6):4151-4156.
 17. Fanfani F, Restaino S, Cicogna S, et al. Preoperative Serum Human Epididymis Protein 4 Levels in Early Stage Endometrial Cancer: A Prospective Study. *Int J Gynecol Cancer.* 2017 Jul; 27(6):1200-1205.
 18. Angioli R, Miranda A, Aloisi A, et al. A critical review on HE4 performance in endometrial cancer: where are we now? *Tumour Biol.* 2014 Feb; 35(2):881-887.
 19. ACOG Committee Opinion No. 734 Summary: The Role of Transvaginal Ultrasonography in Evaluating the Endometrium of Women With Postmenopausal Bleeding. *Obstet Gynecol.* 2018 May;131(5):945-946. doi: 10.1097/AOG.0000000000002626.

Impact of Cervical Infection with Bacteria *Ureaplasma Urealyticum* to Interleukin-1 α -Expression in Pregnant Women

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Abstract

Pregnant women could be at risk of developing complications in genital tract when infected with the bacteria *Ureaplasma urealyticum*. The objective of this study was to assess the impact of genital infection in pregnant women, in Kirkuk city, relevant to both gestational age and level of Interleukine (IL-1 α). Fifty five pregnant women were involved whose ages ranged between 18-45 years. Double swab samples from cervix were collected i.e. the first swab used to detect *U. urealyticum* while the second to assess the level of IL-1 α cytokine. Only 45% of pregnant women were infected with *U. urealyticum*, with the highest positive *U. urealyticum* infection among age group (18-31 years) (40%), while the older women had less infection frequency (5%). The significantly highest ($p \leq 0.05$) distribution percentage was amongst third trimester gestation (33%). Genital expression of IL-1 α had significantly ($p \leq 0.05$) elevated during the infection (189 \pm 3.3pg/mL) in comparison with non-infected pregnant women. The level of IL-1 α was elevated significantly ($p \leq 0.05$) among women in third trimester of pregnancy in comparison with second and first trimester, respectively. A significant correlation between *U. urealyticum* infection and elevation in the level of IL-1 α is established.

Keywords: Bacteria *Ureaplasma urealyticum*, Gestational age, interleukine IL-1 α , pregnant women.

Introduction

Bacterial vaginosis (BV) is one of the most common genital tract infections among reproductive age-group worldwide, in some cases, for unknown reasons. They are parasitic bacteria which need a host i.e. a human or animal to survive. Both social and sexual factors can contribute to the development of bacterial vaginosis¹. The bacteria may exist almost in every woman but as a friendly and in nonpathogenic status. The bacteria *Ureaplasma* (family Mycoplasmataceae) have been found in both men and women with infertility problems. The bacterium is part of the body's bacterial population, and they live in balance, without causing a problem, in most cases; however, they can increase in population, causing infection and health complications. The

Ureaplasma, itself, is a bacterium commonly found in people's urinary or genital tract and can **cause fertility problems in both genders which** can be passed during sexual contact. It may also be found in women who have never been sexually active but might be higher among women who had multiple sexual partners. These bacteria may also be passed to a fetus or newborn if the mother has *Ureaplasma* infection during pregnancy².

Many species of mycoplasmas, do exist but only four are recognized as human pathogens; however, this study deals with only one species e.g. *Ureaplasma urealyticum*. There are other species isolated from humans' genital tract, but their role in disease is not well established yet e.g. *Mycoplasma genitalium* and *Ureaplasma parvum* that may reach colonization rates of up to 80% in healthy, sexually active women³. These species can be detected within vaginal flora in 40% of sexual inactive and 67% of sexually active women at reproductive age and in 25% of postmenopausal women⁴. The known transmission routes involved sexual contact or maternal infant transfer⁵.

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The *Ureaplasma* lacks the cell wall that makes it unique among bacteria represented in its resistant to some common antibiotics, including penicillin while it can be treated with others. The *U.urealyticum*, is also an important opportunistic pathogen during pregnancy⁶. These reproductive tract infections are implicated in medical conditions, i.e. pelvic inflammatory disease, preterm premature rupture of membranes, preterm birth, pregnancy loss, postpartum and postabortal sepsis^{7,8,9}. *Maternal genital colonization with U.urealyticum promotes preterm delivery: association of the respiratory colonization of premature infants with chronic lung disease and increased mortality*¹⁰. The health condition of females is commonly checked by swab samples taken from cervicovaginal tract includes cytokines. The cervico-vaginal fluid proteome reflects the local biochemical milieu and is influenced by the physical changes occurring in the cervix and adjacent overlying fetal membranes^{11,12}. Hence, it can be an excellent media to test the health condition in the female.

Cytokines represent a broad and loose category of peptides i.e. interleukins which cannot cross the lipid bilayer of cells to enter the cytoplasm but are involved in signaling as immuno-modulating agents. They are produced by a broad range of cells, including immune cells like macrophages, B-lymphocytes, T-lymphocytes and mast cells, as well as endothelial cells, fibroblasts, and various stromal cells¹³. The cytokines, similar to hormones, do act through receptors, and are especially important in the immune system as well as in health and disease, specifically in host responses to infection, i.e. immune responses, inflammation, trauma, sepsis, cancer, and reproduction¹⁴. Interleukine-1 (IL-1) is a central mediator for innate immunity and inflammation which includes 7 ligands with agonist activity, three receptor antagonist and an anti-inflammatory cytokine (IL-37). Interleukine-1(IL-1) could therefore play a key role in checking the urogenital health condition of BV in women particularly in pregnant women.

Due to scanty studies to assess the prevalence of this bacterium and its correlation with the hormone interleukine-1 sequence in pregnant women in Iraq this study has been undertaken to address such a correlation.

Materials and Method

Only 55 pregnant women involved were attending Azadi teaching hospital for the period of November 2016-March 2017. Two cervicovaginal swabs from each

pregnant woman were collected i.e. first was tested to diagnose *U.urealyticum* bacteria using mycoview kit (Zeakon diagnostic) (Besancon-france)¹⁵. The second swab was preserved in phosphate buffer saline and then tested to assess for level of IL-1 α using ELISA technique (Diacclone Company, Besancon Cedex, France), and the SPSS (ANOVA) biostatistical analysis was used.

Results

Only 25 out of 55 swabs (45.5%) collected from vaginal cervix were positive to *U. urealyticum* infection divided between 15 urban (27.3%) and 10 rural women (18.2%) indicating a proportion of 3:2 urban to rural (Table -1). The levels of IL-1 α among pregnant women infected with *U. urealyticum* in urban appeared significantly ($p \leq 0.05$) higher (279.7 \pm 17pg/ml) than in rural (246 \pm 6pg/ml) as in (Fig. 1).

Table 1: Details of infection with U.urealyticum according to geographical distribution, percentages and interleukine-1 levels(*): $p \leq 0.05$.

Groups	Ureaplasmaurealyticum		Total
	Positive pg/mL	Control pg/mL	
Urban	15(27.3%)* (279 \pm 17)	21(38.2%)* (158 \pm 5)	36(65.4%)
Rural	10(18.2%) (246 \pm 6)	9(16.3%) (146 \pm 6)	19(34.6%)
Total	25(45.5%)	30(54.4%)	55(100%)

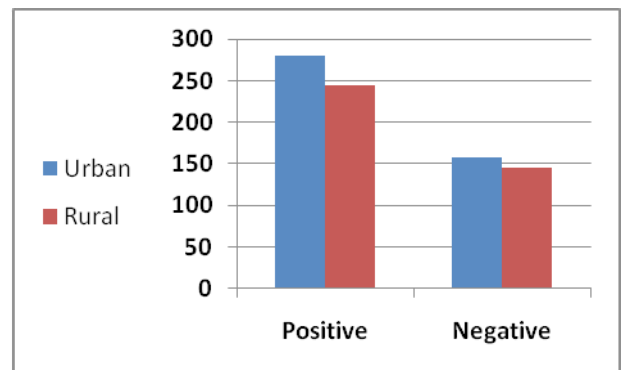


Fig-1: Levels of IL-1 α (pg/mL) in both infected with U. urealyticum and control pregnant women from urban and rural districts. Differences were significant ($p \leq 0.05$).

The highest positive *U.urealyticum* infection was 22(40%), among women whose ages ranged 18-31 years while the older women had less infection frequency 3(5%) [Fig.2]. The significantly highest ($p \leq 0.05$)

distribution percentage was amongst third trimester 18(33%) in comparison with second and first semesters [Fig.3].

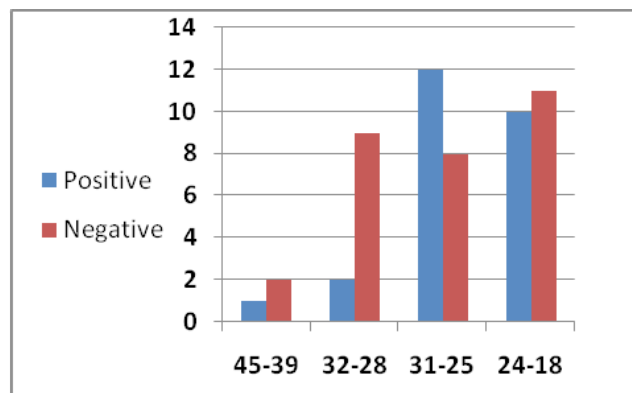


Fig 2: Frequency of U. urealyticum infection in pregnant women according to age groups. The highest group infected was women aged 25-31 and 18-24 years old.

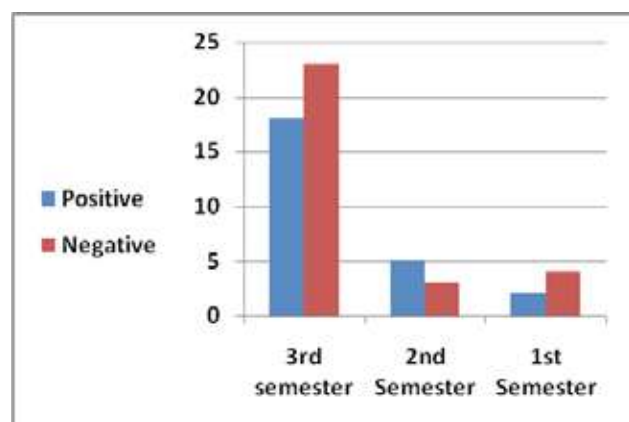


Fig. 3: Frequency of U. urealyticum infection according to gestational trimester of pregnancy. Note the third Trimester recorded the highest ever.

Level of interleukins (IL-1α) has significantly ($p \leq 0.05$) increased in pregnant women infected with *U. urealyticum* that involved almost all age groups. The highest record was at age group 32-38 year old (359±28pg/mL) followed by age group (18-24) years, respectively. However, the elevation in older age groups were less in comparison with control (Table 2).

Levels of IL-1α in different trimester with *U. urealyticum* infection had significantly ($p \leq 0.05$) increased in the third trimester (305.74±13.76 pg/mL) in comparison with the second (176.4±3.8 pg/ml) and first trimester, respectively (Table-3).

Table (2): Level of IL-1α with U.urealyticum infection among pregnant women according age groups (* $p \leq 0.05$).

Age groups	IL-1α level (pg/ml) against U. urealyticum	
	Infected (pg/ml)	Control (pg/ml)
18-24	239.4±7.3*	160.7±12.9
25-31	193.3±5.5*	141.5±5.8
32-38	359±27*	156± 8
39-45	189.4±8*	144±6
Mean	189.3±3.3*	152± 6

Table 3: Distribution of IL-1a (pg/mL) in different trimester with U. urealyticum infection in pregnant women

Groups	U.urealyticum	
	Infective (pg/mL)	Control (pg/mL)
Trimesters		
First trimester	187.4±7.3	167.5±4
Second trimester	176.4±3.8	154.6±6
Third trimester	305.7±13.7*	144.5±8

Discussion

Although the total samples of pregnant women is not high enough due to social Iraqi mentality to donate swap samples to male researcher; however, they might, to certain degree, be indicative to the real frequency of infection. The negative samples that showed no infection were used as control for the comparison purposes. The high prevalence of *U. urealyticum* infection was among pregnant women in rural residence which indicates a rather lesser hygienic awareness differences and consequence lower health education level amongst the urban women. Such result is concomitant with most recent work¹⁶ while other studies had significantly varied in prevalence outcome than ours e.g. 41.1%¹⁷; 69%¹⁸. However, further lower percentages (16.13%) were also reported in Northern Greece¹⁹ and in Iran (15%)²⁰. Much lesser percentage (11.4%) was detected in amniotic fluid samples in a study done on pregnant women in second trimester²¹. An Iranian study found that the prevalence of *U.urealyticum* infection in women (spontaneous abortion and normal pregnancy) was 11.92%²². while the prevalence was significantly ($p \leq 0.001$) higher in Turkey's (HSD)²³. Such a differences might be attributed to geographical distribution of the VB or to genetic factors while the health care awareness differences must not be knocked out.

The *Ureaplasmas* bacterium produces an IgA protease and releases ammonia through urea hydrolysis, both of which are considered possible virulence factors, may lead to immunologic response²⁴. It seems that the middle age group are more sensitive to the infection than other age groups.

The presence of BV during pregnancy become a matter of concern of physicians/gynecologists due to adverse pregnancy outcomes as they increase the risk of late miscarriage, preterm labor, low-birth-weight infants, chorioamnionitis, postpartum endometritis, and postabortion pelvic inflammatory disease²⁵. The BV-associated micro-organisms e.g. bacteria, in amniotic fluid and the placenta originating from the cervicovaginal mucosa are correlated to abortion and preterm labor²⁶.

When BV is identified before 16 weeks of gestation, the highest rates of preterm labor was detected while BV was responsible for 2 fold risk and 3 fold miscarriage detected of miscarriage in the first trimester²⁷, respectively. Other studies showed that BV is related to the late miscarriage in comparison with the first trimester pregnancy loss²⁸. Almost 40% of pregnant women the BV had caused low-birth-weight infant at the second trimester pregnancy²⁹. Other studies contradicted the above findings in fertile women³⁰.

The early age infection in our study is concomitant with a most recent study which was (70.7%) among age group (25-35 years)³¹. Simultaneously, the lower percent of *U. urealyticum* infection of the pregnant women was above 35 years age which may refer to rather a better gynecological experience of sexual transmitted disease prevention in older women than in younger ages. The higher frequency of *U. urealyticum* infection among third trimester might be attributed to the increase in infection rate among age group (25-31) years due to ignorance in health checkout and lack of treatment prior delivery. The latter might burden further risks on pregnant women in defected children e.g. congenital abnormalities. The test of pregnant women for *Ureaplasma* infections, can greatly reduce the chance of any complications by a suitable antibiotic treatment.

The significant increase in the level of IL-1 α in pregnant women at the third trimester may be correlated to the increase in the infection intensity. At late pregnancy, the level of IL-1 α and β concentrations increase to the peak at 4-14 days prior to labor onset³² which is concomitant with the present study, however,

no correlation was made to address the link between the levels of IL-1 α to the intensity of the infection. In other words, the concomitant increase of the interleukine with the infection rate might indicate the involvement of the interleukins in defense mechanisms against ascending infection from the vagina³³. To the best of our knowledge no correlation studies to relate the level of IL-1 α during *U. urealyticum* infection have previously been done to address such a relevancy which may mean that the present study may represent a pioneer one so far.

Conclusions and Recommendation

The BV bacterium *U. urealyticum* infection has relatively high rate among pregnant women represented at third trimester of pregnancy particularly at age groups (25-31 years). Level of IL-1 α elevated among age groups (32-38 years) particularly at third trimester of pregnancy. It is recommended to carry out a obligatory survey of BV during the pregnancy all over the country for prognosis with an early treatment to avoid further risk to the pregnant women and their babies.

Acknowledgement: Data are collected anonymously from routine daily hospital checkup for pregnant women attending the state hospital to which the authors acknowledge. There is no conflict of interest in this research.

Ethical Clearance: The results involved routine data from daily hospital checkup procedure for pregnant women attending the state hospital. Ethical clearance, therefore, deems unrequired as the results are taken anonymously from the hospital records where no patient name is disclosed.

Source of Funding: The whole research is done upon results of checkup at state hospital where it is self-funded. Any other fees spent are all from our pocket money. The authors acknowledged in the manuscript the Hospital officers for their co-operation in proving us the data for research purposes.

Conflict of Interest: There is no conflict of interest in this research of other parties at all and I am liable for any claim otherwise.

References

1. Mengistie, Z; Woldeamanuel, Y; Asrat, D and Adera, A (2014). Prevalence of bacterial vaginosis among pregnant women attending antenatal care in Tikur Anbessa University Hospital, Addis Ababa,

- Ethiopia. *BMC Research Notes*. 7(1): 822-830.
2. Mayer, G (2016). "Bacteriology-Chapter nineteen Mycoplasma and Ureaplasma". *Microbiology and Immunology on line*. University of South Carolina School of Medicine. Also available at: <http://www.microbiologybook.org/mayer/myco.htm>
 3. Kechagia, N; Bersimis S and Chatzipanagiotou, S (2008). Incidence and antimicrobial susceptibilities of genital mycoplasmas in outpatient women with clinical vaginitis in Athens, Greece. *J. Antimicrob Chemother*; 62: 122-125.
 4. Allanson, B; Jennings, B; Jacques, A, et al. (2010). Infection and foetal loss in the mid-second trimester of pregnancy. *Aust N Z J Obstet Gynaecol*;50: 221-225.
 5. Volgmann, T; Ohlinger, R; and Panzig, B (2005). *Ureaplasmaurealyticum*-harmless commensal or underestimated enemy of human reproduction? A review. *Archives of Gynecology and Obstetrics*; 273(3): 133-139.
 6. Randelović, G, Kocić, B, Miljković-Selimović, B, Mladenović-Antić, S, Stojanović, P and Stefanović, M (2006). *Visokstepenkolonizacijecerviksatrudnica*. *Vojnosanitetski Pregled: Military Medical and Pharmaceutical Journal of Serbia*; 63(8): 737-741
 7. Guerra, B; Ghi, T; Quarta, S, et al. (2006). Pregnancy outcome after early detection of bacterial vaginosis. *Eur J Obstet Gynaecol Reprod Biol*; 128: 40-45.
 8. Vogel, I; Thorsen, P; Hogan, VK; et al. (2006). The joint effect of vaginal *Ureaplasmaurealyticum* and bacterial vaginosis on adverse pregnancy outcomes. *Acta Obstet Gynecol*; 85: 778-785.
 9. Kacerovsky, M; Pliskova, L; Bolehovska R; et al. (2011). The microbial load with genital mycoplasmas correlates with the degree of histologic chorioamnionitis in preterm PROM. *Am J Obstet Gynecol*; 205:213-217.
 10. Kafetzis, DA; Skevaki, CL; Skouteri V; et al. Maternal genital colonization with *Ureaplasmaurealyticum* promotes preterm delivery: association of the respiratory colonization of premature infants with chronic lung disease and increased mortality. *Clin. Infect. Dis.*. October 2004, roč. 39, čís. 8, s. 1113–22. Dostupné online. DOI:10.1086/424505. PMID 15486833.
 11. Di Quinzio, MK; Oliva, K; Holdsworth, SJ; Ayhan, M; Walker, SP; Rice, GE; Georgiou, HM; Permezel, M (2007). Proteomic analysis and characterization of human cervico-vaginal fluid proteins. *Aust N Z J Obstet Gynaecol*; 47(1): 9-15.
 12. Curfs, JH; Meis, JF and Hoogkamp-Korstanje, JAA (1997). primer on cytokines: sources, receptors, effects, and inducers. *Clinical Microbiology Reviews*; 10(4): 742-780.
 13. Lackie, J (2010). "Cytokine". *A Dictionary of Biomedicine*. Oxford University Press. 010. ISBN 9780199549351. Also available at: <https://en.wikipedia.org/wiki/Cytokine>
 14. Chokkalingam, V; Tel, J; Wimmers, F; Liu, X; Semenov, S; Thiele, J; Figdor, CG and Huck, WT (2013). "Probing cellular heterogeneity in cytokine-secreting immune cells using droplet-based microfluidics". *Lab Chip*. 13(24): 4740-4744.
 15. Robinson, DP and Klein, SL (2012). Pregnancy and pregnancy-associated hormones alter immune responses and disease pathogenesis. *Hormones and behavior*;62(3): 263-272.
 16. Lee, MY; Kim, MH; Lee, WI; Kang, SY and Jeon, YL (2016). Prevalence and Antibiotic Susceptibility of *Mycoplasma hominis* and *Ureaplasmaurealyticum* in Pregnant Women. *Yonsei Medical Journal*.57(5): 1271-1275.
 17. Barton, PT; Gerber, S; Skupski, DW and Witkin, SS (2003). Interleukin-1 receptor antagonist gene polymorphism, vaginal interleukin-1 receptor antagonist concentrations, and vaginal *Ureaplasmaurealyticum* colonization in pregnant women. *Infection and Immunity*.71(1): 271-274.
 18. Benito, CW and Blusewicz, TA (2001). The relationship of *Ureaplasmaurealyticum* cervical colonization and preterm delivery in high-risk pregnancies. *Obstetrics and Gynecology*.97(4): S45-S46.
 19. Kotrotsiou, T; Exindari, M; Diza, E; Gioula, G; Melidou, A; Kaplanis, K and Malisiovas, N (2013). Prevalence and antimicrobial susceptibility of *Ureaplasmaurealyticum* in asymptomatic women in Northern Greece. *Hippokratia*. 17(4): 319-321.
 20. Sobouti, B, Fallah, S, Mobayen, M, Noorbakhsh, S, & Ghavami, Y (2014). Colonization of *Mycoplasma hominis* and *Ureaplasmaurealyticum* in pregnant women and their transmission to offspring. *Iranian Journal of Microbiology*. 6(4): 219-224.
 21. Gerber, S; Vial, Y; Hohlfeld, P and Witkin, SS (2003). Detection of *Ureaplasmaurealyticum* in

- second-trimester amniotic fluid by polymerase chain reaction correlates with subsequent preterm labor and delivery. *The Journal of infectious diseases*. 187(3): 518-521.
22. Ahmadi, MH; Mirsalehian, A and Bahador, A (2016). Prevalence of urogenital mycoplasmas in Iran and their effects on fertility potential: a systematic review and meta-analysis. *Iranian journal of public health*;45(4): 409-422.
 23. Honestly Significant Difference (HSD)-Test (2019). Tukey's range test. 'a single-step multiple comparison procedure and statistical test'. Also available at: https://en.wikipedia.org/wiki/Tukey%27s_range_test
 24. Waites, KB; Katz, B and Schelonka, RL (2005). Mycoplasmas and ureaplasmas as neonatal pathogens. *Clin Microbiol Rev*. 18: 757-789.
 25. Yoon, BH; Romero, R; Moon, JB, et al., (2001). Clinical significance of intra-amniotic inflammation in patients with preterm labor and intact membranes. *Am J ObstetGynecol*;185: 1130-1136.
 26. Seong, HS; Lee, SE; Kang, JH; Romero, R and Yoon, BH (2008). The frequency of microbial invasion of the amniotic cavity and histologic chorioamnionitis in women at term with intact membranes in the presence or absence of labor. *Am J Obstet Gynecol*; 199(4): 375.e1-5.
 27. Ugwumadu, A; Manyonda, I; Reid, F; and Hay, P (2003). Effect of early oral clindamycin on late miscarriage and preterm delivery in asymptomatic women with abnormal vaginal flora and bacterial vaginosis: a randomised controlled trial. *Lancet*; 361(9362):983-988.
 28. Newton, ER (1993). Chorioamnionitis and intraamniotic infection. *Clin Obstet Gynecol*; 36(4): 795-808.
 29. Ralph, SG; Rutherford, AJ; and Wilson, JD (1999). Influence of bacterial vaginosis on conception and miscarriage in the first trimester: cohort study. *BMJ*. 24: 319(7204).
 30. Llahi-Camp, JM; Rai, R; Ison, C; Regan, L and Taylor-Robinson, D (1996). Association of bacterial vaginosis with a history of second trimester miscarriage. *Hum Reprod*. 11(7): 1575-1578.
 31. Lautenbach, D; Krynienska, K; Kozubowska, K; Rachon, K; Malczewska, B and Preis, K (2014). Wellness of pregnant women with colonization of *Ureaplasma urealyticum*. *University of Gdansk Klinika Położnictwa Gdańskiego Uniwersytetu Medycznego*; 2(62). Also available at:<https://www.google.com/>
 32. Heng, YJ; Liong, S; Permezel, M, et al. (2014). The Interplay of the Interleukin 1 System in Pregnancy and Labor. *Repro Sci*. 21(1): 122-130.
 33. Sagawa, T;Furuta, I; Negishi, H, et al. (1996). Cytokines Concentrations in the Cervical Mucus of Pregnant Women. *The Journal of Obstetrics and Gynecology Research*. 22(5): 517-522.

Short Clinical Outcome of Microscope Assisted Discectomy

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Abstract

Objective: Determine the effectiveness of microscopic assisted discectomy and its application for the patient with disc disease, its efficacy, and its pitfalls.

Materials and Method: A prospective study conducted on 90 patients, which they reviewed prior to the operation by using Oswestry disability index (ODI) and visual analog score (VAS) for the back and leg pain, followed up on a period of 6 months by using the same method which they have been reviewed, all of the patient were operated on by microscopic assisted microdiscectomy discharge on the same day or the day after the procedure.

Results: There was a major improvement of back and leg pain by using VAS, the overall improvement in VAS for back pain was 4.43 points (p-value <0.001) and improvement in VAS for leg pain was 4.51 (p-value <0.001), while the improvement in ODI was 34.85 (p-value <0.001).

Conclusion: Microscopic assisted microdiscectomy offered a successful solution for common health issue with the advantage of small wound better cosmetics, low adverse effect and early rehabilitation and return to daily activity and resume individual function and productivity, good preoperative planning and selection of patient with the meticulous procedure and post-operative care can offer supreme results.

Keywords: *Clinical outcome, microscopic assisted, discectomy, disc herniation, Oswestry index.*

Introduction

Back pain considered an ancient health issue, being describes in the bible and by Hippocrates, it's quite common and international prevalence of back pain reported to be 49-80% annually¹.

Approximately 80% of individuals are affected by the symptoms of lumbar disc herniation at a point in their lives. Impairments of the back and spine are ranked as the most frequent cause of limitation of activity in individuals younger than 45 years old by the National Center for Health Statistics in the united states².

Among of many causes of back pain is lumbar disc herniation which is commonly seen in daily orthopedic

and neurosurgical practice with wide range of presentation from simple back pain to radiculopathy due to nerve compression³, in severe cases of lumbar disc herniation depending on the grade of prolapsed disc, leads to numbness weakness saddle anesthesia urinary and bowel incontinence and even foot drop sometimes which is required an emergency decompression surgery for cauda equina syndrome⁴.

Conventional open discectomy has been prescribed as an effective remedy for this situation and with the advancement of minimally invasive surgery and its implementation in spine surgery, microscopic discectomy has been gaining popularity among surgeons, with its characteristic of small incision less tissue damage clearer operation field and faster recovery as effective as conventional open discectomy⁵.

The objective of this study is to determine the effectiveness of microscopic assisted discectomy in treating patients with symptomatic lumbar and

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lumbosacral disc herniation who failed to respond to conservative treatment, follow them up, and determine functional outcomes using ODI and VAS scores for back and leg pain.

Method

Study design: A prospective study designed to follow up the patient according to ODI and VAS for both back and leg pain who underwent microscopic assisted microdiscectomy.

Study setting: The study was conducted in Erbil province in PAR private hospital and Rozhwa emergency hospital (neurosurgical department).

Period of study: The study was carried out between June 2016 and September 2018

Study sample: A total of 90 patients involved in this study a randomized sampling use

Inclusion criteria: Adult patients between 17 and 50 years of age complaining of lower back pain and/or radiculopathy and neurological symptoms, who failed to respond to a 6-8 weeks period of conservative therapy (lifestyle modification, NSAIDs, and physiotherapy).

The diagnosis carried out by using history, and physical examination; MRI was done for the patient to confirm the diagnosis and the level of disc herniation and determine the direction and extent of disc herniation

Exclusion criteria: Subjects with age group (<17 years and >50 years), any other type of disc herniation apart from L3-L4, L4-L5, L5-S1, multilevel pathology, patients with spondylolisthesis, spondylolysis, patients with scoliosis and kyphosis, patients with cauda equina syndrome, patients with previous back surgery, and with no local infection.

Data Collection: A questionnaire form constructed by the researcher which include:

- Demographic data of the patient.
- Level of activity (sedentary or active).
- Symptoms (back pain, leg pain, neurological deficit, or combination of these).
- Duration of symptoms in months.
- Level of disc herniation confirmed by MRI.
- Oswestry disability index before and after the

operation

- Visual analog scale for back pain before and after the operation
- Visual analog scale for leg pain before and after the operation

All the patients discharged on the same day of operation or a day after, mobilized soon as they were ready. Patients were reviewed in intervals of 2 weeks, 2 months, and 4 months after surgery using VAS score for low back pain and leg pain and ODI score.

Operative procedure: All the patients were operated on in a prone position by using bolsters under chest and pelvis and padding to protect pressure areas, all the patients were generally anesthetized, patients were sterilized using stander sterilization method and draping gave a prophylaxis antibiotic (ceftriaxone 1gm) about 30±15 minutes prior to incision. The level of operation was identified using spinal needle and slandered C-Arm available at operation theatre. Make the incision from the midspinous process of the upper vertebra to the superior margin of the spinous process of the lower vertebra at the involved level. This usually results in (25 to 30 mm) skin incision. This incision may need to be moved slightly higher for higher lumbar levels.

Incise the fascia at the midline. Insert a periosteal elevator in the midline incision. Using gentle lateral movements, elevate the deep fascia and muscle subperiosteally from the spinous processes and lamina on the involved side only. Obtain a lateral radiograph with a metal clamp attached to the spinous process to verify the level. Then surgery carried out by using appropriate depth of tubular retractor which helps to minimize the damage to the surrounding soft tissue.

Sequentially dilate down to the bone with enlarging tubular retractors to expose the interlaminar space. Each dilator can be used as a curette to remove soft-tissue attachments from the interlaminar space.

Identify the lamina and by using high-speed drill bit under visualization using a microscope, which is already been draped, remove part of lamina to allow dissection using Kerrison rongeur

Use a Kerrison rongeur to resect the superficial leaf of the ligamentum flavum to allow identification of the critical angle, which is the junction of the leading edge of the caudal lamina and the medial edge of the superior

articular process. Identifying the critical angle is essential in primary micro lumbar discectomy because it has a constant relationship to the corresponding pedicle, traversing nerve root, and target disc. The pedicle is always just lateral to the critical angle, the traversing nerve is always just medial to the pedicle, and the disc of interest is always just cephalad to the critical angle and pedicle. It sometimes is necessary to drill the medial aspect of the inferior articular process to allow adequate visualization of the critical angle.

Once the ligamentum flavum is removed, the medial wall of the corresponding pedicle is identified, the traversing nerve can be found just medial to it and the target disc can be found just cephalad to it small opening can be made using small size scalpel.

When the nerve root is identified, carefully mobilize the root medially. Gently dissect the nerve free from the disc fragment to avoid excessive traction on the root. Bipolar cautery for hemostasis is helpful. When mobilized, retract the root medially. With the nerve root retracted, the disc is now visible as a white, fibrous, avascular structure. Under magnification, small tears may be visible in the annulus as shown in figure 1. Remove the disc material with the appropriate-sized pituitary rongeur or small size curette. Do not insert the instrument into the disc space too deep, to minimize the risk of anterior perforation and vascular injury.

Remove the exposed disc material. Remove additional loose disc or cartilage fragments. Inspect the root and adjacent dura for disc fragments. Forcefully irrigate the disc space using a syringe and a suction tip inserted into the disc space. Maintain meticulous hemostasis.

Washing carried out muscle debrided fascia closed using double thread nylon suture size 0 or 1 or by using absorbable sutures vycril or PDS size 0 or 1, and the skin closed in interrupted vertical mattress technique.

Statistical analysis: Data were analyzed using the Statistical Package for Social Sciences (SPSS, version 22). The student's t-test of two independent samples was used to compare two means. The paired t-test was used to compare the readings of the scales before and after the operation. One-way analysis of variance (ANOVA) was used to compare three means. A post hoc test (LSD) was used to compare means of each two groups (after doing the ANOVA test). Pearson correlation coefficient

was used to assess the strength of correlation between numerical variables. A p-value of ≤ 0.05 was considered statistically significant.

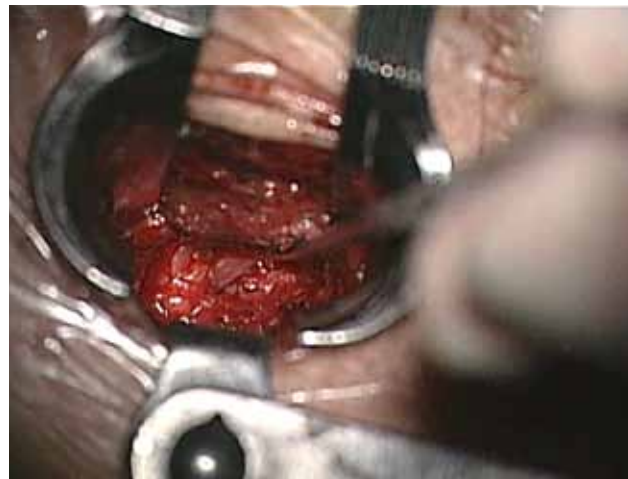


Figure 1: shows retracted nerve root and disc space under microscope magnification

Results

The mean age of patients was 35.67 ± 8.32 years, ranging from 17 to 50 years, 62.2% of the patients were females. More than half (54.4%) of the sample were working in active/manual jobs. Regarding the patients' symptoms, around half (47.8%) of the patients had backache, leg pain, and neurological deficit. The disc herniation level was in L4-L5 in 61.1% of the patients (Table 1). Table 2 shows a significant decrease in the scores of all the studied indicators after the operation.

There is an inverse significant correlation between age and VAS gain ($r = -0.599$), no significant ($p = 0.868$) association was detected between the VAS leg gain and age, there was a significant inverse correlation between age and Oswestry gain ($r = -0.587$), figure 2.

Regarding the duration of symptoms, it is evident in figure 3 that the more the duration of symptoms, the less the gain in the Oswestry scores ($r = -0.674$, $p < 0.001$). figure 3 shows also an inverse significant correlation between the VAS for back pain gain and the duration of symptoms ($r = -0.461$, $p < 0.001$).

Regarding complication we faced during operation, we had 2 cases of incidental dural tear while retracting the cord, both making 2.2% of total cases, both tears were small and treated by using fibrin sealant and a 24 hour of supine backrest, 2 cases of superficial wound infection making 2.2% of the total number of cases.

Table 1: Basic characteristics of the study sample

Variables	Number	(%)
Age (Years)		
<30	23	(25.6)
30-39	29	(32.2)
≥40	38	(42.2)
Gender		
Male	34	(37.8)
Female	56	(62.2)
Activity		
Sedentary work	41	(45.6)
Active work	49	(54.4)
Symptoms		
Backache	2	(2.2)
Leg pain	2	(2.2)
Backache + Leg pain	22	(24.4)
Backache + Neurological deficit	8	(8.9)
Leg pain + Neurological deficit	13	(14.4)
All	43	(47.8)
Disc herniation levels		
L3-L4	16	(17.8)
L4-L5	55	(61.1)
L5-S1	19	(21.1)

Table 2: The studied mean scales before and after the intervention

Scales	Before operation		After operation		P-value
	Mean	(±SD)	Mean	(±SD)	
Oswestry	51.62	(±8.19)	16.77	(±2.80)	< 0.001
VAS back pain	5.72	(±0.87)	1.29	(±0.50)	< 0.001
VAS leg pain	5.78	(±0.67)	1.27	(±0.44)	< 0.001

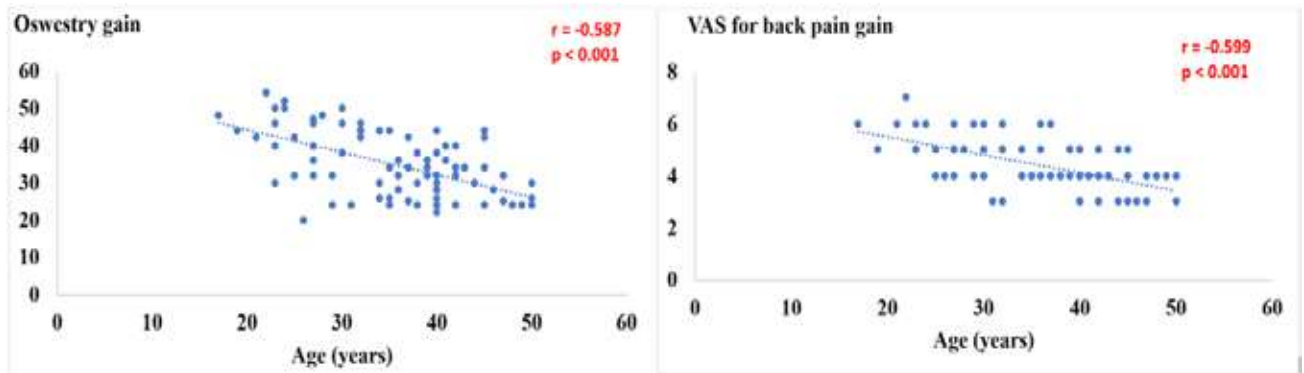


Figure 2: Correlation between the gain in Oswestry scores and age (left), correlation between gain in VAS for back pain scores and age (right)

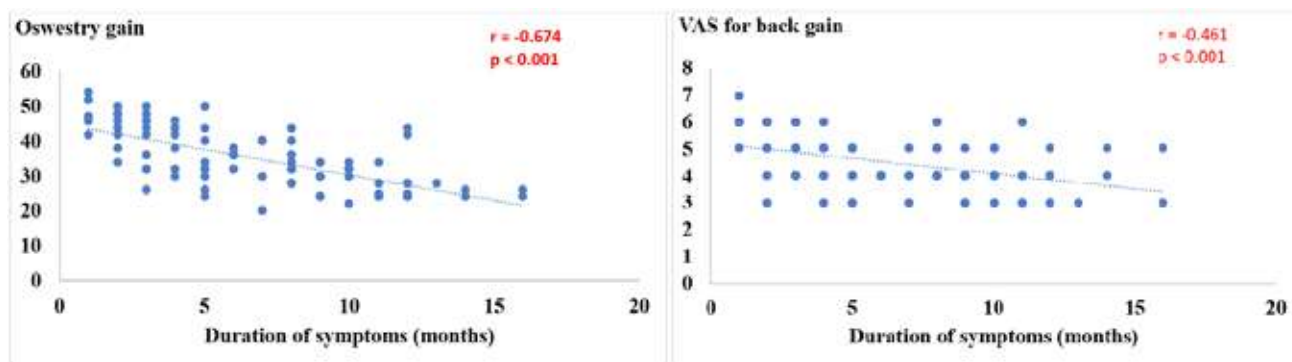


Figure 3: Correlation between the gain in Oswestry scores and duration of symptoms (left), correlation between gain in VAS for back pain scores and duration of symptoms (right)

Discussion

The advantage of microscopic discectomy includes, small incision, better outcomes, early mobilization, less analgesics, and short time to return to work the measurement of CPK level and cross-sectional area (by CT scan, MRI) of paraspinal muscle and intraoperative EMG along with pre and post-operative biochemical markers (CPK, IL, CRP) showed less damage⁶.

Arts et al study showed frequent retraction and relaxation of tube retractor every 15 minutes resulted in lower CPK value⁷, though in another study Mark Arts et al showed no change in cross-sectional area of multifidus and paraspinal muscle comparing conventional open discectomy and microscopic and tubular discectomy after 1 year follow up⁸.

The present study showed that the L4-L5 levels are the most operated level by 61.1%, L3-L4 levels 17.8% and L5-S1 levels were 21.1%, these results are comparable to other studies^{4,6,9-13}. While in other studies the L5-S1 level was the dominant level of herniation^{3,5,10}.

In the present study VAS gain of back pain was about 4.62 points in males and 4.32 in females (p-value 0.190), and VAS gain of leg pain was 4.68 in males and 4.41 in females (p-value 0.132). Additionally, no statistically difference in gain between male and females, in which mean ODI gain in males was 35.74% \pm 9.48, and in females 34.32% \pm 8.12, p-value = 0.454, mean VAS for back pain gain in males was 4.62 \pm 1.13, and in females 4.32 \pm 0.38, p-value = 0.190, which is comparable with results reported by Sedighi et al¹.

The resolution of symptoms correlated with level of disc herniation was similar inpatient with L4-L5 with ODI gain 34.24% \pm 8.82, and for L5-S1 ODI gain was

34.86% \pm 7.32, p-value = 0.337, while the resolution of symptoms with L3-L4 regarding ODI was 40.25% \pm 7.44, had significant improvement in compared to L4-L5 with p-value = 0.013 and with L5-S1, with p-value = 0.005, these findings probably occurred because of the more severe herniation correlated to L3-L4 level.

Regarding the VAS score for back pain the gain, was nearly the same through all levels postoperatively. L3-L4 mean gain was 4.69 \pm 1.01, L4-L5 gain was 4.38 \pm 0.97 and VAS for back pain at L5-S1 was 4.43 \pm 0.96, which is comparable with the results reported by Sedighi et al¹.

Conclusion

Microscopic assisted microdiscectomy is safe procedure, it offered high and significant success rate, offered advantages of early mobilization low pain score after procedure, magnified clear flow with minimal blood loss, it can be done on day base surgery for most of the cases, most of the patient tolerate the pain and mobilization because of minimum muscle dissection and less invasiveness to structures that preserve spinal stability, and its showed low complication rate.

Conflict of Interest: None

Ethical Clearance: Informed written consent was obtained from all the participants in the study, and the study and all its procedures were done in accordance with the Helsinki Declaration of 1975, as revised in 2000. The study was approved by the scientific council of the Iraqi Board of Medical Specializations.

Source of Funding: The work was supported by authors only

References

1. Sedighi M, Haghnegahdar A. Lumbar disk herniation surgery: outcome and predictors. *Global spine journal*. 2014;4(4):233-44.<https://doi.org/10.1055/s-0034-1390010>
2. Wong AY, Karppinen J, Samartzis D. Low back pain in older adults: risk factors, management options and future directions. *Scoliosis and spinal disorders*. 2017;12:14.<https://doi.org/10.1186/s13013-017-0121-3>
3. Bhatia PS, Chhabra HS, Mohapatra B, Nanda A, Sangodimath G, Kaul R. Microdiscectomy or tubular discectomy: Is any of them a better option for management of lumbar disc prolapse. *Journal of craniovertebral junction & spine*. 2016;7(3):146-52.<https://doi.org/10.4103/0974-8237.188411>
4. Abdul Aziz AI, Abdul Aziz AM. Functional outcome of microscopic lumbar discectomy for the treatment of lumbar disc prolapse. *Int J Res Orthop*. 2018;4(3):389-94.<http://dx.doi.org/10.18203/issn.2455-4510.IntJResOrthop20181438>
5. Lu X, Li W, He J, Peng X, Zhao J. A Retrospective Study of Microscope-Assisted Discectomy versus Open Fenestration Discectomy for Lumbar Disc Herniation. *Ann clin Lab Res*. 2016;4(3):112
6. Kogias E, Jimenez PF, Hubbe U. Microendoscopic lumbar discectomy: Technique and results of 188 cases. *Indian journal of orthopaedics*. 2015;49(2):262-3.<https://doi.org/10.4103/0019-5413.152551>
7. Arts MP, Peul WC. Timing and minimal access surgery for sciatica: a summary of two randomized trials. *Acta neurochirurgica*. 2011;153(5):967-74.<https://doi.org/10.1007/s00701-011-0983-8>
8. Arts M, Brand R, van der Kallen B, Lycklama a Nijeholt G, Peul W. Does minimally invasive lumbar disc surgery result in less muscle injury than conventional surgery? A randomized controlled trial. *European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society*. 2011;20(1):51-7.<https://doi.org/10.1007/s00586-010-1482-y>
9. Singh SD, Kale SY, Athar A, Sahni H, Singh S, Dhar SB. Clinical outcomes in patients undergoing microlumbar discectomy for lumbar disc herniation. *International Journal of Orthopaedics Sciences*. 2018;4(1):392-4.<https://doi.org/10.22271/ortho.2018.v4.i1f.57>
10. Solberg TK, Nygaard OP, Sjaavik K, Hofoss D, Ingebrigtsen T. The risk of “getting worse” after lumbar microdiscectomy. *European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society*. 2005;14(1):49-54.<https://doi.org/10.1007/s00586-004-0721-5>
11. Allam Y, El-Fiky T. Early follow-up of microscopy-assisted percutaneous nucleotomy technique for the treatment of lumbar disk prolapse in Egyptian patients. *The Egyptian Orthopaedic Journal*. 2015;50(4):278-81.<https://doi.org/10.4103/1110-1148.182316>
12. Abdulrazaq M, Gorial F, Fawzi H, Hassan A. Prevalence of pulmonary tuberculosis in spinal tuberculosis patients. *European Respiratory Journal*. 2017;50 (suppl 61). <https://doi.org/10.1183/1393003.congress-2017.PA2697>
13. Shawkat AJ, Jwaid AH, Marzouq Awad G, Adnan Fawzi H. Evaluation of osteopathy in patients with beta-thalassemia major using different iron chelation therapies. *Asian Journal of Pharmaceutical and Clinical Research*. 2018;11(11):467-71.<http://dx.doi.org/10.22159/ajpcr.2018.v11i11.29079>

Hyaluronidase Versus Magnesium Sulphate as Adjuvants to Bupivacaine in Ultrasound Guided Supraclavicular Brachial Plexus Block in Upper Limb Surgeries

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Abstract

Introduction: Aim of this trial was to assess the effect of hyaluronidase and MgSo₄ when added separately or in combination to bupivacaine on the onset of sensory and motor block, quality of block and effect on duration of action.

Method: Eighty ASA I, II patients of either sex undergoing upper limb Surgery under ultrasound-guided supraclavicular brachial block were recruited in this prospective randomized double blinded controlled study and divided in to four groups each group contain 20 patients. First group received (28 ml 0.5% bupivacaine and 2 ml 0.9% normal saline). Second group received (28 ml 0.5% bupivacaine and 1000 unit hyaluronidase dissolved in 2 ml 0.9% normal saline). Third group received (28 ml 0.5% bupivacaine and 2 ml of MgSo₄ containing 200 mg). Fourth group received (28 ml 0.5% bupivacaine and 2 ml of MgSo₄ containing 200 mg mixed with 500 unit hyaluronidase).

Results: Hyaluronidase fastened the onset but didn't affect the duration however MgSo₄ prolonged the duration of postoperative analgesia without effect on the onset of block

Keywords: Regional, brachial plexus; local anesthetics, bupivacaine, equipment, ultrasound machines; hyaluronidase; MgSO₄.

Introduction

Supraclavicular nerve block is ideal for procedures of the upper arm, from the mid humeral level down to the hand. It has a rapid onset, with a dense and predictable level of pain control [1].

Hyaluronidase, the mucolytic enzyme which acts on the muco-polysaccharide hyaluronic acid, is generally considered to be "spreading factor". When used with local anesthetics, hyaluronidase hastens the onset of analgesia and shortens its duration of effect [2].

Magnesium sulphate acts as an adjuvant in analgesia due to its properties of calcium channel blocking and N-methyl-D-aspartate antagonism. Magnesium has been shown to decrease peripheral nerve excitability and to enhance the ability of lidocaine to raise the excitation threshold of A-beta fibers [3].

Ultrasound guidance has dramatically improved nerve localization and offers several advantages as direct visualization of nerves and anatomical structures, facilitated visualization of local anesthetic spread in real time, produced good compensation for anatomical variation, reduced incidence of complications [4].

Method

This prospective, randomized, double blind controlled clinical study was carried out after obtaining the local ethics committee of El-Minia university hospital approval and written informed consent was taken from the patients. It was done between September

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2017 to December 2018, 90 patients of both sexes, ASA I and II, aged between 18-65 years old scheduled to undergo elective and urgent distal arm, forearm and hand surgeries under ultrasound guided supraclavicular brachial plexus block, 80 patients were enrolled in this study and ten were excluded due to block failure.

Preoperative Assessment and Preparation: A careful assessment of medical history was done. Routine preoperative general examination and local examination of the site of injection for signs of infection or any other pathology were carried out. Routine investigations were done. Explanation of visual analogue pain scale was done VAPS is consisted of a straight, vertical 10-cm line; the bottom point represented “no pain”= (0 cm) and the top “the worst pain you could ever have. Two mg midazolam IV was given as a premedication 5 minutes before the block.

Equipments: The ultrasound device Sonosite, micromaxx, Lubricating gel, 21-gauge 50 mm length short bevel insulated stimulating needle, 10-ml syringes for injection, Sterile gloves, 25-gauge needle for skin infiltration, Sterile towels and sterile antiseptic solution (Povidone-iodine 10%).

All medications were prepared in similar sterile coated bottles and coded then passed to the anesthesiologist who is blind to its manner. In this prospective randomized double blinded controlled study 80 bottles numbered from 1 to 80 were prepared and divided in to four groups each group containe 20 bottles. Then the patients were randomly assigned to study groups.

Group (I): Received 28 ml bupivacaine (0.5%) + 2 ml saline (0.9%).

Group (II): Received 28 ml bupivacaine (0.5%) + 1000 unit hyaluronidase dissolved in 2 ml saline (0.9%).

Group (III): Received 28 ml bupivacaine (0.5%) + 2 ml MgSo4 containing 200 mg.

Group (IV): Received 28 ml bupivacaine (0.5%) + 2 ml MgSo4 containing 200 mg mixed with 1000 unit hyaluronidase.

Block technique: A 20 G intravenous cannula was inserted in a peripheral vein of unaffected upper limb and standard monitoring was provided. Patient lie down supine with head turned to the contralateral side and ipsilateral arm adducted gently by the assistant. Skin

was sterilized and infiltrated with 1-2 ml of lidocaine 2% at the needle entry site.

The brachial plexus was visualized by placing ultrasound probe in the sagittal plane in the supraclavicular fossa behind the middle-third of the clavicle as 3 hypoechoic circles with hyperechoic outer rings or as a grape like cluster of 5 to 6 hypoechoic circles, lateral and superior to the subclavian artery between the anterior and middle scalene muscles at the lower cervical region.

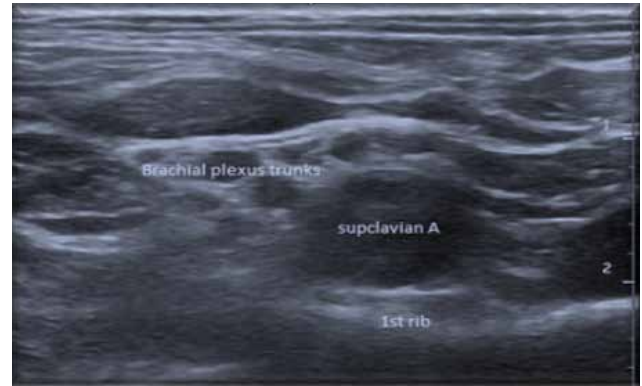


Fig (1): Ultrasonographic imaging of brachial plexus

Parameters assessed: The anesthesiologist who gave the block recorded the onset of sensory and motor block and recorded intraoperative data then the postoperative care physician recorded the duration of block and postoperative data.

The hemodynamic variables were assessed and recorded 5 minutes before the block as a baseline value, immediately after the block 0,10,20,30,60, 90 minutes during the operative time then 1,2,4,6, and 12 hours after the end of operation. Quality of sensory block was assessed by pin prick test using a 3-point scale ^[5] Grade 0 = normal sensation, Grade 1 = loss of sensation of pin prick (analgesia), and Grade 2 = loss of sensation of touch (anesthesia).

Also motor block quality was determined by thumb abduction (radial nerve), thumb adduction (ulnar nerve), thumb opposition (median nerve), and flexion of elbow (musculocutaneous nerve) according to the modified Bromage scale 1997 ^[6] on a 3-point scale. **Grade 0:** Normal motor function with full flexion and extension of elbow, wrist, and fingers. **Grade 1:** Decreased motor strength with ability to move the fingers only. **Grade 2:** Complete motor block with inability to move the fingers.

Pain intensity was assessed using VAPS. It was

measured before starting the nerve block then 15, 30, 60, 90, 120 minutes after nerve block. When it is more or equals 4 cm we gave analgesia or sedation using fentanyl and propofol during operation. Then Patients were asked to rate their pain intensity at 2, 4, 8, 12, and 24 hours postoperative and if it was more than four paracetamol 1000 mg bottle was given. Time of first analgesic request: The time from supraclavicular brachial plexus block administration to the patient’s first request for analgesic medication by hours. Total analgesic requirements in 24 hours: The total amount of intravenous paracetamol which was given to the patient as a rescue analgesia or maintenance during 24 hours. Adverse effects: any adverse effects such as hypotension (i.e. 20% decrease relative to baseline), bradycardia (HR <50 beats/min), nausea, vomiting, hypoxemia (SpO2 <90%), local hematoma, hemothorax, pneumothorax, recurrent laryngeal nerve block, intravascular injection, Horner’s syndrome and signs of local anesthetic toxicity

were recorded during the operation and for 24 hours postoperative.

Results

During studying hemodynamic data changes among groups, The Mean Arterial blood pressure (mmHg) and arterial oxygen saturation changes during intraoperative or postoperative period were statistically insignificant between the four groups. As regard the Heart rate (beat/min) we found it was lower in group (II, IV) than the other two groups (I, III) at time intervals of 10,20,30 and 60 minutes intraoperative but these changes were statistically insignificant.

Sensory, motor block onset and density of block were faster in groups (II & IV) than in groups (I & III) but the duration of sensory and motor block was found to be longer in groups (III & IV) than in groups (I & II) as presented in fig (2, 3, 4).

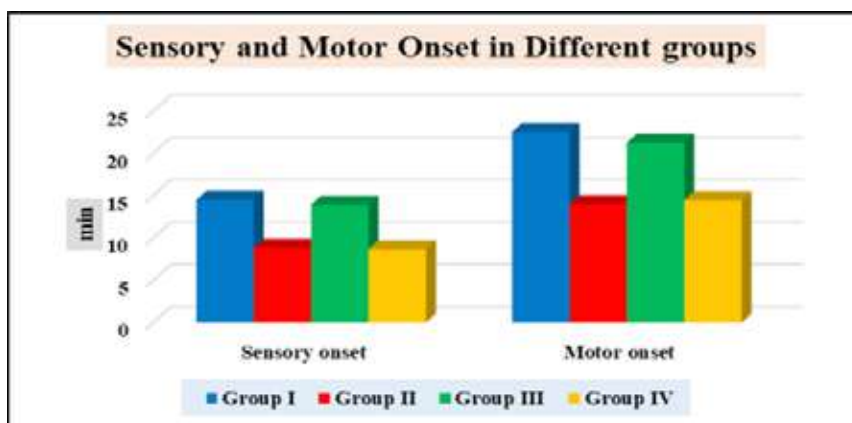


Fig (2)

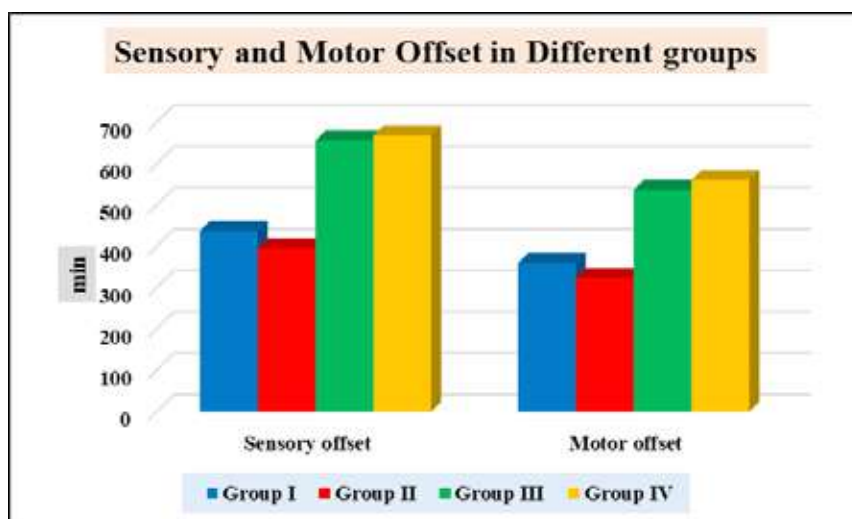


Fig (3)

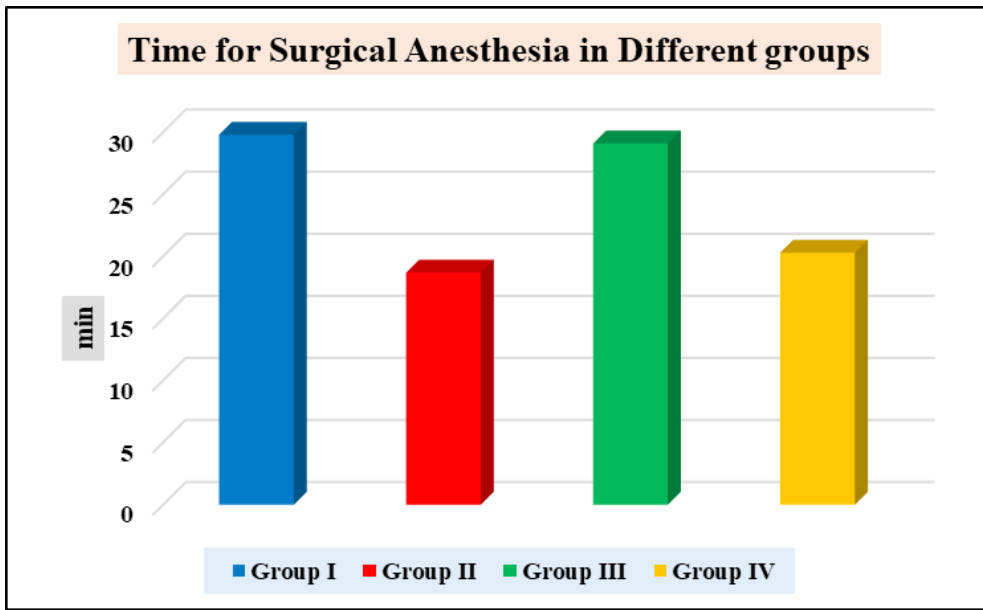


Fig (4)

Pain measurement presented by VASP during intraoperative period at 15 min post injection the pain score was significantly lower in patients received hyaluronidase in groups (II & IV) than in groups (I & III) but no significant difference was found after that during operation. In the postoperative period the VASP was significantly lower at 4, 8, 12, 24 hours in patients received MgSO₄ in groups (III & IV) than in groups (I & II).

Intraoperative need for sedation and fentanyl was insignificantly different between the four groups. But the mean time of for postoperative 1st analgesic request was significantly longer in groups (III & IV) (360-900) and (540-950) minutes in comparison to groups (I & II) (300-620) and (300-700) minute. And total analgesic requirement (mg) in groups (III & IV) was less than groups (I & II).

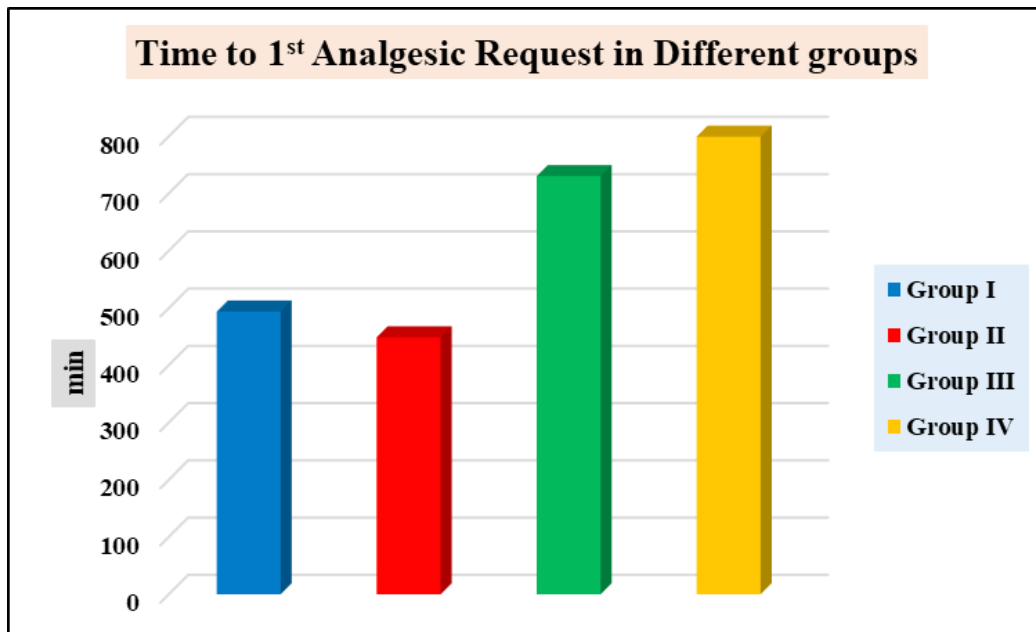


Fig (5)

As regard complications happened during the study no significant differences were found between the four groups.

Discussion

Brachial plexus block is a safe reliable anesthetic technique for upper limb surgery with fewer complications, especially with the introduction of ultrasound which decreased the complications dramatically.

Hyaluronidase the mucolytic enzyme which acts on the muco-polysaccharide hyaluronic acid, is generally considered to be “spreading factor”. When used with local anesthetics, hyaluronidase hastens the onset of analgesia and shortens its duration of effect [7].

A number of studies have shown that addition of hyaluronidase during ocular blocks has beneficial effects including higher quality of anaesthesia and improved success rates.

In a study done by Koh et al investigated the hypothesis that addition of hyaluronidase to ropivacaine may reduce the time to achieve complete sensory block after axillary brachial plexus block. The patients were randomly assigned into a hyaluronidase group (n = 24) and a control group (n = 24). The hyaluronidase group received ropivacaine 0.5% with 100 IU.ml₋₁ of hyaluronidase, and the control group received ropivacaine alone. The primary endpoint was the time to achieve complete sensory block. The hyaluronidase group demonstrated significantly shorter mean (SD) sensory block onset time (13.8 (6.0) min) compared with the control group (22.5 (6.3) min), $p < 0.0001$. Addition of hyaluronidase to ropivacaine resulted in a reduction in the time needed to achieve complete sensory block [8].

Another previous study by Keeler et al reported the effect of the addition of hyaluronidase to bupivacaine 0.5% for axillary brachial plexus blocks. In that study, 3000 IU hyaluronidase mixed with bupivacaine significantly reduced the duration of the sensory and motor block, and had no effect on the number of patients experiencing a complete sensory block after 30 min while the duration of sensory anesthesia was significantly shorter in the hyaluronidase group and the duration of motor block showed a shorter trend [9].

In our study hyaluronidase had obvious effect on decreasing the sensory onset that recorded by pinprick

test at 5 min interval after performing the block till complete sensory block occurred and motor onset detected by detection of complete thumb block also detected at 5 min interval after the block in comparison with control group and Mgso4 group. The mean sensory onset was (8.9 ± 3.3) minutes in hyaluronidase group in comparison to the mean sensory onset (14.5 ± 4.5) , (14 ± 3.8) minutes in control and Mgso4 groups respectively. The mean motor onset was (14 ± 5.1) minutes in hyaluronidase group in comparison to the mean motor onset (22.5 ± 4.9) , (21.3 ± 5) minutes in control and Mgso4 groups respectively, and both results were significant with p value < 0.001 . However it didn't affect the duration of sensory or motor block or the postoperative analgesic requirement in comparison with other groups.

Mgso4 can act as an adjuvant in analgesia due to its properties of calcium channel blocking and N-methyl-D-aspartate antagonism. Magnesium has been shown to decrease peripheral nerve excitability and to enhance the ability of lidocaine to raise the excitation threshold of A-beta fibers [10].

Haghighi et al. in Guilan, Iran, in 2014, investigated the effect of Mgso4 in axillary brachial plexus block when added to lidocaine in upper limb surgeries, and reported that the addition of Mgso4 to lidocaine significantly increased the duration of sensory and motor blocks in comparison with the use of lidocaine alone [11].

Rao et al. found that The addition of MgSo4 to 0.5% bupivacaine increased the duration of motor and sensory supraclavicular brachial block in the upper extremities during surgeries when compared to the use of 0.5% bupivacaine alone, The mean sensory block duration in the group MgsSo4 was 249 ± 9.36 and in control Group was (160 ± 5.62) ($p < 0.39$). The mean motor block duration in the group MgsSo4 was (232 ± 9.64) and in control group was (147 ± 26.52) (both $p < 0.32$). The mean onset of sensory block in group MgsSo4 was (15.5 ± 2.16) and the onset of block in control group was (12.73 ± 1.18) ($p < 0.4$) statistically not significant). Also the mean onset of motor block in group Mgso4 was (23.5 ± 1.1) and the onset block in control Group P was 41 ± 3 ($p < 0.53$; statistically not significant) [12].

In our study the addition of Mgso4 to 0.5% bupivacaine in supraclavicular brachial plexus block for upper limb surgeries increased the duration of sensory and motor blocks with mean sensory block duration (643.1 ± 144.8) in Mgso4 group vs (423.5 ± 89.4) in control

group or (387.2±78.3) in hyaluronidase group and mean motor block duration (546.6±99.8) vs (337.5±77.6) in control group or (310±84.9) in hyaluronidase group with (p value <0.001) for both. Also Mgso4 decreased the postoperative pain with mean VAPS at 4, 8, 12, 24 (0-2.8), (0-3), (2-6), (5-6) vs (2-3), (4-6), (6-7), (7-7.8) in control group vs (2-3), (3.3-6), (6-7), (6-7.8) with (p value <0.001) for all. Also Mgso4 reduced total analgesic requirements in comparison with the use of 0.5% bupivacaine or bupivacaine plus hyaluronidase with mean total analgesic requirement (1-2) in Mgso4 vs (2-3) in both control and hyaluronidase groups and the change was statistically significant with (p value <0.001). However MgSo4 didn't affect the onset of sensory or motor block when compared to the control and hyaluronidase group.

The most recent in our study is the addition of both MgSo4 and hyaluronidase to bupivacaine 0.5% which resulted in significant decrease in the onset of motor and sensory block and also significant increase in the duration of the block which produced rapid surgical anesthesia, reduced postoperative pain and decrease postoperative analgesic requirement, the mean sensory block onset was (8.7±2.7), the mean motor block onset was (14.5±4).mean VAPS at 4, 8, 12, 24 hours was (0-0), (0-2), (2.3-5), (5-6) which was significant in comparison with control and MgSo4 groups with p value < 0.001. Mean sensory duration was (660.3±94.9), Mean motor duration was (546.6±99.8) both was significantly increased than control and hyaluronidase groups with p value < 0.001. Mean total postoperative analgesic request was (1-1.8) also it was significantly less than control and hyaluronidase groups.

Conclusion

The present study shows that the use of hyaluronidase reduces the time to reach complete sensory and motor block and therefore shortens the total anesthetic time before operation, hyaluronidase has no influence on the total analgesic duration or the consumption of postoperative analgesics.

Also the study shows that the use of Mgso4 increases the duration of motor and sensory block, increases the analgesic duration and reduces the postoperative analgesic consumption. However MgSo4 has no effect on the sensory or motor onset of block.

Last conclusion was that the combination of both MgSo4 with hyaluronidase as adjuvants to bupivacaine

produces significant effect on reducing the time to reach complete sensory and motor block and therefore shortens the total anesthetic time before operation, increases the duration of motor and sensory block, increases the analgesic duration and reduces the postoperative analgesic consumption.

The Institutional Ethics Committee approved this study of the School of Medicine, Minia University, Egypt, and all patients gave informed consent before participation in this study. The study conducted in accordance with the ethical guidelines of the 1975 Declaration of Helsinki and International Conference on Harmonization Guidelines for Good Clinical Practice.

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Conflict of Interest: The authors declare that there is no conflict of interests.

References

1. Sadowski M, Tułaza B and Łysenko L. Renaissance of supraclavicular brachial plexus block. *Anaesthesiology intensive therapy*. 2014; 46 (1):37-41.
2. Bailard NS, Ortiz J and Flores RA, Additives to local anesthetics for peripheral nerve blocks: Evidence, limitations, and recommendations. *American Journal of Health-System Pharmacy*, 2014. 71(5): p. 373-85.
3. Vastani N, Seifert B, Spahn DR, et al., Sensitivities of rat primary sensory afferent nerves to magnesium: implications for differential nerve blocks, *European Journal of Anesthesiology(EJA)*. 2013. 30(1): P. 21–28.
4. Price A, Walker KJ, McGrattan K, et al. Ultrasound guidance for upper and lower limb blocks. *The Cochrane of Systematic Reviews*. 2015; (9).
5. Lee I. O., Kim W. K., Kong M. H., et al., No enhancement of sensory and motor blockade by ketamine added to ropivacaine interscalene brachial plexus blockade. *Acta anaesthesiologicascandinavica*. 2002. 46, 821-6.
6. Bromage P, *Epidural analgesia*. st Ed. Philadelphia, WB Saunders; 1997:144.
7. Wohlrab J, Finke R, Franke WG, et al. Efficacy study of hyaluronidase as a diffusion promoter for lidocaine in infiltration analgesia of skin. *Plastic and reconstructive surgery*. 2012; 129 (4):771-772.

8. Koh W. U, Min H. G, Park H. S. et al. Department of: Hyaluronidase for axillary block. *Anesthesiology and Pain*. 2015, 70, 282–289. |
9. Keeler JF, Simpson KH, Ellis FR, et al., Effect of addition of hyaluronidase to bupivacaine during axillary brachial plexus block. *British Journal of Anaesthesia* 1992; 68: 68 –71.
10. Vastani N, Seifert B, Spahn DR, et al., Sensitivities of rat primary sensory afferent nerves to magnesium: implications for differential nerve blocks. *Eur J Anaesthesiology*. 2013; 30(1):21–8. P mid: 23138572.
11. Haghghi M, Soleymanha M, Sedighinejad A, et al. The effect of magnesium sulfate on motor and sensory axillary plexus blockade. *Anesth Pain Med*. 2015; 5(1).
12. Rao LN, Jeyalakshmi V, Nagaraju M, Anitha S. The effect of magnesium sulfate as an adjuvant to 0.5% bupivacaine on motor and sensory supraclavicular brachial plexus blockade. *Int J Basic Clin Pharmacol*. 2015; 4(2):317–21.

Assessment of Asthma Symptoms and Relationship to Obesity among High School Students in Fallujah City, Iraq

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Abstract

Introduction: Asthma attacks all age groups but often starts in childhood. Asthma is a chronic disease characterized by recurrent attacks of breathlessness and wheezing, and occurs in people of all ages. It is the most common chronic disease among children. Many publications have shown an association between severity of asthma symptoms and obesity in children and adults. The aim of the study is to assess the symptoms of asthma and the relationship to obesity among secondary school students in Fallujah City.

Method: A cross-sectional study was done during March 2018. We assessed 47 students with asthma from nine secondary schools across Fallujah city, Anbar governorate, Iraq. Simple random sampling technique has been used to select the nine schools.

Results: With a total of 47 subjects with asthma, 20 (42%) male and 27 (57.4%) female subjects have been included in the study. The age of subjects was between (15-23 years with mean 17 +-1.8).

With a total of 47 participants with asthma, 33 (70.2%) participants had attacks of cough or wheeze more than a couple of times per week in the last month. The corresponding weight categories of those 33 participants were as follows: six were obese, nine of over-weight, 14 were normal-weight and four of under-weight.

Those who had attacks of cough or wheeze less than a couple of times per week in the last month were 14 (29.8%) participants and their corresponding weight class were: None of them were obese, four were over-weight, eight of normal-weight and two were under-weight.

Conclusion: Obesity could be a risk factor for severe asthma symptoms among the subjects.

Recommendation: Further national study is needed for assessment the association between obesity and severity of asthma symptoms among students in secondary schools.

Keywords: Asthma, obesity, high school students, Fallujah City.

Introduction

Asthma is a chronic disease characterized by recurrent episodes of wheezing and breathlessness¹

It is a common chronic disease starting in childhood. World Health Organization (WHO) estimates that 235 million people worldwide have asthma¹

Affected individuals may experience asthma symptoms several times in a day or week, and in some people the symptoms worsen during periods of physical activity or at night. A substantial burden to individuals

and families is the result of asthma being under-diagnosed and under-treated, and this possibly restricts individuals' lifetime activities.¹

Obesity is defined as Body Mass Index (BMI) ≥ 30 kg/m². Pre-obese individuals are those with BMI = 25 – 29.99 kg/m². Further classification of obesity includes obesity class I, BMI from 30.0 to 34.9; obesity class II, BMI from 35 to 39.9; and obesity class III, BMI ≥ 40.0 .²

Many publications have shown an association between obesity and asthma in children and adults.³⁻⁶

A study that conducted on Canadians examined the association between asthma prevalence and BMI, it showing that each 1 unit increase in BMI was associated with an increase of about 6% in the risk of developing asthma in women and a 3% increase in the risk in men.⁷

Obesity was found to be associated with more asthma symptoms, missed days of work, increased rescue bronchodilator use and an increase in asthma severity overall.⁸ With obesity, it is less likely to achieve a good control of asthma and there is a reduced response to current asthma treatment⁸⁻¹⁰

Aim: The aim of the study is to assess the symptoms of asthma and their relation to body weight among secondary school students in Fallujah city.

Method

A cross section study was done during March 2018. We assessed 47 students from nine high schools across Fallujah city, Anbar governorate, Iraq. Considering equal gender participation and avoiding the selection bias, simple random sampling technique has been used to select the nine high schools with five secondary schools for girls and four secondary schools for boys. The study included only the subjects who stated that they were diagnosed with asthma, and are being treated with a chronic drug usage with or without occasionally seeking an emergency medical help for their asthma exacerbations. To minimize confounding by other conditions in which asthma-like symptoms have been reported, those who did not have the asthma diagnosis card and who stated that their symptoms have diminished and undergone remission for many years were excluded from the study.

The assessment has been made through questionnaire-based interviews which carried out by a committee of highly qualified and trained staff from College of Medicine, University of Fallujah.

The questionnaire, derived from the National Institutes of Health, Pediatric Asthma Center at Children's Hospital of Pittsburgh¹¹ and certified by a community medicine specialist at the faculty of College of Medicine, University of Fallujah, and consisted from 5 main sections; these included sociodemographic questions, school's information, details on asthma symptoms and medications, family and social history, and certain anthropometric measurements.

The sociodemographic questions included age, sex, address, school's name and study level. Questions for asthma consisted from the date of diagnosis and asthma events during the last month including the frequency of asthma symptoms, frequency of nighttime asthma symptoms, frequency of exercise-induced symptoms, frequency of missing school, frequency of rescue medication usage, frequency of flare-ups, and patient's physical activity between flare-ups.

At the end of the interview, the patient's weight and height were measured using a battery-powered digital weight scale with the shoes unworn and a height measuring scale while the patient in the upright position, respectively and Body Mass Indices [BMI (kg/m²) = weight (kg)/height (m) squared (ht × ht)] were determined.

After the students with asthma were gathered from the high school classes, they have been grouped together in the meeting room of their respective school and interviewed by the committee using the standard questionnaire. Each interview took an average of 15 minutes. To maintain the privacy of the information collected from the subjects, each interview consisted from one interviewer and one subject and was done in a separate place from other groups of subjects.

After fully explaining the specific objectives of the research, the way of carrying out the study, and verbally informing the participating students that the collected information will be highly secured and only be used for the purpose of researching, appropriate patient and school administrations approvals were obtained.

Statistical analysis: The data collected on the questionnaire-based interviews was computerized using the Microsoft Office Excel 2007 and SPSS version. 20. Chi test has been used as a statistical test and a P value < 0.05 was considered significant.

Results

Table (1) shows the frequency of gender in the study; with a total of 47 subjects with asthma (diagnosed and known cases of asthma), 20 (42%) male and 27 (57.4%) female subjects have been included in the study. Ages of subjects were between 15-23 years with mean 17 ± 1.8 .

42 (89.4%) of the study subjects experienced coughing or wheezing frequently during or after exercise

in the last month while only 5 (10.6%) subjects did not (Table 1).

For the frequency of coughing and wheezing, the results have shown that 33 (70.2%) subjects coughed or wheezed more than a couple of times per week during the last month while 14 (29.8%) subjects experienced coughing and wheezing less frequently in the last month (Table 1).

By measuring the Body Mass Indices (BMI) for the 47 young high school respondents, the results showing the following: Obese (6 people, 12.8%), over-weight (13 people, 27.7%), normal-weight (22 people, 46.8%), and under-weight (6 people, 12.8%) (Table 2).

The results have shown that the number of subjects who stated that rescue medication has been used more than a couple of times per week in the last month for flare-ups of coughing, wheezing, and chest tightness was 37 (78.7%) mainly among obese subjects (100%), over-weight (100%), normal-weight (63.6%), and under-weight (67%).

While those who did not need to use rescue medications more than a couple of times per week in the last month were 10 (21.3%) subjects and their percentages (%) in regard to weight categories were as follows: Normal-weight (36.4%), under-weight (33%), and percentage of those who were obese and overweight was (0%) for both weight classes making significant association between obesity and the usage of rescue medications more than couples of times per week among asthmatic patients, p value of 0.034 (Table 3).

For the frequency of missing school as a severity indicator for asthma symptoms in the study participants, the results have shown that a total of 19 (40.4%) subjects were obligated to missing school because of their asthma symptoms; In regard to weight categories, their percentage were as follows: obese (50%), over-weight (69.2%), normal-weight (31.8%), and under-weight (0%), there was statistically significant association, p value = 0.024 (Table 3).

Table 1: frequency of gender and coughing or sneezing attacks among the participants

		n	%
Gender	Male	20	42.6
	Female	27	57.4
	Total	47	100.0
Coughing or wheezing frequently during or after exercise (last month)	Yes	42	89.4
	No	5	10.6
	Total	47	100.0
Attacks of Coughing or wheezing more than twice a week (last month)	Yes	33	70.2
	No	14	29.8
	Total	47	100.0
Valid			

Table 2: Weight categories among the subjects

	n	%
Under weight	6	12.8
Normal weight	22	46.8
Over weight	13	27.7
Obese	6	12.8
Total	47	100.0

Table 3: Relationships between weight categories and asthma symptoms during the last month

		Coughing or wheezing more than a couple of times a week last month)		Total	P*
		Yes	No		
Weight class	Under weight	4	2	6	0.38 NS
	Normal weight	14	8	22	
	Over weight	9	4	13	
	Obese	6	0	6	
Total		33	14	47	
		Using rescue medication more than twice a week (last month)		Total	
		Yes	No		
Weight class	Under weight	4	2	6	0.034
	Normal weight	14	8	22	
	Over weight	13	0	13	
	Obese	6	0	6	
Total		37	10	47	

		Missing school frequently (last month)		Total	
		Yes	No		
Weight class	Under weight	0	6	6	0.024
	Normal weight	7	15	22	
	Over weight	9	4	13	
	Obese	3	3	6	
Total		19	28	47	
		Coughing in sleep more than twice a month (last month)		Total	
		Yes	No		
Weight class	Under weight	4	2	6	0.42 NS
	Normal weight	12	10	22	
	Over weight	10	3	13	
	Obese	5	1	6	
Total		31	16	47	
		Frequent exercise-induced coughing or wheezing (last month)		Total	
		Yes	No		
Weight class	Under weight	5	1	6	0.65 NS
	Normal weight	21	1	22	
	Over weight	11	2	13	
	Obese	5	1	6	
Total		42	5	47	

* P value of chi square test.

Discussion

The obesity is considered as a serious global problem that may associate with several health disorders and have an economic burden on the individuals and communities. The current study attempted to assess the effect of obesity on symptoms of asthma among adolescents. Obese subjects ($BMI \geq 30 \text{ kg/m}^2$) have been found to have much more severe asthma symptoms than who had a normal-weight ($18.5 < BMI \leq 24.9 \text{ kg/m}^2$). The parameters used in our study to describe a severe asthma included asthma symptoms more than twice per week, using rescue medications more than twice per week, frequent school missing, coughing in sleep for more than twice per month, and frequent asthma symptoms during or after exercise.

In a relationship between weight categories and the frequency of asthma symptoms during the last month, the results revealed that all obese subjects while 63.6% of normal-weight subjects had asthma symptoms, such as coughing, wheezing, and chest tightness with more than twice per week and they used rescue medications more than two times per week. There was statistically significant association between the obesity and using rescue medications more than two times per week, this

finding was consistent with what reported in the literature as many studies showing a relationship between severity of asthma symptoms and frequency usage rescue medication for asthma with obesity and high body mass index (BMI).⁹⁻¹⁴

A nation-wide cross-sectional study carried out on Korean children has recognized high body mass index (BMI) as an important risk factor for asthma.¹² In a study that conducted among adolescents with asthma in UAE, sleeping disturbances due to wheezing, frequency of nocturnal symptoms, wheezing during or after exercise and rate of inhaler use were all apparently higher among obese and overweight asthmatic children¹⁵.

The results demonstrated that there was significant association between the severity of asthma and obesity with missing school which was consistent with what reported in literature as the obesity and asthma had bad effect on health and performance of the subjects⁸⁻¹⁰

Conclusion

Asthma is a serious disease. Obesity has bad effects on asthma symptoms among high school students, especially on rescue medications usage.

Recommendation: Further national study is needed for assessment of association between obesity and severity of asthma symptoms among students in secondary schools.

Conflict of Interest: Nil

Source of Funding: No source of funding.

Ethical Consideration: Ethical approval for this study was obtained from the Scientific Committee of the College of Medicine, University of Falluja. Participants were given the choice to participate in the study. Verbal consent was obtained from the participants, who were permitted to respond in their own time and privacy.

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References

- World Health Organization (WHO)(2018) Asthma <http://www.who.int/respiratory/asthma/en/>(accessed April 2018).
- WHO, 2000, Obesity: preventing and managing the global epidemic [whqlibdoc.who.int/trs/WHO_TRS_894.pdf](http://www.who.int/trs/WHO_TRS_894.pdf)(Accessed April 2018)
- Chen Y, Dales R, Tang M, et al. Obesity in women but not in men may increase the incidence of asthma: longitudinal observation from the Canadian National Population Health Surveys. *Am J Epidemiol* 2002;155:1–7.
- Shaheen SO, Sterne JAC, Montgomery SM, et al. Birth weight, body mass index and asthma in young adults. *Thorax* 1999;54:396–402.
- Luder E, Melnik TA, DiMaio M. Association of being overweight with greater asthma symptoms in inner city black and Hispanic children. *J Pediatr* 1998;132:699–703.
- Chinn S. Obesity and asthma. *Paediatr Respir Rev* 2006;7:223–8.
- Chen Y, Dales R, Jiang Y. The association between obesity nonallergic than allergic adults. *Chest* 2006;130:890–5.
- Boulet LP, Franssen E. Influence of obesity on response to fluticasone with or without salmeterol in moderate asthma. *Respir Med* 2007;101:2240e7.
- Dixon AE, Shade DM, Cohen RI, et al. Effect of obesity on clinical presentation and response to treatment in asthma. *J Asthma* 2006;43:553e8
- Camargo Jr CA, Sutherland ER, Bailey W, et al. Effect of increased body mass index on asthma risk, impairment and response to asthma controller therapy in African Americans. *Curr Med Res Opin* 2010;26:1629e35.
- Children’s Hospital of Pittsburgh, Pediatric Asthma Center, PA, USA <http://www.chp.edu/our-services/pulmonology/services/asthma/resources/questionnaire>(accessed April 2018).
- Ali, Z & Ulrik, CS (2013) Obesity and asthma: a coincidence or a causal relationship? A systematic review. *Respir Med* 107, 1287–1300. CrossRef | Google Scholar | PubMed
- Weinmayr G, Forastiere F, Büchele G, Jaensch A, Strachan DP, Nagel G, et al. (2015) Correction: Overweight/Obesity and Respiratory and Allergic Disease in Children: International Study of Asthma and Allergies in Childhood (ISAAC) Phase Two. *PLoS ONE* 10(4): e0126678. <https://doi.org/10.1371/journal.pone.0126678>
- Suh M, Kim H-H, Choi DP, et al. Association Between Body Mass Index and Asthma Symptoms Among Korean Children: A Nation-Wide Study. *Journal of Korean Medical Science*. 2011;26(12):1541-1547. doi:10.3346/jkms.2011.26.12.1541
- AlBehandy N. S., Hussein H., Al Faisal W., El Sawaf E., Wasfy A., Alshareef N., Altheeb A. A. S. Prevalence of Bronchial Asthma and Its Association with Obesity and Overweight Among Adolescents in Dubai, UAE. *International Journal of Preventive Medicine Research*; 1, 3, 2015, 118-125.

Findings of Cranial Magnetic Resonance Imaging in Neonatal Seizure

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Abstract

Aim of study to know the findings of brain MRI in neonates present with seizure. A retrospective study was done in Maternity & pediatric teaching hospital in Al-Dywanyia city in Iraq, from May 2014 to June 2018. All included neonates diagnosed to have seizure, all of them had cranial magnetic resonance imaging. The standard MRI used protocol T1, T2, diffusion weighted image, gradient echo. Included patients had general anesthesia only 5 patients didn't have anesthesia or sedation as they were in deep sleep during MRI examination. The results that more than half of neonate (58.5%) was male & (41.5%) was female. Term neonate (60.4%) was more than preterm neonate (39.6%). High significant association between preterm & term neonate with MRI findings also there is high significant association between age of neonate at time of 1st attack of convulsion & positive brain MRI findings, abnormal brain MRI was more common in neonate who had 1st onset on seizure in the 1st week of his life.

Keyword: Cranial MRI of neonate, neonatal seizure.

Introduction

Seizure(convulsion) is the commonest central nervous system manifestation during the neonatal life(the first 28 days of life)¹, it can define as attack of alternation in neurological function and usually it shows an underlying problem in the brain², due to brain damage and developmental defect in the central nervous system³. There is high morbidity (25-35%) and high mortality rate in neonatal convulsions although there is no guide line in diagnosis of neonatal convulsion⁴, magnetic resonance imaging (MRI) regarded as the standard imaging technique in diagnosis of development brain disorder⁵, its rapidly became study of choice for diagnosis of central nervous system dysgenesis, MRI provide excellent diagnostic imaging technique in evaluation brain disorder superior to cranial computed tomography & ultrasound⁶. Immature brain in preterm baby seem to prone to seizure more than mature brain in term baby^{7,8}, convulsions are more common in the period of neonate than during other time throughout life & it regard as a commonest neurological emergency especially during 1st days of life^{9,10,11}, in contrast to convulsion in childhood most neonatal convulsion are acute with suspected specific causes, relatively

few neonatal convulsions are idiopathic. The etiology & presentation of neonatal convulsion is different to seizures in childhood & adult^{12,13}. It's important to detect neonatal seizures causes as early as possible for treatment planning & to know the prognosis, as the prognosis of the neonatal seizure depending on the etiology, for example prognosis after hypocalcaemic attack is excellent. Symptomatic hypoglycaemia and meningitis have a 50% chance of survivors¹⁴. Overall survivor in hypoxic ischaemic encephalopathy is 30-50%, while central nervous system dysgenesis are generally associated with poor outcome. Preterm neonates with clinical seizures have a higher incidence of impairment than preterm infants without seizures¹⁵. Aim of study to know the value of brain MRI in neonate present with convulsion in addition to other laboratory investigation

Materials and Method

A retrospective study was done in Maternity & pediatric teaching hospital in AL Dywanyia city in Iraq in a period from May 2014- June 2018. The study included 53 neonates all of them diagnosed to have seizure by pediatrician when the neonate had sudden repeated involuntary movement, abnormal tonic movement. EEG

was done to 27 patients. 1st attack of seizures occurred at different time of neonatal period, all of them had brain MRI at a period few hours – 3days from the onset of seizure when the neonate became stable, only 5 patients didn't have anesthesia or sedation as they were in deep sleep during MRI examination. We exclude the patients when his family refused MRI or refused anesthesia or sedation also we exclude the patient that was not fit for anesthesia according to the recommendation of anesthetic or not stabilized neonate.

MRI system & protocols: We used Philips - Ingenia 1.5 Tesla system & routine MRI sequences were obtained, axial & sagittal spine echo T1 weighted images (TR/TE = 460/10, slice thickness = 4mm, gap = 1mm), axial T2 weighted image (TR/TE 5500/120, slice thickness = 4mm & gap = 1mm), gradient-echo (GRE) sequences (TR/TE/FLIP angle = 800/40/40), axial diffusion weighted image (DWI) (TR/TE/b factor = 5075/84/1000), MRA (magnetic resonance angiography & MRV (magnetic resonance venography) were done not for all cases only when vascular insults like ischemia or hemorrhage are suspected. Brain MRI findings were evaluated by two radiologist to have final diagnosis this findings are classified to normal brain MRI & abnormal brain MRI than abnormal brain MRI classified to different causes.

Statistical analysis: SPSS version 22.0 and Microsoft Office Excel 2010 were used to analyse the data. The numeric variable was expressed as mean ± SD & categorical variables were expressed as number & percentage, the level of significance was considerable at P- value of 0.05.

Results

Table 1: Distribution of study sample of neonate according to the gender

Gender	No. (%)
Male	31(58.5%)
Female	22(41.5%)
Total	53(100%)

According to table 1 more than half of neonate (58.5%) was male & 41.5% was female.

Table 2: Number & percent of preterm & term neonate in our study

Term & Preterm neonates	No. (%)
Preterm neonates	21(39.6%)
Term	32(60.4%)
Total	53(100%)

Table 2 show term neonate (60.4%) was more than preterm neonate (39.6%).

Table 3: Age of neonate at time of fit

Age of fetus at time fit	No. (%)
0-7 days	28(52.7%)
8-14 days	11(20.8%)
15-21 days	11(20.8%)
22-30 days	3(5.7%)
Total	53(100%)

Nearly half of fetus (52.7%) have 1st attack of fit at about 1st week of life swing between few hours to 7 days.

Table 4: Cranial MRI of the neonate present with fit.

Cranial MRI Findings	No. (%)
Normal MRI	31(58.5%)
Abnormal MRI	22(41.5%)
Total	53(100%)

Table 5: The association between cranial MRI findings & gender of the neonate.

Cranial MRI findings	Gender		Total
	Male	Female	
Abnormal MRI	10	12	22
Normal	21	10	31
Total	31	22	53
Chi-square=2.633	DF=1		P=.105

According to table 5 there is no significant association between gender & cranial MRI findings in neonatal convulsion.

Table 6: The association between cranial MRI findings with preterm & term neonate in neonatal convulsion.

Cranial MRI findings	Preterm neonate	Term neonate	Total
Abnormal MRI	2	20	22
Normal MRI	19	12	31
Total	21	32	53
Chi-square=14.656	df=1	P value =.000	

High significant association between preterm & term neonate with MRI findings.

Discussion

The susceptibility of seizure recurrence was extremely low with an absence of major cerebral lesions on MRI, for this reason MRI has a value not only diagnosis the etiology but also for predication of neurological outcome¹⁶. In this study neonate male (58.5%) present with convulsion slightly more than female (41.5%) with no significantly association ($p=.105$) which is go with many study like Moayedi et al¹⁷, Taghdiri et al¹⁸, Sanjeev et al¹⁹, Amjaad et al²⁰ & Weeke²¹ but there is no explanation for this variation Moayedi et al¹⁷.

Percent of term baby (60.4%) was more than preterm baby (39.6%) that's go with many other studies Moayedi et al¹⁷ & Sanjeev et al¹⁹ while Al-Zwaini I et al²² reported that preterm newborn exhibits higher risk for neonatal seizures than term newborn and this difference may be interfere with other factors like body weight, natal & postnatal complication that affect the occurrence of seizure²³, in this study hypoxic ischemic encephalopathy (40.9%) was the commonest cause which related to the natal complication.

First onset of seizure in the neonate most often occur at 1st wk of life^{6,20,21}, in our study about half of neonate (52.7%) have 1st attack of fit at 1st week of life at a period swing between few hours after birth to 7 days with a high significant association (p value =.000) between age of neonate at time of 1st attack of convulsion & MRI findings.

Less than half of our patient (41.5%) have abnormal brain MRI scan of different etiology & (58.5%) of neonate have normal brain MRI, the most common abnormality seen in neonate was hypoxic ischemic encephalopathy (40.9%) follow by brain dysgenesis (36.4%) which is go with many study like Amjaad et al²⁰, Snehalatha et al⁶ &

Shafi M et al.²⁴.

All patient who have normal brain MRI were undergo to laboratory investigation to detect cause of seizure, in those patient metabolic disorder was the commonest cause (38.7%) follow by kernikterus (35.5%) & unknown etiology was in 12.9%. which is go with many study like Tekgul et al¹ & Ronen et al².

Conclusion: MRI is indicated with other tests to diagnose underlying brain pathology in neonatal seizure.

Conflict of Interest: None

Funding: Self

Ethical Clearance: Not required.

Recommendation: Further study is recommended included follow up these neonate to know whether there is recurrence of fit in future. Further study using MRI spectroscopy to predict the severity & prognosis of patients with neonatal seizure.

References

- Ronen GM, Buckley D, Penney S, Streiner DL. Long term prognosis in children with neonatal seizures: a population –based study. *Neurology* 2007; 69:304-11.
- Tekgul H, Gauvreau K, Soul J. The current etiology profile and neurodevelopment outcome of seizure in term newborn infants. *Pediatrics* 2006;117:1270-80.
- Glass HC, Sullivan JE, Neonatal seizure. *Curr Treat Option Neurol* 2009;11:405-13.
- Girard N, Raybaud C. Neonate with seizure what to consider, how to image. *MagnReson Imaging Clin N Am* 2011; 19:685-708.
- Rutherford MA, Ramenghi LC, Cowan FM. Neonatal stroke. *Arch Dis Child Fetal Neonatal Ed* 2012;97:377-84.
- Snehalatha G, Ravikumer N, Sikha M. Magnetic resonance imaging of brain in neonatal seizure. *IOSR Journal of dental & medical sciences volume 14, issue 12, 2015;21-25*
- Miller SP, Weiss J, Barnwell A I. Seizure-associated brain injury in term newborns with perinatal asphyxia. *Neurology* 2002; 58: 542-548.
- Davis AS, Hintz SR, Vanmeurs KP et al. Seizures in extremely low birth weight infants are

- associated with adverse outcome. *J Pediatr* 2010; 157: 720-725.
9. Berga A, Jallon P, Preux P. The epidemiology of seizure disorders in infancy and childhood: definitions and classifications. In: O Dulac et al (Eds), *Handbook of Clinical Neurology. Pediatric Neurology, Part 1* (3rd edition), pp 381-398. Elsevier, Amsterdam, Netherlands, 2013.
 10. Vasudevan C, Levene M. Epidemiology and etiology of neonatal seizures. *Semin Fetal Neonatal Med* 2013; 18(4): 185-191.
 11. Benary Y, Holmes GL. Effects of seizures on developmental processes in the immature brain. *Lancet Neurol* 2006; 5: 1055-1063.
 12. Jensen FE. Neonatal seizures: an update on mechanisms and management. *Clin Perinatol* 2009; 36: 881-900.
 13. Malone A, Ryan CA, Fitzgerald A et al. Interobserver agreement in neonatal seizure identification. *Epilepsia* 2009; 50: 2097-2101.
 14. Pisani F, Piccolo B, Cantalupo G et al. Neonatal seizures and postneonatal epilepsy: a 7-y follow-up study. *Pediatr Res* 2012; 72(2): 186-93.
 15. Uria-Avellanal C, Marlow N, Rennie JM. Outcome following neonatal seizures. *Semin Fetal Neonatal Med* 2013; 18(4): 24-32.
 16. Osmond E, Billetoop A, Jary S, Likeman M, Thoresen M, Luyt . Neonatal seizure: magnetic resonance imaging adds value in the diagnosis and prediction of neurodisability. *Act Paediatr.* 2014;103(8):820-6.
 17. Moayedi AR, Zakeri S, Moayedi F. Neonatal seizure: etiology and type. *Iran J Child Neurology* 2007;Feb:23-26.
 18. Taghdiri MM, Emdadi M, Jabbari M, Tavasoli AR. Plain CT scan in neonatal convulsion. *MJIRC* 2005;7(3):53-55.
 19. . Sanjeev K, Ashok G. Prevalence of seizures in hospitalized neonate. *JK science* 2007;9(1):27-29.
 20. Amjaad M & Nasma N. Findings of brain computed tomography in neonatal seizure. *Medical Journal of Babylon* 2011;8(1):49-58.
 21. Weeke LC, Groenedaal F, Toet MC, Benders MJ, Nievelstein RA . The aetiology of neonatal seizure and the diagnostic contribution of cerebral magnetic resonance imaging. *Dev Med Child Neurol* 2015;57(3):210-1.
 22. AL-Zwaini Isam. Neonatal Seizures, Epilepsy in Children - Clinical and Social Aspects. 2011;27-46
 23. Mosley M, Neonatal Seizure. *Pediatr.* 2010; 31:127-8.
 24. Shafi M, Ezhilarasan R, Umamaheswari B, Saravanan R, Rangasami R. Spectrum of magnetic resonance imaging abnormalities in neonatal seizure in a tertiary care hospital in India. *International Journal of Contemporary pediatrics* 2016;3(4):1150-1155.

Ethyl Acetate Fraction of Papua's Ant Nest Plant (*Myrmecodia Pendens*) Induces Cell Cycle Arrest and Apoptosis of an Oral Malignant Burkitt Lymphoma Cell through Down Regulation of Cyclin E–CDK2 Complex

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Abstract

Efforts to inhibit the growth of oral Burkitt's lymphoma cells require an effective strategy, one of that uses Papua's ant nest plant (*Myrmecodia pendens*) which are natural medicinal plants. In the present study, induction of cell cycle arrest and apoptosis of an oral Burkitt's lymphoma cell (Raji cell)-mediated by an ethyl acetate fraction of Papua's ant nest plant through down regulation of cyclin E-CDK2 complex was examined. For detection of cell cycle arrest was evaluated by flow-cytometer. Induction of apoptosis was detected by colorimetric assay caspase-3, -8 and -9. The level of cyclin E and CDK2 was carried out by Elisa kit. The results revealed the active fraction of the ant nest was markedly induced the cell cycle arrest in the G0-G1 phase according to increased concentration followed by the induction of apoptosis characterized by elevated of proteolytic activity of caspase-3, -8 and -9. Cyclin E and CDK2 level was significantly decreased in cell treated with ant nest fraction. These results suggest the ethyl acetate fraction of the ant nest plant had a strong potential antitumor activity of oral malignant Burkitt's lymphoma cell proofed by the induction of cell cycle arrest and apoptosis through down regulation of cyclin E-CDK2 complex.

Keywords: Burkitt's lymphoma, cell cycle arrest, apoptosis, ethyl acetate fraction, cyclin E, CDK2.

Introduction

Burkitt's lymphoma (BL) is one of the aggressive oral cancers derived from lymphoid with a percentage of events ranging from 3-5% of all lymphoma cancers. BL is a high-stage B cell neoplasm, commonly found in the population of children aged 7-11 years.¹ Almost 40% of BL occur in children includes the type of Non-Hodgkin lymphoma.² The highest incidence is found

in endemic areas in the equatorial regions of Africa and Papua-New Guinea in the amount of 50-70% of all malignancies in children.³ Interestingly, Epstein-Barr virus (EBV) has an important role in the occurrence of BL and most commonly occurs in the maxillary or mandibular regions.⁴ BL causes a lot of deaths in the children population in developing countries due to inadequate treatment or coming to health institutions in advanced stages. So, the effective and potential treatment strategies to suppress the Burkitt's lymphoma malignant cell growth are still very necessary, one of it uses plants medicine is made from natural ingredients that are cheap, easily available and are local products and are widely grown in the tropic areas, namely ant nest plant (*Myrmecodia pendens*) whose its antitumor potential has been empirically and scientifically observed.

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Ant nest plants contain active compounds of flavonoids, polyphenols and tannins, which function

as antioxidants that can prevent the growth of various types of human cancer cells and effectively suppress carcinogens.⁵ Ant nest plants also contains tocopherol and alpha-tocopherol, substances with high activity that can inhibit free radicals.⁶ It was reported that ant nest plants are toxic to several human cancer cells including cervical uterine cancer cells (HeLa), breast cancer cells (MCM-B2),⁶ and oral carcinoma cells (KB).⁷ The mechanism of growth inhibition of cancer cells with ant nest plants is reported through barriers to signaling factors transduction of NF-kB, IL-8 and Vascular Endothelial Growth Factor (VEGF).⁸

In the present study, the ethyl acetate fraction of the ant nest plant induces cell cycle arrest and apoptosis of an oral malignant Burkitt's lymphoma (Raji) cell through down regulation of cyclin E-CDK2 complex was evaluated.

Materials and Method

Cell and cell culture: Raji cells (ATCC CCL-86 B lymphocyte, USA) were cultured in Dulbecco's modified eagle medium (Sigma-Aldrich, St. Louis, MO, USA) supplemented with 10% fetal calf serum, and 100mg/ml streptomycin, 100 U/ml penicillin (Moregate BioTech, Bulimba, Australia). The cultures were incubated in a humidified atmosphere of 95% air and 5% CO₂ at 37°C.⁹

Ethanol Extract of Papua's Ants Nest Plants: Ant nest plants (Wamena, Papua, Indonesia) were washed and dried in an oven at 55°C until it dries and was ground to powder (simplicia). Maceration was done by soaking the simplicia into 96% ethanol (Brataco, Indonesia) and stirred for 30 minutes, then incubated for 5 days. The immersion liquid was filtered to separate the pulp and ethanol extract. The macerated extract was collected in one section and evaporated using a rotary vacuum evaporator at a temperature of 70°C. Thus, the existing water content was removed by heating it in a water bath with a temperature of 70°C.

The process of fractionating ant nest plants: Fractionation is the process of separation between liquid and liquid which is carried out in stages based on the level of polarity, namely from non-polar, semi-polar and polar. The puremethanol (Brataco, Indonesia) extract was suspended with methanol: water (1:1) and partitioned using hexane solvent, producing a hexane fraction. Repeated until the hexane fraction obtained was clear. The n-hexane (Nacalai, Japan) fraction was partitioned using n-hexane solvent obtained by n-hexane

extract. The n-hexane fraction was partitioned with ethyl acetate (EtoAc): Aquades (1:1) to obtain the ethyl acetate fraction. The results of the partition of the fractions were evaporated at a temperature of 30-40°C until fractions were obtained. Furthermore, the fraction obtained can be used for phytochemical tests.

Cell cycle analysis with flow cytometry: Cell cultures were inserted in a 24-well with a concentration of 2.5×10^5 cells/well and incubated for 24 hours. The treated cells (concentration 37.5, 75, 112.5, 150 and 300 µg/mL) were collected in a flow cytometer tubes and centrifuged at 1500 rpm for 5 minutes, then the supernatant is removed. Cells were fixed with 500 µL of 70% ethanol cold, stored at 4°C for 15 minutes and centrifuged for 5 minutes. Cell pellets were suspended with 900 µL PBS and 100 µL Propidium Iodide (Sigma Aldrich, USA), dye analysis of DNA content, and homogenized. Suspended cells were incubated in the dark for 30 minutes and analyzed for cell cycles with flow cytometry (Beckmann coulter, USA).

Apoptosis induction analysis by caspase -3, -8 and -9: Caspase-3,-8 and -9 activities were measured using the colorimetric assay kit according to the manufacturer's directions. Briefly, equal amounts of cell extracts prepared from Raji cell treated with ethyl acetate fraction with concentration 37.5, 75, 112.5, 150 and 300 µg/mL were incubated with the substrate (DVED-pNA and LEHD-pNA; BioVision colorimetric assay kit, CA, USA) in the assay buffer for 2h at 37°C. Absorbance was measured at 450 nm using a microplate reader (Bio-Rad Laboratories, Hercules, CA, USA). Each determination was conducted in triplicate.¹⁰

Cyclin E and CDK2 analysis using Elisa kit: All reagents and samples were prepared in 4°C storage. Fifty micro liter of all sample were added to appropriate wells and 50 µL of the Antibody cocktail was also added to each well. Seal the plate and incubate for 1 hour at room temperature on a plate shaker set to 400 rpm. Each well was washed with 3x350 µL 1X wash buffer. Wash by aspirating or decanting from wells then dispensing 350 µL 1X wash buffer into each well. 100 µL of TMB substrate were added to each well and incubate for 10 minutes in the dark on a plate shaker set to 400 rpm. Further more, 100 µL of stop solution were added to each well. Shake plate for 1 minute to mix and measured at 450 nm.

Statistical analysis: Data was evaluated with Stat View 4.5 (Abacus Concepts, Berkeley, CA) using one-

way ANOVA and *t-test*. The significance level was set at 5% for each analysis.

Results

Proteolytic activities of caspase-3,-8 and -9:

The activity of caspase-3,-8 and -9 in Rajicell treated with various concentrations of ethyl acetate fraction (EAF) were investigated. Raji-EAF 112.5 to 300 µg/mL revealed increased the proteolytic activities of caspase-3, -8 and -9 as compared with that of control. Proteolytic activities of caspase-3 in Raji-EAF 300 µg/mL was found at 1.42 fold increase compared with that of control (Figure 1A). Furthermore, proteolytic activities of caspase-8 in Raji-EAF 300 µg/mL was detected at 1.75 fold increased (Figure 1B). Moreover, caspase-9 proteolytic activities in Raji-EAF 300 µg/mL was confirmed at 1.83 fold increase (Figure 1C). Increased caspase-3, -8 and -9 expressions were followed by in increased in ethyl acetate fraction of *M. pendens* concentration. These results showed that apoptosis can

appear through intrinsic (chemical induced apoptosis) and extrinsic (receptor induced apoptosis) pathways. Interestingly, induced apoptosis through the intrinsic pathway was detected stronger than extrinsic pathway in oral Burkitt's lymphoma cells.

Cell cycle analysis: Cell cycle arrest was examined by flow cytometry. As seen in Table 1, Raji-EAF 150 µg/mL had a potential to arrest of cell cycle in G0-G1 phase by 13.75% and in G2-M phase at 8.54%. However, Raji-EAF 300 µg/mL was only inhibited the cell cycle in G2-M phase.

Level of cyclin E and CDK2: Cyclin E and CDK2 was evaluated by Elisa kit. As seen in Figure 2A and 2B, cyclin E and CDK2 level were significantly decreased according to increased concentration of Ethyl acetate fraction of ant nest. The suppression of cyclin E and CDK2 level in Raji cell treated with EAF 300 µg/mL was found at 68% and 57%, respectively.

Figure 1. Proteolytic activity of caspase-3, -8 and -9 evaluated by colorimetric assay. A. Fold increase in caspase-3. B. Fold increase in caspase-8. C. Fold increase in caspase-9 (*, P < 0.05)

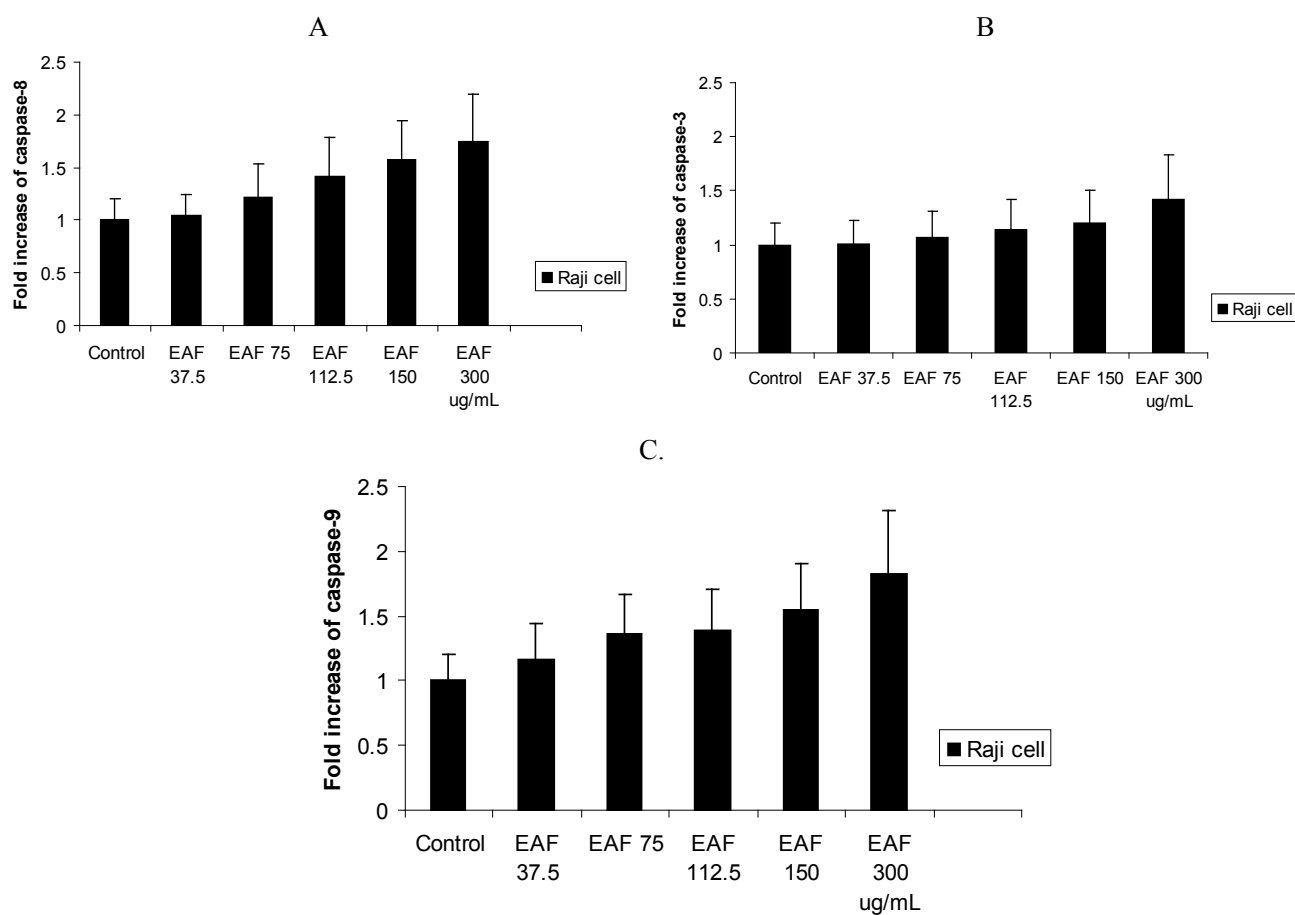
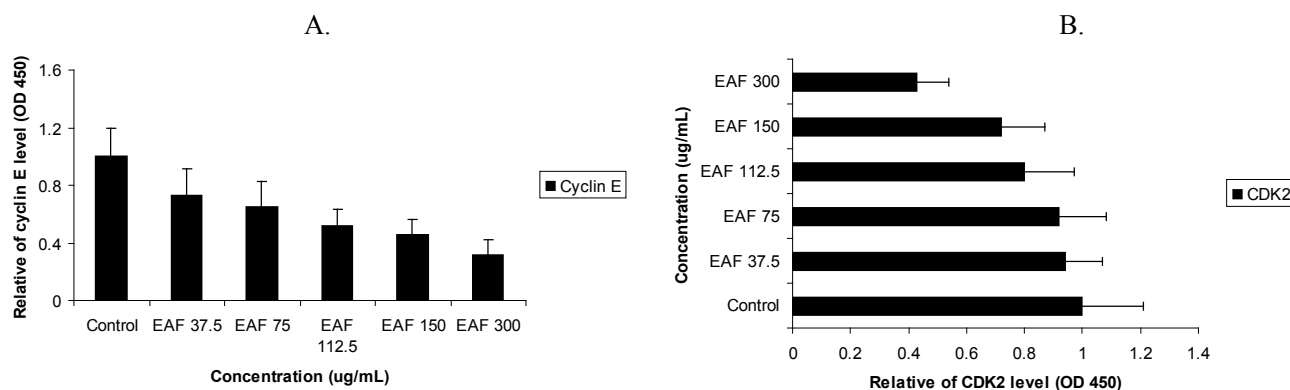


Table 1: Cell cycle arrest was examined by flow cytometri. Raji cell was treated with various EAF of ant nest

	Control (%)	EAF 37.5 (%)	EAF 75 (%)	EAF 112.5 (%)	EAF 150 (%)	EAF 300 (%)
G0-G1	61.31	52.71	48.84	50.82	75.06	45.63
S	18.80	20.62	18.99	21.59	13.56	40.47
G2-M	20.08	26.67	31.84	27.60	11.54	11.95

Figure 2: Cyclin E and CDK-2 level assay was carried out by Elisa kit(*, P < 0.05)



Discussion

The cell cycle requires a delicate balance between positive and negative regulatory factors. Any alteration in this balance can result in abnormal cell proliferation and apoptosis reduction which may contribute to cancer. Cancers of the oral cavity present a major health problem, as indicated by their high incidence in many parts of the world.¹¹ These highlights the necessity for continued efforts to improve the treatment modalities one of them uses superior herbal medicine products in Indonesia, Papua’s ant nest plant (*Myrmecodia pendens*). In the present study, active fraction of ethyl acetate was employed to investigate the effect of cell cycle arrest and apoptosis induction on oral Burkitt’s lymphoma cells. Treatment of various concentration of ant nest into cultured Raji cell was induced the cell cycle arrest and apoptosis effect. In addition, higher concentration of ant nest revealed stronger effect in both examined. These results clearly showed that cell cycle arrest and apoptosis induction was increased by the ant nest effect and not by non-specific effects such as ethyl acetate toxicity. Furthermore, cell cycle arrest in G0-G1 and G2-M phases was showed in Raji cells treated with ethyl acetate fraction of ant nest at concentration 150µg/mL. Interestingly, cell cycle arrest in G2-M phase was only detected at concentration 300 µg/mL. These data

suggest the most effective concentration inhibits the cell cycle was 150-300 µg/mL. Recently reported that phytochemical species of ant nest plants have relatively similar active compounds include tannin, tocopherols, alkaloids and flavonoids.⁶ Flavonoids were reported to have antioxidants effect that activating the cancer cell apoptosis pathway. The mechanism of cell apoptosis in that theory is a result of DNA fragmentation. This fragmentation begins with the release of the proximal DNA chain by reactive oxygen compounds such as hydroxyl radicals. Second, flavonoids as cancer inhibitors are one of them by inhibiting the activity of protein kinase so that it inhibits the signal transduction pathway from the cell membrane to nucleus. Third, flavonoid is inhibiting tyrosine kinase receptor activity because the increased receptor activity of tyrosine kinase plays a role in the growth of malignancy.¹² Recently, Dehay and Kennedy¹³ reported cell cycle control is carried out by CKI which acts as a negative regulator of activation of the cyclin/CDK complex during the G1 and S phases. Cyclin/CDK regulation at each cell cycle phase including the cyclin D/CDK4/6 complex plays a role in the initial transition until mid-phase G1. The beginning of the S phase is characterized by the formation of the cyclin E/CDK 2 complex. In this study, we showed ant nest fraction was markedly induced cell cycle arrest

through down regulation of cyclin E-CDK-2 complex protein. This data was in accordance with the results of this study that induction of cell cycle arrest in G0-G1 or G2-M phases followed by down regulation of cyclin E-CDK-2 complex protein.

As expected from the cell cycle arrest effect, apoptotic induction was also occurred in cells treated with ethyl acetate fraction of ant nest at concentrations of 75-300 µg/mL g/mL. Increased in proteolytic activity of caspase-3, -8 and -9 suggest that apoptosis can occur through the extrinsic and intrinsic pathways. In both pathways there was activation of cystein aspartyl-specific proteases (caspase) which play a role in breaking down cellular substrate which causes changes in cell morphology and biochemistry as a characteristic of apoptosis.¹⁴Intrinsic pathways had the proteolytic activity stronger than extrinsic pathways. It means the ethyl acetate fraction of ant nests was more potent elevating intrinsic pathways which are chemical-induced apoptosis than receptor-induced apoptosis. Moreover, increased activity of caspase-3, -8 and -9 strongly suggest that apoptosis occurred in those cultures. Activation of caspase-3, an executioner caspase in apoptosis pathway, leads to the cleavage of PARP and DNA fragmentation indicating that caspase-3 targets cellular proteins for proteolytic cleavage resulting in cell death.¹⁵ Caspase-3 activity can be activated by either an extrinsic apoptosis pathway, by the activation of caspase-8, or an intrinsic apoptosis pathway, by the release of cytochrome-c from mitochondria. Activated caspase-8 can directly cleave and activate the executioner caspases, such as caspase-3, or it can cleave one of the Bcl-2 family members, such as Bid, to induce the release of mitochondrial cytochrome c, which also leads to activation of caspase-3 via formation of a pop to some consisting of Apaf-1 and caspase-9.¹⁶

In conclusion, the ethyl acetate fraction of the ant nest plant had a strong potential antitumor activity of oral malignant Burkitt's lymphoma cells proofed by the induction of cell cycle arrest and apoptosis through down regulation of cyclin E-CDK-2 complex..

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Ethical Clearance: This research has been

requested by ethical clearance at the faculty of dentistry at Gadjah Mada University with the number 001385/KKEP/FKG-UGM/EC/2018.

References

1. Guimarães AC, de Carvalho GM, Bento LR, Correa C, Gusmão RJ. Clinical manifestations in children with tonsillar lymphoma: A systematic review. *Crit Rev Oncol Hematol* 2014;90(2):146-151.
2. Tewfik TL, Bond M, Al-Ghamdi K. Burkitt's lymphoma of the tonsil in children. *J Otolaryngol* 1996; 25:205-208.
3. Carbone A, Canzonieri V, Gloghini A, Rinaldo A, Gaidano G, Ferlito A. Burkitt's lymphoma: historical background and recent insights into classification and pathogenesis. *Ann Otol Rhinol Laryngol* 2000; 109(7):693-702.
4. Salamon D, Adori M, He M, Bonelt P, Severinson E, Kis LL. Type I interferons directly down-regulate BCL-6 in primary and transformed germinal center B cells: Differential regulation in B cell lines derived from endemic or sporadic Burkitt's lymphoma. *Cytokine* 2012; 57(3):360-371.
5. Subroto MA, Saputro H. *Destroyed Disease with Ants Nest*. Jakarta: Swadaya press. 2008.
6. Soeksmanto A, Subroto MA, Wiajaya H, Simanjuntak P. Anticancer Activity Test for Extracts of Sarang Semut Plant (*Myrmecodia pendens*) to HeLa and MCM-B2 Cells. *J Bio Sci* 2010;13(3):148-151.
7. Yuletnawati SE, Meiyanto E, Agustina D. High antitumor activity of ethanolic extracts of Papuas ant nest plant (*Myrmecodia pendens*) on an oral carcinoma (KB) cell line. *IJSR* 2016; 5(1):1619-1623.
8. Achmad H, Supriatno, Ramadhany S, Singgih M, Samad R, Chandra MH. Apoptosis induction (caspase-3, -9) and human tongue squamous cell carcinoma VEGF angiogenesis inhibition using flavonoids ethyl acetate fraction of Papua ant hill (*Myrmecodia pendans*). *J Int Dent Med Res* 2018; 11(1):276-284.
9. Supriatno, Yuletnawati SE. Antitumor Activity of Chronic Heart Failure Drug Quinolinone Derivate-Vesnarinone On An Oral Malignant Burkitt's Lymphoma Cell (Study on proliferation, chemotactic migration and cell apoptosis). *J Int Dent Med Res* 2018; 11(3):834-839.

10. Supriatno. S-Phase Kinase-Associated Protein-2 and Nuclear Factor-kappa Beta as Molecular Targets of Oral Burkitt's Lymphoma Cell Induced by Quinolinone Derivate-Vesnarinone. *Curr Signal Transduction Ther* 2018; 13:1-6.
11. Almofti A, Uchida D, Begum NM, Tomizuka Y, Iga H, Yoshida H, et al. The clinico-pathological significance of the expression of CXCR4 protein in oral squamous cell carcinoma. *Int J Oncol* 2004; 25:65-71.
12. Lee S, Kim YJ, Kwon S, Lee Y, Choi SY, Park J. Inhibitory effects of flavonoids on TNF- α -induced IL-8 gene expression in HEK 293 cells. *BMB reports* 2008;265-270.
13. Dehay C, Kennedy H. Cell cycle control and cortical development. *Nat Rev Neurosci*.2007; 8(6):438-450.
14. Igney FH, Krammer PH. Death and anti-death: tumour resistance to apoptosis. *Nat Rev Cancer*. 2002; 2(4), 277-288.
15. Harada K, Kawaguchi S, Supriatno, Onoue T, Yoshida H, Sato M. Enhancement of apoptosis in salivary gland cancer cells by the combination of oral fluoropyrimidine anticancer agent (S-1) and radiation. *Int J Oncol* 2004; 25: 905-911.
16. Azuma M, Harada K, Supriatno, Tamatani T, Motegi K, Ashida Y, *et al.* Potentiation of induction of apoptosis by sequential treatment with cisplatin followed by 5-fluorouracil in human oral cancer cells. *Int J Oncol* 2004; 24: 1449-1455.

Space-Time Analysis for Dengue Surveillance: A Case Study in Sleman, Yogyakarta, Indonesia

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Abstract

Introduction: Surveillance is a dynamic activity that needs a continuous update to perform their function such as monitoring, evaluating, identifying high risk and supporting disease policy making. Geographic Information System (GIS) is a system for capture, store, analysis and visualise a phenomenon related to the geographical position including related particular disease. This tool is claimed powerful to support disease surveillance.

Objective: This study aims to apply retrospective space-time analysis using GIS on dengue cases to identify the clustering that may occur during the data period for supporting dengue surveillance.

Method: This research was a descriptive study by employed GIS technique-Satscan retrospective space-time permutation model. 159 confirmed dengue case sourced from Sleman District Health Office (Sleman DHO) between January 2017 to September 2018 was used as an input data. Geographical Positioning System (GPS) was employed to collect the coordinate location of the cases. The map was generated using Arc GIS.

Results: A most likely cluster and eight secondary clusters were detected in this study. The most likely cluster was found in Depok subdistrict during the middle of March to the middle of April 2018.

Conclusions: GIS shown as a powerful tool for dengue surveillance. Identification of space and time related to dengue is an alarm for related stakeholder on dengue prevention to prepare and prevent outbreak occurrence.

Keywords: *Dengue, Scan statistic, Space-Time cluster detection, GIS, Sleman, Indonesia.*

Introduction

Dengue is caused by DEN virus that transmitted by female *Aedes aegypti* that it is estimated responsible to 390 million infections each year¹. Dengue is an infectious disease that closely associated with environmental condition and time pattern. In Sleman dengue-related to environmental aspects such as land cover, humidity and rainfall². Understanding the space and time pattern is essential for surveillance action on monitoring and

preventing the dengue transmission.

Geographical Information System (GIS) is an instrument for capture, store, analysis and visualise a phenomenon related to the geographical position of particular object^{3,4}. GIS is a powerful tool on surveillance activity, as stated by some researches before. John Snow introduced this tool in 1854. On that time, he used GIS to study cholera outbreak in London⁵. Since then, GIS is widely used in public health study in many diseases' cases. A review from Jennifer et al. discussed the role of GIS for surveillance purpose⁶, for example, recognising the triggers of dengue by assessing the correlation among the variable visually and geographical phenomenon. The important of GIS also said by another review that GIS could support dengue control program, such as by generating the vulnerable risk map⁴.

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According to Sleman government information, Sleman is divided into seventeen subdistricts that located in the north of Yogyakarta province, Indonesia. This district spreads over 574.82 Km², with more than 800.000 resident living over there⁷. Dengue in this district has been receiving attention from the local authority. The case number fluctuated throughout the year from 2013 to the middle of 2018 (Figure 1). Dengue case information in Sleman is captured through Integrated Disease Surveillance System or called as Surveilans Terpadu Penyakit (STP) and Hospital Information system or called as (SIRS). All of which are based on the patient visit in the hospital, primary health centre and other health facilities. A monthly report was generated from this activity to calculate the top 10 disease status⁸.

Space-time permutation statistic is an algorithm which required case date of illness and coordinate position. This formula is a promising tool for early detection of particular disease outbreak⁹. Currently, information about the place and time of the disease occurrence is pivotal for preparing the disease prevention program by the stakeholder involved. There is growing evidence the usage of GIS method in disease-related environmental. However, information regarding space and time simultaneously is lacking, particularly in dengue. This research aims to apply retrospective space-time analysis using GIS on dengue cases to identify dengue cluster that may occur during the data period for supporting dengue surveillance.

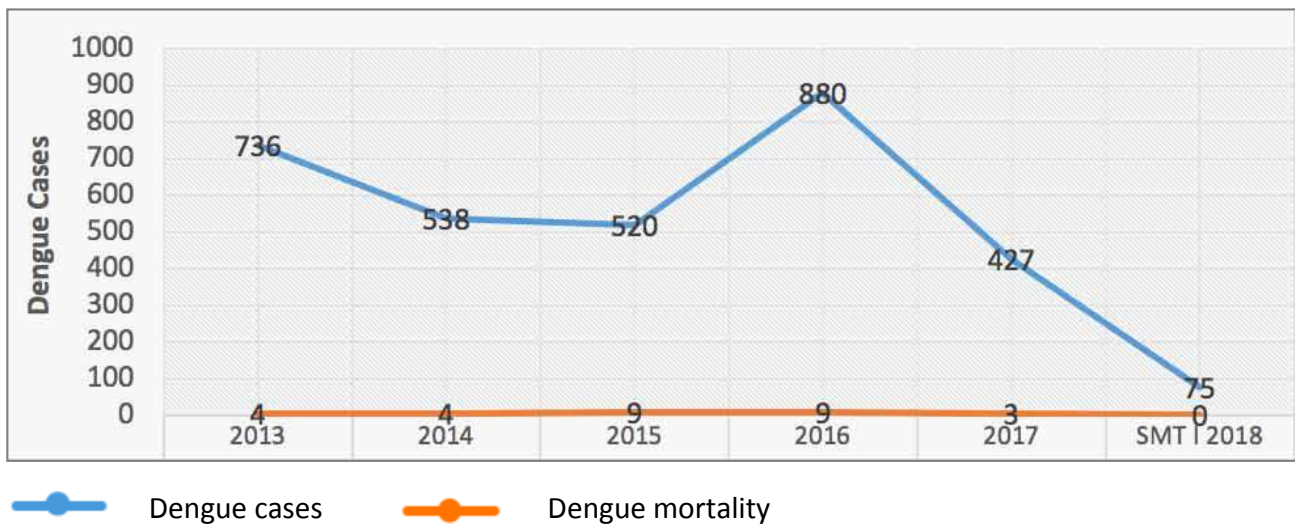


Figure 1: Dengue case and mortality in Sleman district from 2013 to the middle of 2018

Material and Method

This research is a descriptive study to detect space and time cluster of dengue cases in Sleman, Yogyakarta (January 2017 to November 2018). Data collection and analysis was done in the end of 2018. Secondary data from Sleman District Health Office (Sleman DHO) was collected as input data of the study. Of 159 confirmed dengue cases who had a complete home address and date of illness was included. Geographical Positioning System (GPS) was employed to collect the coordinate location of the cases. For analysis purposes, we used the Retrospective Spatial Scan Statistic (Satscan) software. The Kulldorf space-time permutation model was used to discover the dengue cluster by using five days of Time

Aggregation Length. The map was generated using Arc GIS.

Results

According to our research, space-time analysis can be used on dengue surveillance study to inform where and when the dengue transmission potentially occurred. This information is essential to influence dengue program stakeholder to determine appropriate prevention of dengue outbreak.

During the data period - from January 2017 to November 2018, Satscan statistics detected nine clusters of dengue cases in Sleman, Yogyakarta. Among which, one cluster was significant ($p\text{-value} \leq 0.05$). This cluster

centred at Depok subdistrict, in adjacent with the city of Yogyakarta and some other district in Central Java Province. The other eight clusters are spread over the

Sleman, and they were not significantly space time associated. Complete information is summarised in Table 1 and Figure 2.

Table 1. Cluster detection according to retrospective space time permutation model

Cluster ID	Data range	Cluster locations	Cluster radius (km)	Actual cases	Expected cases	P-value
1	3/12/18-4/15/18	-7.78311, 110.3928	2.34	8	1.19	0.022*
2	7/5/17- 9/2/17	-7.80071, 110.2959	2.78	13	3.65	0.176
3	7/30/17-8/18/17	-7.69815, 110.4208	1.57	3	0.11	0.337
4	1/1/18- 1/10/18	-7.66529, 110.3271	7.95	6	0.82	0.36
5	6/5/18- 6/19/18	-7.81873, 110.4561	1.80	2	0.03	0.471
6	1/31/18- 2/19/18	-7.74006, 110.3479	0.31	4	0.35	0.783
7	3/2/18- 3/6/18	-7.74064, 110.3123	0.01	2	0.05	0.991
8	9/8/17- 10/2/17	-7.72644, 110.4851	6.73	5	0.75	0.996
9	4/21/18- 5/5/18	-7.76558, 110.3429	2.01	3	0.22	0.999

*significant cluster

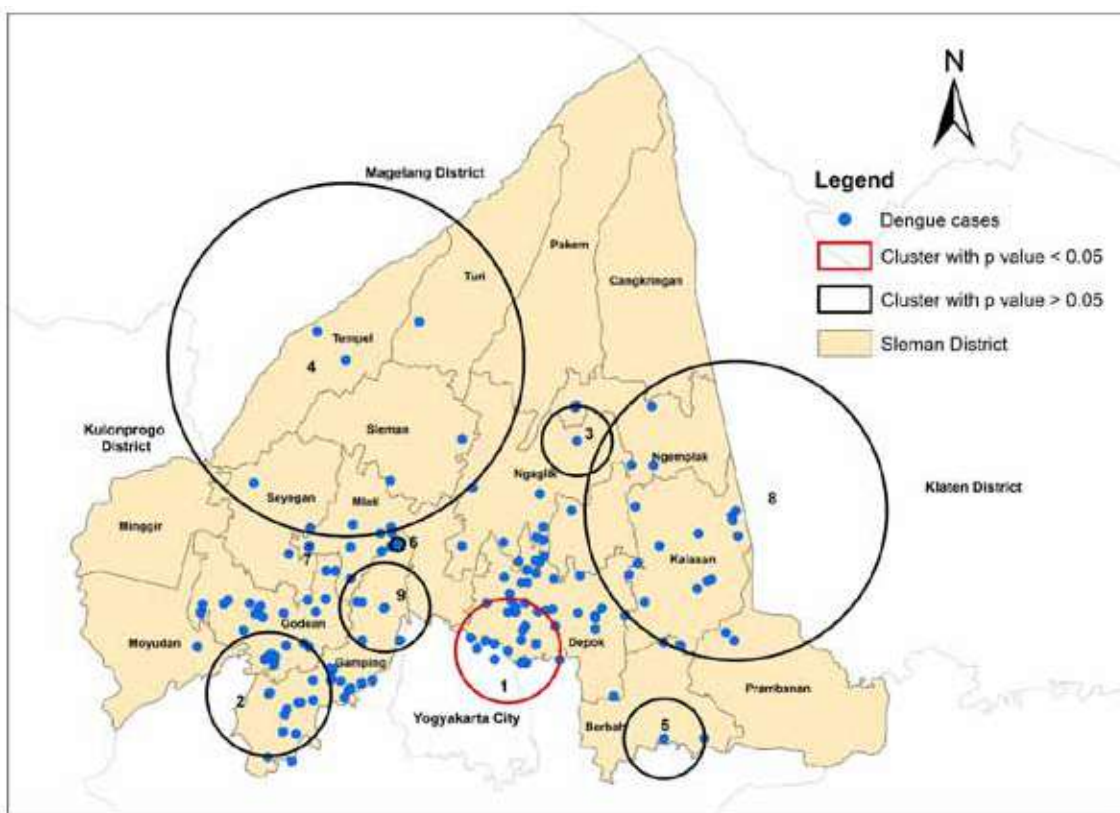


Figure 2: Cluster map of dengue cases in Sleman, Yogyakarta, during 2017-2018.

Discussion

Geographic Information System (GIS) is a highly recommended tool on disease surveillance to monitor, control and prevention. Currently, many researchers use this method to study disease pattern to support the

decision maker for taking the policy. However, dynamic and continuous analysis is needed to update the disease situation because of Dengue as one of environmental disease that changes over time. Identification following space and time will facilitate the development of dengue

monitoring and may improve the response to the dengue outbreak.

In this study, we measured the using of space-time GIS analysis to identify dengue cluster that may occur during the data period. Through Satscan, we found 9 clusters; one of them significantly associated with space and time. Our study in Yogyakarta city also found a similar result, that dengue case was corresponding to space and time¹⁰. In Sleman during 2017-2018, a significant dengue cluster is detected centred in Depok sub-district from March 12 to April 15 of 2018. Since several years, Depok has received attention about dengue transmission in this area. According to Sleman DHO information, this area has been predicted as a vulnerable subdistrict in 2019 due to the high population density^{11,12}. The previous study proved about the correlation between dengue incidence and population density, one of which in Sri-Lanka¹³. While in São Paulo-Brazil, dengue incidence clustered in an area that has a high population density because it increases the possibility of contact between infected mosquito and human¹⁴.

The most likely cluster in Depok was at March 12 to April 15 of 2018. This occurrence is guessed coincided with the rainfall intensity in this location. According to the Meteorology Climatology and Geophysics Council, on March 2018. Depok subdistrict had high-intensity rainfall (301-400 mm)¹ while in April 2018 had medium rain between 150-200 mm¹. A combination of high-intensity precipitation and proper temperature highly contributed to increasing dengue risk¹⁷. Rainfall is an essential aspect of *Aedes* development as they need stagnant water for breeding¹⁸, rain builds breeding sites for larvae develop before it grows to adult mosquitos¹⁹. From this information shows when high-intensity rainfall occurred, it could potentially increase of dengue incidence if the prevention system is not ready.

Three clusters were detected in Gamping sub-district, while Mlati, Tempel, Ngaglik, Berbah and Kalasan subdistrict, on each of them was found one secondary cluster. Even though it was not significant, this result needs to pay attention for the stakeholder involved as part of dengue prevention. In our observation, there was also unique spot that we found dengue cases in high altitude that is > 500-999 m above sea level 2, namely in Tempel and Turi subdistrict. This information needs to be considered as part of climate change phenomenon that potential to extent the vulnerable area for *Aedes*

development due to temperature increases²¹, including in high altitude which is in a normal situation having a lower temperature. When the temperature is rising, it has implication to mosquito growth rate, reduces the interval on blood feeds, shortens the incubation period and contributed to virus evolution rate^{22,23}. Accordingly, this information also provides an early warning on dengue transmission in the future.

Conclusion

From this paper, we can see the power of GIS through space-time permutation analysis on surveillance activity. Cluster detection can help on dengue surveillance to providing early detection of dengue outbreak by knowing the association both space and time. This identification can lead to seeking the possible aspect that in uences the incidence. Future study is proposed to conduct a research related to the dynamic of rainfall and the association with dengue incidence. Secondly, to do research related to the changing of temperature and vector longevity in the research area.

Conflict of Interest: The authors declare no conflicts of interest

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Ethical Clearance: This research was approved by the advisory board of Public Health Faculty, Universitas Ahmad Dahlan, Indonesia. Anonymity and confidentiality of participants were managed.

References

1. WHO. Dengue and severe dengue [Internet]. Fact sheet. 2018 [cited 2016 Jan 1]. p. 1. Available from: <http://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue>
2. Kesetyaningsih TW, Andarini S, Sudarto, Pramoedyo H. Determination of environmental factors affecting dengue incidence in Sleman District, Yogyakarta, Indonesia. *African J Infect Dis*. 2018;12(Special Issue 1):13-25.
3. Wieczorek WF, Delmerico AM. Geographic Information Systems. *Public Access NIH Public Access*. 2009;1(2):167-86.
4. Eisen L, Lozano-Fuentes S. Use of mapping and spatial and space-time modeling approaches in operational control of *Aedes aegypti* and dengue. *PLoS Negl Trop Dis* [Internet].

- 2009;3(4). Available from: <http://www.ncbi.nlm.nih.gov/pubmed/19399163> <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC2668799>
5. Stout CM. GIS as a Tool in the Study of Diseases [Internet]. Canada: ESRI; 2011. p. 1–24. Available from: https://www.academia.edu/2582371/GIS_as_a_Tool_in_the_Study_of_Diseases_The_Great_Cholera_Outbreak_in_the_Soho_District_of_London_England_1854_?auto=download
 6. Duncombe J, Clements A, Hu W, Weinstein P, Ritchie S, Espino FE. Review: Geographical information systems for dengue surveillance. *Am J Trop Med Hyg.* 2012;86(5):753–5.
 7. Sleman Government. Sleman profiles [Internet]. Web. 2019 [cited 2019 Jun 3]. Available from: <http://www.slemankab.go.id/profil-kabupaten-sleman/geografi/letak-dan-luas-wilayah>
 8. Yogyakarta Provincial Government. Profil Kesehatan Provinsi di Yogyakarta Tahun 2017 [Internet]. Yogyakarta; 2017. Available from: http://www.depkes.go.id/resources/download/profil/PROFIL_KES_PROVINSI_2017/14_DIY_2017.pdf
 9. Kulldorff M, Heffernan R, Hartman J, Assuncao R, Mostashari F. A space-time permutation scan statistic for disease outbreak detection. *PLoS Med.* 2005;2(3):0216–24.
 10. Sulistyawati S, Astuti FD, Ramadona AL. Exploring spatio-temporal cluster for dengue prevention in urban area of indonesia. *Int J Public Heal Clin Sci.* 2019;6(1):176–85.
 11. Nto, Lufianti G. Kecamatan Depok Sleman Paling Berpotensi Diserang DBD. *Tribun Jogja* [Internet]. 2019 Jan 22; Available from: <http://jogja.tribunnews.com/2019/01/22/kecamatan-depok-sleman-paling-berpotensi-diserang-dbd>
 12. Sulistyawati S, Sukesi TW, Mulasari SA, Sulistyawati S, Med JC, Health P. Spatiotemporal mapping of dengue cases in Sleman district, Indonesia year 2014-2017. *Int J Community Med Public Heal.* 2019;6(3):971–5.
 13. Sirisena P, Noordeen F, Kurukulasuriya H, Romesh TA, Fernando LK. Effect of climatic factors and population density on the distribution of dengue in Sri Lanka: A GIS based evaluation for prediction of outbreaks. *PLoS One.* 2017;12(1).
 14. Araujo RV, Albertini MR, Costa-da-Silva AL, Suesdek L, Franceschi NCS, Bastos NM, et al. São Paulo urban heat islands have a higher incidence of dengue than other urban areas. *Brazilian J Infect Dis.* 2015;19(2):146-55.
 15. Meteorology Climatology And Geophysics Council. Buletin Prakiraan Hujan Bulanan [Internet]. Yogyakarta: Meteorology Climatology And Geophysics Council; 2017. Available from: https://diperpautkan.bantulkab.go.id/filestorage/berkas/2017/12/Buletin_Prakiraan_Curah_Hujan_DIY_Januari_-_Maret_2018.pdf
 16. Ridwan M. Analisis Curah Hujan dan Sifat Hujan Bulan April 2018 [Internet]. Meteorology Climatology And Geophysics Council. 2018 [cited 2019 Jun 4]. Available from: <https://www.bmkg.go.id/iklim/informasi-hujan-bulanan.bmkg?p=analisis-curah-hujan-dan-sifat-hujan-bulan-april-2018&lang=ID>
 17. Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, et al. The global distribution and burden of dengue. *Nature* [Internet]. 2013 Apr 25 [cited 2014 Jul 11];496(7446):504–7. Available from: <http://dx.doi.org/10.1038/nature12060>
 18. Benedum CM, Seidahmed OME, Eltahir EAB, Markuzon N. Statistical modeling of the effect of rainfall flushing on dengue transmission in Singapore. *PLoS Negl Trop Dis.* 2018;12(12):1–18.
 19. Valdez LD, Sibona GJ, Condat CA. Impact of rainfall on *Aedes aegypti* populations. *Ecol Modell.* 2018;385(November 2017):96–105.
 20. Sleman Government. Sleman Topography [Internet]. Web. 2018. Available from: <http://www.slemankab.go.id/profil-kabupaten-sleman/geografi/topografi>
 21. Ramasamy R, Surendran SN. Global climate change and its potential impact on disease transmission by salinity-tolerant mosquito vectors in coastal zones. *Front Physiol.* 2012;3 JUN(June):1–14.
 22. Kilpatrick AM, Meola MA, Moudy RM, Kramer LD. Temperature, viral genetics, and the transmission of West Nile virus by *Culex pipiens* mosquitoes. *PLoS Pathog.* 2008;4(6).
 23. Reisen WK, Fang Y, Martinez VM. Effects of temperature on the transmission of west nile virus by *Culex tarsalis* (Diptera: Culicidae). *J Med Entomol* [Internet]. 2006;43(2):309–17. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/16619616>

Influence of Social Cultural Capital and Marketing on Skin Whitening Products Use among Higher Education Female Students in the Northeast of Thailand

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Abstract

Introduction: There have been increasing trends of skin whitening products use globally. Social cultural capital has been identified as one of a significant determinants of skin whitening products use. However, there was no study on these issues in Thailand. Therefore, this study aimed to identify skin whitening products use situation and the association between social cultural capital, marketing, and skin whitening products use among female higher education students in the Northeast of Thailand.

Method and Materials: This cross-sectional study was conducted in the Northeast of Thailand among 1,143 female higher education students. Data was collected using a self-administered structured questionnaire. The Generalized Linear Mixed Model (GLMM) was used to identify the associations between social cultural capital, marketing and skin whitening products use when controlling other covariates.

Results: Most of the respondents ever used skin whitening products (84.95%; 95%CI: 82.88–87.03), of which 52.66% (95%CI: 49.77–55.57) were current users, and 17.41% (95%CI: 15.21–19.61) were inappropriate use. The social cultural capital factor that were associated with skin whitening products use were those who were not satisfied with skin colors (Adj. OR=3.48; 95%CI=2.18–5.55; $p<0.001$), had friends using skin whitening products (Adj. OR=2.63; 95%CI=1.71–4.04; $p<0.001$), had thin to normal figures (Adj. OR=2.53; 95%CI=1.54–4.15; $p<0.001$), and had family members using skin whitening products (Adj. OR=1.86; 95%CI=1.10–3.15; $p=0.020$), studied in humanities and social sciences (Adj. OR=2.07; 95%CI=1.25–3.45; $p=0.005$) and product marketing (Adj. OR=1.92; 95%CI=1.15–3.20; $p=0.012$). Moreover, other factors that were also associated with skin whitening products use were family monthly income.

Conclusion: Majority of the higher education female students were current skin whitening products users of which about one-sixth was inappropriate users. Both social cultural capital, marketing had influence on skin whitening products use.

Keywords: Skin whitening, Social cultural capital, Marketing, Female students.

Introduction

Skin whitening products use is an ancient and widespread practice in many cultures ⁽¹⁾, and is one of the most popular products of the global beauty industry,

particularly in Asia. Marketing forecasters predict the business will be worth about USD 31.2 billion by 2024⁽²⁾. In several Asian countries, particularly India, Japan, Korea, China, and Thailand, women face pressure to lighten their skin due to the social perception that light skin is considered to be a cultural marker of beauty, class, and wealth, and has been reflective of high social status for many decades⁽³⁻⁴⁾. The social cultural capital refers to social, political, economic, cultural assets, and imperceptible health resources⁽⁵⁻⁶⁾, with a growing recognition of the socioeconomic

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status and social determinants of health⁽⁷⁾. It has been described as a feature of trust, norms, networks, skill, cultural knowledge, and education that can improve the efficiency of society by facilitating coordinated actions⁽⁸⁾. In addition, previous studies reported that the advertising industry has recently created a market on notions of beauty, and enhance social cultural capital for the improvement in confidence and career prospects through the use of products advertised to promote white skin⁽⁹⁾.

However, skin whitening products frequently contain toxic ingredients that are directly associated with adverse health and skin problems⁽¹⁰⁾. A study on the use of skin whitening products among university students indicated that 70.7% of females reported using skin whitening products⁽¹¹⁾ of which their use was associated with adverse skin effects, lack of personal control, risky sexual behaviors, and low social support⁽¹²⁾. In Thailand, as well as the Northeast region, the country biggest region both in term of land areas and population, there are still lack of research specifically concerned with social cultural capital, skin whitening products use, and their relationship to female higher education students.

Hence, this study aimed to describe skin whitening products use situation and to identify the association between social cultural capital, marketing, and skin whitening products use among female higher education students in the Northeast of Thailand. The findings of this study will provide evidence for health, education and relevant sectors to formulate appropriate measures to improve inequalities in health and reduce the use of skin whitening products.

Method

This cross-sectional analytical study was conducted between March to July 2019. The population were female higher education students in the Northeast of Thailand. The inclusion criteria were female higher education students aged 18 years old and older, currently studying for a bachelor's degree in universities of the Northeast of Thailand, able to verbally communicate, and agreed to participate in the study with written informed consent. The sample size was calculated by using the formula to estimate the sample size for a logistic regression analysis of Hsieh⁽¹³⁾. The estimated sample size was 1,143. We recruited students from 18 universities of the Northeast by using a multi-stage random sampling method. The sampling frame was all 18 universities in the Northeast

of Thailand. The first stage was a random selection of 4 universities, followed by randomly selecting 3 fields from each university. Then, one faculty from each field was randomly selected. Therefore, a total of 12 faculties were included in the study. Simple random sampling was applied to select participants proportional to the size of the estimated total samples. A total number of 1,143 individuals were chosen to participate in this study.

Research Tools: A structured questionnaire was developed based on the research questions and relevant literatures. The structured questionnaire consisted of 4 parts including: 1) Demographic and socioeconomic: age, university level, field of study, residence, allowance, family monthly income, adequacy of expense, and family members. 2) Skin whitening products use included; Have you ever used skin whitening products in your lifetime? Do you currently use skin whitening products? Inappropriate use was assessed by using a list of dangerous cosmetics from the FDA (Food and Drug Administration, Ministry of Public Health, Thailand), defined as those who reported any use of dangerous cosmetics. 3) Social cultural capital included; satisfied with skin color, have a friend using skin whitening products, have any family members using skin whitening products, Figures were assessed by using BMI (Body Mass Index). The scores were categorized into four groups according to the WHO (World Health Organization)⁽¹⁴⁾ for Asian-Pacific cutoff points, as follows: Underweight (<18.5 kg/m²), Normal (18.5–22.9 kg/m²), Overweight (23–24.9 kg/m²), and Obese (≥25 kg/m²). Finally, the scores were dichotomized as thin/normal (<23) and overweight/obesity (≥23). 4) Marketing: Product, Price, Place, and Promotion. Using the 5 scores (Very Low, Low, Moderate, High, Very high). After summing up the total marks, according to Best's theory, the scores were categorized into 3 groups (Low, Moderate, High). Finally, the scores were dichotomized as low/moderate (<3.68) and high (≥3.68) by using the mean as the cutoff point.

The questionnaire was undergone content validation by 5 experts and was revised to improve its validity. The Cronbach's alpha coefficient of social cultural capital was 0.80, marketing was 0.87. A self-administer questionnaire was used for data collection. The researcher responded to possible questions raised by the respondents, and assisted them when necessary. The completed questionnaires of each student were placed into an individual envelope, sealed, and put into a box. Confidentiality of all data was fully assured.

Data analysis: The data was analysed using STATA® (ver. 13; College Station, TX, USA: Stata Corp). Frequency and percentage were presented to describe the categorical variables. Continuous variables were described as mean and standard deviation, median and range. The generalized linear mixed model (GLMM) was performed to model the random effects and correlations within clusters. In the modelling, the universities were set as random effects. Bivariate analysis was used to determine the association of each independent variable with skin whitening products use. The variable that had p-value<0.25 were proceeded to multivariable analysis, of which the backward elimination method was used for model fitting. The final model results were presented as adjusted Odds Ratio (Adj. OR), 95% CI, with the levels of significance of 0.05.

Results

The average age of female higher education students was 20.67 ± 1.25 years old. Almost equal proportion of students were from each 4 universities (about 25%) and were from freshman (24.06%), sophomore (24.41%), junior (27.91) and senior: 23.62%. Majority of the student lived in private accommodation. Their median family monthly income was USD 940 with the ranged of USD 163 to USD 6,528. Nearly half of the respondents had adequate financial support but were unable to save any money. Most of respondents (84.51%) had thin and normal figure, and had friends (71.22%) using skin whitening products. Almost one-third had family members using skin whitening products and were not satisfied with their skin colors. Majority of respondents (53.81%) perceived a moderate level of overall marketing strategies and about 60% perceived a high level of product marketing.

Most of the respondents used skin whitening products (84.95%), 52.66% were current use and 17.41% were inappropriate use.

Table 1: Number and percentage of skin whitening products use among female higher education students in the Northeast of Thailand (n = 1,143)

Characteristics	Number	Percent	95%CI
Use of skin whitening products			
Never	172	15.05	13.09 – 17.24
Ever	971	84.95	82.76 – 86.91
Current Use			
No	541	47.34	44.44 – 50.24
Yes	602	52.66	49.76 – 55.56
Inappropriate Use			
No	944	82.59	80.28 – 84.68
Yes	199	17.41	15.32 – 19.72

The bivariate analysis indicated that social cultural capital factor including satisfied with skin colors, had friends using skin whitening products, figures, had family members using skin whitening products, and field of study, product marketing and marketing on place, age, family members, family monthly income, and allowance might associated with skin whitening products use (p-value <0.25). These variable were proceeded to the multiple variable analysis using GLMM. The results indicated that satisfied with skin colors (adj. OR=3.48: 95% CI; 2.18-5.55), had friends using skin whitening products (adj. OR= 2.63: 95% CI; 1.71- 4.04), were thin-normal (adj. OR= 2.53: 95% CI; 1.54- 4.15), studied in the field of humanities and social sciences (adj. OR= 2.07: 95% CI; 1.25- 3.45), had product marketing level (adj. OR= 1.92: 95% CI; 1.15- 3.20), and had monthly family income ≥ 980 USD (adj. OR= 2.13: 95% CI; 1.41-3.20).

Table 2. Factors Associated with Skin Whitening Products Use among Female Higher Education Students: A multivariable analysis (n = 1,143)

Influence of Social Cultural Capital and Marketing on Skin Whitening Products Use	N	% of Use	OR	AdjOR	95% CI	p-value
Satisfied with skin colors						<0.001
Yes	618	81.42	1	1		
No	353	91.93	2.60	3.48	2.18 – 5.55	
Had friends using skin whitening products						<0.001
No	226	68.69	1	1		
Yes	745	91.52	4.92	2.63	1.71 – 4.04	

Had family members using skin whitening products						0.020
No	591	80.19	1	1		
Yes	380	93.60	3.61	1.86	1.10 – 3.15	
Figures						<0.001
overweight-obesity	136	76.84	1	1		
thin-normal	835	86.44	1.92	2.53	1.54 – 4.15	
Field of study						0.005
Science and technology & health sciences						
Sciences	278	82.74	1	1		
Humanities and Social						
Sciences	693	85.87	1.27	2.07	1.25 – 3.45	
Product marketing						0.012
Low-moderate	380	81.02	1	1		
High	591	87.69	1.67	1.92	1.15 – 3.20	
Family monthly income						<0.001
< 980 USD	464	80.70	1	1		
≥ 980 USD	507	89.26	1.99	2.13	1.41 – 3.20	

Discussion

Skin whitening products use among female higher education students was 84.95%. This finding is consistent with previous studies reporting a high prevalence of skin whitening products use^(1,15). However, this was inconsistent with a study among African women, observed only 60% the respondents using skin whitening products⁽¹⁶⁾. Our study observed that 52.66% of students were current users, which was higher than the 37.60% found in India. It probably due to the greater range of ages (16-60 years) as well as the cultural setting of the study⁽¹⁷⁾. About one sixth were using the products inappropriately, a little lower than 46.7% of teenage females reported using harmful cosmetics⁽¹⁸⁾.

The multivariable analysis of this study confirmed that social cultural capital was significantly associated with skin whitening products use. Regarding social cultural capital and satisfaction with skin colors, students who were dissatisfied with their skin colors were 3.48 times more likely to use skin whitening products. This finding was consistent with a previous study⁽¹⁵⁾. Social and cultural notions connected females using skin whitening products⁽¹⁵⁾. The presence of social cultural capital among university students was associated with their entire health and individual life⁽¹⁹⁾. Shroff, H et al suggested enhanced social cultural capital for prevention of use among women⁽¹⁷⁾. Students who had friends using skin whitening products were 2.63 times more likely to

use skin whitening products as well as having family members using skin whitening products were 1.86 times more likely to use them. It might be that both peers and families could have direct communication with the students that could have influence on their behaviors. These findings were consistent with another study⁽²⁰⁾. Students with thin to normal figures were 2.53 times more likely to use skin whitening products compared to those in the overweight and obese group. This was in similar with the study in India⁽¹⁷⁾, but inconsistent with the study in Sudan⁽¹⁵⁾. This might be due to the body image and beauty concerns of female students engaged in weight control. Students who studied in humanities and social sciences were 2.07 times more likely to use skin whitening products than students who studied science and technology. The finding was also consistent with another study⁽²¹⁾. Students with a high level of product marketing were 1.92 times more likely to use skin whitening products, which was similar with a study in United Arab Emirates⁽²²⁾. Students with family monthly income ≥ USD 980 were 2.13 times more likely to use skin whitening products. This was also similar with a study conducted in Southeast Asia⁽¹⁹⁾. It might be that they had money to spend on nonessential items.

Conclusion

As high as 84.95% of the higher education female students ever used skin whitening products of which more than half were current skin whitening products

users. About one-sixth was inappropriate users. Both social cultural capital, marketing had influence on skin whitening products use.

Limitation of the study

Since this is a cross-sectional study, it could not identify the causal relationship between independent variables with skin whitening products use.

Conflicts of interest

The authors declare no conflicts of interest.

Ethics clearance

After explaining the study objective, written informed consent was taken from all the participated in the study. Confidentiality of the data was fully assured. The Khon Kaen University Ethics Committee in Human Research approved the exemption for ethical approval of this study (reference no. HE 612343).

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References

1. Olumide YM. Use of skin lightening creams. *BMJ*. 2010;341:c6102.
2. Global Industry Analysts I. Skin Lighteners: A Research Brief [Internet]. 2018. Available from: https://www.strategyr.com/MarketResearch/Skin_Lighteners_Market_Trends.asp
3. Chaudhri SK, Jain NK. History of cosmetics. *Asian J Pharm*. 2009;3(3):164–7.
4. Alghamdi KM. The use of topical bleaching agents among women: A cross-sectional study of knowledge, attitude and practices. *J Eur Acad Dermatology Venereol*. 2010;24(10):1214–9.
5. Bourdieu P. The forms of capital. In: Richardson J, editor. *Handbook of Theory and research for the society of Education*. Greenwood: Westport, CT; 1986.
6. Pillai TR, Ahamat A. Social-cultural capital in youth entrepreneurship ecosystem: Southeast Asia. *J Enterprising Communities*. 2018;12(2):232–55.
7. Story WT. Social capital and health in the least developed countries: A critical review of the literature and implications for a future research agenda. *GPH*. 2013;8(9):983–99.
8. Putnam R, Leonadri R, Nanetti R. *Making Democracy Work: Civic Traditions in Modern Italy*. Princeton: Princeton University Press; 1993.
9. Kavita K. Obsessions with Fair Skin: Color Discourses in Indian Advertising. *Adv Soc Rev*. 2008;9(2):1–19.
10. Ladizinski B, Mistry N, Kundu RV. Widespread use of toxic skin lightening compounds: medical and psychosocial aspects. *Dermatol Clin*. 2011;29(1):111–23.
11. Ofili A, Eze E, Onunu A. Prevalence of use of skin lightening agents amongst University of Benin undergraduates in Benin City, Nigeria. *Niger Med Pract*. 2006;49(1).
12. Adbi A, Chatterjee C, Kinias Z, Singh J. Women’s Disempowerment and the Market for Skin Whitening Products: Experimental Evidence from India [Internet]. 2016 [cited 2019 Sep 13]. Available from: <https://ssrn.com/abstract=2866336>
13. Hsieh FY, Bloch DA, Larsen MD. A simple method of sample size calculation for linear and logistic regression. *Stat Med*. 1998;17(14):1623–34.
14. Pan WH, Yeh WT. How to define obesity? Evidence-based multiple action points for public awareness, screening, and treatment: an extension of Asian-Pacific recommendations. *Asia Pac J Clin Nutr*. 2008;17(3):370–4.
15. Anwar EA, Mohamed EH. Use of skin-whitening products by sudanese undergraduate females: A survey. *J Racial Ethn Heal Disparities*. 2017;4(2):149–55.
16. Dlova N, Hamed SH, Tsoka-Gwegweni J, Grobler A, Hift R. Women’s perceptions of the benefits and risks of skin-lightening creams in two South African communities. *J Cosmet Dermatol*. 2014;13(3):236–41.
17. Shroff H, Diedrichs PC, Craddock N. Skin Color, Cultural Capital, and Beauty Products: An Investigation of the Use of Skin Fairness Products in Mumbai, India. *Front Public Heal*. 2018;5.
18. Kongwong R, Wattananamkul V. A Study of “Harmful Cosmetics” Usage Behavior Among Female Teenagers in Ubon Ratchathani Province. *IJPS*. 2011;7(1):76–87.

19. Peltzer K, Pengpid S, James C. The globalization of whitening: prevalence of skin lighteners (or bleachers) use and its social correlates among university students in 26 countries. *Int J Dermatol.* 2016;55(2):165–72.
20. Mojdeh K, Fariba M. Socio-economic factors influencing cosmetic products use by females under 20 years old in Yazdanshahr NajafAbad. *Dermatology Cosmet.* 2013;4(1):1–9.
21. Alshima SA. Knowledge, attitude and practice of female university students towards skin lightening agents in Khartoum Sudan 2016. *J Clin Exp Dermatol Res.* 2017;8(6):74.
22. Salim KH. The Influence of Brand Loyalty on Cosmetics Buying Behavior of UAE Female Consumers. *Int J Mark Stud.* 2011;3(2):123–33.

Knowledge Management Based Performance Improvement on Certified Health Workers in Health Center of South Sulawesi

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Abstract

Introduction: The aim of this research was to determine the effect of Knowledge Management on improving the performance of health workers force at Primary Health Center of South Sulawesi.

Material and Method: The research used qualitative method. The informants were 12 health workers. Data collection used was in-depth interviews. The tools used were tape recorders and camcorders.

Finding and Discussion: This study found that the Knowledge Management method was relevant to be used in increasing the performance of health workers force in a group of health workers (Doctors, Nurses, Midwives, and SKM (Bachelor of Public Health) who come from different functional health positions) at the South Sulawesi Community Health Center.

Conclusion: Performance of health work force could be done using one method which was knowledge management.

Keywords: Health workers force, Knowledge management, Performance.

Introduction

Global Health Workforce Alliance (GHWA) Conference reported that the quality of Human Resources Health is still a problem at the global level. In Indonesia, various efforts to improve the quality of health human resources to achieve sustainable competitive advantage and increase profitability were carried out through education and training. However, the education and training system have been criticized for years. The quality of the results of education and training of health workers in general is still inadequate¹. According to various studies showed that health workers are the main key in the success of achieving health development

goals. Health workers contribute up to 80% in the success of health development. In 2006, WHO reported that Indonesia was one of 57 countries that faced a health HR crisis, both in number and distribution.

Competence is an ability possessed by someone in carrying out a task or a job based on skills and knowledge. The development of human resource competencies in the health sector is a strategic component of health development in order to accelerate the distribution of health services and the achievement of health development goals. The performance of an organization will be determined by one of the main elements, which is the quality of human resources².

The implementation of non-quality training will have an impact on the low competency of graduates which ultimately affects the performance of institutions/ organizations. According to Hendry, the practice of improving the quality of human resources (training, job design, employee skills, employee attitudes, work motivation, etc.) has an impact on the performance of various business units³. Likewise, Sule findings

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showed a significant positive relationship between competency-based training and development and employee performance⁴. Knowledge management is a concern of what is called Knowledge Management (KM). According to Qwaider, Knowledge Management helps manage knowledge individually or in group within organizations or between organizations that can affect the quality and benefits of knowledge⁵.

Several studies were conducted on knowledge management related to variables such as performance, competence, training, learning, and others. Research conducted by Tongsamsi discovered the effect of knowledge management and training on manager competencies⁶. Knowledge management positively influences organizational performance. Another study was conducted by Chandavimol, which is the development of a mixed training model by applying the principles of knowledge management and learning actions, in order to develop the design competency of health human resource development staff training programs in the government sector⁷. Furthermore, the working team will form collaboration between participants in education and training⁸. The aim of this

research is to improve the performance of the health work force at the Primary Health Center of South Sulawesi. In the era of knowledge-based society in the 21st century, the way people learn has changed. New knowledge is gained by learning from training, work and exchange of experiences. The US Department of Labor estimated that more than 70% of knowledge occurs from experience and 30% from education and training⁹.

Knowledge of each individual in the organization or the company is certainly different so it causes the knowledge does not develop evenly with in the environment. Knowledge Management is one solution to assist knowledge processing, so that individuals in training or learning classes can have the same knowledge⁹, then with the same knowledge it can help to develop an organization or company. Knowledge management is formed from a knowledge, where knowledge is divided into two types, those are Tacit Knowledge and Explicit Knowledge. This knowledge can be in the form of: books, journals, scientific works, references or others. This knowledge is obtained and developed from the content and information contained in it.

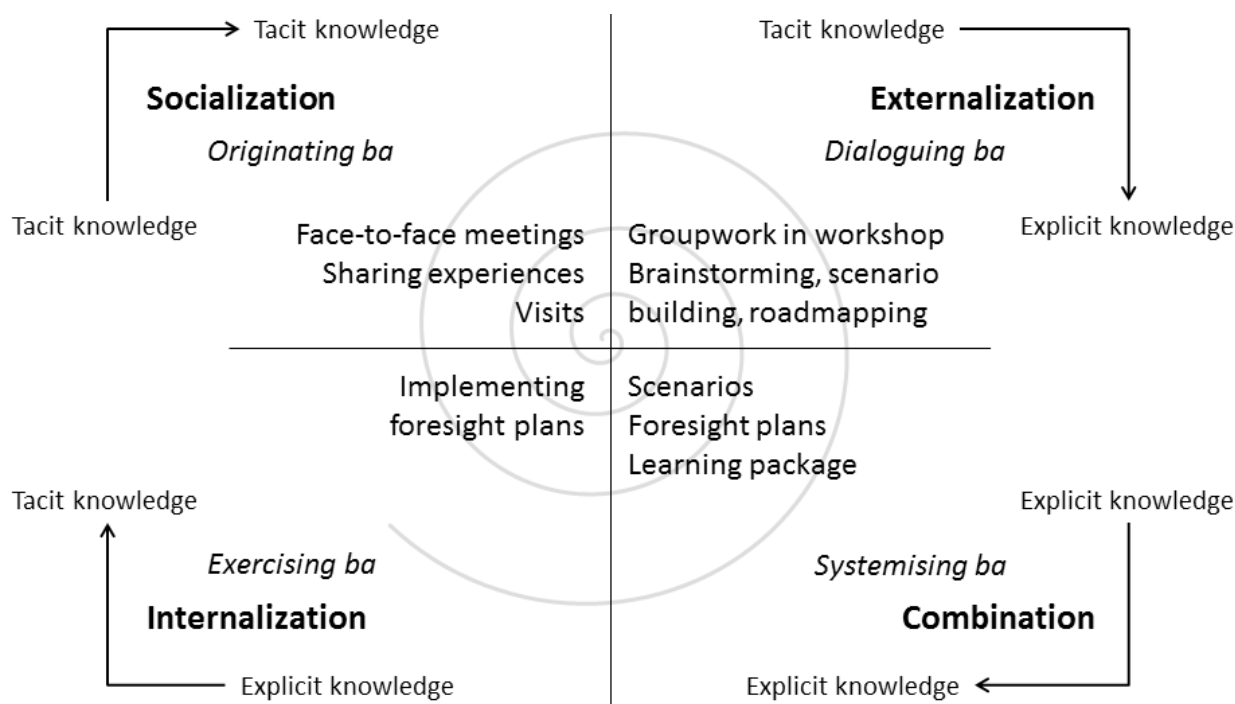


Figure 1. SECI Model

Figure 1 is known as the SECI Model¹⁰, in the figure where there are two types of knowledge, those are tacit knowledge and explicit knowledge. In

university education activities, knowledge management can improve administrative services related to the improvement of curriculum, teaching and learning

processes using technology, as well as improving response by monitoring and combining lessons from student experience and evaluation¹¹. Nawaz and Gomez, presented two Knowledge Management Model Concepts. The first model concentrates on how knowledge sources are transformed into strategic knowledge, where the process of converting tacit and explicit knowledge into knowledge diffusion converts it again as the application of knowledge. Participants develop their knowledge by understanding the concept of subject matter and converting it into strategic knowledge. The second

model strategic knowledge is a source of knowledge for students, while learning knowledge learners diffuse knowledge and choose strategic knowledge. This enhances procedural knowledge owned by the students, generates core subject skills and algorithms, core subject techniques and method as well as formula knowledge to determine when and how to use appropriate procedures to solve problems. The Strategic Knowledge Model can be implemented in universities, then for Knowledge Models can be implemented in advanced training institutions.

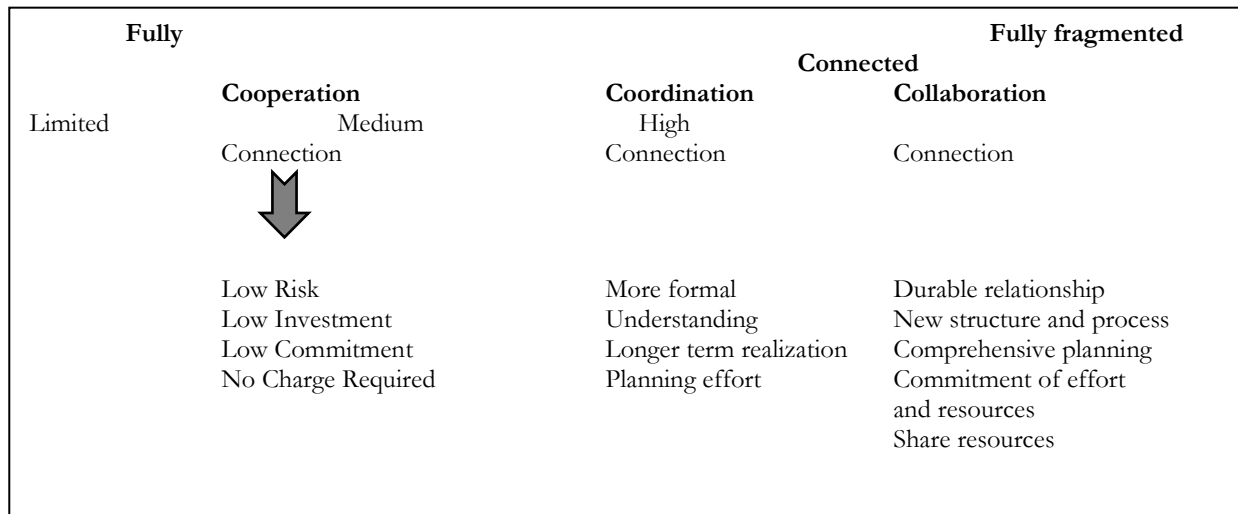


Figure 2. The Victorian council and social services

Knowledge Management strategy is very much needed to cooperate or collaborate, namely Cooperation, Coordination and Collaboration. Simple horizontal integration between cooperation, coordination and collaboration is shown in Figure 2.

Material and Method

Based on the conceptual framework, the variables in this study consisted of: Knowledge Management Strategy as an independent variable, and Enhancing Performance and competency as the dependent variable. This study used qualitative research method to obtain comprehensive, valid and objective data.

Finding and Discussion

The results of in-depth interviews showed that the application of knowledge management in the form of face-to-face socialization had a positive impact and benefits for the health workers in the Primary Health

Center. Thus, it was very well implemented for every training attended by the health workers in the Primary Health Center, since knowledge management is very helpful in understanding the management of the health center. In addition it is also able to be directly held.

Knowledge management can improve organizational performance¹² even though not all knowledge resources affect organizational performance directly. However, it cannot be ignored because they work in combination with other supporting sources, including knowledge acquisition and application knowledge that can contribute directly to the organizational success.

Based on the results of research at the Primary Health Center that have implemented knowledge management, it shows that it indirectly affects the performance of health workers so that it can encourage the management of the health center to improve the function of health services. The following are the results of the interview:

-*Socialization of training results improved performance, seen from the document management of the health center that had been produced....*

Performance is a work achievement that can be measured based on the standards or criteria set by the Primary Health Center. The completion of basic tasks and functions is the performance of a health worker who is physically and mentally attached.

.....*At our place (Primary Health Center), every employee who participated in the training must be trained to conduct socialization of training in meeting each patient in the Primary Health Center...*

Knowledge Management focuses on the identification, acquisition, distribution and maintenance of substantial and relevant knowledge. Rush (2005) described the term of Knowledge Management related to the exploitation and development of knowledge assets of an organization with the intention of improving the organizational goals. Knowledge management has been implemented in many organizations with the expectation that they will have a positive effect on performance¹¹.

Conclusion

The results showed that knowledge management had an effect on performance, and it could be concluded that health workers in the Primary Health Center who were committed to organizing had an impact on completing their main tasks and functions as health workers. Knowledge management provides development and the ability to think, work and manage work well so as to produce performance that affects the health services. Furthermore, research on learning strategies and knowledge management are suggested to be combined because they can facilitate the learning well.

Conflict of Interest: There is no conflict of interest to be declared.

Source of Funding: Self or other source

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Ethical Clearance: The ethical approval of this research was based on the letter Number: 3598/UN4.14.8/TP.02.02/2019), Faculty of Public Health, Hasanuddin University, Makassar, Indonesia.

References

1. Report M. Global Health Workforce Alliance. 2006;(April).
2. Harper K, Armelagos G. The changing disease-scape in the third epidemiological transition. *Int J Environ Res Public Health*. 2010;7(2):675–97.
3. Hendry C, Pettigrew A. The Practice of Strategic Human Resource Management. *Pers Rev*. 1986;15(5):3–8.
4. Sule BA. Assessment of implementation of competence based: Effect of Competence Based Management Approache on employee performance in UNHCR Kenya. 2015; Available from: erepo.usiu.ac.ke/bitstream/handle/11732/627/BSULE_PROJECT.pdf?sequence...
5. Qwaider WQ. Integrated of Blended Learning System (BLs) and Knowledge Management System. *Int J e-Learning Secur*. 2011;1(2):89–95.
6. Tongsamsi K, Tongsamsi I. Influence of training and knowledge management on competency among quality managers at Rajabhat Universities in Thailand. *J Psychol Educ Res*. 2015;23(2):54–72.
7. Chandavimol P, Natakatoong O, Tantrarungroj P. Blended Training Model with Knowledge Management and Action Learning Principles to Develop Training Program Design Competencies. *Int J Inf Educ Technol*. 2013;3(6):619–23.
8. Trivellas P, Akrivouli Z, Tsifora E, Tsoutsas P. The Impact of Knowledge Sharing Culture on Job Satisfaction in Accounting Firms. The Mediating Effect of General Competencies. *Procedia Econ Financ [Internet]*. 2015;19(15):238–47. Available from: [http://dx.doi.org/10.1016/S2212-5671\(15\)00025-8](http://dx.doi.org/10.1016/S2212-5671(15)00025-8)
9. Chandavimol P, Natakatoong O, Tantrarungroj P. Knowledge Management and Action Learning in Blended Training Activities. *Creat Educ*. 2013;04(09):51–5.
10. Gourlay S, Hill K. shortcomings. 1995; (Figure 1): 1–10.
11. Ramakrishnan K, Norizan MY. Knowledge Management System and Higher Education Institutions. *Int Conf Inf Netw Technol*. 2012;37(Icint):67–71.
12. Nonaka I. The knowledge-creating firm. *Harv Bus Rev*. 1991;69(6):96–104.

Hearing Impairment among Primary School Children in Nasiriya City/Iraq During 2018

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Abstract

Across-sectional and comparative school-based study was carried out through multistage systematic random sampling for 9 public primary schools in Al-Nasiriya city from 1st of February/2018 -3th of May/2018. Primary information was obtained through prepared questionnaires including the socio-demographic characters of studied pupils. A total of 355 pupils were screened, 228(64.2%) of them were males and 127(35.8%) were female that ratio of male to female was 1.8 :1. Nearly half of pupils were within 6-7 years at (55.2%),and least one were within age group >10 years (15.2%). Majority of pupils were within high socio-economic status (87.6%), and the remaining were within moderate (8.2%) - low class (4.2%). The extent of hearing impairment among pupils in Nasiriya city was 16% .Unilateral (9.2%) was more prevalent than bilateral (7%). of 58 pupils with hearing impairment,52(14.7%) of studied pupils had mild hearing impairment, and 6(1.7%) had moderate hearing impairment. Non showed moderately severe or sever or profound hearing loss. There was significant association between age, socio-economic status of studied population and Prevalence of hearing impairment by logistic regression analysis.

Keywords: *Hearing impairment, primary school children, public school, tuning fork test, screening audiometry, hearing assessment.*

Introduction

Hearing impairment in pediatric is a common and serious disability¹. Hearing loss can come from inherited problem, some infections affecting ear, infections during pregnancy; complicated birth of child, use of ototoxic medications, chronic, infection of middle ear and excessive exposure for noise². In 2018 WHO estimated disabling hearing impairment to be more than 5% of the world's population which is about 466 million people, 34 million of them are children, and greatest of those were found in Southern area of Asia, Eastern area of Asia and sub-Saharan area of Africa² Which was in continuous rising that in 1995, WHO shown that peoples with hearing problems were 120 million³, in 2000, 250 million people and in 2011 they involved about 360 million with disabling hearing loss; 32 million of them were children within age less than 14 years⁴. South and East Asia and sub-Saharan Africa remain the world regions with the highest prevalence of hearing impairment in both adults and children⁵. Unrecognized

hearing loss, even of a mild severity can significantly affect educational achievement, language, social and emotional development of children⁶⁻⁸. Hearing impairment can be classified according to its severity of mild, moderate to severe or profound and also classified as conductive, sensorineural and mixed⁹. WHO developed a set of excellent and well-illustrated training guidelines for hearing care, aimed to provide primary health care workers and communities in developing countries with effective and simple method from preconception to adulthood in order to lower the burden of hearing disorders¹⁰. Early interventions through primary prevention, early detection, and assessing hearing impairment can overcome this problem. Management for children who have hearing problem that showing benefit include earlier identification; hearing aids usage, surgery of cochlear implants; and in educational and communicational field is encouraging use the language of sign and/or comment.

Materials and Method

Study Setting: This study was conducted in Al-Nasiriya; Thi-Qar Governorate's city center about 370Km southeast of Baghdad Where:

Ethical Consideration: The ethical clearance was obtained from committee of Department of Family medicine and Community/Thi-qar university. Thi-qar office of education and head teachers of recruited schools were notified and permission obtained from them to carry out the study. Informed verbal consent was obtained from parents of children, their teachers, and from children themselves, whenever applicable.

The Study Population: They were primary school children of 9 public primary school in Nasiriya City aged between 6-13 years of both sexes.

Inclusion criteria; all pupils aged 6-13 years.

Exclusion criteria; excluded were pupils who refused to participate, and those who were out of studied age group.

The study design: It was a cross-sectional descriptive-comparative school based-study carried out in primary schools in Nasiriya during the period from 1st day of February/2018- 4th of May/2018.

Sample size and Sampling process: The sample size was calculated according to the following equation¹¹

$$N = (1.96)^2 \times P(1-P)/d^2$$

Where: N: Sample size, P: Estimated prevalence rate from other studies which would be (8%)²¹

d: Maximum tolerated error, the value of 0.03 was chosen as an acceptable limit.

$$N = (1.96)^2 \times 0.08 \times 0.92 / (0.03)^2 \approx 314$$

At the initial time in conducting the pilot study, there was a very high unresponsive rate (13%) ... even though it might be acceptable to some extent... so the reviewers add a further 41 cases to overcoming this high refusal rate and at the end the sample size estimated totally as 355 pupils. Multistage random sampling was carried out.

Firstly Nine primary schools were randomly selected (by simple random sampling from a list of primary schools obtained from Thi-Qar Education Directorate; 5 primary school from the first area and 4 primary school from 2nd area, those were be labeled then) from 9 primary health care sectors in Al Nasiriya city.

Data collection: The research team consisted of the researcher, consultant otolaryngology surgeon, and audiologist with his assistant. The researchers explained the aim of the study to school management and pupils and assured them of data confidentiality. Each selected school pupil was asked a special designed questionnaire (about hearing impairment approved by ethical committee for purpose of the study, before starting the study) and examined by direct observation and a special screening test (Tuning fork test and screening Audiometry).

Data analysis: Statistical analysis was performed using SPSS package (version 23). Descriptive data statistics expressed [in form of frequencies, percentages, and graphs], inferential statistics for testing of association by using tests of significance [Chi-square or Fisher exact test which are used for analysis of variables].

Results

A cross-sectional, school based-study was conducted on 355 pupils with mean age of 8 years; ranging from 6-13 years and male to female ratio was 1.8:1. According to age and sex distribution of studied population, a total of 355 pupils screened; 228(64.2%) of them were male and 127(35.8%) were female. Nearly half of them were within 6-7 years (55.2%), and least one were within age group >10 years (15.2%). No statistically significant difference in the age of the studied population according to sex was found. In respect to socioeconomic distribution with no statistically significant difference, majority of pupils were within high socio-economic status as (87.6%), and the minority one within low class as (4.2%). Regarding family size with no statistically significant difference, most of studied population were within family size <5 as (83.9%) and the remaining were within family size ≥ 5 as (16.1%).

Table 1: Socio-demographic characters of studied population.

Variables		Sex		Total Count (%)	p-value, x2 test
		Female Count (%)	Male Count (%)		
Age	(6-7)years	68(53.5%)	128(56.1%)	196(55.2%)	0.838, 0.354
	(8-10)years	40(31.5%)	65(28.5%)	105(29.6%)	
	>10 years	19(15.0%)	35(15.4%)	54(15.2%)	
Socio-economic status	High	109(85.8%)	202(88.6%)	311(87.6%)	0.340, 2.586
	Moderate	14(11.0%)	15(6.6%)	29(8.2%)	
	Low	4(3.1%)	11(4.8%)	15(4.2%)	
Family size	<5	106(83.5%)	192(84.2%)	298(83.9%)	0.854, 0.034
	≥5	21(16.5%)	36(15.8%)	57(16.1%)	
Total		127(100.0%)	228(100.0%)	355(100.0%)	

Prevalence of hearing impairment according to screening audiometry: Prevalence of hearing impairment in primary school children in Nasiriya city is illustrated in **Figure 1**. Among the 355 studied pupils, 58(16.3%) was with HI, giving the prevalence rate of 16.3%.

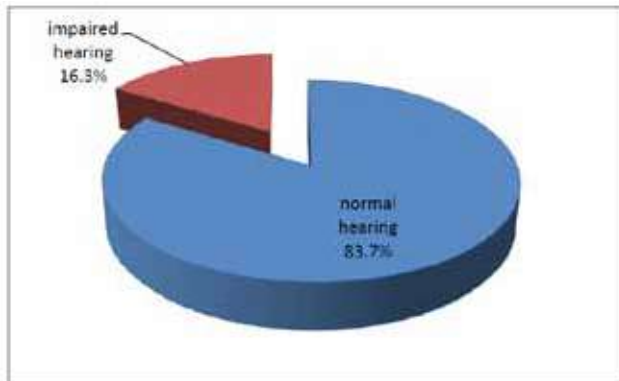


Figure 1.

Prevalence of hearing impairment according to severity based on audiometry: **Figure. 2** demonstrates prevalence of audiometric-based severity of hearing impairment. of 58 pupils with hearing impairment, 52(14.7%) of studied pupils had mild hearing impairment, and 6(1.7%) had moderate hearing impairment. Non showed moderately severe or severe or profound hearing loss.

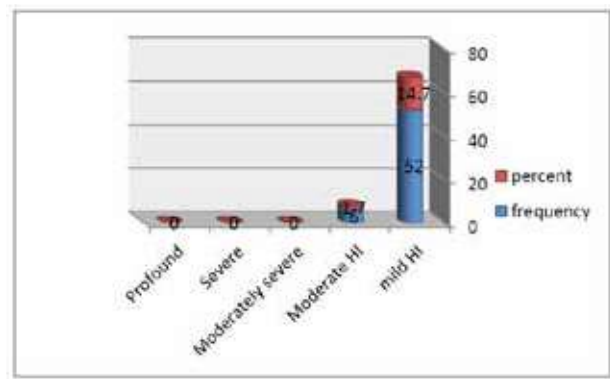


Figure 2.

Prevalence of audiometric-based HI according to selected socio-demographic characteristic: Table 2 shows the prevalence of hearing impairment was highest among pupils aged >10 years (24.1%), and least in pupils aged 6-7 years (13.3%)with no statistically significant association between HI and pupil’s age. The prevalence of HI among females (21.3%) was higher than that for males (13.6%), however, the association was statistically not significant.

The prevalence of HI according to socio-economic status was highest among low socioeconomic pupils (46.7%), followed by moderate class (24.1%) . The prevalence of hearing impairment was lowest among those of high socio-economic class (14.1%). The association between socio-economic class and HI was statistically highly significant.

The prevalence of HI according to family size showed a lower prevalence among pupils of small family size (14.4%),compared to those of large family size (26.3%). The association between family size and HI was statistically significant.

Table 2: Prevalence of audiometric-based HI according to selected socio-demographic characteristic.

Variables		Hearing impairment		Total	p-value, x2 test
		Normal hearing	Impaired hearing		
Age (Years)	6 -7	170 (86.7%)	26 (13.3%)	196 (100.0%)	0.138,3.955
	8-10	86(81.9%)	19(18.1%)	105(100.0%)	
	>10	41 (75.9%)	13 (24.1%)	54 (100.0%)	
Sex	Female	100 (78.7%)	27 (21.3%)	127 (100.0%)	0.061,3.504
	Male	197(86.4%)	31(13.6%)	228(100.0%)	
Family size	<5	255(85.6%)	43(14.4%)	298(100.0%)	0.026,4.946
	≥5	42(73.7%)	15(26.3%)	57(100.0%)	
Total		297(83.7%)	58(16.3%)	355(100.0%)	

Table 3. Demonstrated that mild HI was more prevalent in pupils aged 6-7 years (42.3%) but without significant statistical association. It was of equally prevalence in females and in female. Mild HI was more

prevalent in high socioeconomic status (75%) and this association was not statistically significant. It was more in pupils living within large family (66.7%) and this association was also statistically significant.

Table 3. Socio-demographic relationship with prevalence of hearing impairment severity according to Audiometry examination

Variables		Mild HI	Moderate HI	Total	p-value, x2 test
Age (Years)	6 -7	22(42.3%)	4(66.7%)	26 (100.0%)	0.078, *7.486
	8-10	91(36.5%)	0(0.0%)	19(100.0%)	
	>10	11(21.2%)	2(33.3%)	13(100.0%)	
Sex	Female	26(50.0%)	1(16.7%)	27(100.0%)	3.467, *2.635
	Male	26(50.0%)	5(83.3%)	31(100.0%)	
Socio-economic status	High	39(75.0%)	5(83.3%)	44(100.0%)	0.431, *1.683
	Moderate	12(13.5%)	0(0.0%)	7(100.0%)	
	Low	6(11.5%)	1(16.7%)	7(100.0%)	
Family size	<5	42(19.2%)	1(16.7%)	43(100.0%)	0.002, *9.987
	≥5	10(66.7%)	5 (83.3%)	15 (100.0%)	
Total		52(100%)	6(100.0%)	58(100.0%)	

Discussion

Strengths of the study: It is the first study about hearing impairment implemented in Nasiriya city, and it was conducted for three classes (grades) in primary schools of Al- Nasiriya city/Thi-Qar Governorate.

Limitations of the study: The cross-sectional design of this study allowed only for single observation and for short period (limited to school time), to assess the hearing acuity among primary school children, and cannot follow selected pupils with hearing impairment for any changes in prevalence rate over time (it may be with temporary or permanent cause). The referred suspected cases of HI to differentiate them as CHL or

SNHL by diagnostic audiometry and tympanometry in Al- Habboby hospital were not attend. Also Prevalence of ear infections associated with hearing impairment were limited mostly for particular season, so this promotes short period for their estimation (underestimation). Screening audiometry is used only for determining prevalence of hearing impairment and hearing threshold, but it wasn't done to determine type of hearing loss whether conductive, sensori-neural or mixed type that could be done only in presence of the diagnostic audiometry which was available in hospital.

Extent of hearing impairment: A cross sectional study extended over 4 months including 355 pupils

of primary school children in Al- Nasiriya city who were selected randomly with male: female ratio 1.8:1 as comparable to study in Port Harcourt, Nigeria¹³, to estimate extent of hearing impairment among pupils in primary school as 16.3%, as comparable to study which was conducted in Aligarh, Uttar Pradesh, that was found to be 17.9%¹⁴. It is compared with study conducted in Egypt (20.9%)¹⁵ [total of 555 children aged 6-12 years from both a rural and an urban school in El-Kom District of Egypt]. In Nigeria (29.4%)¹³ [the study conducted from January 10th to May 21th]; a higher percentage of HI among primary school children than in Al- Nasiriya city. In comparing with study conducted in Tikrit city/ Iraq (5.14%) [it was conducted in period from September through to 15 of December for 1420 pupils and the pure tone audiometry was done for pupils who have HI], a lower than the present estimation for the extent of the problem in Al-Nasiriya city. The extent of unilateral impaired hearing (9.3%) had been higher than extent of bilateral impaired hearing (7%). It is comparable to study done by Obukowho et al and also Khairi et al who reported that unilateral hearing loss as being more common (61.1%)¹³.

Age specific-prevalence of hearing impairment:

The Prevalence of hearing impairment was shown to be higher in pupils aged >10 years (24.1%) and least in pupils aged 6-7 years (13.3%) but this was statistically significant by logistic regression analysis. Comparable to study conducted in Nigeria (32.8%)¹³ [that was HI more in those aged more than 10 years(32%) than those who aged 5-7 years(24%)].

Sex specific-prevalence of hearing impairment: The present study showed that the prevalence was higher in females (21.3%) than in males (13.6%) and this sex difference is statistically not significant. Comparable to study in Nigeria¹³.

Socio-economic status specific- prevalence of hearing impairment: The prevalence of hearing impairment had been more in low socio-economic class(26.7%) and lowest among high class of pupils(7.4%). This association between HI and the socio-economic class was statistically significant. It is comparable to study done in India¹⁵ (where prevalence of HI was more in those with low standard of living).

Family size specific- prevalence of hearing impairment: Prevalence of hearing impairment was higher in large family size (14%) than in smaller family

size (7.7%). This difference is not statistically not significant. This was comparable to study by Parvez et al¹⁵ (that family with overcrowding showed more prevalence of HI that was 18.5%).

Conclusions

This study had shown a high prevalence of hearing impairment(16.3%) among primary school children, higher prevalence in female gender, in pupils aged > 10 years, in families with low socioeconomic class, significant independent association was found between HI and age and socioeconomic status, the most common ear diseases associated with hearing impairment were ear wax impaction and otitis media with effusion, the majority had mild HI.

Conflict of Interest: None

Funding: Self

Ethical Clearance: Not required.

References

1. Schoem SR, Darrow DH. Pediatric Otolaryngology. American Academy of Pediatrics; 2012 Jun 15.
2. World Health Organization. Deafness and hearing loss, Fact sheet N^o 300. Geneva, Switzerland: WHO Media Centre. 2015 Mar.
3. Smith AW. The World Health Organization and the prevention of deafness and hearing impairment caused by noise. *Noise and Health*. 1998 Oct 1;1(1):6.
4. Mathers C, Smith A, Concha M. Global burden of hearing loss in the year 2000. *Global burden of Disease*. 2000;18(4):1-30.
5. Duthey B. Background paper 6.21 hearing loss. Geneva: WHO Int. 2013 Feb 20.
6. Yoshinaga-Itano C, SedyAl, Coulter DK, et al . language of early and later identified children with hearing loss. *Pediatrics*. 1998;102:1161-71.
7. Moller MP. early intervention and language development in children who are deaf or hard of hearing *pediatrics*. 2000;106:43-46.
8. Westberg BD, Showronski DM, Stewart IF, et al. prevalence of hearing loss children in Zimbabwe. *Int J pediatr Otorhinolaryngol*. 2005;69(4):517-25.
9. Dhingra PL, Dhingra S. *Diseases of Ear, Nose and Throat-E-Book*. Elsevier Health Sciences; 2014 Jun 5: 21.

10. WHO G. WHO method and data sources for global burden of disease estimates 2000-2011. Geneva: Department of Health Statistics and Information Systems. 2013 Nov3.
11. Julious, S.A., (2009), *Sample Sizes for Clinical Trials*. Boca Raton: CRC Press. Dobson, A. J. and Gebski, V. J. (1986). Sample sizes for comparing two independent proportions using the continuity-corrected arc sine transformation. *The Statistician*:1986; 35, 51-53.
12. Absalan A, Pirasteh I, Khavidaki GA, Asemi rad A, EsfahaniAA, Nilforoush MH, A Prevalence Study of Hearing Loss among Primary School Children in the south east of Iran, *Int. J. Otolaryngol.* 2013; 138935: 4.
13. Obukowho O L, Enekole O, Ifeoma A. Risk Factors of Hearing Impairment among Lower Primary School Children in Port Harcourt, Nigeria. *Glob J Otolaryngol.* 2017 March;5(5).
14. Parvez A, Siddiui A R, Khan Z, Hashim SF, Khan M S. Prevalence of hearing impairment among primary school children in rural and urban areas of Aligarh, Uttar Pradesh, India. *International Journal of community medicine and public health*, 2016 My 3 : (3) 5:1273-1277.
15. Taha AA, Pratt SR, Farhat TM, Abdel-RasoulGM, Albtanony MA, Elrashiedy AL, et al. Prevalence and risk factors of hearing impairment among primary-school children in Shebin El-kom District, Egypt. *Am J Audiol.*2010; 19(1) 46-60 .
16. Al-Rowaily MA, AlFayez Al, AlJomiej MS, Al Baber AM, Abolfotouh MA. Hearing impairment among Saudi preschool children. *International Journal of pediatric otorhinolaryngology.* 2012 Nov; 76(11):1674-1677.
17. Karatas E, Karilikama M, Mumbuc S (2006) Auditory functions in children at schools for the deaf. *JNati Med Assoc* 2010;98(2):204.

In Silico Comparative Studies on Cytokine Receptor “Interleukin-11 Receptor” of Human, Rat and Mouse

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Abstract

Objectives: Interleukin-11 receptor with an imperative multifunctional role in normal cell signals and also in different pathologies, Interleukin-11 receptor with many statistical methods obviously show how this protein is estimated to include possibly disordered regions in association with normal bonding partnerships.

Method: The Interleukin-11 receptor conducted a concise comparative bioinformatic analysis of three different types of human, mouse and rat. The study was conducted using numerous statistical methods to examine the function-correlation and structure of their corresponding amino acid sequences and the associated protein sequences. Physico-chemical properties, sequence conservation, and secondary structural details are studied on the basis of specific bioinformatics tools and techniques. Findings: in order to recognize both structural diversity and sequence, different bioinformatics techniques were used. Interleukin-11 receptor's initial sequence analysis showed that they shared 86.1% similarity of the mouse and 81.9% identification of 85.4% and 80.5% identity of the rat similarity. With few exceptions, all sequences presented a high level of sequence survival. The physico-chemical analysis verified that there was no high evolutionary distance between mouse, rats and humans. Analysis of retained domains showed a clear structure of clustering, which also indicated the ancestral relationship among mouse, rat and human. The results suggest that IL may have originated from a common ancestor and may have diverged genetically in the course of evolution. Those studies will help the researchers to investigate the IL receptors functional differentiation and substratum binding process. Applications: Understand the evolutionary relationship and the sequence survival among humans, rats and mouse, which may lead to further studies in proteomics.

Keywords: *Silico, Cytokine Receptor, Interleukin-11 receptor.*

Introduction

Interleukins (ILs) are hematopoietic immunomodulatory proteins that belong to the subfamily of cytokines and serve as diverse immunological functions. Cytokines are biomolecules that play a vital role in infections, hematopoiesis and homeostasis, revealed their multi-functional position in regulating infectious disease reaction and even tumor genesis by growth, cellular sprouting and controlling tissue renewal. Both chronic inflammatory responses and acute, interleukins are involved. These work as a response to specific receptor stimulus conveyed in the cell surfaces, triggering every time a different signaling pathway. Interleukin-11 is followed by its IL-11 receptors- α (IL-11R α) transmembrane receptor and induces breast neoplastic cell proliferation with the parallel development of primary cancer cells

and the diffusion of cancer cells into distant organs¹. The cytoplasmic domain of IL-11 predicts to be strongly disordered, and there is a significant volume of dysfunction even in the broad extracellular protein domain². The ability to bind IL-11 with high affinity (K_d = 300-800 pM). The discovery that some cytokines that associate with complexes of receptors which contain common components.^{3,4,5} In this way, three groups of cytokines are identified. IL-3, IL-5 and GM-CSF are special low-affinity binders α -chains and associate with a common γ -chain producing a high-affinity signal transduction receptor^{3,5}. Similarly, it is believed that IL-2, IL-4, IL-7, IL-9 and IL-13 bind both to unique receptor chains and to a general subunit, initially isolated as the IL-2 receptor γ -chain⁴. The third group is even more complicated with IL-6, IL-11, LIF, OSM and CNTF receptors⁶.

An attempt was made here to describe and contrast the properties of 3 types of human, rat and mouse receptors using various bioinformatics method.

Materials and Method

For this study, sequence extraction and evaluation was called three separate forms of IL receptors from three types of mouse, rat and human. NCBI Gen Bank (www.ncbi.nlm.nih.gov/genbank) obtained three sequences in Fast format (NCB Accession Numbers: person (Q14626), rat (Q99MF4) and mouse (Q64385). Protparam was used to measure the physico-chemical properties off selected IL receptor proteins. (<http://web.expasy.org/Protparam>) The amounts of aminoacidcomposition are determined in version 6.06 of MEGA. Hydrophobicity/Hydrophobicity Protein research was carried out on the web database Peptide 2.0. (http://peptide2.com/N_peptide_hydrophobicity_hydrophilicity.php) For pair sequence analysis, sequence synchronization and secondary structure estimation EMBOSS (<http://imed.med.ucm.es/EMBOSS/>) needle was used.

The arrangement of the amino acid sequence was

performed using PROMALS3D (<http://prodata.swmed.edu/promals3d/promals3d.php>) to figure out the pattern of preservation and secondary structural information. PROMALS3D generates protein sequence alignments based on sequence database knowledge, secondary structure prediction, accessible 3D structure homologues and user-defined constraints^[6].

Conserved domains are calculated to use the NCBI Batch Web CDs Searching features within protein sequences (<http://www.ncbi.nlm.nih.gov/Structure/bwrpsb/bwrpsb.cgi>) within an E-Valuecut-off:0.01.

Result and Discussion

The amino acid concentration percentage was estimated and shown in Figure 1. In IL11, for all sequences, the amount of metabolites, including proline, leucine. Serine, Valin residues are lower in rat and can note arginine higher in rat comparing with human and mouse. Alanine is high in human and lowest in comparing with mouse and rat. Glycine is high in human, rat when compared to the mouse. Simultaneously, aspartic acid, Glutamic acid in both rat and mouse higher than human.

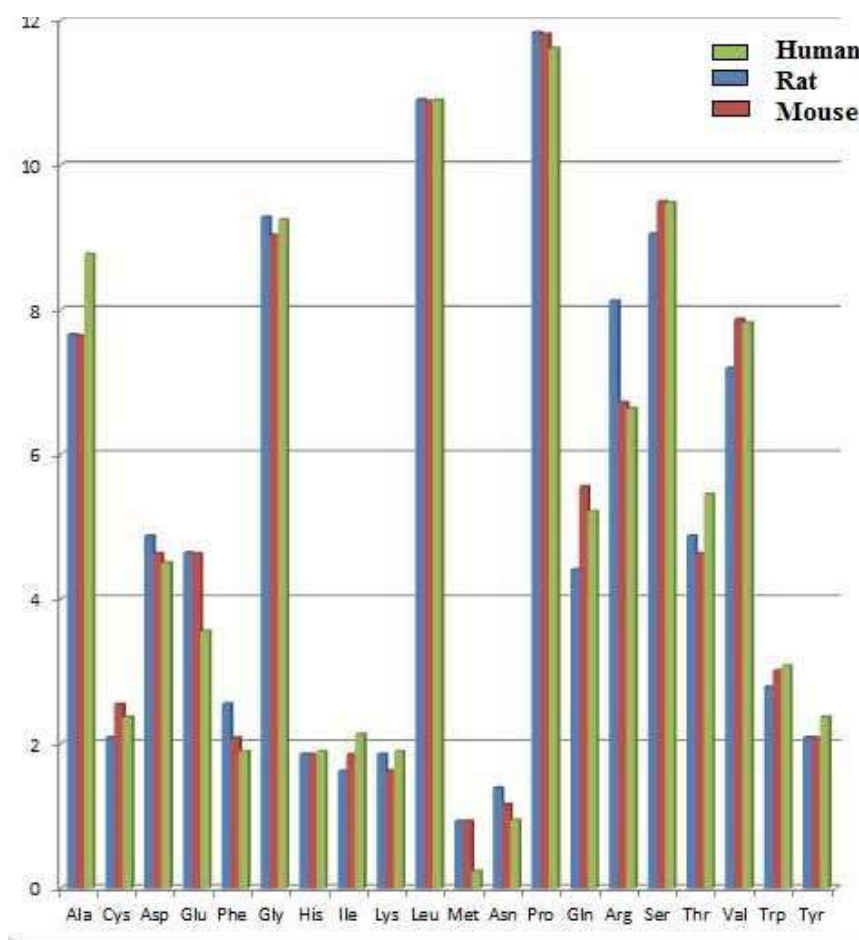


Table 1: Physico-chemical analysis

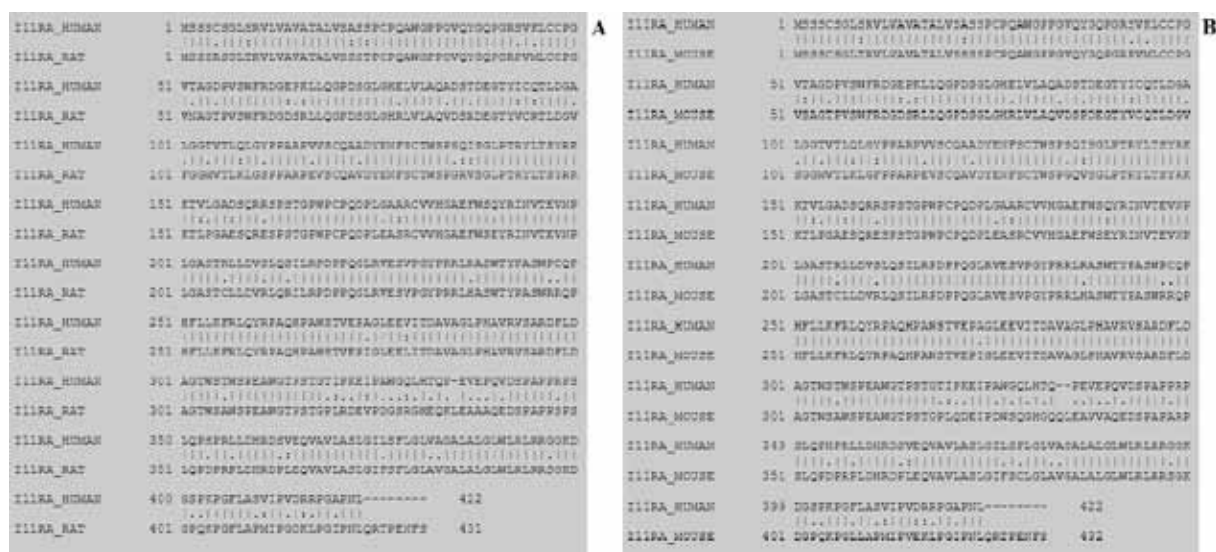
Physico-chemical	Hu	Mouse	Rat
Number of amino acids	422	432	431
Molecular weight	45222.36	46654.94	46784.08
Theoretical pI.	8.03	6.09	8.07
Instability index	51.03	54.23	51.42
Aliphatic index	82.27	80.12	77.38
Hydrophobic residues	46.45%	46.06%	45.48%
Acidic residues	8.06%	9.26%	9.51%
Basic residues	10.43%	10.19%	11.83%
Neutral residues	35.07%	34.49%	33.18%
The total number of residues that have been adversely labeled (Asp + Glu):	304	40	41
The total number of residues positively charged (Arg + Lys):	36	36	43

Table of physico-chemical analysis (1) revealed the hydrophobic existence of the proteins. The expected parameters are given in Table 1 and there is not that much difference in their properties when comparing the physicochemical characters. Isoelectric point (pI) seems to be a pH where the amino acid net charge is null. pI of human 8.03 and rat 8.07 was higher than mouse 6.09. From the Instability Index study, which has found that mouse 54.23, while the rest of the proteins were in lower in rat and human. Therefore, the Aliphatic index (AI) corresponds to the relative amount of a protein that its aliphatic side chains share. The lower the protein Aliphatic level, the more the proteins stable thermally. Human Aliphatic index 82.27, mouse 80.12 and rat 77.38 ranged from 46.45% to 45.48% (hydrophilic).

Secondary Structure: Sequence similarity (Figure 2) indicated a high level of residue retention for amino acids. Among the retained residues (disulfide bonds), the cysteine (C) disulfide bonds in place may have profound effects on the folding mechanism and a protein stability; thus the entropy of the unfolded system, thereby increasing its suitability for survival in the extra cellular

Disulfide bonds can stabilize the protein⁷⁸. In addition, they may make the journey to thenativestate smoother when they connect parts of a protein that must come into contact early during a folding reaction and can make it less likely to unravel when they happen in especially labile areas of a protein⁹. Native intra- or inter-molecular disulfide bonds that develop translationally during the folding of secretory pathway proteins well before further protein C-terminal regions join the ER¹⁰. This can happen if the bonds are formed between neighboring cysteines^{11,12} or if the protein comprises of autonomously folded domains¹³.

These substitutions in il11 structure Mouse compared with human sequence the are (T9, S22, P43, M45, S52, T55, D64, S65,R66, R78, V84, P87, V93, V100, S101, M104, K108, F111, E117, L153, P 154, E157, E161, E176, S178, E190, C206, R211, H237, R247,R248, I274, A306, P319,L320, Q321, D322, D326, S328, G330, G332, Q334,L335, E336, A337, V339, A340, E342, A348, D355, P358, P364,L365, F377, C379, A383,V384, S398, P403,Q404, L408, P411, M412, E416,K417,L418, I421, QRTPENFS).fig(z).



Also these substitutions in Rat sequence compared with human fig (z) (R5, T9,s22, T24, P43, M45,N52,T55, D64,S65,R66,R78, V84,R87,V93,R95,V100, F101, M104,K108,S111, E117,V123, G135,R136,V137, L153, P154, E157, E161, E176,S178, E190, C206,R211,R214, H237, R247,R248, I274,L279, A306, P319,L320,R321, D322,V324, D326, G327,S328,R329, G330, E332, K334,L335, A337, A338, A339, E341,S348, D354, P357, P363,L364, F376, A382,V383, S397, P402,Q403, P410, M411, G414, K416,L417, I420, QRTPENFS). Additionally among substituted residues,a specific residue is replaced with hydrophobic.

Hydrophobic activity is recognized as one of the key drivers for protein folding and is also a key factor

in stabilizing single protein, multi-protein, and protein–ligand matrix globular and binding structures¹⁴. The hydrophobicity in proteins maybe related with the amino acid residues sides chain that are the protein base functional elements, according to previous studies. Differences in amino acid residues of the residue region can reduce or decrease the active site cavity size when substituted by smaller residues or bulkier which may contribute to operational divergence processes ¹⁵. Structural key section. (Z) details are also shown in the organization of different sequences (Figure 3). The generic series of CHS from alfalfa. It is clear from the results that the protein is relatively stable and consists of most beta-strands and less alpha-helices.



Conserved Domains Database (CDD): From 3 protein receptor sequences, they investigate how they consist of a well-annotated series of several sequence coordination templates for ancient domains and full-length proteins. These are accessible as position-specific score matrices (PSSMs) (214653,238020) for rapid recognition by RPS-BLAST of retained domains in protein sequences. CDD material contains NCBI-curated

domains¹⁶, that use 3D-structure data to specifically identify domain boundaries and offer insight in to sequence, structure and feature relationships; As well as IG-related domain models such as human sequence 33 to 109, rat and mouse sequence 33 to 95, human and mouse sequence FN3 sequence 216 to 310, superfamily rat sequence 111 to 202 fn3 (cl21522). (Fig. 4).

	Hit type	PSSM-ID	From	To	E-Value	Bitscore	Accession	Short name	Incomplete	Superfamil
A_HUMAN	specific	214653	33	109	1.8525e-07	48.2705	smart00410	IG_like	-	cl29242
	specific	238020	218	310	2.22173e-06	45.5651	cd00063	FN3	-	cl21522
A_MOUSE	specific	214653	33	95	7.25133e-07	46.7297	smart00410	IG_like	-	cl29242
	specific	238020	218	310	2.46526e-06	45.5651	cd00063	FN3	-	cl21522
A_RAT	specific	214653	33	95	1.2452e-07	48.6557	smart00410	IG_like	-	cl29242
	specific	238020	218	310	4.28922e-06	44.7947	cd00063	FN3	-	cl21522
	superfamily	354851	111	202	0.00133455	37.7858	cl21522	FN3 superfamily	-	-
A_BOVIN	specific	238020	217	309	4.55927e-07	47.4911	cd00063	FN3	-	cl21522
	specific	214653	33	94	4.50271e-05	41.7221	smart00410	IG_like	-	cl29242

Conclusion

Human, rat and mouse sequence and structural analysis revealed regions that are evolutionarily and structurally related. In addition to the range of retained Residues of amino acids from physico-chemical properties at the active site, Retention at the respective site in a few amino acid substitutions that result in functional divergence. Because interleukin is very essential proteins that play a role in inflammatory conditions, bone homeostasis, hematopoiesis, and fertility, more proteomics work will be supported by the studies on it.

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Ethical Clearance: Not required.

References

1. Fasoulakis Z, Kolios G, Papamanolis V, Kontomanolis EN. Interleukins Associated with Breast Cancer. *Cureus*. 2018;10(11):1-11. doi:10.7759/cureus.3549
2. Permyakov EA, Uversky VN, Permyakov SE. Interleukin-11: A Multifunctional Cytokine with Intrinsically Disordered Regions. *Cell BiochemBiophys*. 2016;74(3):285-296. doi:10.1007/s12013-016-0752-7
3. Miyajima A. Molecular structure of the IL-3, GM-CSF and IL-5 receptors. *Int J Cell*

Cloning. 1992;10(3):126-134. doi:10.1002/stem.5530100302

4. Kishimoto T, Taga T, Cell SA-, 1994 undefined. Cytokine signal transduction. Elsevier. <https://www.sciencedirect.com/science/article/pii/0092867494903336>. Accessed August 7, 2019.
5. Nicola N, Cell DM-, 1991 undefined. Subunit promiscuity among hemopoietic growth factor receptors. *cell.com*. [https://www.cell.com/cell/pdf/0092-8674\(91\)90564-F.pdf](https://www.cell.com/cell/pdf/0092-8674(91)90564-F.pdf). Accessed August 7, 2019.
6. Hilton DJ, Hilton AA, Raicevic A, et al. Cloning of a murine IL-11 receptor alpha-chain; requirement for gp130 for high affinity binding and signal transduction. *EMBO J*. 1994;13(20):4765-4775. doi:10.1002/j.1460-2075.1994.tb06802.x
7. Trivedi M, ... JL-... P and P, 2009 undefined. The role of thiols and disulfides on protein stability. *ingentaconnect.com*. <https://www.ingentaconnect.com/content/ben/cpps/2009/00000010/00000006/art00008>. Accessed August 7, 2019.
8. Khoo K, Peptides RN-F of AA and, 2011 undefined. Role of disulfide bonds in peptide and protein conformation. *research.monash.edu*. <https://research.monash.edu/en/publications/role-of-disulfide-bonds-in-peptide-and-protein-conformation>. Accessed August 7, 2019.
9. Feige M, biology LH-C opinion in cell, 2011 undefined. Disulfide bonds in ER protein folding and homeostasis. Elsevier. <https://www.sciencedirect.com>

- com/science/article/pii/S0955067410001833. Accessed August 7, 2019.
10. Chen W, Helenius J, ... IB-P of the, 1995 undefined. Cotranslational folding and calnexin binding during glycoprotein synthesis. *Natl Acad Sci*. <https://www.pnas.org/content/92/14/6229.short>. Accessed August 7, 2019.
 11. Peters T, Chemistry LD-J of B, 1982 undefined. The biosynthesis of rat serum albumin. In vivo studies on the formation of the disulfide bonds. *ASBMB*. <http://www.jbc.org/content/257/15/8847.short>. Accessed August 7, 2019.
 12. Braakman I, Hoover-Litty H, ... KW-TJ of cell, 1991 undefined. Folding of influenza hemagglutinin in the endoplasmic reticulum. *jcb.rupress.org*. <http://jcb.rupress.org/content/114/3/401.abstract>. Accessed August 7, 2019.
 13. Bergman L, Chemistry WK-J of B, 1979 undefined. Formation of an intrachain disulfide bond on nascent immunoglobulin light chains. [pdfs.semanticscholar.org](#). <https://pdfs.semanticscholar.org/a46e/939881fe6ce1df895149209be314c2d1e50c.pdf>. Accessed August 7, 2019.
 14. Zhu C, Gao Y, Li H, Meng S, ... LL-P of the, 2016 undefined. Characterizing hydrophobicity of amino acid side chains in a protein environment via measuring contact angle of a water nanodroplet on planar peptide network. *Natl Acad Sci*. <https://www.pnas.org/content/113/46/12946.short>. Accessed August 7, 2019.
 15. Austin M, reports JN-N product, 2003 undefined. The chalcone synthase superfamily of type III polyketide synthases. *pubs.rsc.org*. <https://pubs.rsc.org/en/content/articlehtml/2003/np/b100917f>. Accessed August 7, 2019.
 16. Marchler-Bauer A, ... MD-N acids, 2014 undefined. CDD: NCBI's conserved domain database. *academic.oup.com*. <https://academic.oup.com/nar/article-abstract/43/D1/D222/2439461>. Accessed August 7, 2019.

Psychosocial Characteristics of Human Trafficking: A Systematic Review

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Abstract

The phenomenon of human trafficking is one of contemporary issue being seriously concerned. Its characteristics are repressive to human exploitation destination (individual or group) as well as a direct implication on human rights violations. Victim of *trafficking* has characteristics social typical for trading. The purpose of systematic review was to identify the psychosocial characteristics of human trafficking victims. Systematic search on March 12, 2019, in the data of Proquest, Springer Link, Scopus by key word Psychosocial Characteristics of Victims of Human Trafficking during 2013 -2018. The results found 13 appropriate journal that included into inclusion criteria, they were peer-reviewed journals in English, all forms of exploitation, the samples were aged >15 years old. The results based on a). Demographic data Age (adults/children), gender, marital status, education level, place of residence (urban/rural), regional trade (national/international), religion, type of work, economic conditions before trading. b) Variable of exposures (smuggling status, the process of departure, detention in camps, forgery/fraud documents, employment status, obscure country of work, type of work). c) Method of recruitment using social media (Backpage, Facebook, dating website) and invited directly by recruiters. d) Type of exploitation (household slavery, exploitation of labor, financial exploitation, sexual exploitation). e) Characteristics of the exposure (restriction of movement, drug use, sexual abuse, psychological abuse, restriction/confinement, physical violence, the background to the incident trafficking, race, home life, relationships with parents/carers/ family members, economic opportunities, the recruiters-victim relationship, trust in strangers, lack of social support), f). Psychosocial variables as the impact of trafficking (the abuse of alcohol/drugs, involved in crime and a fugitive/police targets). Required a prevention effort to group or individual who had the same characteristics, thus, they did not fall to the incidence of trafficking.

Keyword: *Psychosocial characteristics, Human trafficking.*

Introduction

Crime Human trafficking is a serious problem and became the center of world attention. Trafficking itself very influential impact on the environment social, Human rights violations to one's mental disorders. The crime of trafficking is said to be a form of modern

slavery, where exploitation is financially beneficial for the group of perpetrators. The UN has sought to suppress, prevent and punish perpetrators of trafficking crimes by forming units of protection for victims who received exploitation⁽¹⁾. Accepted forms of exploitation including victims of violence, fraud, forced labor and sex workers⁽²⁾ with the aim of earning a lot of money and the benefits of being an offender profit trafficking⁽²⁾. The phenomenon of trafficking involving an individual, family, and local network criminal/Supra-regional organized. There are about 45.8 million people in the world of human trafficking with the same psychosocial characteristics⁽³⁾. Trafficking crime makes vulnerable groups of aspects social and the economy as a operandi target. Indonesia is ASEAN countries included in the Country economic

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range and has a high population⁽⁴⁾. Increasing population effect on increasing employment requirements, so that Indonesia is reported by IOM as the country to 13 with most trafficking cases throughout the year⁽⁴⁾. Various efforts have been made by governments, organizations local and International to address trafficking problems, but these problems do not go over, because it does not touch directly on the subject matter. This study provides empirical evidence of characteristics of human trafficking and networks exploiting victims⁽⁵⁾. Its impact on mental health psychosocial⁽⁶⁾. Psychosocial characteristics of vulnerable victims of trafficking in terms of sociodemographic among others folly, no school, live in rural areas, the lack of global information⁽⁴⁾. Lack of jobs and low of human resources⁽⁷⁾. This systematic review aimed to identify the psychosocial characteristics of trafficking victims were vulnerable to exploitation and trafficking.

Methodology

Search criteria: Systematic search using electronic with NHS evidence (electronic information resources, research, evidence, and best review). Search on March 12, 2019, by databases Proquest, Spinger Link, and Scopus. Health care data bases chosen because it allowed advanced search of relevant articles with keywords characteristics of psychosocial.

Inclusion and Exclusion Criteria: The inclusion criteria were peer-reviewed journals in English by year of publication from 2013 to 2018. Articles include any form of exploitation (sexual abuse, violence, selling organs, etc.). Samples were age 15 to adult. Psychosocial characteristics focused on survivors. Articles that were not selected are Dissertations & Theses (ProQuest), the Conference of COS, ProQuest Index, Conference Proceedings, Citation Index (Thomson Reuters), Thesis & Dissertation website Open Access, OpenGrey, report the results.

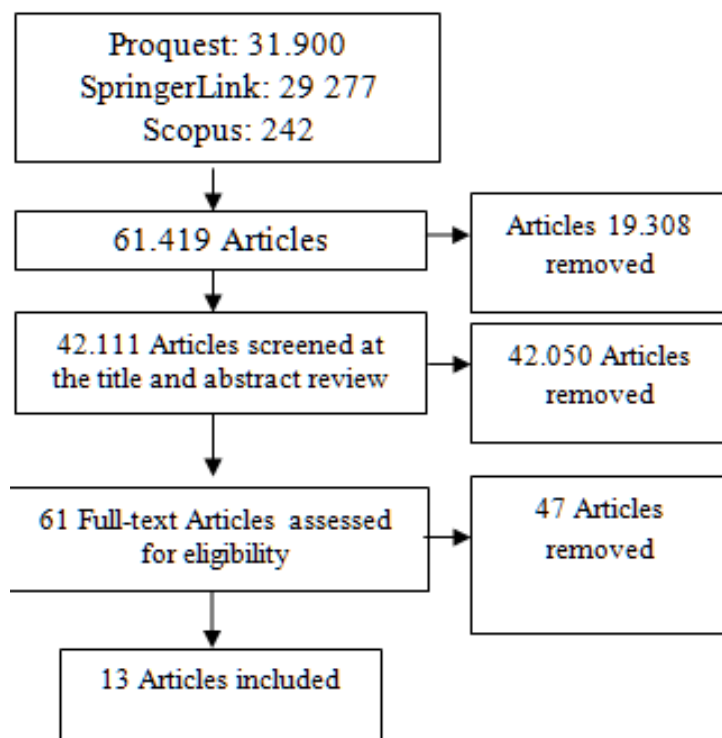


Figure 1: Process of Taking and Abstracting Journal

The initial search was obtained 61.419 articles that consisted of 31.900 of Proquest, 29.277 of Spingerlink and 242 of Scopus. 19 308 articles removed because it did not fit the inclusion criteria. The review process was

selected based on reviews of article titles, abstracts and full text. Researcher extracted 61 studies of the titles and abstracts and 47 studies of full-text review. Finally 13 articles selected for this study.

Outcomes Measures:

Summary of Characteristics: The search yielded 13 articles. Five articles using qualitative design, three articles using quantitative designs: cross-sectional and RnD, five articles using cohort study. Total of 455.392 participants consisting of 5.248 direct participants and 450.134 tracked from electronic medical records and database of CRIS.

Characteristics Participants: Characteristics of participants in 13 studies were described as follows: characteristics of study participants in Ethiopia were male and female under the age of 18 years old⁽⁸⁾. Cambodia, Thailand, Vietnamese were male, female, adolescents and children aged 10-17 years^(1,7), Moldova special for female aged >18 years⁽⁹⁾, Ghana special for girls and female without mentioning age⁽¹⁰⁾, US to keep track of medical records of patients <18 years⁽⁶⁾. South London and East London in search of medical records of children and women up to 30 years^(2, 5), India, Laos, Nepal without specifying gender and age, East Nusa Tenggara for women aged 21-37 years⁽⁴⁾ and the rest did not mention the place, age, or gender of the participants⁽¹¹⁾.

Context: The research data was collected in 2006-2012⁽¹²⁾, 2006-2012⁽¹⁰⁾2013⁽¹¹⁾, 2006-2012⁽¹³⁾, 2013⁽¹³⁾, 2016⁽⁸⁾. Four were taken using electronic medical records and databases CRIS years 2007-20012⁽¹⁵⁾.

Recruitment and sampling: The sampling method on 13 studies were differentiated by design research undertaken. In quantitative research using consecutive sampling, and cohort was used while using a qualitative research study of medical records in accordance with the criteria of the UN Protocol and purposive sampling. Four studies with a cohort design was conducted by checking the electronic medical record or database CRIS at hospital⁽¹⁶⁾. 9 studies took the sample directly in places where human trafficking occurred. In-dept qualitative data collection through interviews with open-ended questions in person or over the phone. While quantitative questionnaire or implement interventions to participants.

Study design and analysis: Article qualitative used semi-structured interviews in a special group. Three articles used quantitative questionnaire design and five articles using a cohort study with Electronic Medical Record or database CRIS⁽¹⁶⁾. Two studies using logistic

regression analysis^(9,12). Two studies using SEM^(1,8), one study using multiple regression⁽⁵⁾, one study using descriptive analysis⁽⁶⁾, four studies using thematic analysis⁽¹⁷⁾ and three studies using retrospective interviews with UN standard protocol. Among the studies did not found that reported the normality assumption test and data.

Ethical considerations: There were 13 studies reported ethical approval to use ethical standards of WHO and Recommendations Safety⁽¹⁾. Ethical approval was obtained from Kings College Research Ethics Committee (CREC/07/08-56) and from the State of N. Testemitanu Institutional Review Board of the Medical and Pharmaceutical University⁽⁸⁾, Research Ethics Committee (Oxfordshire C, reference 08/H0606/71)⁽³⁾ and Ethical approval from the University of South Wales⁽⁴⁾. One study did not report on the ethical approval.

Mains Findings: Human trafficking identified in accordance Optional Protocol to the United Nations (UN), which prevent, suppress and punish trafficking in persons, especially women and children⁽⁸⁾. According to the 13 studies, found the psychosocial characteristics of victims such as: a) The demographic data; age (adults, children), gender, marital status, education level, place of residence (urban/rural), regional trade (national/international⁽⁵⁾, religion, type of work, economic conditions before trading. b) Variable of exposure; smuggling status, the process of departure, detention in camps⁽⁸⁾ counterfeiting and document fraud, employment status⁽⁹⁾ unclear country the purpose of employment, and the type of work presented⁽⁵⁾, c) Method of recruitment using mediasocial (Backpage.com, Facebook.com, dating website) and invited directly by recruiters⁽⁶⁾, d) Type of exploitation; domestic slavery, exploitation of labor, financial exploitation, sexual exploitation⁽⁷⁾, e) Characteristics of exposure to experience during the work; restriction of movement, drug use (shisha, marijuana, alcohol)⁽⁸⁾, sexual abuse, psychological abuse, restriction and confinement, physical violence⁽⁶⁾. The background incidence of trafficking, race, home life, relationships with parents/carers/family members, economic opportunities, the recruiters-victim relationship, trust in strangers, lack of social support⁽⁸⁾, f) Variables of psychosocial on the impact of trafficking; abuse of alcohol/drugs, engage in crimes that require incarceration, a fugitive/police targets⁽⁷⁾.

Discussion

Victims of trafficking are vulnerable to trafficking has characteristics that may be invoked to think of society to recognize the psychosocial characteristics trafficking events that begins from the neighborhood sociodemographic, factor which affects the incidence of trafficking, trafficking process, type of exploitation is accepted⁽⁹⁾. Exposure to events experienced problems as well as the victim is also a psychosocial characteristics that must be observed to prevent mental health disorders⁽⁶⁾. Effort early prevention of the root of the problem by fixing all the characteristics that led to trafficking thereby minimizing the incidence of trafficking and mental disorders.

Conclusion

Psychosocial characteristics of trafficking victim based on the literature search found a few characteristics: a) the demographic characteristics b) variable trafficking process. c) method of recruitment d) exploitation type e) characteristics of the exposure. f) the background of the trafficking g) psychosocial variables that appear. Further research is more focused on prevention through campaigns for the public to minimize the incidence of mental disorders.

Conflict of Interest: None

Ethical Clearance: This study has passed the ethical test held at committee ethics Faculty of Medicine, University of Brawijaya with number 302/EC/KEPK-S2/11/2018.

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References

1. Lisbeth Iglesias-Rios SDH, Sarah A. Burgard, Ligia Kiss and Cathy Zimmerman. Mental health, violence and psychological coercion among female and male trafficking survivors in the greater Mekong sub-region: a cross-sectional study. *BMC Psychology*. 2018;6:56.
2. Siân Oram MK, Melanie Abas, Matthew Broadbent, Louise M Howard. Characteristics of trafficked adults and children with severe mental illness: a historical cohort study. *Lancet Psychiatry*. 2015.
3. Elizabeth K. Hopper PD. Trauma Informed Psychological Assessment of Human Trafficking Survivors. Beacon St., Brookline: The Trauma Center at Justice Resource Institute; 2016.
4. Indra Yohanes Kiling BNK-B. Motif, Dampak Psikologis dan Dukungan pada Korban Perdagangan Manusiadi Nusa Tenggara Timur. *Jurnal Psikologi Ulayat*. 2019; X(X), XXX-XXX e-ISSN: 2580-1228 DOI: 10.24854/jpu02019-218.
5. Maria Cary SO, Louise M. Howard, Kylee Trevillion and Sarah Byford. Human trafficking and severe mental illness: an economic analysis of survivors' use of psychiatric services. *BMC Health Services Research* 2016;16:284.
6. Jessica L. Moore B, Christopher Houck, PhD, Priyadarshini Hirway, ScM,, Christine E. Barron M, and Amy P. Goldberg, MD. Trafficking Experiences and Psychosocial Features of Domestic Minor Sex Trafficking Victims. *Journal of Interpersonal Violence* 2017;16.
7. Zimmerman CAaC. Access to mental health and psychosocial services in Cambodia by survivors of trafficking and exploitation: a qualitative study. *International Journal of Mental Health Systems*. 2015;9:16 DOI 10.1186/s13033-015-0008-8
8. Lemma Derseh Gezie AWY, Yigzaw Kebede Gete, Telake Azale, Tilman Brand, Hajo Zeeb. Socio economic, trafficking exposures and mental health symptoms of human trafficking returnees in Ethiopia: using a generalized structural equation modelling. *International Journal of Mental Health Systems*. 2018;12 62.
9. Melanie Abas NVO, Martin Prince, Viorel I Gorceag, Carolina Trigub and Siân Oram. Risk factors for mental disorders in women survivors of human trafficking: a historical cohort study. *BMC Psychiatry*. 2013;13 : 204.
10. David Okech NH, Waylon Howard, John K. Anarfi & Abigail C., Burns. Social Support, Dysfunctional Coping, and Community Reintegration as Predictors of PTSD Among Human Trafficking Survivors. *Behavioral Medicine*. 2018;44:3, 209-218 .
11. Rafferty Y. Mental Health Services as a Vital Component of Psychosocial Recovery for Victims of Child Trafficking for Commercial Sexual Exploitation *American Journal of Orthopsychiatry*. 2018;Vol. 88, No. 3, 249-260 <http://dx.doi.org/10.1037/ort0000268>
12. Siân Oram MA, MD, Debra Bick, PhD, Adrian Boyle, MD, Rebecca French, PhD, Sharon Jakobowitz, PhD, Mizanur Khondoker,, PhD NS, MSc, Kylee Trevillion, PhD, Louise Howard,

- MRCPsych, and Cathy Zimmerman, PhD. Human Trafficking and Health: A Survey of Male and Female Survivors in England. *AJPH RESEARCH*. 2016;June 2016, Vol 106, No. 6 *AJPH*.
13. Jill Domoney LMH, Melanie Abas, Matthew Broadbent and Sian Oram. Mental health service responses to human trafficking: a qualitative study of professionals' experiences of providing care. *BMC Psychiatry* 2015;15:289 DOI 10.1186/s12888-015-0679-3
 13. Livia Ottisova PS, Hitesh Shetty, Daniel Stahl, Johnny Downs, Sian Oram. Psychological consequences of child trafficking: An historical cohort study of trafficked children in contact with secondary mental health services. *PLoS ONE* 13 : 3 2018.

Risk Factors for Obesity in Patients with Hypertension

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Abstract

Introduction: Non-communicable diseases (NCDs) are a leading cause of death worldwide. In 2018, NCDs' prevalence had reportedly increased since 2013. Hypertension was the biggest cause of NCDs diagnosed in health facilities, from 25.8% to 34.1%. Patients with hypertension and obesity are at increased risk of complications from diabetes mellitus and kidney disease.

Objective: The present study aimed to determine risk factors for obesity in patients aged 25–69 years with hypertension.

Materials and Method: This was an observational study with a cross-sectional design, using secondary data from the 'Cohort Study of Risk Factors of Non-communicable Diseases', conducted in Bogor City, Kebon Kelapa Village in 2017. The population in this study included adult patients with hypertension aged 25–69 years.

Results: The prevalence of obesity in patients with hypertension was 47.4%. Risk factors that were significantly related to obesity in patients with hypertension included age groups 25–44 and 45–59, female gender and excessive energy intake ($p = 0.009, 0.050, 0.025$ and 0.039 , respectively and odds ratio = 2.43, 1.73, 1.85 and 1.85, respectively).

Conclusions: Risk factors associated with obesity in patients aged 25–69 years with hypertension included age, gender and energy intake.

Keywords: Obesity, hypertension, adult, elderly.

Introduction

Non-communicable diseases (NCDs) are the leading cause of death worldwide. Around 15 million people aged 30–69 years die each year from NCDs, with 85% occurring in low and middle-income countries.¹ NCDs' prevalence increased in Indonesia between 2013 and 2018.²

Hypertension is a leading cause of cardiovascular disease that can lead to strokes, coronary heart disease, kidney failure and premature death.^{3–6} It is estimated to

cause 12.8% of deaths worldwide.⁷ In 2018, hypertension was the main cause of NCDs diagnosed in health facilities. Hypertension's prevalence increased from 25.8% in 2013 to 34.1% in 2018.²

Studies have reported that the prevalence of obesity among patients with hypertension is increasing. A study by Ford et al. using data from the National Health and Nutrition Examination Survey showed that obesity's prevalence increased from 25.7% from 1976–1980 to 50.8% from 1999–2004 in adults with hypertension.⁸ Qin et al. also reported an increase in the prevalence of obesity and central obesity in hypertensive adults in China.⁹ A study by Sartika et al. showed that obesity's prevalence in Indonesian patients with hypertension was 40.7% in urban areas and 18.9% in rural areas.¹⁰

Patients with hypertension and obesity are at increased risk of complications of type 2 diabetes mellitus

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and kidney disease.^{11,12} Obesity status in patients with hypertension is associated with a significant difference in the average onset age of type 2 diabetes mellitus.¹² In patients with hypertension, obesity and insulin resistance also play major roles in the genesis of kidney failure, which is known as ‘nephrosclerotic hypertension’.¹¹

Risk factors such as age, gender, education, income, diet, physical activity, hypertension treatment, smoking and stress contribute to the incidence of obesity in patients with hypertension. Risk factors for obesity complications in patients with hypertension vary greatly among regions.

The present study aimed to determine the risk factors for obesity complications in patients with hypertension aged 25–69 years in Bogor City in 2017. This study’s results are expected to provide an evidence base for appropriate health programmes to prevent obesity in patients with hypertension.

Materials and Method

The present study was cross-sectional in design and analysed secondary data from the ‘Cohort Study of Non-communicable Diseases’, conducted by the National Institute of Health Research and Development, Republic of Indonesia, in Bogor City, Kebon Kelapa Village, in 2017. This study’s population were all patients with hypertension aged 25–69 years who were respondents in 2017. Hypertension was defined as systolic blood pressure >140 mmHg and/or diastolic blood pressure >90 mmHg, doubling of blood pressure within 5 min under appropriate conditions, diagnosis of hypertension by a health professional or undergoing treatment for hypertension. A population of 489 patients with hypertension aged 25–69 years was selected from the ‘Cohort Study of Non-communicable Diseases’, conducted in 2017. This research sample was selected using total population sampling. Respondents with heart disease (n = 50), stroke (n = 44), diabetes mellitus (n = 118) and pregnancy (n = 1) were excluded from the study sample. Thus, 318 respondents were included in the study.

The dependent variable in this study was obesity status, with a body mass index (BMI) parameter >27 kg/m². BMI was calculated as body weight in kilograms divided by the height in metres squared and categorised as: underweight (<18.5 kg/m²), normal weight (18.5–25.0 kg/m²), overweight (25.1–27.0 kg/m²) and obese

(> 27 kg/m²).¹³ Independent variables were age, gender, education, conversation, nutrition intake, physical activity, hypertension treatment, smoking and stress. Nutrient intake was measured as the amount of energy, carbohydrate, protein, fat and sodium consumed daily compared with dietary recommendations for people with hypertension (DASH).¹⁴ Intake of nutrients was categorised as low (<90%), moderate (90%–119%) and high (≥120%).¹⁵

Data processing involved cleaning and transforming data and was performed by univariate and bivariate using chi Square test with a 95% confidence interval (CI) (α = 0.05) and odds ratios (ORs).

Results

Characteristics of patients with hypertension:

Analysis of nutritional status in patients hypertensive aged 25–69 years showed malnutrition in 1.6%, normal nutrition in 35.3%, with 15.7% overweight and 47.4% obese. The prevalence of hypertension was greatest (53%) among those aged 45–59 years (pre-elderly). The incidence of hypertension was highest (72.6%) among females compared with males. Most (65.1%) patients with hypertension were of low education status. The patients’ characteristics are presented in Table 1.

Table 1: Characteristics of patients with hypertension aged 25–69 years

Variables	Category	N	%
Nutritional status (n = 312)	Underweight	5	1.6
	Normal	110	35.3
	Overweight	49	15.7
	Obese	148	47.4
	Missing	6	
Obesity (n = 312)	No	164	52.6
	Yes	148	47.4
	Missing	6	
Age (years) (n = 318)	25–44 (adult)	67	21.1
	45–59 (pre-elderly)	168	53.0
	60–69 (elderly)	82	25.9
Gender (n = 318)	Male	87	27.4
	Female	231	72.6
Education status (n = 318)	High	111	34.9
	Low	207	65.1
Income (n = 318)	Low	159	50.0
	High	159	50.0

Source: secondary data processed

Prevalence and risk factors for obesity in patients with hypertension: The prevalence of obesity in patients with hypertension was quite high (47.4%) and was higher in females compared with males (51.5% vs. 36.5%). Obesity in patients with hypertension mostly occurs in adulthood, from age 25 to 44 years. The prevalence of obesity was higher in patients with a low education status compared with those who were highly educated (50.2% vs. 42.3%). Nutrient intake in obese hypertensive patients showed high energy (58.2%), high carbohydrate (54.8%), adequate protein (61.4%), moderate fat (52.4%) and low sodium (50.3%) intake.

The bivariate analysis showed that factors were significantly related ($p < 0.05$) and the risk factors for

obesity in patients with hypertension were age, gender and energy intake. Adult patients with hypertension aged 25–44 years showed a 2.43-fold higher risk of obesity compared with that of elderly patients (aged 60–69 years), and pre-elderly patients (aged 45–59 years) showed a 1.73-fold higher risk of obesity compared with that of elderly patients (aged 60–69 years). There were 1.85 times more female than male patients with hypertension. High energy intake in patients with hypertension was 1.85 times higher than low energy intake. The results of the bivariate analysis of risk factors for obesity in patients with hypertension are presented in Table 2.

Table 2. Risk factors for obesity in patients with hypertension aged 25–69 years

Variables	Obesity				Total		OR	P-value
	No		Yes		N	%		
	N	%	N	%				
Age (years)								
25–44 (adult)	28	42.4	38	57.6	66	100.0	2.433	0.009*
45–59 (pre-elderly)	84	50.9	81	49.1	165	100.0	1.729	0.050*
60–69 (elderly)	52	64.2	29	35.8	81	100.0		
Gender								
Male	54	63.5	31	36.5	85	100.0		
Female	110	48.5	117	51.5	227	100.0	1.853	0.025*
Education								
High	64	57.7	47	42.3	111	100.0		
Low	100	49.8	101	50.2	201	100.0	0.792	1.375
Income								
Low	83	53.9	71	46.1	154	100.0		
High	81	51.3	77	48.7	158	100.0	1.111	0.725
Energy intake								
Low	85	57.0	64	43.0	149	100.0		
Moderate	40	50.0	40	50.0	80	100.0	1.328	0.308
High	28	41.8	39	58.2	67	100.0	1.850	0.039*
Carbohydrate intake								
Low	91	54.2	77	45.8	168	100.0		
Moderate	34	51.5	32	48.5	66	100.0	1.112	0.714
High	28	45.2	34	54.8	62	100.0	1.435	0.226
Protein intake								
Low	129	54.2	109	45.8	238	100.0		
Moderate	17	38.6	27	61.4	44	100.0	1.880	0.060
High	7	50.0	7	50.0	14	100.0	1.183	0.759
Fat intake								
Low	51	55.4	41	44.6	92	100.0		

Variables	Obesity				Total		OR	P-value
	No		Yes		N	%		
	N	%	N	%				
Moderate	30	47.6	33	52.4	63	100.0	1.368	0.339
High	72	51.1	69	48.9	141	100.0	1.192	0.514
Natrium intake								
Low	71	49.7	72	50.3	143	100.0		
Moderate	33	55.0	27	45.0	60	100.0	0.807	0.487
High	49	52.7	44	47.3	93	100.0	0.885	0.648
Hypertensive medication								
No	60	37.3	101	62.7	161	100.0		
Yes	48	34.0	93	66.0	141	100.0	1.151	0.643
Type of hypertensive medication								
Captopril	6	33.3	12	66.7	18	100.0		
Amlodipine	35	32.1	74	67.9	109	100.0	1.057	
Nifedipine	6	46.2	7	53.8	13	100.0	0.583	
Bisoprolol	1	100.0	0	0.0	1	100.0	0.000	0.396
Low physical activity								
Yes	50	32.7	103	67.3	153	100.0		
No	59	40.4	87	59.6	146	100.0	0.718	0.205
Moderate physical activity								
Yes	105	36.1	186	63.9	291	100.0		
No	4	57.1	3	42.9	7	100.0	0.423	0.456
High physical activity								
Yes	9	47.4	10	52.6	19	100.0		
No	100	35.8	179	64.2	279	100.0	1.611	0.445
Smoking								
No	121	51.7	113	48.3	234	100.0		
Yes	43	55.1	35	44.9	78	100.0	0.872	0.695
Stress								
No	144	52.0	133	48.0	277	100.0		
Yes	11	52.4	10	47.6	21	100.0	0.984	1.000

* p < 0.05

Source: Secondary data processed

Discussion

Our results indicate that the prevalence of obesity in patients with hypertension aged 25–69 years in Bogor City in 2017 was high (47.4%). This high prevalence is in line with findings from previous studies by Ford et al. (2008), Qin et al. (2013) and Sartika (2015).^{8,9,10} The cause of obesity among patients with hypertension is multifactorial. The level of hypertension, socioeconomic status, residential area, consumption of red meat, physical activity, hypertension treatment, family history of diabetes, hypertension and heart disease, which is associated with obesity among people with hypertension.⁹

In the present study, risk factors for obesity complications in patients with hypertension were found to be age, gender and energy intake. Residential area, consumption of red meat, family history of diabetes, family history of hypertension and family history of heart disease could not be analysed due to limited secondary data.

The prevalence of obesity in patients with hypertension was higher in adults aged 25–44 years than in pre-elderly (45–59 years) and elderly (60–69 years) patients. Under normal conditions, age is associated with obesity as metabolism decreases with age, which increases the risk of obesity. However, in the present

study with a population of patients with hypertension, adults (25–44 years) showed a higher risk of complications of obesity that was 2.43-fold higher than elderly (60–69 years) patients, whereas this value was 1.73-fold higher in pre-elderly (45–59 years) compared with elderly patients.

The prevalence of obesity in female patients with hypertension was higher than that of males. These findings reveal a significant relationship between gender and incidence of obesity in patients with hypertension. Females with hypertension showed a 1.85-fold higher risk of obesity compared with males with hypertension. This study's results are in line with those reported by Qin et al. (2013).⁹ They conducted a study in Lianyungang, China from October 2008 to September 2009 and showed that the prevalence of obesity in females with hypertension was higher than that of males.⁹ Females are at greater risk of obesity since they generally have more fat than males, including a higher amount of subcutaneous fat and more fat deposits in the gluteal–femoral area or peripherals that determine the typical pear-shaped female (peripheral or gynoid type obesity).¹⁶

Excessive energy intake is related to obesity in patients with hypertension and is associated with a 1.85-fold increased risk of obesity compared with those with low energy intake. When energy intake exceeds energy expenditure, a positive energy balance occurs, leading to an increase in body mass. A 60%–80% increase in body mass is associated with an increase in body fat.¹⁷ An imbalance between excess energy intake and output results in weight gain, both under normal conditions and in patients with hypertension.

Conclusion

The prevalence of obesity in patients with hypertension aged 25–69 years in Bogor City in 2017 was 47.4%. Risk factors that were significantly related to obesity in patients with hypertension included age (adults aged 25–44 and pre-elderly aged 45–59 years), female gender and excessive energy intake ($p = 0.009, 0.050, 0.025$ and 0.039 , respectively and $OR = 2.43, 1.73, 1.85$ and 1.85 , respectively). The high prevalence of obesity in patients with hypertension is a health problem requiring appropriate treatment since controlling weight gain is fundamental to improving quality of life in patients with hypertension. Our results are expected to be used to plan appropriate health programmes and prevent obesity in patients with hypertension.

Conflict of Interest Statement: The authors declare that there is no conflict of interest.

Ethical Clearance: The present study obtained approval from 'The Research and community engagement Ethical Committee Faculty of Public Health Universitas Indonesia', Ket-593/UN2.F10/PPM.00.02/2019.

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References

1. World Health Organization. Noncommunicable disease. 2018.
2. National Institute of Health Research and Development. Indonesia basic Health Research 2018. Jakarta: Indonesian Ministry of Health; 2018.
3. StaessenJA, WangJ, BianchiG, BirkenhägerWH. Essential hypertension. *Lancet*. 2003;361(9369):1629-41. doi: 10.1016/S0140-6736(03)13302-8. PMID 12747893.
4. FieldsLE, BurtVL, CutlerJA, HughesJ, Roccella EJ, Sorlie P. The burden of adult hypertension in the United States 1999-2000: Arising tide. *Hypertension*. 2004;44(4):398-404. doi: 10.1161/01.HYP.0000142248.54761.56. PMID 15326093.
5. Kearney PM, Whelton M, ReynoldsK, Muntner P, Whelton PK, HeJ. Global burden of hypertension: analysis of worldwide data. *Lancet*. 2005;365(9455):217-23. doi: 10.1016/S0140-6736(05)17741-1. PMID 15652604.
6. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with 19.1 million participants. *Lancet* 2017; 389: 37–55. doi: 10.1016/S0140-6736(16)31919-5.7. World Health Organization. Raised blood pressure. 2018.

8. FordES, ZhaoG, LiC, PearsonWS, MokdadAH. Trends in obesity and abdominalobesity among hypertensive and nonhypertensiveadults in the United States. *AmJ Hypertens.* 2008;21(10):1124-8. doi: 10.1038/ajh.2008.246. PMID 18772861.
9. Qin X, Zhang Y, CaiY, HeM, Sun L, FuJ, LiJ, WangB, XingH, TangG, WangX, XuX, XuX, HuoY. Prevalence of obesity, abdominalobesity and associatedfactors in hypertensiveadultsaged 45-75 years. *ClinNutr.* 2013;32(3):361-7. doi: 10.1016/j.clnu.2012.08.005. PMID 23084742.
10. Sartika RAD, Wulandari RA, Ompusunggu IJ, Sutrisna B. Risk factors of dyslipidemia in hypertensive patients in selectedurban and ruralareas in Indonesia. *J Food NutrDisord.* 2015;4(2). doi:10.4172/2324-9323. PMID 1000168.11. Kincaid-SmithP. Hypothesis: obesity and the insulin resistance syndrome play a majorrole in end-stage renal failure attributed to hypertension and labelled 'hypertensivenephrosclerosis'. *J Hypertens.* 2004;22(6):1051-5. doi: 10.1097/00004872-200406000-00001. PMID 15167435.
12. Channanath AM, Farran B, Behbehani K, Thanaraj TA. Impact of hypertension on the Association of BMI with Risk and Age at Onset of Type 2 diabetesmellitus: age- and gender-mediated modifications. *PLOS ONE.* 2014;9(4):e95308. doi: 10.1371/journal.pone.0095308. PMID 24743162.
13. Indonesian Health Ministry. *Pedoman Praktis Memantau Status Gizi Orang Dewasa*; 2011.
14. United States Department of Health and Human Services. *Your guide to lowering your blood pressure with DASH. DASHeatingplan*; 2006.
15. Gibson SR. *Principal of nutritional assessment.* UK: Oxford University Press; 2005.
16. Karastergiou K, Smith SR, Greenberg AS, Fried SK. Sex Differences in Human Adipose Tissues—the Biology of Pear Shape. *Biol Sex Differ.* 2012;3(1):13. doi: 10.1186/2042-6410-3-13. PMID 22651247.
17. HillJO, Wyatt HR, Peters JC. Energy balance and obesity. *Circulation.* 2012;126(1):126-32. doi: 10.1161/CIRCULATIONAHA.111.087213. PMID 22753534.

HIV and Zonke-bonke Syndrome in Mthatha Region of South Africa: Case Reports

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Abstract

Introduction: South Africa is an African rainbow nation, not only in its color of population, but also in the mixture of HIV infection. There is all three combinations are of HIV infection such as HIV-1, HIV-2, and both of them. This is matter of concern.

Objective: To highlight the problem of HIV-1 and HIV-2 (combined) infection in Mthatha region of South Africa.

Case History: First time four cases of HIV-1/2, mixed infection were reported within period of 1-year (2009). They were reported at Sinawe Center for examination for their sexually assaulted. The HIV screening tests were carried out for HIV infection. There were four patients were found positive for both HIV1 & 2. Surprisingly, one was a child of 8-years of age. Multiple sexual partners some or other time crossed with West African who were harboring the type 2 HIV could be the cause of this mixed infection. This kind of promiscuous behavior with multiple partners is called as “*Zonke-bonke syndrome*”. The history, mode of transmission of HIV infection, and the consequences of mixed HIV infections is discussed in this case reports.

Conclusion: There is prevalence of HIV-1 & HIV-2 (mixed) infection in Mthatha region of South Africa. It is a serious matter of concern.

Keywords: *HIV type 1 & 2, Promiscuous behavior, and multiple partners.*

Introduction

South Africa has one of the highest rates of sexual assaults in the world as well as one of the highest prevalence rates of HIV infection.¹ In Bantustan (Transkei), the young people were allowed to come and engage in free sexual experimentation.² Young women actively seek partners who are willing to spend money and often-initiate relationships with older men. The girl goes out there and positions herself in a place where she knows she will get the man. They do not see themselves as victims. This is all about power and authority, with teenage boys and girls involved in these relationships on an unequal footing. “The sugar daddy or mommy is in a better position, and is therefore able to entice the young girl or boy. They are reluctant to be identified because “people will think we are doing these things” Although everyone agrees it is a common practice, cross-generational relationships are not often addressed

in HIV/AIDS prevention campaigns, despite a growing awareness that they are driving much of the epidemic.³

HIV-2 infections are predominantly found in Africa. West African nations with a prevalence of HIV-2 of more than 1% in the general population are Cape Verde, Côte d’Ivoire (Ivory Coast), Gambia, Guinea-Bissau, Mali, Mauritania, Nigeria, and Sierra Leone. Other West African countries reporting HIV-2 are Benin, Burkina Faso, Ghana, Guinea, Liberia, Niger, São Tomé, Senegal, and Togo. Angola and Mozambique are other African nations where the prevalence of HIV-2 is more than 1%.⁴

Differentiating between HIV-1 and HIV-2 infection is the first step to understanding HIV transmission, epidemiology and pathogenesis in geographical areas where both viruses circulate.⁵ HIV is a highly variable virus, which mutates very readily. This means there are

many different strains of HIV, even within the body of a single infected person. Both types (HIV-1 and HIV-2) are transmitted by sexual contact, through blood, and from mother to child, and they appear to cause clinically indistinguishable AIDS. However, it seems that HIV-2 is less easily transmitted, and the period between initial infection and illness is longer in the case of HIV-2. Worldwide, the predominant virus is HIV-1, and generally, when people refer to HIV without specifying the type of virus they will be referring to HIV-1. The relatively uncommon HIV-2 type is concentrated in West Africa and is rarely found elsewhere.⁶ A recent (2014) study showed that HIV-2 is intrinsically resistant to nonnucleoside reverse transcriptase inhibitors. Therefore it is mandatory to discriminate between HIV types before initiating antiretroviral treatment. Guinea-Bissau has the world's highest prevalence of HIV-2 and HIV-1/HIV-2 dually infected individuals.⁷ The purpose of these case reports is to highlight the problem of HIV1 and HIV-2 (combined) infection in this community, and to make aware to the health care professionals for its management.

Methodology

This is a retrospective study done in Sinawe Centre over 1-year (January to December, 2009). This unit is a part of Nelson Mandela Academic Hospital, and caters to a population of about 400 000 in the OR Tambo Municipality area. All the cases of rape, and sexual assaults are reported in this center. It is now a 'One Stop Center' providing a multidisciplinary management of victims of rape and sexual assaults. It is open from Monday to Friday from 08h00 to 16h00. On weekends and after hours, the victims were examined in Accident and Emergency (A & E) section of Nelson Mandela Academic Hospital. It is policy of the center to provide HIV testing after counseling to all victims of sexual assault and rape. Blood for HIV screening is taken with the consent of the victims. It is later confirmed by ELISA test in laboratory. HIV1 and HIV2 (combined) infection in four cases who were presented to the center for an examination. Post-exposure Prophylaxis (PEP) was started at the beginning of 2003, and is offered to all the victims except those who came later than 72 hours after the incident.

Case history 1: AM, a 19 years female presented with history of sexual assault by known person, her boyfriend's cousin. It was happened in morning hours. She was with her boyfriend who was intoxicated in his

aunt's home in the guest room. Perpetrator pushed the door, entered in the room, and dragged her in outside bedroom. She tried to resist but the perpetrator assaulted her. He forcefully undressed her and raped her. He used a condom.

The victim has a boyfriend who worked in Cape Town and had a consensual sex in August 2008. She wanted a sex as she met her friend after a long time, but he was drunk. The perpetrator took advantage. The victim had multiple injuries such as lacerations on left knee, and bruises on left hand and on back.

On genital examination, there was old ruptured hymen with fresh tears on 9 O'clock position. There is increased friability with bruised introitus. Rapid test was reactive to both HIV1 and 2. HIV Ag/Ab Combination Assay reactive suggestive of that both HIV antibody and antigen (p24).

Case history 2: PM 26 years old single woman is living 40 kms from Mthatha. A known person has sexually assaulted her on 26.03.2009. This is happened in the perpetrator's bedroom at Qumbu. She was talking with another colleague. The perpetrator has shown a knife and grabs her to his bed. She has a boyfriend and had a consensual intercourse about 2 weeks before. She is having two children of the age 9 and 4 years old.

On genital examination, there were no sign of any injury. There is increased friability, but no whitish discharge visible. Rapid test was reactive to both HIV1 and 2. HIV Ag/Ab Combination Assay reactive suggestive of that both HIV antibody and antigen (p24).

Case history 3: Police with history of sexual assault on 10.04.2009 brought BB 18 year female. She is a learner in standard 10. She was waiting for transport for going to Easter Church Service. Four unknown men were approached her, and asked her name. One of them starts assaulting her, and drag in nearby bushes and raped her. He robbed her R15. BB is having a boyfriend, and had a consensual sex on 20th March 2009. She had two boy friend earlier as well. They did not use condom. She is menstruating now. There is no injury identified. She was counseled for HIV test in January, and she was negative. HIV screening test conducted on 10 April 2009 at Sinawe Center, and she found HIV positive for both HIV1 & HIV 2. She is stick to only one boyfriend from last 3-years.

Case history 4: IT, an 8-year learner referred

from Ngangelizwe Health Center with history of being sexually abused by a known eight-year-old boy on 03.04.2009 at about 3 pm. Her grandmother on 24.04.2009 at Sinawe center brought her. Her mother is staying in Johannesburg. She was coming from school, and on the way, she was overpowered by the perpetrator, and raped her. Counseling and reassuring therapy was done.

On examination child is scared of mother. There was yellowish, offensive dark, vaginal discharge with ruptured hymen. Pus swab taken for microscopy and culture. Gram stain showed on microscopy gram-positive cocci, yeast cells with neutrophils. On culture, klebsiella pneumonie extended spectrum β -lactamase producer and proteus mirabilis.

Rapid HIV test found to be positive for both types HIV-1 and HIV-2.

Discussion

This is believed to be the first case of HIV-2 infection in this region. There is no case as such found in literature reported in South Africa. It provides important information that justifies expanded efforts to initiate and develop a program for the HIV-2 screening in this region. Mthatha (Umtata) was a capital of former Republic of Transkei. Mthatha region is the least developed of the former black homelands. It is also a region where majority of workers go for their earning in far-flung richer areas of South Africa. This has contributed directly the spread of HIV in the rural areas of South Africa.

The sole cause of HIV transmission is the poverty. Older men, who use their power and money in return for sex from younger women, are among the drivers of the HIV and AIDS infections in this region. Several studies showed that there was a positive correlation between HIV prevalence and poverty globally especially in sub-Saharan Africa. The infection is increasing. South Africa. Research organizations dealing with testing and counseling say it is not only men but women, too, who are out to attract younger colleagues. The fact is that older, affluent professionals, previously thought to be at low risk of HIV infection, are increasingly becoming vulnerable to infection because of risky sexual behaviour with younger partners.⁴

Changes in sexual behaviour among the wealthy have led to a worrying swell in HIV and AIDS infections among those who had previously been considered low risk. Several behavioral factors have been aligned to

this development, among them inter-generational sex, where older, affluent men and women were having sex with the higher-risk younger group. It is the arrogance, not ignorance that contributing in the spread of HIV infection.⁸ In United States, HIV-2 infection was diagnosed in 1987. Since then, the Centers for Disease Control and Prevention (CDC) has worked with state and local health departments to collect demographic, clinical, and laboratory data on persons with HIV-2 infection. of the 79 infected persons, 66 are black and 51 are male. Fifty-two were born in West Africa, 1 in Kenya, 7 in the United States, 2 in India, and 2 in Europe. The region of origin was not known for 15 of the persons, although 4 of them had a malaria-antibody profile consistent with residence in West Africa. AIDS-defining conditions have developed in 17, and 8 have died.⁴ It is not known in this area, but there national of almost all African countries are residing in South Africa. There should be a screening system in place before they immigrate to South Africa. These case counts represent minimal estimates because completeness of reporting has not been assessed. Although AIDS is reported uniformly nationwide, the reporting of HIV infection, including HIV-2 infection, differs from state to state according to state policy.⁴ There is hardly any estimate available in South Africa despite of the fact that HIV-2 infection is increasing.

Because epidemiologic data indicate that the prevalence of HIV-2 in the United States is very low, CDC does not recommend routine HIV-2 testing at U.S. HIV counseling and test sites or in settings other than blood centers. However, when HIV testing is to be performed, tests for antibodies to both HIV-1 and HIV-2 should be obtained if demographic or behavioral information suggests that HIV-2 infection might be present.⁴ The first victim has reported that her boyfriend is working in Cape Town, could be the source of infection with HIV-2. The second case is mutipara young women who have given history of having multiple sexual partners one of them was a West African. The third victim was a school girl, and had relationship with boyfriend without using a condom. Most surprising is the case of child (case 4) who is only 8 years and sexually abused. She was having history of poring foul smelling fluid through vagina. This was notice by her grand mother. The perpetrator could be the close relative of this child as mother is staying in Johannesburg.

Among all HIV-infected people, the prevalence of HIV-2 is very low compared with HIV-1.⁴ However, the

potential risk for HIV-2 infection in some populations may justify routine HIV-2 testing for all people for whom HIV-1 testing is warranted.⁵ The decision to implement routine HIV-2 testing requires consideration of the number of HIV-2-infected persons whose infection would remain undiagnosed without routine HIV-2 testing compared with the problems and costs associated with the implementation of HIV-2 testing. The development of antibodies is similar in HIV-1 and HIV-2. Antibodies generally become detectable within 3 months of infection. Since 1992, all U.S. blood donations have been tested with a combination HIV-1/HIV-2 enzyme immunoassay test kit that is sensitive to antibodies to both viruses. This testing has demonstrated that HIV-2 infection in blood donors is extremely rare. All donations detected with either HIV-1 or HIV-2 is excluded from any clinical use, and donors are deferred from further donations.⁴

Little is known about the best approach to the clinical treatment and care of patients infected with HIV-2. Given the slower development of immunodeficiency and the limited clinical experience with HIV-2, it is unclear whether antiretroviral therapy significantly slows progression. Not all of the drugs used to treat HIV-1 infection are as effective against HIV-2.⁷ In vitro (laboratory) studies suggest that nucleoside analogs are active against HIV-2, though not as active as against HIV-1. Protease inhibitors should be active against HIV-2. However, non-nucleoside reverse transcriptase inhibitors (NNRTIs) are not active against HIV-2. Whether any potential benefits would outweigh the possible adverse effects of treatment is unknown.⁴ Monitoring the treatment response of patients infected with HIV-2 is more difficult than monitoring people infected with HIV-1. Viral load assays used for HIV-1 are not reliable for monitoring HIV-2. Response to treatment for HIV-2 infection may be monitored by following CD4⁺ T-cell counts and other indicators of immune system deterioration, such as weight loss, oral candidiasis, unexplained fever, and the appearance of a new AIDS-defining illness. More research and clinical experience is needed to determine the most effective treatment for HIV-2.⁴

In conclusion, there is a lack of knowledge regarding HIV-2 infection in Mthatha region of South Africa. It needs surveillance study to know the population infected of HIV-2. This will help in the management of patients as well as to curtail the infection on its grassroots levels. Physicians caring for patients with HIV-2 infection

should be empowered to initiate antiretroviral therapy after discussing with their patients what is known, what is not known, and the possible adverse effects of treatment. Continued surveillance is needed to monitor HIV-2 in the population because the possibility for further spread of HIV-2 exists. Programs aimed at preventing the transmission of HIV-1 also can help to prevent and control the spread of HIV-2.

Ethical Consideration: Prior consent for HIV testing was taken from all the victims of sexual assaults. Their names and identity has kept confidential, and not allow to divulge to anybody. The author has been have ethical permission for collecting data and publication from ethical committee of University.

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References

1. Abrahams N, Jewkes R, Lombard C, Meel B. The development and evaluation of an intervention to improve post exposure prophylaxis adherence after a sexual assault incident to prevent HIV transmission. Findings from Cape Town and Mthatha. MRC technical report to the Department of Health in the Western and Eastern Cape Provinces, October 2008.
2. Reuther RR. Sexual Illiteracy. Catholics for Choice in Good Conscience. catholicsforchoice.org/conscience/.../c2004sum_sexualilliteracy.asp (accessed 31.10.2008).
3. AEGIS-IRIN AFRICA. The 'sugar daddy' phenomenon. www.aegis.org/news/irin/2003/ir030735.html (Accessed 02.11.2008).
4. CDC. Human Immunodeficiency Virus Type 2. Fact sheets HIV/AIDS. www.cdc.gov/hiv/resources/factsheets/hiv2.htm (Accessed 01.11.2008).
5. Diaz DF, Ortiz E, Martin D, Nibot C, Rizo A, Silva E. HIV-2 antibody detection after indeterminate or negative HIV-1 Western blot in Cuba, 2005-2008. *MEDICC Rev.* 2012; 14(1):25-9.

6. Avert Organization. HIV types, subtypes, groups & strains. Differences between HIV types 1 and 2, HIV groups, HIV subtypes, CRFs and strains including implications for transmission, testing, treatment and vaccine research. www.avert.org/hivtypes.htm (Accessed 01.11.2008).
7. Honge BL, Bjarnason Obinah MP, Jespersen S, Medina C, Te Dda S, da Silva ZJ, Ostergaard L, Laursen AL, Weise C, Erikstrup C, et al. Performance of 3 rapid tests for discrimination between HIV-1 and HIV-2 in Guinea-Bissau, West Africa. *J Acquir Immune Defic Syndr.* 2014; 65(1):87-90.
8. International Planned Parenthood Federation (IPPF). South Africa: older men fuel third wave of HIV and AIDS. Website: ippf.org/en/News/Intl+news (Accessed 02.11.2018).

Performance of Midwives with Self Management as a Mediator from the Influence of Individual Factors

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Abstract

The performance of midwives is very influential on the performance of the organization in an effort to achieve its goals optimally. This study aims to prove that individual factors in the form of knowledge and skills with self management as mediation influence the performance of midwives in midwifery services at Kupang District Health Centers. Quantitative research with a cross-sectional study design conducted in 26 Puskesmas in Kupang Regency, with a sample of 220 implementing midwives, using the sampling method by simple random sampling. Descriptive statistical analysis, hypothesis testing with PLS. The results of this study prove that the skills of midwives have a significant effect on self management and midwife performance. Knowledge and skills of midwives with self management as mediation have a significant effect on the performance of midwives. Individual factors (knowledge and skills) directly and indirectly influence the performance of midwives with self-management as mediation.

Keywords: *Performance of Midwives, Self Management.*

Introduction

Health workers who function to provide quality health services are required to play an optimal role according to their main tasks, roles and functions⁽¹⁾. Health workers as health care providers can be measured in performance through various indicators, one of which is through patient satisfaction as recipients of health services⁽²⁾.

Performance is the result of work that has a strong relationship with the objectives of organizational strategy, customer satisfaction and economic contribution. Willingness and skill are not effective enough to do something without a clear understanding of what is done and how to do it⁽³⁾. Human resources

who are talented, qualified, highly motivated and willing to cooperate in teams will be the key to the success of the organization. Therefore the leader must be able to set work goals that will produce high-quality, highly motivated and productive employees. Specific target setting in a certain period of time is not only quantitative but also qualitative. Strategies to achieve performance targets, for example by self-development to master the knowledge and expertise needed with an improved level of competence. One effort to find out the ability of an individual in his work is to measure performance according to competency standards carried out continuously and effectively and efficiently. Performance measurement that is commonly used is the measurement of employee performance assessed by direct supervisor, peer rating and self-rating⁽⁴⁾.

Midwives as one of the leading health workers are also required to show optimal performance. Midwifery is a science that is formed from the synthesis of multi-disciplines related to midwifery services including medicine, nursing, social, behavioral, cultural, public health, and management.

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Kupang Regency with a population of 305,548 people, couples of childbearing age 46,404 couples, the number of pregnant women in 2014 was 8115 mothers. The proportion of village midwives reached 83.33% (289 midwives) with placements that were almost evenly distributed in all villages in the Kupang Regency area. Nonetheless, the coverage of delivery assistance by health workers is still very low at 50.79% with the number of mothers giving birth as many as 7746 people. The low coverage of delivery assistance by health workers can result in high MMR and IMR. Maternal mortality in Kupang Regency in 2014 was 4 people (absolute number) with the cause of death due to post partum bleeding and preeclampsia. While infant mortality in kupang district in 2014 was 52 people (absolute numbers). Causes of death of newborns due to neonatal asphyxia, LBW, aspiration, and congenital abnormalities. It was also reported that K1 coverage was 4760 people (58.66%) and V4 coverage was 3758 people (46.31%). Early detection of risks to mothers and infants by health workers was 679 people (41.84%) and by the public as many as 451 people (27.79%), and referral of neonatal maternal cases was 149 (9.31%)⁽⁵⁾.

Human factors are determinants of public service providers in producing quality services. The quality of service to the community is very dependent on the individual and the system used. Doctors and medical and non-medical support staff serving in health services must understand how to serve consumers well, especially for patients and families, because they are the main consumers of health services. Patient and family complaints about the quality of midwifery services can be caused by various factors, among others, one of them is the low performance of midwives. Assessment of performance includes several factors including observation, size, development and assessment of effectiveness. In individual factors which are one of the factors that influence performance, there are self-management factors that are very important to improve their performance, among others: 1) how individuals determine the behavior of the target to be changed; 2) then individuals are able to monitor their own behavior; 3) individuals choose the procedure to be determined; 4) individuals carry out procedures that have been set by themselves and 5) individuals are able to evaluate the procedures they have carried out continuously. Self management is an effort to manage individuals in order to organize themselves in improving their performance to achieve organizational goals.

According to Quintero et al.⁽⁶⁾ who examined the self leadership and effectiveness though in self management teams, found that the ability of a person to lead himself was effective against individual work in the team.

According to Young K (2018)⁽⁶⁾ there are 18 components of self management skills, namely: self assessment, building self confidence, identifying risk factors, choosing good activities, goal setting, building possession.

Material and Method

This study used an analytical cross sectional design. The target population in this study were all health workers working in the Kupang Regency area. This study took the total population with inclusion criteria: 1) Midwives, 2) worked in the scope of Kupang district health center 3) Willing to be respondents 4) Physical and spiritual health. While the exclusion criteria in this study were respondents who were originally willing to later resign for certain reasons. Sampling using Role of Thumbs, totaling 220 respondents.

Independent variables in this study are individual factors of knowledge and skills. Dependent variable is the performance of midwives in midwifery services including the quality of performance of midwives in the implementation of midwifery care for pregnant women, maternity, newborns and postpartum mothers. Mediator variables are self management, namely self assessment, self analysis, goal setting, self planning, self-implementation, finding social support, self monitoring and self evaluation modified with Varney 7 step midwifery management including the assessment of basic data, interpretation of basic data, anticipate diagnosis/potential problems, immediate action, planning, implementation and evaluation⁽⁷⁾. The tool used for this study was a closed questionnaire. In the closed questionnaire the answers are available, with a blue print. This research was carried out in the Kupang District work area which covered a total of 26 Puskesmas in Kupang District, NTT Province of Indonesia.

Very good knowledge of midwives tends to show very good self management (52.3%), good midwife knowledge tends to show good self management (77.8%), sufficient knowledge of midwives tends to show good midwife self management (87.5%), knowledge of midwives who are less likely to show good midwife self management (36.4%), poor midwife knowledge tends to show balanced good and bad midwives self management (39.2%).

Excellent midwife skills tend to show very good midwife self management (60.5%), good midwife skills tend to show good midwife self management (67.3%), midwife skills that tend to show good midwife performance (70, 3%), skills of midwives who were less likely to show good midwife performance (78.9%), poor midwife skills tended to show poor midwife self management (60.6%).

The knowledge of midwives about excellent self management tends to have excellent midwifery service performance (62.6%), good knowledge, tends to perform very well (63.0%), sufficient knowledge of performance tends to be good (45.8%), lack of knowledge tends to perform very well (45.5%) and poor knowledge of performance tends to be very good (29.4%).

The skills of a very good midwife tend to show very good performance (77.6%), good midwife skills tend to show good performance (47.3%), sufficient skills of midwives tend to perform very well (40.5%), skills midwives who are less likely to perform very well (42.1%), poor midwife skills tend to be balanced between good and very good performance, each (27.3%).

Very good midwife self management tends to midwife’s performance in midwifery services is also very good (87.7%), good midwife self-management midwife performance also tends to be good (45.8%), midwife self-management that is quite midwife performance tends to be good (39, 1%), midwives’ self-management that lacked the performance of midwives tended to be lacking (40.0%) and poor self management the performance of midwives tended to be very good (40%).

The inner model is including the goodness of fit, which is the value of the R Square of the dependent latent variable as in table 1:

No	Variable	R Square	R Square Adjusted
1	Y. Performance of Midwives	0.792	0.784
2	Z. Self Management	0.795	0.788

The influence between variables is as follows:

a. Knowledge of midwives has a significant effect on midwife’s self management, self management has a significant effect on midwife’s performance, meaning that knowledge of midwives has a significant effect on midwife’s performance through self management. The results of this study indicate

that the knowledge of very good midwives tends to influence excellent self-management, which can also influence the tendency of midwives’ performance to be very good. This shows that the better the knowledge of midwives about self management can encourage the better implementation of self management, which can influence the performance of midwives to be better.

- b. The skills of midwives significantly influence midwife’s self management, self management significantly influences the performance of midwives, meaning that the skills of midwives significantly influence the performance of midwives through self management. The results of this study indicate that the skills of very good midwives tend to influence self-management which is very good, which can also influence the tendency of midwives’ performance to be very good. This shows that the better the skills of midwives can encourage better self management, which can influence the performance of midwives to be better
- c. Self management has a significant effect on the performance of midwives, the results of this study indicate that self management which tends to be very influential also affects the tendency of midwives’ performance to be very good. This shows that the better the midwife’s self management can encourage the performance of the midwife to be better
- d. Knowledge of midwives mediated by self management has a significant effect on the performance of midwives. This shows that the knowledge of midwives mediated by good self management can encourage the performance of midwives to be better.
- e. The skills of midwives mediated by self management significantly influence the performance of midwives. This shows that the skills of midwives mediated by good self management can encourage the performance of midwives to be better.

Discussion

Individual factors (knowledge) of midwives about self management, the results of the study showed that the knowledge of midwives about self-management was mostly good. According to Sharma et al (2015)⁽³⁾ the assessment is based on a criterion that is self-determined or uses existing criteria. In this study the measured knowledge of midwives about self management. The

knowledge of midwives in Kupang District Health Center is mostly good, meaning that most midwives already know about self management, have understood it, have applied it, have the ability to analyze and have the ability to evaluate what they are doing.

The individual factors (skills) of midwives about self management, the results of the study showed that the skills of midwives in implementing self management were mostly very good. Skills are the ability to do a physical or mental work. Allan et al (2013)⁽⁸⁾ say that skills are aspects of behavior that can be learned through exercises that are used to fill the workplace; skills not only require training, but the basic abilities that each person has can help produce something more valuable faster. Skills are the capacity needed to carry out a series of tasks that develop from the results of training and experience. A person's expertise is reflected by how well someone is carrying out a specific activity, such as operating an equipment, communicating effectively or implementing a business strategy. Most midwives have excellent skills in implementing self management in carrying out Varney's 7-step midwifery management. This can be interpreted that most midwives already have expertise in solving midwifery problems using their logic.

The influence of individual factors (knowledge) midwives on self management gets p values = 0.013, the knowledge ability of midwives to develop self management is very significant, where there are 6 self management skills, namely: problem solving, decision making, resource utilization, the formation of a patient-provider⁽⁹⁾ partnership, action planning and self-tailoring, this is in line with those recommended by the International Confederation of Midwives

The influence of individual factors (skills) midwives on self management get p values = 0.015, Midwives who have self management will be able to build Building performance skills, do exercises to improve their ability to work. In carrying out the work that is the main task of each employee, performance is displayed in the form of achievement. Effective and efficient performance management is carried out as an activity to help employees discover their potential abilities that are followed up by providing opportunities to make them become achievement through their placement in the field of work or position in accordance with their potential abilities. The performance of individuals is not something that is static, but always dynamic in the sense

that it can increase in height or vice versa to decrease or be low. So that everyone wants to achieve progress in work. Progress can only be achieved if someone is able to display satisfactory performance, including higher work productivity.

The influence of individual factors (knowledge) on midwives in implementing self management on the performance of midwives obtained p values = 0.02. This is in accordance with the results of the study from Moattari, et al (2012)⁽¹⁰⁾ who wrote that there was a correlation between physiological factors of knowledge, motivational factors, leadership factors, incentive/reward factors and co-worker factors with midwives' performance in Iranian services.

The effect of individual midwives (skills) in implementing self management on the performance of midwives obtained p values = 0.02. In line with the study of Karvande, et al (2018)⁽¹¹⁾ who wrote that the skills of midwives who are often honed make their self-management fundamentally improve performance

The effect of the implementation of self management on the performance of midwives in the health service obtained p values = 0.02. Self management in education, psychology, and business terminology is a method, skill and strategy that can be done by individuals in effectively directing the achievement of the objectives of the activities they perform, including goal setting, planning, scheduling, task tracking, self evaluation, self intervention, self development. In addition, self management is also known as the execution process (decision making).

This study, Varney's 7-step midwifery management was modified with the aim that midwives can provide midwifery services well by doing self-management on their own by modifying self management adapted from Corbin and Charles (2017)⁽¹²⁾ consisting of 8 cell steps

Conclusions

Individual factors (knowledge and skills) directly and indirectly influence the performance of midwives with self-management as mediation.

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References

1. Kementerian Kesehatan. PERMENKES No. 28 Tahun 2017. 2017. p. 1–48.
2. Ghahramanian A, Rezaei T, Abdullahzadeh F, Sheikhalipour Z, Dianat I. Quality of healthcare services and its relationship with patient safety culture and nurse-physician professional communication. *Heal Promot Perspect* [Internet]. 2017;7(3):168–74. Available from: <http://dx.doi.org/10.15171/hpp.2017.30>
3. Sharma B, Hildingsson I, Johansson E, Prakasamma M, Ramani K V., Christensson K. Do the pre-service education programmes for midwives in India prepare confident “registered midwives”? A survey from India. *Glob Health Action*. 2015;8:1-9.
4. Franklin N, Melville P. Competency assessment tools: An exploration of the pedagogical issues facing competency assessment for nurses in the clinical environment. *Collegian* [Internet]. 2015;22(1):25–31. Available from: <http://dx.doi.org/10.1016/j.colegn.2013.10.005>
5. Dinas Kesehatan Prov. NTT. Profil Kesehatan Prov. NTT Tahun 2015. 2016;12.
6. Young K, Young K. *Theories of Personality. Personality and Problems of Adjustment*. 2018. 276–300 p.
7. Helen Varney, Jan M. Krlebs CLG. *Varney’s Midwifery*. 2004.
8. Alan S, Ozturk M, Gokyildiz S, Avcibay B, Karatas Y. An evaluation of knowledge of pharmacovigilance among nurses and midwives in Turkey. Vol. 45, *Indian Journal of Pharmacology*. 2013. p. 616.
9. International Confederation of Midwives. *Model Curriculum Outlines for Professional Midwifery Education*. 2012;(June 2012):15.
10. Moattari M, Shafakhah M. Assessing Stages of Exercise Behavior Change, Self Efficacy and Decisional Balance in Iranian Nursing and Midwifery Students. 2013;1(2):121–9.
11. Karvande S, Sonawane D, Samal J, Mistry N. Family planning training needs of auxiliary nurse midwives in Jharkhand, India: Lessons from an assessment. *Natl Med J India*. 2018;31(2):73–8.
12. Corbin CB, Masurier GC Le, Lambdin DD, Charles B, Masurier GC Le, Dolly D. *Fitness For Life*. 2007;117.

Health Literacy on Weighing Control and Use of Weight Loss Products among Working-age Women in the Northeast of Thailand

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Abstract

This cross-sectional study aimed to describe weight loss products' use patterns and identify the association of health literacy on weight control and weight loss products use among working-age women in the Northeast of Thailand. The study was conducted among 1,190 respondents who were multistage randomly selected from 4 provinces of the Northeast region. Data were collected using a self-administered structured questionnaire. The generalized linear mixed model (GLMM) was used to identify the association between health literacy and weight loss products use when controlling the effects of other covariate presenting adjusted OR and 95% confidence interval. The results indicated that 23.19% (95% CI = 20.79-25.59) of the respondents ever used weight loss products, of which 11.60% (95% CI = 9.77-13.41) were current users. Levels of health literacy on weight control was statistically significant with weight loss products use including having; sufficient level of health literacy (adj. OR = 2.62: 95% CI=1.59-4.31, p-value <0.001), problematic level of health literacy (adj. OR = 4.71: 95% CI=2.87-7.72, p-value <0.001) and inadequate level of health literacy (adj. OR = 10.97: 95% CI=6.17-19.51, p-value <0.001) when compared with having excellence level. The significant covariate was had waist circumference \geq 80 cm. (Adj. OR = 4.12: 95% CI = 2.79-6.11, p-value =0.025), finished lower than bachelor degree (adj. OR = 2.11, 95% CI = 1.78-3.70, p-value <0.001), had average monthly income \geq 15,000 THB =(adj. OR = 3.08: 95% CI = 2.20-4.31, p-value <0.001), About twenty three percent of working-age women ever used weight loss products. Health literacy was highly associated with used weight loss products.

Keyword: *Weight loss products, Health literacy, working-age women.*

Introduction

Overweight and obesity cause various health problems all over the world¹, obesity particular is one of the main causes of morbidity and mortality² especially cardiovascular disease (CVD). Awareness of the serious health consequences, people turn their attention to weight control to be within the standard³. It is widely accepted that lifestyle modification, such as healthy dietary habits and regular physical activity is necessary for weight control, however, with a long term effort⁴. Therefore,

many people use various weight loss products because they are quicker and easier than exercising or dieting⁵. Although this method is dangerous or has many side effects⁶, as well as being unable to confirm the weight loss results as to whether or not effective⁷. The main target groups of these products are working women⁸. Because he or she is a person with financial readiness, able to make independent purchase decisions and pay attention to the shape⁹.

Health literacy is linked to the ability of individuals to understand and apply health information to practice for disease prevention and health promotion¹⁰. People with an excellent level of health literacy should be less likely to use weight loss products since they are well aware of their complications than those with inadequate health literacy. Social-cognitive factors also play an important role in behavioral determination¹¹.

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Although different health behavior theories have been used to explain weight management, roles of social-cognitive factors on weight loss remain poorly understood¹². Also, there is limited evidence concerning the influence of socio-demographic gradients on dieting and attempts at weight loss¹³ such as women are more likely to concern about their shape.

The Northeastern region of Thailand is the biggest region both in terms of areas and population. Most of the labor forces of the country are from this region. With the long term continuously economic expansion, there has been an increasing trend of overweight and obesity among northeastern women. Therefore it is essential to the determinants of weight loss products use among them.

Objective: To describe the weight loss products use and identify the association between health literacy on weight control and weight loss products use among working-age women in the Northeast of Thailand.

Materials and Method

This cross-sectional study was conducted in 2019. The population was working-age women aged 20 to 59 years old in the Northeast of Thailand. The sample size was calculated by using the sample size estimation formula for the logistic regression analysis of Hsieh¹⁴. The estimated sample size was 1,190. The respondent was recruited from 4 provinces of the Northeast of Thailand by using multi-stage random sampling method to respond to a structured questionnaire.

Data Analysis: All analyses were performed using Stata version 10.0 (Stata Corp, College Station, TX). Descriptive statistics including frequency and percentage to describe categorical data whereas mean, standard deviation, median, and maximum-minimum for continuous data. A simple logistic regression was used to identify individual the association between each independent variable and weight loss products use. The independent factors that had p-value <0.25¹⁵ were processed to the multi variable analysis using the generalized linear mixed model (GLMM) to identify the association between health literacy and weight loss products use when controlling the effect of other covariates, of which 4 provinces were selected to include as random effects. The magnitude of association was presented as adjusted odds ratio (Adj. OR), 95% confidence interval (CI) and p-value <0.05 as statistical significant level.

Result

Socio-demographic: The average age of the respondents was 39.46 ±10.71 years old, 58.74 were married, 67.15 percent had education lower than a bachelor’s degree. the occupation was employee 25.04 percent, an average monthly income 10,000-19,999 baht, average monthly expenditures less than 10,000 baht, normal body mass index 40 percent, waist circumference exceeds the standard threshold 50.25 percent without chronic disease 86.47 and healthy status of 81.26 percent.

Almost a quarter of the respondents ever used weight loss products (23.19%: 95% CI = 20.79-25.59) of which 11.60% (95% CI = 9.77-13.41) were current users. The most common type of weight loss product use were diet pills which were consumed by 7.84% of the respondents, followed by diet coffee (6.68%) and fiber products (4.50%), see table 1

Table 1: Number and percentage of weight loss products use pattern (n = 1,190 people)

Weight loss products use pattern	Number	Percent
1. Weight loss products use		
Currently, use	138	11.60
Used for less than 6 months and stop using	39	3.28
Used for more than 6 months and stop using	99	8.32
Never used but would like to use in the future	90	7.56
Never used and want to use	824	69.24
2.Type of weight loss product use (Can answer more than 1 question)		
Diet pills	101	7.84
Diet coffee for weight loss	86	6.68
Fiber products	58	4.50
Konjac Extract	55	4.27
Wearable products for weight loss	12	0.93
Tea products	11	0.85
A traditional procedure such as massage	10	0.78
Chitosan	9	0.70
Weight loss program	8	0.62
Equipment	7	0.54
Garcinia extract	5	0.39
Increased metabolism products	4	0.31
Other weight loss products	8	0.62
Do not use weight loss products	914	70.96

Association between health literacy and weight loss products use among northeastern working women when controlling other covariates: a multivariable analysis: Association between health literacy and weight loss products use among northeastern workingwomen were identified by using the Generalized Linear Mixed Model (GLMM) to control the clustering effect in each health zone. The results indicated that levels health literacy were associated with weight loss products use including had sufficient level of health literacy (adj. OR = 2.62 :95% CI=1.59-4.31, p-value <0.001), had problematic level of health literacy (adj.

OR = 4.71:95% CI=2.87-7.72, p-value <0.001) and had inadequate level health literacy 10.97 times the use of weight loss products for those with excellent health literacy (adj. OR = 10.97: 95% CI=6.17-19.51, p-value <0.001) when compared with those with excellent level of health literacy. The other significant covariates were, those with waist circumference ≥ 80 cm. (adj. OR = 4.12: 95% CI = 2.79-6.11, p-value =0.025), graduated bachelor **degree or higher** (adj. OR = 2.11,95% CI = 1.78-3.70, p-value <0.001), had average monthly income $\geq 15,000$ THB (adj. OR = 3.08:95% CI = 2.20-4.31, p-value <0.001), see Table 2.

Table 2: Association between health literacy and weight loss products use among northeastern working women when controlling other covariates: a multivariable analysis using GLMM

Factors	Number	Percent	Crude OR	Adj. OR	95%CI	P-value
Health literacy						
Excellent	320	9.69	1	1	1.60-4.24	<0.001
Sufficient	407	18.92	2.17	2.61	2.88-7.61	<0.001
Problematic	331	30.32	4.15	4.68	6.04-18.62	<0.001
Inadequate	132	50.00	9.32	10.60		
Education level						
\geq Bachelor Degree	391	18.41	1	1	1.78-3.70	<0.001
<Bachelor Degree	799	25.53	1.52	2.57		
Income per month (THB)						
<15,000	667	15.59	1	1	2.20-4.31	<0.001
$\geq 15,000$	523	32.89	2.65	3.08		
Waist circumference(cm.)						
<80	588	10.54	1	1	4.48-8.98	<0.001
≥ 80	602	35.55	4.68	6.31		

Discussion

This present study observed that about 23% of working-age women ever used weight loss products. This proportion was a little lower than those found in a study in 2015 in Bangkok, Thailand indicated that 27.7% of the respondents used weight loss products¹⁶. However, it was higher than those found in a study in 2017 in Ratchaburi Province, Thailand that observed that 19.6% of the participants used weight loss products¹⁷. A possible explanation was that there was a higher level of economic development in Bangkok, people have higher income and might concern about shape more than the northeasterners. Ratchaburi, on the other hand, had a lower income. The multivariable analysis of this study also indicated that higher income had a high influence on weight loss products use (adj. OR = 3.08) which was similar to a study in Sweden¹³.

Health literacy (HL) played an important role in weight loss products use. Our finding indicated that those who had excellence level of health literacy on weight control were less likely to use weight loss products when compared to those who had sufficient, problematic, and inadequate levels of HL (adj. OR= 2.61, 4.68, and 10.60 respectively). A study of Cheong et al. Indicated that HL had a positive impact on weight loss behaviors. There was also evidence that interventions focusing on improving knowledge and HL skills could effectively control the weight¹⁸. HL influences reach and moderates weight effects. These findings underscore the need to integrate recruitment strategies and further evaluate programmatic approaches that attend to the needs of low-HL audiences. HL is necessary and an important indicator when making decisions about weight loss products. Having HL can influence the choice and

decision not to use weight loss products. Therefore, encouraging the public to have good HL will help people to avoid using weight loss products and choose to use the right weight control¹⁹. Our finding also observed that there were socioeconomic gradients to overall health and showed that those with lower levels of education had poorer health and higher mortality. A previous study of Barbering et.al¹³ also indicated that proper dietary regimen and overweight were associated with higher education levels. Similarly a studied of Ball observed that males who were married, living in households with shared income and who had less education were more likely to use weight loss products²⁰. Waist circumference(WC) is one of the conditions of metabolic syndrome, which is an important risk factor of cardiovascular disease²¹. Women with higher WC have a bigger belly which made them looked fat. This might lead to more concern about weight loss. They might try to reduce the WC as quick as possible by using weight loss products²². Therefore, it requires effective measures to improve health literacy on appropriate weight control especially among those with lower education having a big belly and had a higher income that has more purchasing power.

Conclusion

The study indicated that about 23 percent of working-age women never used weight loss products. Health literacy was highly associated with used weight loss products when considering the influenced of waist circumference, educational level, and income.

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References

1. Organization WH. Obesity and Overweight [Fact Sheet No 311], 2012. Geneva: World Health Organization. 2015.
2. Lopez-Gomez JJ, Izaola-Jauregui O, Primo-Martin D, Torres-Torres B, Gomez-Hoyos E, Ortola-Buigues A, et al. Effect of weight loss on bone metabolism in postmenopausal obese women with osteoarthritis. *Obes Res Clin Pract.* 2019;13(4):378-84.
3. Unick JL, Ross KM, Wing RR. Factors associated with early non-response within an Internet-based behavioural weight loss program. *Obes Sci Pract.* 2019;5(4):324-32.
4. Rao G. Office-based strategies for the management of obesity. *American family physician.* 2010;81(12):1449.
5. Burns RD. Energy balance-related factors associating with adolescent weight loss intent: evidence from the 2017 National Youth Risk Behavior Survey. *BMC Public Health.* 2019;19(1):1206.
6. Yang N, Chung D, Liu C, Liang B, Li XM. Weight loss herbal intervention therapy (W-LHIT) a non-appetite suppressing natural product controls weight and lowers cholesterol and glucose levels in a murine model. *BMC Complement Altern Med.* 2014;14:261.
7. Manore MM. Dietary supplements for improving body composition and reducing body weight: where is the evidence? *International journal of sport nutrition and exercise metabolism.* 2012;22(2):139-54.
8. Vitalone A, Menniti-Ippolito F, Moro PA, Firenzuoli F, Raschetti R, Mazzanti G. Suspected adverse reactions associated with herbal products used for weight loss: a case series reported to the Italian National Institute of Health. *Eur J Clin Pharmacol.* 2011;67(3):215-24.
9. Grogan S. *Body image: Understanding body dissatisfaction in men, women and children:* Routledge; 2016.
10. Sørensen K, Van den Broucke S, Fullam J, Doyle G, Pelikan J, Slonska Z, et al. Health literacy and public health: a systematic review and integration of definitions and models. *BMC public health.* 2012;12(1):80.
11. Hansen S, Huttunen-Lenz M, Sluik D, Brand-Miller J, Drummen M, Fogelholm M, et al. Demographic and Social-Cognitive Factors Associated with Weight Loss in Overweight, Pre-diabetic Participants of the PREVIEW Study. *Int J Behav Med.* 2018;25(6):682-92.
12. Byrne S, Barry D, Petry NM. Predictors of weight loss success. Exercise vs. dietary self-efficacy and treatment attendance. *Appetite.* 2012;58(2):695-8.

13. Barebring L, Winkvist A, Augustin H. Sociodemographic factors associated with reported attempts at weight loss and specific dietary regimens in Sweden: The SWEDIET-2017 study. *PLoS One*. 2018;13(5):e0197099.
14. Hsieh FY, Bloch DA, Larsen MD. A simple method of sample size calculation for linear and logistic regression. *Statistics in medicine*. 1998;17(14):1623-34.
15. Hosmer David W, Stanley L. *Applied logistic regression*. New York: Wiley; 2000.
16. Vinijchaiyanun C. Factors Affecting Weight Control Dietary Supplements Consumption of People in Bangkok. *WMS Journal of Management Walailak University*. 2017;Vol.6 (No.1 (Jan – Apr 2017)): 84-90.
17. Kanogporn Maneemas PM. Factors Associated with Consumption of Food Products with the Claim of WeightControl amongFemale Students in Vocational Certificate Level: Case Study of Ratchaburi Technical College. *Thai Journal of Pharmacy Practice*. 2019;11(1(Sep – Nov 2019)):775-86.
18. Faruqi N, Spooner C, Joshi C, Lloyd J, Dennis S, Stocks N, et al. Primary health care-level interventions targeting health literacy and their effect on weight loss: a systematic review. *BMC Obes*. 2015;2:6.
19. Zoellner J, You W, Almeida F, Blackman KC, Harden S, Glasgow RE, et al. The Influence of Health Literacy on Reach, Retention, and Success in a Worksite Weight Loss Program. *Am J Health Promot*. 2016;30(4):279-82.
20. Zhu S, Wang Z, Heshka S, Heo M, Faith MS, Heymsfield SB. Waist circumference and obesity-associated risk factors among whites in the third National Health and Nutrition Examination Survey: clinical action thresholds. *The American journal of clinical nutrition*. 2002;76(4):743-.
21. Hou X, Lu J, Weng J, Ji L, Shan Z, Liu J, et al. Impact of waist circumference and body mass index on risk of cardiometabolic disorder and cardiovascular disease in Chinese adults: a national diabetes and metabolic disorders survey. *PLoS one*. 2013;8(3):e57319.
22. Klein S, Allison DB, Heymsfield SB, Kelley DE, Leibel RL, Nonas C, et al. Waist circumference and cardiometabolic risk: a consensus statement from shaping America's health: Association for Weight Management and Obesity Prevention; NAASO, the Obesity Society; the American Society for Nutrition; and the American Diabetes Association. *Obesity*. 2007;15(5):1061-7.

Oko Mama Culture Betel Nut Consuming Habit in Kupang District and its Effect toward Salivary Ph and Flow Rate

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Abstract

Public health always associated to culture and lifestyle. Lifestyle itself constitutes a concept that commonly used to define “The way people live”, reflecting the whole social value, attitude, and activity. One of long-term culture that become personal habit is chewing betel nut. Oko Mama culture is the local culture of the Timorese tribe who consider it as the symbol of philosophy, dignity, enjoyment, beauty, also as a means of communication in society, political means, and delaying hunger. Several studies revealed several unbeneficial of chewing betel nut, such as acute betel nut toxicity, cardiovascular disease, respiratory disorder, and congenital defect. Besides, betel nut may also alter oral health. This study is aiming to analyse the correlation of habitual chewing betel nut toward salivary pH and flow rate. This was an observational analytic study, by means of cross sectional design involving both on male and female aging 17-50 years old in 4 sub-district, consisting of 2 remote areas and 2 urban areas. The correlation between variables was analysed using path analysis by means of Smart PLS 3.2.7. The analysis revealed a positive correlation between Oko Mama culture toward behaviour ($p=0.316$) and intention ($p= 0.454$), also a negative correlation between the culture toward oral hygiene knowledge ($p=-0.185$) and the effect of chewing betel nut knowledge ($p = -0.111$). A positive correlation also recorded toward perceived norm ($p=0.931$). While intention had a positive correlation toward behaviour ($p=0.429$). Regarding oral health, chewing betel nut had negative effect toward salivary pH ($p=-0.167$) and salivary flow rate ($p=-0.210$).

Keywords: *Community habit, betel nut, salivary pH, flow rate.*

Introduction

Public health is an integrated matter with the local culture. The society in each region have their own concept of health, as the important part of the culture. Betel nut chewing denotes an old habit of the society in Kupang. A prior study revealed that in Oelnaineno, sub district Takari, Kupang, 94% people aged 17-60 years old chew betel nut. The betel nut usually mixed with betel, areca nut, lime, sometimes the other ingredients were added, such as nutmeg, cloves, and even tobacco⁽¹⁾.

The Oko Mama culture, that used betel nut in various occasion in daily life, thus, it can be found in every household in Timor. Oko Mama is the Timorese tribes culture, that chew the betel nut as the symbol of philosophy, dignity, enjoyment, beauty, also as a means of communication in society, political means, and

delaying hunger. This culture denotes the factor that drives the society to chew betel nut to date⁽²⁾.

Studies revealed that chewing betel nut might induce oral precancerous lesion which highly tend to become cancer. The areca nut itself has been classified as class I carcinogenic agent by the International Research Agency for Research Cancer⁽³⁾. Areca nut only, has significant impact toward health, thus, tobacco addition may rise worsen health consequence, even death. After chewing betel nut, several symptoms may appear, such as headache, tachycardia, hot sensation and sweating, epigastric discomfort, hyperventilation, thirst and hunger diminish, relax, and overexcited⁽¹⁾. Areca nut contain arecolin, that possibly toxic toward periodontal tissue, thus, may worsen the periodontal status⁽⁴⁾.

The betel nut is addictive to its chewers. The tint

from betel nut can penetrate into oral mucosa, and teeth, yet may disappear if strongly rubbed by areca skin⁽⁵⁾. The tooth discoloration due to betel nut chewing may prevent tooth demineralization. Several studies had proved that betel nut could reduce the caries prevalence⁽⁶⁾⁽⁷⁾⁽⁸⁾.

Considering the high number of betel nut chewers and its effect toward health, thus, it is important to analyse the Oko Mama culture, related to the habit of chewing betel nut and its effect toward caries. It is expected to be able to help the attempt to reduce betel nut chewers in Kupang, East Nusa Tenggara as it is dangerous to their health, especially their dental health. This research aiming to syntheses a theory of Fishbein Integrated Behaviour Model with Dunn Behavioural theory which including culture as the factor that influence someone behaviour.

Material and Method

This observational analytic study employed a cross sectional design. The sub district South Amfoang and Takari, denotes remote areas, while the urban areas were sub district Nekamese and Kupang Centre. Those selected areas had the most population. The subject of this study were the inhabitants aged 17-50 years old. As much as 363 peoples were randomly chosen from 146.597, calculated using estimated proportion population formula.

The criteria for the respondents were male and female who chewed betel nut, and those who did not from those 4 selected areas. The respondents were asked to fill a questionnaire. The acquired data were

analysed by means of path analysis by PLS 3.2.7 to find a correlation among variables. We hypothesized eleven theories; 1) there is a correlation between attitude and intention; 2) there is a correlation between perceive norm and intention; 3) self-efficacy affect the intention; 4) Oko Mama culture affect intention; 5) Oko Mama culture affect behaviour; 6) intention affect behaviour; 7) oral health knowledge affect behaviour; 8) disease knowledge affect behaviour; 9) habit affect behaviour; 10) behaviour affect salivary flow rate; 11) behaviour affect salivary pH.

Results

The respondents participated in this study consisted of 51.5% female and 48.5% male. The total of betel nut chewers was dominated by female (52.8%). Among the population, the betel nut chewers (79.9%) were more than those who do not chew betel nut (20.1%). Mostly respondents were aged 41-50 years old (43.8%), while the respondents aged less than 20 were the minority (11.3%). The younger the respondents, the less they chew betel nut. Most of the respondents were farmers (82.6%), with the last education was elementary school (59.2%).

The habit of betel nut chewing more than 5 times a day were done by 37.5% of the respondents. The average frequency of betel nut chewing was twice a day. A portion of 51.8% the respondents has been chewing betel nut for 10 years or more, with 58.1% of them chewed betel nut with lime and areca nut. The majority of the respondents learn to chew betel nut form their parents (96,9%).

Table 1. Result from Path Analyzes

Path	Original Sample (O)	Mean (M)	SD	T Statistic (O/STDEV)	P Values
Attitude → Intention	0,290	0,293	0,058	4,978	0,000
Behavior → SFR	-0,210	-0,208	0,053	3,933	0,000
Behavior → pH	-0,167	-0,166	0,046	3,617	0,000
Intention → Behavior	0,428	0,415	0,099	4,323	0,000
Oko Mama → Behavior	0,316	0,315	0,058	5,467	0,000
Oko Mama → Intention	0,463	0,453	0,098	4,739	0,000
Oko Mama → Perceived Norm	0,931	0,931	0,013	73,796	0,000
Habit → Behavior	0,232	0,246	0,098	2,378	0,018
Oral Health Knowledge → Behavior	-0,020	-0,019	0,016	1,213	0,226
Betel nut knowledge → Behavior	-0,013	-0,013	0,018	0,718	0,473
Perceived Norm → Intention	-0,202	-0,202	0,080	2,522	0,012
Self-confidence → Intention	0,414	0,422	0,096	4,296	0,000

Similar to TRA/TPB, the most important predisposing factors in Integrated Behaviour Model (IBM) is intention. Intention defined as individual decision indicator to do a certain behaviour. Without intention, behaviour will not be built. The intention itself was determined by attitude, perceived norm, and self-efficacy to start doing betel nut chewing as habit. This study used 4 variables based on the IBM that affect the intention to chew betel nut, that are attitude, perceived norm, self-confidence and Oko Mama culture. Based on the result from table 1, there were 2 rejected hypotheses, that are 1) oral health knowledge have no effect toward behaviour ($p > 0.05$), and 2) disease knowledge have no effect toward betel nut chewing ($p > 0.05$).

Attitude had significant correlation toward intention as much as 0.278 ($p < 0.05$), while perceived norm also had significant correlation toward intention as much as -0.191 ($p < 0.05$). Self-confidence significantly affect intention as much as 0.417 ($p < 0.05$). Intention had significant effect toward betel nut chewing as much as 0.429 ($p < 0.05$). Oko mama's culture significantly affects the intention to consume betel nut at 0.454 (p value 0,000). The Oko mama culture significantly affects the Behavior of consuming betel nut by 0,316 (p value 0,000). The habit of consuming betel nut significantly affects the salivary pH of -0.167 (p Value 0,000). The habit of consuming betel nut significantly affects the salivary flow rate of -0,210 (p value 0,000). The Behaviour Hypothesis influences the Saliva Flow Rate in the habit of consuming betel nut analysed by looking at the Path Coefficients (table 1). This hypothesis is accepted significantly because Path Behaviour to the Saliva Flow Rate has a p-value of 0,000 and the value of t-statistics 3,933 and Path Coefficients -0,210. The hypothesis is accepted because p-value is less than 0.05 and t statistic is more than 1.96. From these results it can be concluded that the Behaviour has a negative effect of -0.210 on the salivary flow rate.

Discussion

The behaviour of chewing betel nut affects salivary flow rate, may possibly due to the reduce in salivary secretion or salivary properties changes while they are not chewing betel nut. This condition may contribute to several oral and dental diseases, that directly affect the quality of life. Several studies stated that the normal unstimulated salivary flow rate is 0.3-0.5 ml per minute⁽⁹⁾⁽¹⁰⁾, while stimulated salivary flow rate is 10ml per minute⁽¹¹⁾⁽¹²⁾. The significant changes of salivary

flow rate affect dental and oral health⁽¹²⁾. The functional changes of salivary gland, is related to oral cavity, throat, oesophagus, neoplasm, nutrition metabolism, inflammation, genetic disease, auto-immune disease, and nervous system damage. The varied salivary flow rate also depends on the time of measurement. Those variations in 24hours depends on the circadian rhythm. Besides, other factors also contribute, such as age and gender.

Several studies recorded that unstimulated normal salivary pH ranged from 5.5 to 7.9, the higher pH, the higher salivary flow rate⁽¹²⁾⁽¹³⁾. Salivary pH is controlled by carbonate/bicarbonate acid system, phosphate system, and protein system. A study revealed several rate of salivary flow from chewing 4 kinds of betel nutmixture, and raw areca nut only, which resulted the highest mean of salivary flow rate recorded was 4.18ml in 10 minutes⁽¹¹⁾. A decrease of salivary secretion or changes in saliva properties may also contribute to several oral and dental problems, that directly affect the quality of life. Some of those problems are speak and eat difficulty, taste perception changes, increase plaque formation, increase risk of caries, tooth erosion and periodontal disease, increase of plaque formation, mucosal irritation, halitosis, and candidiasis, also decrease the retention of full denture. Those aforementioned oral and dental problems may also affect general health, since the affected individual may experience lost appetite, that leading to malnutrition⁽¹⁴⁾.

There is a significant correlation between chewing betel nut with salivary flow rate. A study revealed unstimulated salivary flowrate in betel nut chewers was basically same to those who do not, yet the when stimulated, the chewer group had a higher flow rate⁽¹⁵⁾. This is possibly caused by the increase of sensitivity and salivary mechanism due to areca nut and tobacco. There is an opinion, that this also probably due to salivary gland hyperplasia, and masticatory muscle hypertrophy in long-term betel nut chewer⁽¹⁶⁾. Besides, oral mucosa also become more sensitive due to toxic effect of betel nut⁽¹¹⁾⁽¹⁵⁾. However, those changes do not affect masticatory efficacy⁽¹⁵⁾⁽¹⁷⁾. Another study showed that the salivary flow rate and pH of the carious and free-caries subject were not significantly different⁽¹⁸⁾. Also no significant differences of salivary flow rate between those subjects. Enamel demineralization may occur in $pH < 5.5$ ⁽¹⁹⁾. The mean pH of the respondents chewing betel nut was 6.6, while those who don't was 6.78⁽¹⁸⁾.

There was a significant correlation found between betel nut behaviour with the salivary pH ($p=0.000$; t -statistic 3.617 and path coefficient -0.167). Behaviour had negative correlation to salivary pH (-0.21). The current study found changes of salivary pH and flow rate in betel nut chewer, which may lead to various oral diseases⁽²⁰⁾. Betel nut chewing denotes socio-cultural expression (Okó Mama), which significantly affect the perceived norm (0.931). The importance of culture affect how the society will behave. Besides, betel nut chewing also noted as social identifier, to be considered as cultured and ethical individual. Some individuals do betel nut chewing in order to be recognized as the member of society⁽²¹⁾.

That the areca nut availability promotes betel nut chewing behaviour. Since betel nut is easily found in every household, makes it easier to consume and mostly the chewer firstly learnt from their parents⁽²²⁾. That in several cases, betel nut chewing was done due to the social pressure, and the desire to be recognised⁽²¹⁾. WHO summarized that betel nut is correlated to oral cancer prevalence⁽²³⁾. Oral carcinoma due to betel nut chewing denotes aggressive malignancy that required intensive treatments⁽²⁴⁾. While the society have not fully understood about cancer, thus, this need a long-term attempt of prevention. Betel nut chewing was not an oral and pharynx potentially malignant disorder (OPMD) only, but also may be the predisposing factors of other diseases. The high prevalence of betel nut chewing increase the incidence of hepatic cancer. Besides, betel nut chewing also affect cardiovascular, nervous system, digestive system, metabolism, respiratory system, and reproductive system⁽²⁵⁾.

To date, there has not any global policy regarding betel nut chewing. Multidisciplinary research is required to control this phenomenon, and further studies to get a better understanding in basic biology, mechanism, and epidemiology of betel nut chewing. This may encourage the prevention, also, stop the betel nut chewing for a better health. Those attempts are betel nut uses monitoring, continuous educate the society to stop the habit, by utilizing advertisement board, and increase areca nut tax.

Conclusion

Okó Mama culture affects intention to chew betel nut, and also affect the behaviour to chew betel nut. The betel nut chewing behaviour affects salivary pH and flow

rate. The habit of betel nut chewing shows a change in salivary pH and flow rate. Those changes contribute in the occurrence of oral diseases. Complex behaviour of betel nut chewing is reflected in varied salivary pH and flow rate.

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References

1. Thavarajah R, Joshua E, Anusa A, Kumar Govind G. Health hazards of chewing areca nut and products containing arecanut. *Calicut Med J.* 2005;3(2).
2. Nome Y. Okó Mama as an Timorese Tradition (Okó Mama sebagai tradisi Orang Timor). *Pos Kupang.* Kupang, NTT; 2015 Sep 12;
3. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. *Betel Quid and Arecanut Chewing. Other Data Relevant to an Evaluation of Carcinogenicity and Its Mechanisms.* France: Lyon; 2004.
4. Trivedy CR, Craig G, Warnakulasuriya S. The Oral Health Consequences of Chewing Areca Nut. *Addict Biol.* 2002;7(1):115–25.
5. Norton SA. Betel: Consumption and Consequences. *J Am Acad Dermatol.* 1998;38(1):81–8.
6. Möller I, Pindborg J, Effendi I. The Relation Between Betel Chewing and Dental Caries. *Scand J Dent Res.* 1977;85(1):64–70.
7. Howden GF. The Cariostatic Effect of Betel Nut Chewing. *Papua New Guinea Med J.* 1984;27(3–4):123–31.
8. Nigam P, Srivastava AB. Betel Chewing and Dental Decay. *Fed Oper Dent.* 1990;1(1):36–8.

9. Garrett JR. The Proper Role of Nerves in Salivary Secretion: A Review. *J Dent Res.* 1987;66:387–97.
10. Ghezzi EM, Lange LA, Ship JA. Determination of Variation of Stimulated Salivary Flow Rates. *J Dent Res.* 2000;79(11):1874–8.
11. Thavarajah R, Mishra G, Elizabeth J, Ranganathan K. Effect of Habitual Areca Nut Chewing on Resting Whole Mouth Salivary Flow Rate and pH. *Indian J Med Sci.* 2006;60(3):95–105.
12. Choo RE, Huestis MA. Oral Fluid as a Diagnostic Tool. *Clin Chem Lab Med.* 2004;42(11):1273–87.
13. Drobitch RK, Svensson CK. Therapeutic Drug Monitoring in Saliva. An Update. *Clin Pharmacokinet.* 1992;23(5):365–79.
14. Walsh M, Kuhn S. Developments in Personalised Nutrition. *Nutr Bull.* 2012;37(4):380–3.
15. Khan GJ, Ishaq M. Salivary Flow Rates in Paan “Tobacco-Betel-Lime Quid” Chewers. *J Med Sci.* 2012;20(1):29–32.
16. Ono K, Marimoto Y, Inoue H, Masuda W. Relationship of The Unstimulated Whole Saliva Flow Rate and Salivary Gland Size Estimated by Magnetic Resonance Image in Healthy Young Humans. *Arch Oral Biol.* 2006;51(4):345–9.
17. Gomes SG, Custódio W, Cury AA, Garcia RC. Effect of Salivary Flow Rate on Masticatory Efficiency. *Int J Prosthodont.* 2009;22(2):168–72.
18. Ahmadi-Motamayel F, Goodarzi MT, Hendi SS, Kasraei S, Moghimbeigi A. Total Antioxidant Capacity of Saliva and Dental Caries. *Med Oral Patol Oral Cir Bucal.* 2013;18(4):553–6.
19. Lenander-Lumikari M, Loimaranta V. Saliva and Dental Caries. *Adv Dent Res.* 2000;14:40–7.
20. Kantak Y, Kadashetti V, Shivakumar KM, Baad R, Vibhute N, Belgaumi U, et al. Consequences of Habitual Arecanut Chewing on Unstimulated Whole Mouth Salivary Flow Rate and pH. *Int J Curr Res.* 2017;9(5):51237–40.
21. Yvette C. Paulino, Novotny R, Miller MJ, Murphy SP. Areca (Betel) Nut Chewing Practices in Micronesian Populations. *Hawaii J Public Heal.* 2011;3(1):19–29.
22. Murphy KL, Herzog TA. Sociocultural Factors that Affect Chewing Behaviors among Betel Nut Chewers and Ex-Chewers on Guam. *Hawaii J Med Public Heal.* 2015;74(12):406–11.
23. Bhandary S, Bhandary P. Cancer of The Oral Cavity - a Growing Concern in The Micronesia: a case report from the Marshall Islands. *Pac Health Dialog.* 2003;10(1):76–8.
24. J. M. Carpenter, Syms MJ, Sniezek JC. Oral Carcinoma Associated With Betel Nut Chewing in The Pacific: an impending crisis? *Pac Health Dialog.* 2005;12(1):158–62.
25. Chen P-H, Mahmood Q, Mariottini GL, Chiang T-A, Lee K-W. Adverse Health Effects of Betel Quid and the Risk of Oral and Pharyngeal Cancers. *Biomed Res Int.* 2017;1–25.

Ethanol Extract with Black Cumin (*Nigella Sativa*) Against sFlt-1 Level and VEGF Serum on Laboratory Mice with Preeclampsia

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Abstract

Introduction: Preeclampsia is one of the complications that occur in pregnancies. This study was aimed to study the factors that affect the of giving ethanol extract with black cumin (*Nigella sativa*) against sFlt-1 level and VEGF serum on laboratory mice induced preeclampsia.

Method: Laboratory experimental research with posttest only control group design. This study used 30 BALB/C laboratory mice, divided into 6 groups, namely negative controls: pregnant mice injected serum from normal pregnant women, positive controls; mice modeled preeclampsia, and treatment groups 1, 2, 3 and 4 are preeclampsia mice received a dose of 500 mg, 1000 mg, 1500 mg and 2000 mg/kg weight of *Nigella sativa* ethanol extract for 5 days. Statistical analysis using ANOVA

Result: The mean serum sFlt-1 level in mice modeled preeclampsia and treatment group dose 500mg, 1000mg, 1500mg and 2000mg (2510.3±182.2 pg/mL, 2142.5±171.9 pg/mL, 1309±161.3 p/mL, and 1500±169.9, respectively) pg/mL) showed a significant difference ($p<0.05$) and found a decrease in serum sFlt-1 levels with increasing doses. The mean serum VEGF levels in preeclampsia mice and treatment groups were 500 mg, 1000 mg, 1500 mg and 2000 mg (50.25±2.85b pg/mL, 60.18±4.81c pg/mL respectively, 71.89±2.38d pg/mL, 66.51±1.87 e pg/mL) showed a significant difference ($p<0.05$) and found an increase in serum VEGF levels as the dose increased.

Conclusion: Giving of Black Cumin extract (*Nigella sativa*) decreases serum sFlt-1 levels and increases serum VEGF levels in preeclampsia mice model and the effect is dependent dose.

Keywords: sFlt-1, VEGF, *Nigella sativa*, preeclampsia.

Introduction

Preeclampsia is one of the complications that occur in pregnancies of more than 20 weeks which is characterized by an increase in systolic blood pressure greater or equal to 140 mmHg or diastolic pressure greater than or equal to 90 mmHg and the amount

of proteinuria 300 mg or more than 30 mg/dL per 24 hours¹. Preeclampsia occurs in about 3-5% of pregnant women worldwide and the number two cause of death for pregnant women. In the United States, 15% of maternal deaths are caused by preeclampsia^{2,3}.

The pathogenesis of preeclampsia occurs with a variety of mechanisms, but placental ischemia/hypoxia is likely to be a major factor due to disruption of trophoblast invasion⁴. Placental ischemia will stimulate excessive production of sFlt-1 or VEGFR-1. The presence of sFlt-1 as a competitor for surface VEGF receptors (Flt-1), causes VEGF cannot attach to receptors on the cell surface. This situation causes serum VEGF levels

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to decrease and induce endothelial cell damage in the glomerulus, producing a urine protein^{5,6}.

Black cumin has been used as a traditional medicine for thousands of years for various diseases such as asthma, coughing, bronchitis, headaches, fever, and rheumatism⁷. Seed extracts of both water and oil have the potential to be anti-tumor, antioxidant, anti-inflammatory, anti-hypertensive, anti-diabetic and anti-seizure. Thymoquinone (TQ) is the main constituent of Black Cumin essential oil^{8,9}. As an antioxidant, thymoquinone synergizes with other compounds such as dithymoquinone and thymol as a free radical scavenger¹⁰. As TQ Anti-inflammatory inhibits activation of NFκβ. In cases of preeclampsia where placental hypoxia occurs, activation of NFκβ will affect the expression of hypoxia-inducible factor 1-α (HIF1-α)¹¹ which is a VEGF¹² transactivator.

By referring to the above facts because Black Cumin (*Nigella Sativa*) has the potential as an antioxidant and anti-inflammatory, it is necessary to conduct research on the molecular mechanism of Black Cumin extract (BC-e) on serum sFlt-1 and VEGF levels in preeclampsia mice.

Design and Method

This research is a laboratory experimental study with a posttest only control group design. This study measured serum sFlt-1 and VEGF levels in the mice model of preeclampsia after being given several doses of *Nigella sativa* extract. A total of 30 pregnant BALB/C mice

were used in this study, divided into 6 groups: pregnant mice injected with serum of normal pregnant women were used as negative controls, preeclampsia mice were as positive controls, and 4 groups of preeclampsia mice were treated with BC-e with a dose of 500 mg, 1000 mg, 1500 mg and 2000 mg/kg of body-weight/day for 5 days. Mice model preeclampsia made by injecting serum of preeclamptic pregnant women on the 10th and 11th days of gestation each 0.1cc intraperitoneally^{13,14}. The manifestation of preeclampsia in mice is obtained by finding hypertension and proteinuria on the 15th day of gestation. Maintenance of mice and modeling of preeclampsia were carried out at the Pharmacology Laboratory of the Faculty of Medicine, University of Brawijaya and got standard food and drink.

Mice are terminated at 20 weeks’ gestation and blood and kidney organs are collected. Examination of sFlt-1 and VEGF levels in mice serum was measured using an ELISA kit, pg/MI unit.

Result

The comparison test results showed a difference (p = 0.000 <) the mean serum sFlt-1 level between the negative control group (healthy mice) (579.8 ± 114.8 pg/mL) and the positive control group (preeclampsia mice) (2752.8 ± 188.7 pg/mL)) Likewise there was a significant difference (p = 0.000 <) mean serum VEGF levels between healthy groups (88.56 ± 5.58 pg/mL) with preeclampsia mice model (44.85 ± 2.15 pg/mL). As shown in table 1.

Table 1. Results of comparison of control groups

Variable	Negative Control (Healthy) Mean ± SD	Positive Control (Eclampsia) Mean ± SD	p-value
sFlt-1 serum level (pg/mL)	579.8±114.8	2752.8±188.7	0.000
VEGF serum level(pg/mL)	88.56±5.58	44.85±2.15	0.000

Based on the results of the one way ANOVA test on serum sFlt-1 level data, there were significant differences in the mean serum sFlt-1 level in the five observation sample groups (p-value<0,000). Furthermore, the Multiple Comparisons with the Least Significant Difference (LSD) showed that there was a difference between the mean serum sFlt-1 levels between the positive control group (model preeclampsia mice) (2752.8±188.7apg/mL) and the

treatment group gave ethanol extract *Nigella sativa* doses 500mg (2510.3±182.2b pg/mL), with a dose of 1000mg (2142.5±171.9cpg/mL), with a dose of 1500mg (1309±161.3dpg/mL), and also with a dose of 2000mg (1500±169.9dpg/mL). This means that there is a treatment effect of giving 500mg, 1000mg, 1500mg and ethanol *Nigella sativa* extracts to serum sFlt-1 levels in preeclampsia mice.

Table 2. The influence of Nigella sativa ethanol extract on mean serum sFlt-1 levels and VEGF levels

Intervention Group	Mean serum sFlt-1 levels (pg/mL)	Mean serum VEGF (pg/mL)
Negative control	579,8	88,56
Positive control	2752,8	44,85
Preeclampsia Mice + Ethanol Extract 500 mg	2510,3	50,25
Preeclampsia Mice + Ethanol Extract 1000 mg	2142,5	60,18
Preeclampsia Mice + Ethanol Extract 1500 mg	1309,0	71,89
Preeclampsia Mice + Ethanol Extract 2000 mg	1500,0	66,51

Based on the results of the One Way ANOVA test on VEGF level data, there were significant differences in the mean VEGF levels of the five observation sample groups (p -value=0,000). Furthermore, the Multiple Comparisons with the Least Significant Difference (LSD) showed that there were significant differences in the mean VEGF levels between the positive control group (preeclampsia mice) (44.85 ± 2.15 pg/mL) and the treatment group administered ethanol extract Nigella sativa at a dose of 500mg, 1000mg, 1500mg and 2000mg ($50.25 \pm 2.85b$ pg/mL, $60.18 \pm 4.81c$ pg/mL, $71.89 \pm 2.38d$ pg/mL and $66.51 \pm 1.87e$ pg/mL). There appears to be an increase in serum VEGF levels along with an increase in the dose of ethanol extract except at doses of 2000 mg. If based on the average value of VEGF levels, the treatment group doses 1500mg show the highest value of the average VEGF level ($71.89 \pm 2.38d$ pg/mL) compared to the group in other doses and can be considered the fastest dose in increasing VEGF levels in mice models preeclampsia.

The occurrence of a decrease in serum sFlt-1 levels and an increase in VEGF in line levels in increasing doses. The 1500mg dose seems to be the optimal dose of reducing serum sFlt-1 levels and increasing serum VEGF levels.

Discussion

This study showed that sFlt-1 serum levels in pregnant mice injected with pre-eclampsia maternal serum (2752.8 ± 188.7 pg/mL) significantly increased compared with negative control mice. The administration of pre-eclampsia serum intraperitoneal injection with high TNF levels in pregnant mice increase blood pressure and serum sFlt-1 levels¹⁴ which caused by an increase in angiotensin II¹⁵.

The previous study reported that the administration of IgG injection of preeclampsia mothers increase TNF serum levels in pregnant mice. Increased levels

of sFlt-1 in preeclampsia patients can reduce levels of free VEGF and PlGF in the circulation resulting in the onset of symptoms of preeclampsia^{16,17}. Soluble Fms-like tyrosine kinase-1 (sFlt-1), also known as Soluble vascular endothelial growth factor receptor 1 (sVEGFR-1) which is a soluble receptor for VEGF and PlGF¹⁸ which acts as VEGF and PlGF against by binding and inhibiting interactions both of them against endogenous receptors¹⁹.

This study showed the serum VEGF levels of preeclampsia mice have a significant decrease compared to control mice. The injection of serum for pregnant women PEB in pregnant mice causes pre-eclampsia-like symptoms because TNF- α found in maternal serum binds to TNF type 1 receptors (TNFR-1) mice which in turn activate the NF- κ B²⁰ transcription factor. NF- κ B activation by TNF α may play a role in inducing HIF-1 α ²¹ which is a transcription factor for sFLT formation in the placenta²². sFlt does not have a transmembrane domain and membrane⁶ cytoplasmic domain, so the bond between VEGF and PlGF to sFlt-1 cannot provide a second messenger for angiogenic and has an antiangiogenic effect⁵. The presence of sFlt-1 as a competitor for surface VEGF receptors (Flt-1) causes VEGF cannot attach to receptors on the cell surface. This condition causes serum proangiogenic VEGF levels to drop by 5/6. Decreasing levels of free VEGF can also indirectly increase in blood. The low levels of free VEGF in serum could decrease in nitric oxide (NO) which cause in blood vessel vasoconstriction followed by an increase in blood pressure.

There was a significant difference in serum sFlt-1 levels in preeclampsia mice with a treatment group given a dose of BC-e dose of 500 mg, 1000 mg, 1500 mg, and 2000 mg. Antioxidant supplements to preeclampsia patients able to reduce serum sFlt-1 levels and increase serum PlGF levels. Black cumin with the main content of Thymoquinone (TQ) has the potential as

an antioxidant so that it can reduce serum sFlt-1 levels in preeclampsia mice significantly²³. TQ is able to inhibit organ damage caused by free radicals¹⁰. The antioxidant effects of TQ, dithymoquinone, and thymol be able to inhibit some reactive oxygen species (ROS). TQ and dihydrothymoquinone (DHTQ) have the ability as free radical scavengers with a half inhibitory concentration (IC50) in nanomolar concentrations and micromolar¹⁰. All ingredients of black cumin have a strong antioxidant effect, where thymol works by quelling single oxygen production, while TQ and dithymoquinone show activities such as superoxide dismutase (SOD)²⁴.

There was a significant difference in the mean serum VEGF levels of preeclampsia mice with a treatment group that was given a dose of 500 mg, 1,000 mg, 1500 mg, and 2000 mg of BC-e. The effect of BC-e on increasing serum VEGF levels in preeclampsia mice is not fully understood. TQ has the ability to inhibit transcription factors, nuclear factor kappa β (NF κ β) is thought to be the cause. TQ as an inflammatory inhibitor works through anti-inflammatory and proapoptotic action²⁵.

TQ can inhibit the bonding of NF κ β to DNA through direct interaction with sub-unit p65. TQ will inhibit activation by I κ B α kinase which in turn will inhibit degradation and phosphorylation of I κ B α thereby inhibiting the activation and translocation of NF κ β from the cytoplasm to the cell nucleus²⁶. Barriers to activation of NF- κ β cause decreased HIF1- α expression. In preeclampsia placenta, the inhibition of activation of HIF1- α can reduce the synthesis of sFlt anti-angiogenic factors, and ultimately increase the VEGF angiogenic factor that enters the maternal circulation.

The role of BC-e as an antioxidant is also thought to play a role in increasing VEGF levels. Antioxidant supplementation caused a significant decrease in the concentration of sFlt-1 and increased PlGF in plasma. Whereas in vitro studies showed beneficial effects of antioxidants on VEGF. BC-e has considerable antioxidant properties both in vivo and in vitro^{8,24}. In its activity as an antioxidant, thymoquinone synergizes with other compounds such as dithymoquinone and thymol to capture free radicals¹⁰.

The average increase in serum VEGF levels along with the increase in the dose of black cumin extract given and the optimal dose of NS in increasing VEGF levels in serum is 1500 mg. At a dose of 2000 mg, there

is a decrease in serum VEGF levels. This is presumably because the effect of hormesis is found in the effects of the response dose²⁷, where at low doses black cumin ethanol extract has a beneficial effect while at high doses it has a detrimental effect.

Conclusion

Giving of Black Cumin extract (*Nigella sativa*) decreases serum sFlt-1 levels and increases serum VEGF levels in preeclampsia mice model and the effect is dependent dose.

Ethical Clearance: Ethical approval was obtained from the ethics committee of Brawijaya University.

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Conflict of Interest: None

References

1. Noris M, Perico N, Remuzzi G. Mechanisms of Disease: pre-eclampsia. 2005;1(2):98-114. doi:10.1038/ncpneph0035.
2. Cindrova-davies T. The therapeutic potential of antioxidants, ER chaperones, NO and H₂S donors, and statins for treatment of preeclampsia. 2014;5(May):1-13. doi:10.3389/fphar.2014.00119.
3. Conti E, Zezza L, Ralli E, et al. Growth factors in preeclampsia: A vascular disease model: A failed vasodilation and angiogenic challenge from pregnancy onwards Cytokine Growth Factor Rev. 2013;24(5):411-425. doi:10.1016/j.cytogfr.2013.05.008.
4. Gilbert JS, Ryan MJ, Lamarca BB, et al. Pathophysiology of hypertension during preeclampsia: linking placental ischemia with endothelial dysfunction. 2008;4505. doi:10.1152/ajpheart.01113.2007.
5. Shibuya M. JB Review Vascular endothelial growth factor and its receptor system: physiological functions in angiogenesis and pathological roles in various diseases. 2013;153(1):13-19. doi:10.1093/jb/mvs136.
6. Levine RJ, Maynard SE, Qian C, et al. Circulating angiogenic factors and the risk of preeclampsia. N Engl J Med. 2004;350(7):672-683. doi:10.1056/NEJMoa031884.
7. Meziti A, Meziti H, Boudiaf K, Mustapha B,

- Bouriche H. Polyphenolic Profile and Antioxidant Activities of *Nigella Sativa* Seed Extracts In Vitro and In Vivo. *World Acad Sci.* 2012;64:24-32.
8. Paarakh PM. *Nigella sativa* Linn. – A comprehensive review. 2010;1(December):409-429.
 9. Ahmad A, Husain A, Mujeeb M, et al. A review on therapeutic potential of *Nigella sativa*: A miracle herb. *Asian Pac J Trop Biomed.* 2013;3(5):337-352. doi:10.1016/S2221-1691(13)60075-1.
 10. Mansour Nagi, M.N. El-Khatib, A.S. Al-Bekairi, A.M M a. Effects of Thymoquinone on Antioxidant Enzyme Activities, Lipid Peroxidation and Dt-Diaphorase in Different Tissues of Mice; A Possible Mechanism of Action. *Cell Biochem Funct.* 2002;20(October 2001):134-151.
 11. Görlach A, Bonello S. The cross-talk between NF-kappaB and HIF-1: further evidence for a significant liaison. *Biochem J.* 2008;412(3):e17-e19. doi:10.1042/BJ20080920.
 12. Fukuda R, Hirota K, Fan F, Jung Y Do, Ellis LM, Semenza GL. Insulin-like growth factor 1 induces hypoxia-inducible factor 1-mediated vascular endothelial growth factor expression, which is dependent on MAP kinase and phosphatidylinositol 3-kinase signaling in colon cancer cells. *J Biol Chem.* 2002;277(41):38205-38211. doi:10.1074/jbc.M203781200.
 13. Kalkunte S, Boij R, Norris W, et al. Sera from preeclampsia patients elicit symptoms of human disease in mice and provide a basis for an in vitro predictive assay. *Am J Pathol.* 2010;177(5):2387-2398. doi:10.2353/ajpath.2010.100475.
 14. Wicaksono BA, Candra S, Baktiyani W, Fitri LE. Intraperitoneal Injection of High Tumor Necrosis Factor (TNF- α) Serum Increase Soluble Fms-like Tyrosine Kinase 1 (sFlt-1) and Blood Pressure of Pregnant Mice. 2015;5(1).
 15. Murphy SR, Cockrell K. Regulation of soluble fms-like tyrosine kinase-1 production in response to placental ischemia/hypoxia: role of angiotensin II. *Physiol Rep.* 2015;3(2):e12310-e12310. doi:10.14814/phy2.12310.
 16. Zhou CC, Ahmad S, Mi T, et al. Autoantibody from women with preeclampsia induces soluble Fms-like tyrosine kinase-1 production via angiotensin type 1 receptor and calcineurin/nuclear factor of activated T-cells signaling. *Hypertension.* 2008;51(4 PART 2 SUPPL.):1010-1019. doi:10.1161/HYPERTENSIONAHA.10
 17. Irani R a, Zhang Y, Zhou CC, et al. Autoantibody-mediated angiotensin receptor activation contributes to preeclampsia through tumor necrosis factor-alpha signaling. *Hypertension.* 2010;55(5):1246-1253. doi:10.1161/HYPERTENSIONAHA.110.150540.7.097790
 18. Chen Y. Novel Angiogenic Factors for Predicting Preeclampsia: sFlt-1, PlGF, and Soluble Endoglin~! 2008-08-29~!2008-12-15~!2009-01-02~! *Open Clin Chem J.* 2009;2(1):1-6. doi:10.2174/1874241600902010001.
 19. Wang A, Rana S, Karumanchi SA. Preeclampsia: the role of angiogenic factors in its pathogenesis. *Physiology (Bethesda).* 2009;24:147-158. doi:10.1152/physiol.00043.2008.
 20. Parameswaran N, Patial S. Tumor necrosis factor- α signaling in macrophages. *Crit Rev Eukaryot Gene Expr.* 2010;20(2):87-103. doi:10.1016/j.bbi.2008.05.010.
 21. Jung Y, Isaacs JS, Lee S, Trepel J, Liu Z-G, Neckers L. Hypoxia-inducible factor induction by tumour necrosis factor in normoxic cells requires receptor-interacting protein-dependent nuclear factor kappa B activation. *Biochem J.* 2003;370(Pt 3):1011-1017. doi:10.1042/BJ20021279.
 22. Nevo O, Soleymanlou N, Wu Y, et al. Increased expression of sFlt-1 in in vivo and in vitro models of human placental hypoxia is mediated by HIF-1. *Am J Physiol Regul Integr Comp Physiol.* 2006;291(4):R1085-R1093. doi:10.1152/ajpregu.00794.2005.
 23. Poston L, Igosheva N, Mistry HD, et al. Role of oxidative stress and antioxidant supplementation in pregnancy. *Am J Clin Nutr.* 2011;94:1980-1985. doi:10.3945/ajcn.110.001156.1.
 24. Leong X, Mustafa MR, Jaarin K. *Nigella sativa* and Its Protective Role in Oxidative Stress and Hypertension. 2013;2013.
 25. Chehl N, Chipitsyna G, Gong Q, Yeo CJ, Arafat H a. Anti-inflammatory effects of the *Nigella sativa* seed extract, thymoquinone, in pancreatic cancer cells. *Hpb.* 2009;11(5):373-381. doi:10.1111/j.1477-2574.2009.00059.x.

26. Sethi G, Ahn KS, Aggarwal BB. Targeting nuclear factor-kappa B activation pathway by thymoquinone: role in suppression of antiapoptotic gene products and enhancement of apoptosis. *Mol Cancer Res.* 2008;6(6):1059-1070. doi:10.1158/1541-7786.MCR-07-2088.
27. Mattson. MP. NIH Public Access. *Natl Institutes Heal.* 2008;18(9):1199-1216. doi:10.1016/j.micinf.2011.07.011. *Innate.*

Biochemical Studies of Oxidative Stress During Ischemia Induce Myocardial Injuries

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Abstract

The study was designed as a biochemical study of the oxidative stress during hypotension caused by cardiac injury, the world's first cause of death, using biomarkers and their role in laboratory diagnosis. The study included three sets of 40 blood samples from each people with myocardial infarction, angina pectoris and healthy people as a control group. Different biochemical variables such as ROS, GPX1, Troponin, C.K, and lipid profile were measured, and the results showed a significant increase in the level of concentration of Reactive Oxygen Species ROS (P-value 0,045) in patients with MI, (7.326 ± 1.143 ng/mL), and the Angina Pectoris was (6.037 ± 1.669 ng/mL) compared with the control group (1.046 ± 5.158 ng/mL). A significant decrease in the level of Glutathione peroxidase GPX1 at the level of (P-value 0.038) in patients with myocardial infarction (1890 ± 391 pg/mL) was observed, while in Angina Pectoris was (2109 ± 600 pg/mL) and in control was (2386 ± 401 pg/mL). Furthermore, a varying rises in the level of troponin and creatine kinase in patients with myocardial infarction (29.03 ± 22.99 ng/mL, 110.62 ± 45.71 u/L) respectively, while in patients with Angina was (2.181 ± 2.186 ng/mL, 39.730 ± 12.79 u/L) compared with the control (0.139 ± 0.1717 ng/mL, 16.283 ± 5.133 u/L). The results of the study showed a significant increase of lipid profile (cholesterol, triglycerides, HDL) in patients with MI and AP, with an average concentration (344.6 ± 67.4, 240.3 ± 58.5, 43.00 ± 6.89 mg/dL) for MI and (303.6 ± 86.1, 232.8 ± 65.8, 39.10 ± 5.86) for AP compared with the control group, with an average concentration Mean ± SD (159.2 ± 50.30, 102.9 ± 35.60, 31.00 ± 3.085) respectively.

Keywords: Cardiac injury, myocardial infarction, angina pectoris, Glutathione peroxidase 1, Reactive Oxygen Species.

Introduction

Cardiovascular diseases (CVD) are the leading cause of death globally⁽¹⁾. This is a fact in all areas of the world except Africa⁽¹⁾. Together CVD resulted in 17.9 million deaths (32.1%) in 2015.^(2,3) Deaths, at a given age, from CVD, are more common and have been increasing in much of the developing world, while rates have declined in most of the developed world since the 1970s.^(4,5) In the United States, 11% of people between 20 and 40 have CVD.⁽⁶⁾

There are many risk factors for heart diseases: age, sex, tobacco, alcohol, obesity, raised hypertension, raised diabetes mellitus, raised hyperlipidemia.⁽⁷⁻¹¹⁾ Myocardial Infarction MI also known as a heart attack⁽¹²⁾ it is acute, threatening heart disease. Most MI are caused by coronary artery disease.⁽¹³⁾ Risk

factors include Hypertension, Smoking, Diabetes, and others.^(1,13) Ischemia⁽¹⁴⁾ is a relative or absolute failure or retention of blood supply to body tissues,⁽¹⁵⁾ causing oxygen and glucose deficiency needed for cellular metabolism⁽¹⁶⁾ Ischemia is usually caused by vascular problems, resulting in damage.

Oxidative stress is an imbalance between free radicals and antioxidants in the body. Free radicals can cause large chain chemical reactions in the body because they react so quickly with other molecules so they can be beneficial or harmful.⁽¹⁷⁾ Chemically, oxidative stress is associated with increased production of oxidizing species or a significant decrease in the effectiveness of oxidant defense's, such as glutathione.⁽¹⁸⁾ Reactive oxygen species (ROS) is a collective term used for a group of oxidants, which are either free radicals or molecular species capable of generating free radicals.

Uncontrolled generation of ROS can lead to their accumulation causing oxidative stress in the cells.⁽¹⁹⁾

The study is designed to studying oxidative stress during ischemia caused by the cardiac injury. Find out the presence of oxidative stress and diagnose it by an imbalance between the levels of oxidants (ROS) and antioxidants (GPX1). Know the importance of antioxidants and oxidative damage because of the serious diseases caused by oxidative stress. Identify the importance of cardiac proteins such as troponin and enzymes such as CK-MB as vital indicators for serious heart disease. Predict the severity of high blood lipid levels as risk factors for heart disease. Minimizing serious heart disease by taking care of its risk factors and thus reducing the oxidative stress caused by it, which causes many dangerous diseases.

Materials and Method

1. **Blood Samples:** Forty samples were collected at age (45-90) years (20) of the male and (20) female for both who was had IM and AP after being diagnosed by specialist doctors at Azadi Teaching Hospital and Kirkuk General Hospital. The sample collection period from 1/2 to 30/4 2019.
2. Five mL of blood was withdrawn from the vein and placed in the gel tube and placed in the centrifuge for five minutes at 4000 rpm and then separated the serum divided into three parts and was kept in small plastic pipes dry and clean and kept in freezing at -20 °C until it is used to measure variables.

Measurement of biochemical variables

Measurement of Reactive Oxygen Species (ROS):

The ELISA kit uses the Sandwich-ELISA principle. The micro ELISA plate provided in this kit has been pre-coated with samples are added to the micro ELISA plate wells and combined with the specific antibody. Then a biotinylated detection antibody specific for Human ROS and Avidin-Horseradish Peroxidase (HRP) conjugate plate well and incubated. The optical density (OD) is measured spectrophotometrically at a wavelength of 450 nm. The OD value is proportional to the concentration of Human ROS. The concentration of Human ROS in the samples can calculate by comparing the OD of the samples to the standard curve.

Measurement of Glutathione Peroxidase 1 (GPX1)

The same method above was used.

Measurement of Troponin: The test uses a sandwich immunodetection method the detector antibody in buffer binds to antigen in the sample, forming antigen-antibody complexes, and migrates onto nitrocellulose matrix to be captured by the other immobilized-antibody on the test strip. The more complex leads to stronger intensity of fluorescence signal detector antibody, which is processed by instrument for ichroma tests to show Tn-I concentration in the sample.

Measurement of Creatine Kinase (CK-MB): CK-NAC modified reagent contains a polyclonal antibody which so completely inhibits CK-MM activity. Only the activity of the non-inhibited B monomer subunit, representing half of the CK-MB activity, is measured. The method assumes that CK-BB activity in the specimen is essentially zero^(20, 21)

Measure of Cholesterol: The enzymatic method described by Allain⁽²²⁾ and al., which is the Cholesterol esters reacts

Measure of Triglycerides: Fossati⁽²³⁾ and Principle method associated with Trinder⁽²⁴⁾ reaction.

The absorbance of the coloured complex (quinoneimine), proportional to the amount of triglycerides in the specimen, is measured at 500 nm.

Measure of High-Density Lipoprotein (HDL): This reagent is only for the treatment of specimens before determination of HDL-Cholesterol with a reagent for total cholesterol. (LDL), (VLDL) and chylomicrons from specimens are precipitated by phosphotungstic acid (PTA) and Magnesium chloride.⁽²⁵⁾

Results and Discussion

Level of (ROS) in Serum of Two Groups of Patients (MI, AP): The results in Table (1) and Figure (1) showed a Rise in the ROS level at (P-Value 0.045) in the serum of the two groups of patients with MI, AP compared to the control group. The reason for the rise is that it has been already established that ROS play a vital role in the progression of CVDs.^(26, 27)

Table (1): Level (Mean ±St.d) of (ROS, GPX1, Troponin, C.K) in serum samples for the two groups of patients with MI, AP and control group

Group	ROS	GPX1	Troponin	C.K
Myocardial Infarction	7.326±1.143A	1890±391c	29.03±22.99A	110.62±45.71A
Angina Pectoris	6.037±1.669B	2109±600b	2.181±2.186B	39.730±12.79B
Control	5.158±1.046C	2368±401a	0.139±0.1717B	16.283±5.133C
P-Value	0.045	0.038	0.0008	0.00003

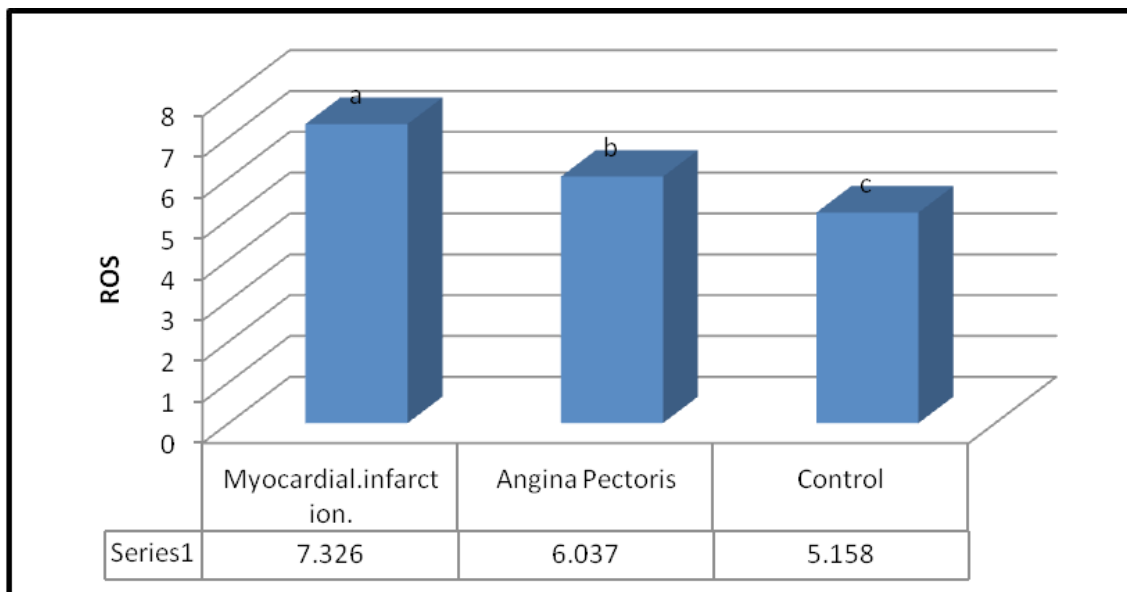


Figure (1): Shows the level of ROS in serum samples for the two groups of patients with MI, AP and control group

Level of Glutathione Peroxidase 1 (GPX1) in Serum of Two Groups of Patients MI, AP Compared to Control Group: The results in Table (1) and Figure (2) showed a Decline in the GPX1 level at (P-Value 0.038) in the serum of the two groups of patients MI, AP compared to the control group and the reason for the decrease in the level of GPX1 denote the increased oxidative stress⁽²⁸⁻³⁰⁾.

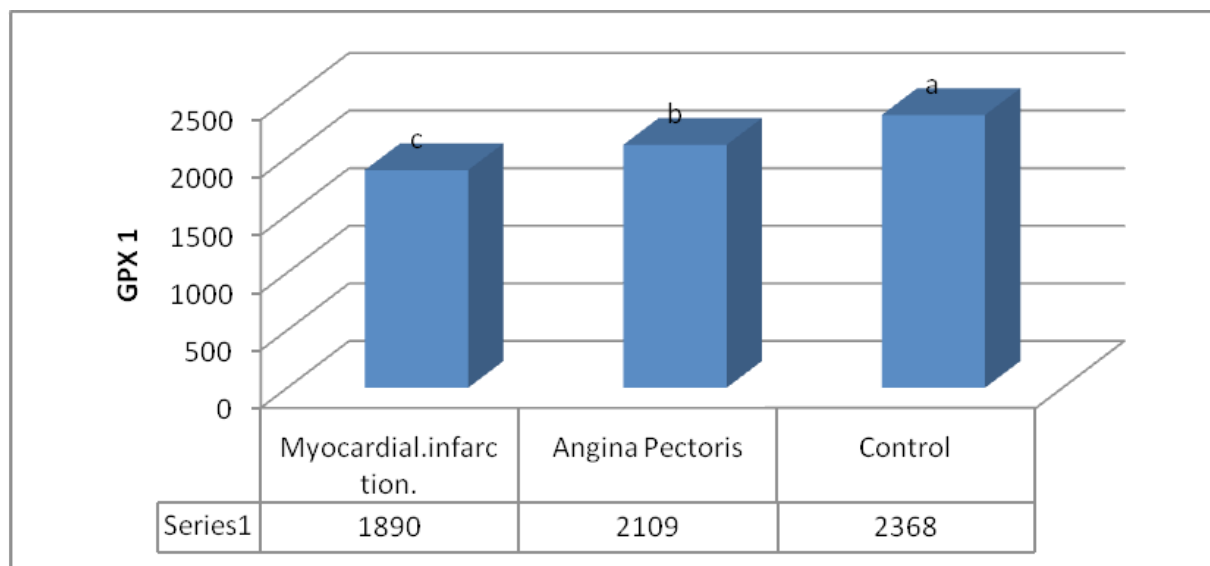


Figure (2): Shows the level of GPX1 in serum samples for the two groups of patients with MI, AP and control group

Measurement of Creatine Kinase (C.K.): The results in Table (1) showed a significant rise in the level of C.K at (P-Value 0.00003) in the serum of patients with MI compared with AP and the control group. The reason is that the enzyme CK -MB regulates adenosine triphosphate within cells to provide increased energy and the measurement of CK - MB was found to detect myocardial infarction and then used as a diagnostic marker for myocardial infarction.⁽³¹⁾

Measurement of Troponin (Tn-I): The results in Table (1) showed a significant rise in the level of troponin at (P-Value 0.0008) in the serum of MI compared to AP and control group, The reason is that troponins excreted into the bloodstream after necrosis of the heart muscle and are free proteins or complicated forms. After that, degradation of muscle fibres continues and once released into the bloodstream; troponin is subject to various biochemical modifications including phosphorylation, oxidative stress and proteolysis. In the

case of myocardial infarction, there is an increase in the concentration of troponin when increased demand of oxygen to the heart muscle such as arrhythmias, high heart pressure and reduced oxygen supply as a result of increased tension on the heart muscle⁽³²⁾

Measurement of Serum Lipid Levels in Patients with MI, AP comparison with control:

Cholesterol: The results in the table (2) showed a significant rise in the level of cholesterol (P-Value 0.0009) in the serum of the two groups of patients with MI, AP compared to the control group. The reason is that cholesterol contributes to the formation of platelets that begin to clump and take place in the walls of the arteries between the inner and outer layers,⁽³³⁾The increase in blood cholesterol causes a high risk that leads to the deposition of cholesterol in the blood vessels, causing partial or complete blockage of the vessels and the occurrence of strokes heart or brain.⁽³³⁾

Table (2): Level (Mean ±St.d) of (Cholesterol, Triglyceride, HDL) in serum samples for the two groups of patients with MI, AP and control group

Group	Ch	T.G	HDL
Myocardial Infarction	344.6±67.4 A	240.3±58.5 A	43.00±6.89 A
Angina Pectoris	303.6±86.1 A	232.8±65.8 A	39.10±5.86 B
Control	159.2±50.30 B	102.9±35.60 B	31.00±3.085 C
P-Value	0.0009		0.0007

Triglycerides: The results in a table (2) showed a significant rise in the level of Triglycerides (P-Value 0.0008) in the serum of the two groups of patients with MI, AP compared to the control group. The reason is due to in the human body, high levels of triglycerides are associated with the risk of heart disease and stroke. This risk can be partially calculated by the relationship between triglyceride level and HDL level⁽³⁴⁾

High Density Lipoprotein (HDL): The results in Table (2) showed a minimal rise in the level of HDL at the level (P-Value 0.0007) in the serum of the two groups of patients with MI, AP compared to the control group and the reason is due to an increased HDL in the blood gets a lower risk of heart disease and a very lower mortality rate in cardiovascular disease and that

high-density lipoprotein is a protection and its presence prevents LDL oxidation. Epidemiological and clinical trials confirm an inverse relationship between HDL and heart disease risk⁽³⁵⁾

Conclusion: ROS rises and GPX1 decline in cases of MI and AP this indicates oxidative stress which gives this test a high importance diagnostic. Troponin and creatine kinase rise slightly or within normal limits in the case of AP while they rise very significantly in the case of MI. Lipid levels are significantly elevated in both MI and AP and may be one of the reasons for these diseases.

Ethical Clearance: Taken from the ethical committee of Chemistry Department, College of Science, Mustansiriyah University.

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References

- Mendis S, Puska P, Norrving B, Organization WH. Global atlas on cardiovascular disease prevention and control: Geneva: World Health Organization; 2011.
- Vos T, Abajobir AA, Abate KH, Abbafati C, Abbas KM, Abd-Allah F, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *The Lancet*. 2017;390(10100):1211-59.
- Abubakar I, Tillmann T, Banerjee A. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet*. 2015;385(9963):117-71.
- Iyngkaran P, Chan W, Liew D, Zamani J, Horowitz JD, Jelinek M, et al. Risk stratification for coronary artery disease in multi-ethnic populations: Are there broader considerations for cost efficiency? *World journal of methodology*. 2019;9(1):1.
- Mensah GA, Wei GS, Sorlie PD, Fine LJ, Rosenberg Y, Kaufmann PG, et al. Decline in cardiovascular mortality: possible causes and implications. *Circulation research*. 2017;120(2):366-80.
- Karlson BW, Nicholls SJ, Lundman P, Barter PJ, Palmer MK. Modeling statin-induced reductions of cardiovascular events in primary prevention: a VOYAGER meta-analysis. *Cardiology*. 2018;140(1):30-4.
- Kelly BB, Fuster V. Promoting cardiovascular health in the developing world: a critical challenge to achieve global health: National Academies Press; 2010.
- Finks SW, Airee A, Chow SL, Macaulay TE, Moranville MP, Rogers KC, et al. Key articles of dietary interventions that influence cardiovascular mortality. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*. 2012;32(4):e54-e87.
- De Souza RJ, Mente A, Maroleanu A, Cozma AI, Ha V, Kishibe T, et al. Intake of saturated and trans unsaturated fatty acids and risk of all cause mortality, cardiovascular disease, and type 2 diabetes: systematic review and meta-analysis of observational studies. *Bmj*. 2015;351:h3978.
- Almuhawwis AGA, el-Fetoh NM, Almalki MAM, Alanazi MSZ, Alshammari NSH, Alruwaili AK, et al. Risk factors of cardiovascular diseases among population of Arar City, Northern Saudi Arabia. *Al-Azhar Assiut Medical Journal*. 2017;15(2):104.
- Ciaccio EJ, Lewis SK, Biviano AB, Iyer V, Garan H, Green PH. Cardiovascular involvement in celiac disease. *World journal of cardiology*. 2017;9(8):652.
- Koh YY, Ki YJ, Kim SS, Kim HW, Park KH, Choi DH, et al. Acute Myocardial Infarction in a Young Adult during Vigorous Physical Activity. *The Medical Journal of Chosun University*. 2017;42(4):124-9.
- Ávila P, Chaix M-A, Mondésert B, Khairy P. Sudden cardiac death in adult congenital heart disease. *Cardiac electrophysiology clinics*. 2017;9(2):225-34.
- Ibanez B, Heusch G, Ovize M, Van de Werf F. Evolving therapies for myocardial ischemia/reperfusion injury. *Journal of the American College of Cardiology*. 2015;65(14):1454-71.
- Al Badarin F, Aljizeeri A, Almasoudi F, Al-Mallah MH. Assessment of myocardial blood flow and coronary flow reserve with positron emission tomography in ischemic heart disease: Current state and future directions. *Heart failure reviews*. 2017;22(4):441-53.
- Patel MR, Calhoun JH, Dehmer GJ, Grantham JA, Maddox TM, Maron DJ, et al. ACC/AATS/AHA/ASE/ASNC/SCAI/SCCT/STS 2017 appropriate use criteria for coronary revascularization in patients with stable ischemic heart disease: a report of the American College of Cardiology appropriate use criteria task force, American Association for Thoracic Surgery, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society of Thoracic Surgeons. *Journal of the American College of Cardiology*. 2017;69(17):2212-41.

17. Sies H, Berndt C, Jones DP. Oxidative stress. Annual review of biochemistry. 2017;86:715-48.
18. Schafer F, Buettner G. Redox Environment of the Cell as Viewed Through the Redox State of the Glutathione Disulfide/Glutathione Couple. Free Radical Biology and Medicine. 2005;39(10):1274-5.
19. Bhattacharya S. Reactive oxygen species and cellular defense system. Free radicals in human health and disease: Springer; 2015. p. 17-29.
20. Mattenheimer H, editor CK-MB method and clinical significance. Proceedings of the CK-MB symposium, Philadelphia; 1981.
21. Stein W, editor CK-MB method and clinical significance. Proceedings of the CK-MB symposium, Philadelphia; 1981.
22. Allain CC, Poon LS, Chan CS, Richmond W, Fu PC. Enzymatic determination of total serum cholesterol. Clinical chemistry. 1974;20(4):470-5.
23. Atta AH, Soufy H, Nasr SM, Soliman AM, Nassar SA, Al Maweri A, et al. Hepatoprotective and antioxidant effects of methanol extract of Moringa oleifera leaves in rats. Wulfenia Journal. 2017;24(3):249-68.
24. Ricketts EF, Calvin J, Hedgpeth JW, Phillips DW. Between pacific tides: Stanford University Press; 1985.
25. NCEP-NIH Publication N95-3044 (1995) p 72-74.
26. Panth N, Paudel KR, Parajuli K. Reactive oxygen species: a key hallmark of cardiovascular disease. Advances in medicine. 2016;2016.
27. Gessi M, Capper D, Sahm F, Huang K, von Deimling A, Tippelt S, et al. Evidence of H3 K27M mutations in posterior fossa ependymomas. Acta neuropathologica. 2016;132(4):635-7.
28. Patil N, Chavan V, Karnik N. Antioxidant status in patients with acute myocardial infarction. Indian journal of clinical biochemistry. 2007;22(1):45-51.
29. Červinková z. Selective antioxidant enzymes during ischemia/reperfusion in myocardial infarction. Physiol Res. 2000;49:315-22.
30. Goyal MR, Ayeleso AO. Bioactive Compounds of Medicinal Plants: Properties and Potential for Human Health: CRC Press; 2018.
31. Ahmad AJ, Al-Mukhtar SB. Comparison between quantitative and qualitative biochemical markers in the diagnosis of acute coronary syndrome. Iraqi Journal of Pharmacy. 2011;11(2):102-10.
32. Korff S, Katus HA, Giannitsis E. Differential diagnosis of elevated troponins. Heart. 2006;92(7):987-93.
33. Blesso CN, Fernandez ML. Dietary cholesterol, serum lipids, and heart disease: are eggs working for or against you? Nutrients. 2018;10(4):426.
34. Naif WR. Study of The relationship between uric acid level and some lipid profile for heart disease patients in Alnasseriya city. Al-qadisiyah medical journal. 2014;10(17):224-33.
35. Al-Asadi JN, Habib OS, Al-Naama LM. Lifestyle determinants of high-density lipoprotein cholesterol (HDL-C) in young adults. The Medical Journal of Basrah University. 2008;26(1):37-41.

Cell free DNA in Maternal Blood as an Indicator of Fetal Complications

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Abstract

Cell-free DNA (cfDNA) is a new biomarker that has been used in different aspects, especially in prenatal diagnosis and pregnancy complications. The aim of the study is to investigate the role of cfDNA in the prediction of fetal complications. Ninety women had been enrolled recruited from AL-Karkh Hospital from March to September 2018. Thirty of with diabetes mellitus and the other 60 with hypertension. The mean age of study sample was 29.7 ± 6.33 years. History was taken from all women. Blood samples were collected and cfDNA was measured using PCR. No significant association was found between the primers for autism or the presence of SeritI gene and age or BMI in hypertensive and diabetic patients. It was concluded that there is no difference in the presence of autism gene primers and SitrI gene primers between different age groups of pregnant women and different BMI index groups except for primer 3 in both hypertensive and diabetic ones.

Keywords: Cell free DNA, Pregnancy, Fetal complications.

Introduction

cfDNA is DNA parts which are found outside the nucleus. They are formed by apoptotic or necrotic mechanisms; they are also present in fluids of the body, so they can be used as indicators of pathological states⁽¹⁾.

cfDNAs that circulates in the maternal blood of healthy pregnant women is 3.4 to 6.2% of the whole DNA amount in the beginning and the end of pregnancy respectively. The sources of fetal DNA in maternal circulation are from a direct transfer of fetal DNA, placenta and blood cells⁽²⁾.

The cfDNA vanishes from the blood of the mother maternal after labor except for those pregnant women with liver disease where high levels of fetal DNA are seen even after childbirth⁽³⁾.

A possibility of having congenital problem is about 3-4% in all pregnancies⁽⁴⁾. So cfDNA is measured as a non invasive prenatal diagnosis especially in chromosomal aneuploidies, sex-linked diseases, blood diseases- fetal RhD type, preeclampsia, and paternally inherited problems⁽⁵⁾. Recently, the estimation of cf-DNA is used in clinical practice for the prenatal detection and

screening of some fetal aneuploidies⁽⁶⁾.

The elevation in the levels of cfDNA can predict the complications related to pregnancy before symptoms appear⁽⁷⁾, although most of the studies showed the increase in cfDNA was early in the disease, but others proved the sustained increase in all stages, so it can be used to predict intrauterine growth retardation, placental previa, preterm labor, and hyperemesis gravidarum⁽⁸⁾.

The aim of the study is to investigate the role of cell free DNA in the prediction of some fetal complications.

Materials and Method

Ninety pregnant women were enrolled, recruited from AL-Karkh Hospital from March to September 2018. Women with complicated pregnancy were included in this study (33%) were diabetics (DM) and (67%) were hypertensive (HPT). The mean age was 29.7 ± 6.33 .

History was taken from all women. Medical examination was done. BMI was calculated by the equation $(\text{Wight}/(\text{Hight})^2)$ ⁽⁹⁾

Blood samples were collected in EDTA tubes and stored in (-20C^0) .

Procedure of DNA extraction was done by adding proteinase K and four buffers . The DNA purity was determined by nanodorp spectrophotometer.

Two µl of DNA sample was added, the software calculated the nucleic acid concentration (ng/µl) at 260 nm.

The ratio of absorbance at 260 nm and 280 nm is used to assess the purity of DNA, the accepted ratios must range between 1.8-2.0⁽¹⁰⁾.

Primers of FMR1, C16, SEZ6L2 (forward F and reverse R) for detection of Autismgene, prepared by adding 100µl of de ionized water to the powder of the primer.

FMR1

Forward	5, _ GCT CAG CTC CGT TTC GGT TTC ACT TCC GGT – 3,	900 bp
Reverse	5, _ AGC CCC GCA CTT CCA CCA CCA GCT CCT CCA -3,	900 bp

C16

Forward	5- ACT GCC CCA GCG AAG ATG -3'	500 bp
Reverse	5'-CCG ACC ACC CAG ACC -3'	500 bp

SEZ6L2

Forward	5'-CCT CTC TCT TCC CCA CAA AGG- 3'	1000 bp
Reverse	5· TGG ACA GCC TGG TTC TCT CT-3'	1000 bp

Primers of A allele 1, A allele 2, G allele, G allele 2 (forward F and reverse R), for detection of SIRT1 gene were prepared by adding 100µl of de ionized water to the powder of the primer.

A allele 1

Forward	5· CCC AGG GTT CAA CAA ATC TAT GTT G-3'	900 bp
Reverse	5· - GCT TCC TAA TCT CCA TTA CGT TGA C-3'	900 bp

A allele 2

Forward	5- GGT GGT AAA AGG CCT ACA GGA AA-3'	500 bp
Reverse	5- CCT CCC AGT CAA CGA CTT TAT C -3'	500 bp

G allele 2

Forward	5'-GAG AAG AAA GAA AGG CAT AAT CTC TGC -3'	500 bp
Reverse	5'-GAT CGA GAC CAT CCT GGC TAA G -3'	500 bp

G allele

Forward	5'-GTA GCA GGA ACT ACA GGC CTG -3'	700 bp
Reverse	5'-CTA TCT GCA GAA ATA ATG GCT TTT CTC -3'	700 bp

The PCR mixture was done in a volume of 25 µl containing the DNA extracted primers, and PCR premix (**Accupowder** ® by Bioneer Company).

The Primers DNA were added into the PCR PreMix tube. Distilled water was put. The blue pellet was

dissolved and spin down by pipetting. The reaction was maintained at 4°C and stored at (-20°C). The mixture (8µ) was loaded on gel to analyze the product of PCR.

For Autism gene all forward and reverse primers of C16 and FMR1 were added in one Gold multiplex

PCR Premix tube, the same way all forward and reverse primers of SEZ6L2 were added in another tube.

For SirtI genes all forward and reverse primers of G allele and G allele 2 were added in one Gold multiplex PCR Premix tube, the same way all forward and reverse primers of A allele 1 and A allele 2 were added in another tube.

PCR reaction tubes were centrifuged. The tubes were placed in the thermal cycler where DNA was amplified.

To detect the size of the amplicons, agarose gel electrophoresis was done.

Gel visualized in in gel documentation system/UV transilluminator revealing bands(primers).

All data were analyzed using SPSS 17.0 .All values were in mean ± SD, chi-square test was. A P value of less than 0.05 is significant.

Results

The study included 90 women, 30 of them with diabetic millets and other 60 were with hypertensive.

Table 1 shows no significant difference in age and BMI between hypertensive and diabetic patients.

Table 1: Comparison of age and BMI between pregnant women with diabetes and hypertension

			Disease		Total	P value	
			DM	HPT			
Age	18-29 years	Count	13	33	46	0.297	
		% within disease	0.28	0.72	0.51		
	30-45 years	Count	17	27	44		
		%	0.39	0.61	0.49		
Total		Count	30	60	90		
		%	1.0	1.0	1.0		
BMI	Normal	Count	12	24	36		0.592
		% within disease	0.33	0.67	0.40		
	Overweight	Count	18	36	54		
		%	0.33	0.67	0.60		
Total		Count	30	60	90		
		%	1.0	1.0	1.0		

The appearance of autism primers was shown in table 2 in all age and BMI groups in hypertensive patients and it was found that there was no significant difference between the groups except for primer 3.

Table 2: The presence of Autism primers in hypertensive pregnant women.

Disease			APRI1		APRI2		APRI3	
			N	P	N	P	N	P
HPT	Age	18-29 years	5	28	24	9	6	27
		30-45 years	1	26	21	6	0	27
	Total		6	54	45	15	6	54
P value			0.245		0.600		0.028 *	
HPT	BMI	Normal	3	21	20	4	1	23
		overweight	3	33	25	11	5	31
	Total		6	54	45	15	6	54
P value			0.213		0.412		0.201	

*p is significant at ≤ 0.05, N = Negative, P = Positive

Table 3 shows the differences in same primers that were in table 2 but in diabetic women and it was found that there was no significant difference between the groups.

Table 3: The presence of Autism primers in diabetic pregnant women

Disease			APRI1		APRI2		APRI3	
			N	P	N	P	N	P
DM	Age	18-29 years	1	12	9	4	0	13
		30-45 years	0	17	14	3	3	14
	Total		1	29	23	7	3	27
P Value			0.433		0.666		0.238	
DM	BMI	Normal	1	11	10	2	0	12
		overweight	0	18	13	5	3	15
	Total		1	29	23	7	3	27
P value			0.400		0.696		0.123	

The differences between age groups and BMI index groups regarding Sirti gene primers in hypertensive and diabetic women was shown in table 4 and 5, again there was no significant difference between the groups.

Table 4: The presence of Sirti gene primers in hypertensive pregnant women

Disease			SPRI1		SPRI2		SPRI3	
			N	P	N	P	N	P
HPT	Age	18-29 years	6	27	10	23	8	25
		30-45 years	2	25	4	23	8	19
	Total		8	52	14	46	16	44
P value			0.222		0.159		0.771	
HPT	BMI	normal	2	22	6	18	4	20
		overweight	6	30	8	28	12	24
	Total		8	52	14	46	16	44
P value			0.354		0.803		0.153	

Table 5: The presence of Sirti gene primers in diabetic pregnant women

Disease			SPRI1		SPRI2		SPRI3	
			N	P	N	P	N	P
DM	Age	18-29 years	0	13	4	9	2	11
		30-45 years	2	15	2	15	6	11
	Total		2	28	6	24	8	22
P value			0.206		0.197		0.407	
DM	BMI	normal	1	11	4	8	4	8
		overweight	1	17	2	16	4	14
	Total		2	28	6	24	8	22
P value			0.765		0.136		0.500	

Discussion

Diabetes mellitus and hypertension are two of the commonly seen pregnancy complications that adversely affect fetal outcomes ⁽¹¹⁾.

The results of this study reveal that there is no difference between hypertensive and diabetic women in regard to age and BMI. Unlike other studies which found that obesity is accepted to affect the pregnancy process

and it is risk factors for perinatal complications⁽¹²⁾. This result may be explained by the number of patients with high BMI in this study that were 54 out of 90 patients.

There was significant association between hypertension and age in increasing the probability of autism especially in primer 3, this was in agree with other studies which show relation of older parental age with the causes of neurodevelopmental conditions including autism⁽¹³⁾. Also an updated review documented the relation between hypertension in pregnancy and risk of neurodevelopmental problems in the children. While parental age associated risk in ASD has been reported in different regions, with a prove that it is a risk for ASD, found separately for maternal and paternal age. It was shown that parental age-related risk is at its maximum in children where both the mother and father are old in age, and if the couples with high age differentials⁽¹⁴⁾.

Concerning BMI and what was reached to in this study, the results were unlike that was found by other study which documented that maternal obesity was proposed to affect the brain growth cognition of offspring⁽¹⁵⁾. Obesity in mothers might affect fetal neurodevelopment, through low-grade neuroinflammation, high oxidative stress, insulin resistance, glucose, and leptin signaling, non regulated serotonergic and dopaminergic signaling, and changed DNA methylation patterns⁽¹⁶⁾.

Concerning diabetic pregnant women the results in this study were similar to the study which does not support the suggestion about the link between diabetes and ASD⁽¹⁷⁾, also another study did not find an increased risk of autism for babies born to women who were already diagnosed with diabetes before getting pregnant. This might be in part because women with diabetes who become pregnant have made lifestyle modifications that keep their sugar levels in check and may also be taking medications to control their blood sugar. Similarly, those diagnosed with gestational diabetes after 26 weeks did not have an increased risk. The study authors speculated that being exposed to untreated high blood sugar during critical brain development early in the pregnancy may have contributed to the autism risk⁽¹⁸⁾.

Studies examining the effect of diabetes in mothers on autism in offspring have shown variable results. A review collecting 16 studies⁽¹⁹⁾ showed additional risk for autism in the presence of maternal diabetes, while high levels of variation in study outcomes and

publication bias were detected; these disappeared when meta-analysis was restricted to case-control studies, with the risk of ASD increasing by 62% among diabetic mothers, compared with non-diabetic mothers. There is evidence that timing might be significant in the association between maternal diabetes and offspring with ASD⁽²⁰⁾.

There is no significant influence of hypertension and diabetes in relation with age and BMI on the presence of SIRT1 gene primers. Although the positive results in primers 1,2,3,4 were much more than the negative results but it is not significant and this may be due to small sample size.

Accumulating studies have revealed that deacetylase Sirtuins exert protective functions against pathologies like diabetes and hypertension⁽²¹⁾.

In obesity, mitochondrial dysfunction may direct fatty acid to intracellular lipid accumulation, leading to insulin resistance. Sirt1 activation can protect the neuron cells exposed to neurotoxic insult. During cerebral hypoxia, the level of ATP and oxygen are lowered, which stimulate bioenergetic and oxidative stress leading to Sirt1 activation⁽²²⁾. This was shown in the results of this study which illustrate the increasing positive number of Autism primers associated with positivity of Sirt1 gene primers because it is neurodegenerative protective gene.

Conclusion: There is no difference in the presence of autism gene primers and Sirt1 gene primers between age groups BMI index groups of pregnant women except for primer 3 in both hypertensive and diabetic ones.

Conflict of Interest: There is no conflict of interest to be mentioned.

Source of Funding: The study was done with personal funding.

Ethical Clearance: The study was approved by the ethical committee of the medical college of university of Baghdad. An informed consent was taken from patients.

References

1. Heidi Schwarzenbach, Dave S. B. Hoon & Klaus Pantel. Cell-free nucleic acids as biomarkers in cancer patients. *Nature Reviews Cancer*. 2011; 11: 426–437.
2. Bianchi D. W., Williams J. M., Sullivan L. M., Hanson F. W., Klinger K. W., and Shuber A. P..

- “PCR quantitation of fetal cells in maternal blood in normal and aneuploid pregnancies”. *American Journal of Human Genetics*. 1997; 61(4): 822–829
3. Avent N. D., Madgett T. E., Maddocks D. G., and Soothill P. W.. “Cell-free fetal DNA in the maternal serum and plasma: current and evolving applications” *Current Opinion in Obstetrics and Gynecology*. 2009; 21 (2): 175–179.
 4. Bansal V., Suresh S., Suresh I., Jagadeesh S., and Fazal G..“Genetic counseling in chromosomal abnormalities”. *Journal of Prenatal Diagnosis and Therapy*. 2010; 1 (1): 14–19.
 5. Chan K. C. A., Ding C., Gerovassili A. et al..“Hypermethylated RASSF1A in maternal plasma: a universal fetal DNA marker that improves the reliability of noninvasive prenatal diagnosis”. *Clinical Chemistry*. 2006; 52 (12): 2211–2218.
 6. Sifakis S, Papantoniou N, Kappou D, Antsaklis A. Noninvasive prenatal diagnosis of Down syndrome: current knowledge and novel insights. *J Perinat Med*. 2012;40:319–327.
 7. Stavros Sifakis, Zeta Koukou, and Demetrios A. Spandidos . Cell-free fetal DNA and pregnancy-related complications (Review). *Mol Med Rep*. 2015; 11(4): 2367–2372.
 8. Lo YM, Corbetta N, Chamberlain PF, Rai V, Sargent IL, Redman CW, Wainscoat JS. *Lancet*. 1997; 350(9076):485-487.
 9. Garabed E.. Obesity, Diabetes, and Chronic Kidney Disease. *Current Diabetes Report*. 2007; 7: 449.
 10. Li X., Wu Y., Zhang L., Cao Y., Li Y., Li J., et al.. Comparison of three common DNA concentration measurement method. *Analytical Biochemistry*. 2014; 451: 18-24.
 11. Damm P, Houshmand-Oeregaard A, Kelstrup L, Lauenborg J, Mathiesen ER, Clausen TD. Gestational diabetes mellitus and long-term consequences for mother and offspring: a view from Denmark. *Diabetologia*. 2016; 59: 1396–1399.
 12. Silva JC, Amaral AR, Ferreira BD, Petry JF, Silva MR, Krelling PC. Obesity during pregnancy: gestational complications and birth outcomes. *Rev Bras Ginecol Obstet*. 2014;36: 509- 513.
 13. Janecka M, Mill J, Basson MA, Goriely A, Spiers H, Reichenberg A, Schalkwyk L, Fernandes C. Advanced paternal age effects in neurodevelopmental disorders-review of potential underlying mechanisms. *Transl Psychiatry*. 2017;7.
 14. Sandin S, Schendel D, Magnusson P, Hultman C, Surén P, Susser E, et al.. Autism risk associated with parental age and with increasing difference in age between the parents. *Mol Psychiatry*. 2016; 21:693–700
 15. Rivera HM, Christiansen KJ, Sullivan EL. The role of maternal obesity in the risk of neuropsychiatric disorders. *Front Neurosci*. 2015; 9: 194.
 16. Edlow AG. Maternal obesity and neuro developmental and psychiatric disorders in offspring. *Prenat Diagn*. 2017; 37:95–110.
 17. Valma H, Jaakka T. Type1 diabetes and Autism: Is there is a link ?. *Diabetes care*. 2006; 29 (2): 484-485.
 18. Laurie T. Gestational diabetes: A risk factor for Autism?. *American Medical Association*. 2017
 19. Wan H, Zhang C, Li H, Luan S, Liu C. Association of maternal diabetes with autism spectrum disorders in offspring: a systemic review and meta-analysis. *Medicine (Baltimore)*. 2018; 97.
 20. Xiang AH, Wang X, Martinez MP, Walthall JC, Curry ES, Page K, Buchanan TA, Coleman KJ, Getahun D. Association of maternal diabetes with autism in offspring. *JAMA*. 2015; 313:1425–1434.
 21. Haigis MC, Guarente LP. Mammalian sirtuins – Emerging roles in physiology, aging, and calorie restriction. *Genes Dev* 2006;20:2913-2921.
 22. Seo KS, Park JH, Heo JY, Jing K, Han J, Min KN, et al. SIRT2 regulates tumor hypoxia response by promoting HIF-1a hydroxylation. *Oncogene* 2015;34:1354-1362.

Modified Early Warning Score Performance in Predicting the Outcome of Head Trauma Patients in Emergency Department

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Abstract

Modified Early Warning Score (MEWS) is a useful scoring system that detects physiological changes in identifying adult medical surgical patients at risk for deterioration and death. Although it is a good predictor of deterioration and mortality in hospitalized patients, the performance of MEWS in the ED and specifically in head trauma patients is still untested. The purpose of this study was to assess the performance of MEWS in predicting the outcome of head trauma patients in ED. We conducted a retrospective observational study at RSUD dr. Soedono Madiun, East Java Province, Indonesia. The sample using the medical record of patients with moderate-severe head trauma adjusted to the inclusion and exclusion criteria and used purposive sampling technique as many as 181 respondents. Multivariate analysis of ordinal logistic regression to determine the MEWS parameters that most influenced the outcome of head trauma patients, while the ability to predict outcomes was assessed using The Area Under Receiver Operating Characteristic (AUROC) analysis. The ordinal logistic regression results show that AVPU parameters show an Odd Ratio (OR) value of =2.89, meaning that the poor AVPU parameter measurement results have a risk of obtaining a death outcome of 2.89 greater than the outcome of moderate disability, severe disability, vegetative state persistence. The AUC MEWS value to predict the outcome of head trauma patients was 0.777 (95% CI; 0.710-0.836) so that based on the AUC value the level of accuracy of MEWS's scoring predictions was in good classification. In conclusion, MEWS's ability shows good performance in predicting the outcome of head trauma patients.

Keywords: ED, Modified Early Warning Score, Outcome of Head Trauma Patients

Introduction

Head trauma is the third largest cause of death in the world after cardiovascular disease and neoplasm¹. Head trauma results in high costs in the treatment system. Early detection and proper management will provide optimal results and reduce maintenance costs². The outcome of trauma patients depends on the severity, the accuracy of the initial assessment and the time to reach the place of care. Rapid and appropriate assessment can reduce long-term mortality and disability³.

The initial evaluation of a patient with trauma is influential for the management of patients with head trauma. Mortality may decrease if head trauma patients are immediately evaluated for proper treatment at the hospital. Preliminary assessments that only use the Glasgow Coma Scale (GCS) to identify the severity of head trauma lack accurate results, so they often fail

to detect the risk of worsening conditions in some age groups^{4,5}. In recent years, several scoring systems have been developed to determine whether patients need intensive care, medication, and appropriate treatment⁶. Scoring system was also developed to evaluate the severity of patients with trauma and will also provide an objective assessment of the patient's initial clinical condition as part of determining trauma management⁷.

MEWS is a simple and fast physiological scoring system that can be applied by nurses. MEWS is performed by summing physiological data which includes systolic blood pressure, pulse, respiration, body temperature and level of consciousness. A higher MEWS score at the time of admission to an Emergency Departement (ED) is correlated with an increase in the need for hospitalization and the risk of death in the hospital⁸.

The ability of MEWS to predict prognosis is very

good. MEWS is also used as a communication facility between nurses and the medical team when the patient's condition worsens⁹. The research conducted by Chang et al (2018) stated that MEWS has a good predictive value for the mortality of renal abscess patients. The value of Area Under Curve (AUC) of MEWS in predicting hospital mortality was 0.7826¹⁰. Similar results were also obtained from the results of the study from Xie et al (2018), discrimination of MEWS in patients with an AUC value of 0.9, this means that MEWS is very good at predicting mortality in ED¹¹.

Various studies related to the validity of MEWS score in the trauma population have been carried out. However, as far as the researchers know there has been no research on the validity of MEWS in populations that are specific to head trauma patients. Whereas, head trauma is a type of trauma that most often causes mortality and morbidity compared to other types of trauma. The aim of the study was to determine the validity of the MEWS in predicting the outcome of patients with head trauma in ED.

Material and Method

This study used analytic observational design with retrospective cohort approach in RSUD dr. Soedono, Madiun, East Java, Indonesia, on March 2019. There were 181 medical records data selected by inclusive and exclusive criteria. Samples were obtained using purposive sampling method where researchers choose some samples according to researchers' preference which meet the inclusion and exclusion criteria. The variables of this study were MEWS scoring and the outcome of head trauma patients. Data collected included age, sex, education, occupation, causes of head trauma, MEWS parameters and outcome of head trauma patients. In MEWS calculation, five parameters were each scored from 0 to 3 (table 1). Data was analyzed with the help of SPSS For Windows Version 20 and Medcalc Software. Ordinal logistic regression analysis used to determine the MEWS parameters that most influential to the outcome of head trauma patients. The AUROC was used to assess the ability of MEWS to distinguish good outcomes and poor outcomes.

Table 1: The Modified Early Warning Score

	3	2	1	0	1	2	3
Systolic Blood Pressure	<70	71-80	81-100	101-199		≥200	
Heart Rate		<40	41-50	51-100	101-110	111-129	≥130
Respiration		<9		9-14	15-20	21-29	≥30
Temperature		<35		35-38.4		≥38.5	
Score AVPU				Alert	Reaction to voice	Reaction to pain	Unresponsive

AVPU: A: alert; V: responding to voice, P: responding to pain; U: unresponsive.

Source: Kruisselbrink et al., 2016¹²

Findings:

Table 2: Characteristics

Variable	Classification	N	%
Gender	Male	128	71
	Female	53	29
Age	16-25	41	23
	26-35	21	12
	36-45	20	11
	46-55	37	20
	56-65	36	20
	>65	26	14
Education	No school	1	1
	Elementary School	71	39
	Junior High School	25	14
	Senior High School	72	40
	College	12	7

Variable	Classification	N	%
Job	Unemployed	19	10
	Salesman	4	2
	Employee	66	36
	Entrepreneur	8	4
	Farmer	45	25
	PNS/TNI/POLRI	9	5
	Student	30	17
Cause of Head Trauma	Traffic Accident	155	86
	Falling down	26	14

Table 2 shows most of the patients were male with 128 people (71%). Based on the characteristics of age, the highest respondent age with a percentage of 23% was the age group 16-26 years. The job of respondents with the percentage of 36% from the total respondents was private employees. The cause of head trauma, almost all of which was a traffic accident with the percentage of 86%.

Table 3: Respondent Frequency Distribution Based on the Results of MEWS Scoring

No	Variable	Classification	Frequency (n)	Percentage (%)
1	MEWS	Low Risk (0-2)	33	18
2		Medium Risk (3-4)	72	40
3		High Risk (≥5)	76	42
Total			181	100

Table 3 shows that out of 181 patients, 76 or 42% included in the high-risk classification, while 33 (18%) included in the low risk classification.

Table 4: Respondent Frequency Distribution Based on the Outcome of Head Trauma Patients

Variable	Classification	Frequency (n)	Percentage (%)
The outcome of Head Trauma Patients	Good recovery	0	0
	Moderate Disability	36	20
	Severe Disability	54	30
	Persisten Vegetative State	3	2
	Death	88	48
Total		181	100

From table 4, the results show that 88 or 48% of the respondents classified in death, whereas none of the respondents classified in good recovery.

Table 5: Multivariate Test for MEWS Parameters

		Estimate	Std. Error	Wald	Sig.	Odds Ratio
Threshold	[Outcome = 2]	3,850	1,286	8,958	0,003	
	[Outcome = 3]	5,590	1,323	17,853	0,000	
	[Outcome = 4]	5,673	1,325	18,333	0,000	
Location	SBP	0,018	0,006	8,328	0,004	1,02
	PULSE	0,005	0,008	,362	0,547	1,01
	RESPIRATION	0,028	0,027	1,098	0,295	1,03
	TEMPERATURE	-0,005	0,006	0,677	0,411	1,00
	AVPU	1,060	0,184	33,150	0,000	2,89

Table 5 showed AVPU parameter OR = 2.89, meaning that the poor AVPU parameter measurement results have a risk of getting a death outcome of 2.89 greater than the outcome of moderate disability, severe disability, persistent vegetative state.

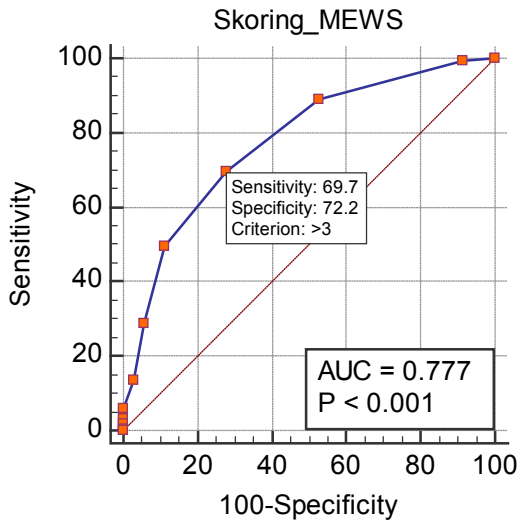


Figure 1: ROC MEWS

Figure 1 showed that the ROC curve is generated from various cut of point values. It can be seen that the ROC curve is above the reference line. The AUC value produced is equal to 0.777 (95% CI; 0.710-0.836), therefore, based on the AUC value the level of accuracy of the predictions of MEWS scoring considered as good classification.

Discussion

Based on the results of the study it was found that almost all respondents (128.71%) were male. This result is almost the same as the research conducted by Hartoyo, Raharjo, & Budiayati (2011) which found 75.4% of respondents were male¹³. Factors that may caused high moderate-to-severe head trauma in men include physical activity and work that is riskier than women. But according to Marcolini, et al (2018) the high incidence of head trauma in men was not only due to physical activity and work, there were hormonal factors in men that will trigger stress and lead to risky behaviors of head trauma such as drinking alcohol while driving¹⁴.

The results of this study indicated that moderate-to-severe head trauma is most experienced by the age range of 16-25 years. This finding is in accordance with the findings of previous studies showing that the age group of 15-24 years was the most group experiencing head trauma, in which this is a group of young adults who

have high productivity and activity¹⁵. Motor vehicle accidents are the most common cause of head trauma in the age group 15-19 years and 20-24 years¹⁶. The high rate of head trauma in this age group due to traffic accidents is possible because of the high mobility and psychological development, where young adults have an unstable psychological development so they often fails to control emotions. This situation caused a lack of awareness in driving.

Based on the type of job, in this study the highest number was private employees with 66 respondents (36%). The results of this study are somewhat different from the results of the study by Krisandi, Utomo, & Indriati (2011) which stated that the type of job of head trauma respondents is students¹⁷. From the results of the study and the fact in previous research, it can be assumed that the type of job had a connection with the incidence of head trauma, and this can be seen from the factors causing head trauma in this study, most of which were traffic accidents (86%). So, it can be concluded that the more often jobs require activities on the road such as riding motorbikes, cars, rickshaws and pedestrians, the higher the possibility of head trauma.

The multivariate test results, AVPU parameter OR= 2,89, meaning that the poor AVPU parameter measurement results have a risk of getting a death outcome was 2,89 and greater than getting moderate disability, severe disability, and vegetative persistence state. AVPU is a simple method of measuring the level of consciousness and used during initial contact with patients. According to Lumbantobing & Anna (2015) the level of awareness can be used as one of the indicators of emergency and prognosis in head trauma. This decrease in awareness can affect the fulfillment of the patient’s basic needs¹⁸. Maas & Steyerberg (2014) stated that the prognosis model of head trauma using level of consciousness showed good prognostic performance¹⁹.

MEWS discrimination scoring performance in this study is good, indicated by the AUC value of 0.77 (95% CI, 0.710-0.836). The AUC value in this study is different compared to the findings in previous studies. In the study of Ghanem-zoubi, Vardi, Laor, Weber, & Bitterman (2011) who examined sepsis patients with predictions of ED mortality, it was obtained AUC score of 0.69 or in the fair prediction category²⁰. Bulut et al (2014) who examined the medical case population and surgery for patients who came to the emergency department on mortality received an AUC value of 0.568²¹. The

same finding was also obtained from the results of the Kruisselbrink et al (2016) study with an AUC value of 0.692¹².

These difference in the performance of discrimination can be explained because the types of cases used in this study were more focused on patients with head trauma. In head trauma patients, physiological status which includes systolic blood pressure, pulse, respiration, body temperature tends to be unstable as a result of auto regulation after experiencing head trauma. Findings that contradict the previous findings provide direction that in the initial assessment of head trauma patients, the doctor cannot only rely on neurological status in determining the degree of mild weight and predictions of head trauma outcomes but also must consider physiological changes.

Conclusion

This study found that MEWS's ability to predict the outcome of head trauma patients showed good performance, so it is necessary to use MEWS scoring as one of the early detection systems or Early Warning Score System (EWSS) in head trauma patients in ED.

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References

1. Weber KT, Guimarães VA, Pontes-Neto OM, Leite JP, Takayanagui OM, Santos-Pontelli TEG. Preditores de qualidade de vida após trauma crânio-encefálico moderado a grave. *Arq Neuropsiquiatr*. 2016;74(5):409–15.
2. Imhoff BF, Thompson NJ, Hastings MA, Nazir N, Moncure M, Cannon CM. Rapid Emergency Medicine Score (REMS) in the trauma population: A retrospective study. *BMJ Open*. 2014;4(5):1–7.
3. Miller RT, Nazir N, McDonald T, Cannon CM. The modified rapid emergency medicine score: A novel trauma triage tool to predict in-hospital mortality. *Injury [Internet]*. 2017;48(9):1870–7. <http://dx.doi.org/10.1016/j.injury.2017.04.048>
4. Scheetz LJ, Horst MA, Arbour RB. Early neurological deterioration in older adults with traumatic brain injury. *Int Emerg Nurs [Internet]*. 2018;37:29–34. <http://dx.doi.org/10.1016/j.ienj.2016.11.003>
5. Najafi Z, Zakeri H, Mirhaghi A. The accuracy of acuity scoring tools to predict 24-h mortality in traumatic brain injury patients: A guide to triage criteria. *Int Emerg Nurs*. 2018;36(May 2017):27–33.
6. Gizem R, Gök Y, Gök A, Bulut M. Assessing prognosis with modified early warning score, rapid emergency medicine score and worthing physiological scoring system in patients admitted to intensive care unit from emergency department-ClinicalKey for Nursing. *Int Emerg Nurs [Internet]*. 2018;(September 2017):0–1.
7. Park HO, Kim JW, Kim SH, Moon SH, Byun JH, Kim KN, et al. Usability verification of the Emergency Trauma Score (EMTRAS) and Rapid Emergency Medicine Score (REMS) in patients with trauma. *Medicine (Baltimore)*. 2017;1–5.
8. Wang AY, Fang CC, Chen SC, Tsai SH, Kao WF. Periarrest Modified Early Warning Score (MEWS) predicts the outcome of in-hospital cardiac arrest. *J Formos Med Assoc [Internet]*. 2016;115(2):76–82. <http://dx.doi.org/10.1016/j.jfma.2015.10.016>
9. Rocha TF da, Neves JG, Viegas K, Rocha TF da, Neves JG, Viegas K. Modified early warning score: evaluation of trauma patients. *Rev Bras Enferm [Internet]*. 2016;69(5):906–11.
10. Chang S, Hsieh C, Weng Y, Hsieh M, Ning Z, Goh L, et al. Performance Assessment of the Mortality in Emergency Department Sepsis Score, Modified Early Warning Score, Rapid Emergency Medicine Score, and Rapid Acute Physiology Score in Predicting Survival Outcomes of Adult Renal Abscess Patients in the Emergency Department. 2018;2018.
11. Xie X, Huang W, Liu Q, Tan W, Pan L, Wang L, et al. Prognostic value of Modified Early Warning Score generated in a Chinese emergency department : a prospective cohort study. 2018;1–8.
12. Kruisselbrink R, Kwizera A, Crowther M, Fox-Robichaud A, O'Shea T, Nakibuuka J, et al. Modified Early Warning Score (MEWS) Identifies Critical Illness among Ward Patients in a Resource Restricted Setting in Kampala, Uganda:

- A Prospective Observational Study. *PLoS One*. 2016;11(3):e0151408.
13. Hartoyo M, Raharjo SS, Budiyati. Predictor's Factors of Mortality of Patients Suffering from Severe Head Injury in Emergency Department at General Hospital Tugurejo Semarang. 2011;175–82.
 14. Marcolini EG, Albrecht JS, Sethuraman KN, Napolitano LM. Gender Disparities in Trauma Care : How Sex Determines Treatment, Behavior, and Outcome. *Anesthesiol Clin*. 2018;37(1):107–17.
 15. Lisnawati, Kwandou L, Akbar M, Muis A, Kaelan C, Patellongi I. Relationship between Cognitive Test For Delirium (CTD) score and outcome based on Glasgow outcome scale (gos) in patients with mild to moderate closed head injuries. *JTS Kesehatan*. 2012;2(2):163–70.
 16. Peeters W, van den Brande R, Polinder S, Brazinova A, Steyerberg EW, Lingsma HF, et al. Epidemiology of traumatic brain injury in Europe. 1st ed. Vol. 157, *Acta Neurochirurgica*. Elsevier B.V.; 2015. 1683–1696 p.
 17. Krisandi E, Utomo W, Indriati G. Description of cognitive status in head injury patients who have been allowed to go home at RSUD Arifin Achmad Pekanbaru. 2011;1–8.
 18. Lumbantobing V, Anna A. The Effect of Sensory Stimulation on the Value of Glasgow Coma Scale in Head Injury Patients in the Neurosurgical Critical Unit Room, RSUP Dr. Hasan Sadikin Bandung. *J Ilmu Keperawatan*. 2015;III(2):105–11.
 19. Maas AIR, Steyerberg EW. Monitoring prognosis in severe traumatic brain injury. 2014;1–2.
 20. Ghanem-zoubi NO, Vardi M, Laor A, Weber G, Bitterman H. Assessment of disease-severity scoring systems for patients with sepsis in general internal medicine departments. 2011;
 21. Bulut M, Cebicci H, Sigirli D, Sak A, Durmus O, Top AA, et al. The comparison of modified early warning score with rapid emergency medicine score: A prospective multicentre observational cohort study on medical and surgical patients presenting to emergency department. *Emerg Med J*. 2014;31(6):476–81.

Contraception Counseling to Reduce Postpartum Unmet Needs: A Qualitative Study at Samarinda, Indonesia

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Abstract

Introduction: Family planning (FP) counseling has a large potential as a strategy for reducing postpartum unmet needs. This study aimed to explore the present-day implementation of FP counseling, and the expectations of providers and recipients of FP counseling.

Method: The research design was a qualitative phenomenological study conducted at Samarinda City, East Kalimantan Province, Indonesia. The research participants were selected with a maximum variation of purposive sampling. The data analysis used thematic analysis.

Results: This study found that FP counseling is currently integrated with ANC. All available method are explained so that clients are confused and forgetful. The choice of method is based on medical questions only. FP counseling is expected to adjust to reproductive needs by cooperation a partner. The clients need more information about the method chosen using practical media counseling. Necessary additional health information and counseling media that can be taken home.

Conclusion: At present there are still weaknesses in FP counselling. It is expected that counseling sessions are more practical, integrated with ANC, concise, easy to remember, meet reproductive needs, cooperation partners and be accompanied by other additional information. The use of a modified Balanced Counseling Strategy (BCS) for pregnant women is a wise and strategic choice.

Keywords: *FP counseling, postpartum unmet needs, balanced counseling strategy.*

Introduction

In developing countries, approximately 214 million women in 2017 at childbearing age wanted to avoid pregnancy but did not use modern contraceptive method.¹ Unmet needs for contraception in Indonesia are relatively low compared to other developing countries. The results of the Indonesian Health Demographic Survey (IDHS)

in 2012 showed that unmet needs in Indonesia was about 11.4%, consisting of 4.5% of spacing pregnancies and 6.9% of limiting pregnancy. High unmet need areas in Indonesia are spread in 10 provinces. One of those is Samarinda City in East Kalimantan Province. Based on data from the 2017 Population and FP Control Board (DPPKB), the unmet needs in Samarinda City was 19.7%, consisted of 9.37% of spacing pregnancy and 10.33% of limiting pregnancy.

The largest proportion of unmet needs for contraception was found in women in the first year after giving birth.² Two-thirds of postpartum women do not want to get pregnant, but do not use contraception. The average postpartum unmet needs in Indonesia from 2007 to 2015 was 26.4%. However, only 50% of Indonesian women start using contraception after 6 months of labor.³

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FP counseling has a high potential as a strategy to reduce postpartum unmet needs by improving the service quality. The main element for improving service quality is improving the interaction between clients and FP service providers.⁴ So, the best strategy to reduce unmet needs is to improve the quality of FP counseling.

Strategy to reduce postpartum unmet needs through FP counseling has been performed, but there are still women who do not want to get pregnant but do not use contraception. Therefore, needed qualitative study aimed to explore the implementation of FP counseling and identify the expectations of providers and recipients of FP counseling.

Subjects and Method

We used a qualitative phenomenological approach to explore views and opinions about FP counseling in Samarinda City, East Kalimantan Province, Indonesia.

The subjects were 8 people selected by purposive sampling considering the maximum sample variation. The selected subjects represented 3 groups of participants: 1) The policy makers(the head of the publichealthdepartment, the head of the development and FP participation section of the Population and FP Control Board (DPPKB), and the head of the primary health care), 2) The counselors namely the midwife in charge of FP clinic, and 3) The clientsare pregnant womens who have received FP counseling.

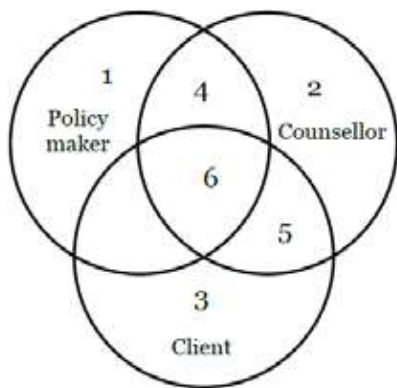


Figure 1: Participants and explored data

Interviews are conducted by someone who works as a midwife and lecturer and has completed education in the field of public health at the master level. Data were collected by interviewer through semi-structured interviews and observing the implementation of FP counseling. The instrument consisted of three interview guides to support the triangulation method. The group

of participants and the data collected are illustrated in Figure 1. Data that were explored included: 1) Policy support, 2) Training of FP counselors, 3) Willingness to receive FP counseling 4) Strategies to reduce postpartum unmet needs, 5) Information on contraceptive method, contraceptive needs, cooperation with partners, and addition of other health information, and 6) Expected FP counseling.

The data were analyzed thematically, using the six steps of qualitative data analysis according to Creswell (2014), namely 1) Transcribe of interview recording results and notes of important events during the data collection process, 2) Coding data, 3) Building categories and themes (using OpenCode 4.03), 4) Describing data, 5) Making comparison between findings and literature, and 6) Ensuring accuracy of findings which are validated by applying triangulation and reflexivity.

Results

From the results of interviews, we classified the quotations into two themes are presented in Table 1. and Table 2.

Current FP Counseling: In Samarinda city, FP counseling received support from policy makers through integration with ANC services and written in standard operating procedures (SOP). The counseling about postpartum contraception is not only done in the FP clinic, but is routinely delivered when the ANC conducts pregnant women class. FP counseling is delivered by midwives, however not all midwives have received FP counseling training.

Table 1: Examples of Quotes from Current FP Counseling Theme

<p>Integrated with ANC: “It has been integrated, we still delivered the postpartum birth control materials at ANC, also in the class of pregnant”.(P.3, head of primary health care)</p>
<p>All method are explained: “All of them are explained, I don’t remember, I forgot a little, I was explained but a bit confused actually “. (P.8, pregnant woman)</p>
<p>Basic method selection</p>
<p>a. Medical question: “We asked about age, date of birth, period, how many children, history of illness here we already have it in accordance with the existing form”. (P.6, midwife).</p>
<p>b. Reproductive needs are not asked: “Counseling is lacking as needed, so sometimes the goal is not achieved, the pregnancy that is too close is still there”. (P.2, Health Office)</p>

The research showed that midwives explained the types and contra indications of various method available at the primary health care. Clients felt that they have received too much information on contraceptive method so that clients felt confused and forgetful. Midwives also felt that FP counseling is currently less effective because the media used seems to require the midwife to explain all the method before helping the clients make choices.

The choice of contraceptive method has not been based on fulfilling the client’s reproductive needs. Midwives use medical questions available on the form as the number of children, history of labor, and history of illness. The questions about fulfilling reproductive needs such as “Do clients still want to have more children or not?” were often ignored. The partner cooperation for method selection was not discussed during FP counseling.

FP counseling that is expected: Some participants argued that FP counseling is better delivered since ANC, because when the mother gave birth was constrained by physical changes, and the psychological condition of mothers who gave birth such as breast pain and baby blues. Some mothers were late for post-natal care (PNC). There are mothers who are pregnant again because they think they will not get pregnant before menstruation returns.

Table 2: Examples of Quotes from the Expected FP Counseling Theme

<p>Integrated with ANC “It’s better for FP counseling since from ANC because she waits for the menstruation occur, she comes for post-natal care, as soon as we check the pregnancy test, the result is positive”. (P.5, Midwife)</p>
<p>According to reproductive needs and cooperation partner “I think it is necessary asking for the purpose of using the method and cooperation from their husbands because it is indeed adjusted, leading to wanting to have more children, yes or no more”. (P.6, Midwife).</p>
<p>Counseling material</p> <p>a. Practical: “I think, the old method may be okay, but it is not implemented well, or maybe there must be a more practical method”. (P.4, Head of Primary health care)</p> <p>b. Compact and easy to remember: “More concisely, she keeps on remembering it, so she can choose it more precisely, because she understands, not because she merely said yes.” (P.1, DPPKB)</p> <p>c. There is additional information: “It could be, we explain the prevention of HIV, or cervical cancer, only if there is a guideline”. (P.6, Midwife)</p>

Counseling media can be taken home:
 “It is necessary, would be happy, so that we can read at home right, so later we will be able to, I mean that it can be thinking about it first”. (P.7, Pregnancy women).

The choice of method should be adapted to the reproductive needs of the client (spacing or limiting pregnancy) and cooperation the partner in determining the choice of method. The informant stated that there were still women who did not want to have a child anymore but chose a short-term contraceptive method because they considered only the best method.

Practical counseling is needed so that the information delivered is concise and easy to remember. Information about the additional benefits of FP may increase motivation for FP. Other health information such as HIV prevention and cervical cancer make it possible to add to this. The addition of counseling time is not a problem for clients or midwives because other health information is also needed.

The clients being given print media to learn at home is considered a good idea that makes it possible to try to help clients recall information that has been delivered. The clients also stated that it is necessary and they are happy to be given counseling media to read at home.

Discussion

Current FP counseling: This study found that Samarinda City FP counseling to promote contraception immediately after birth has been integrated with the maternal and child health (MCH) program. MCH program serves as a “gateway” to reach women throughout the reproductive period to increase access and use of contraception.⁵FP counseling at the ANC has repeatedly been shown to increase post-natal birth control.⁶The counseling is given after delivery but the the client planning to use contraception should be identified since the ANC.⁷

This study showed that current FP counseling has weaknesses. Midwives seem to have explain all available method while clients feel that they receive too much information that is not relevant to the method of choice. Submission of information that is irrelevant by the service provider is one of the barriers to fertility regulation.⁸This is a major cause of unmet needs and continuity barriers to contraceptive use.⁹⁻¹¹

The providers did not discuss the client’s wishes in determining the choice of contraceptive method,

but preferred medical questions in the available forms. The provider did not ask about the client's reproductive intentions (the number of children she wants and the willingness of the partner to cooperate).

FP counseling is expected to reduce unmet needs for postpartum: FP counseling is better began since the ANC rather than PNC. Previous studies found a relationship between PNC and postpartum contraceptive use was lacking, this may be due to limited PNC intensity.¹² Promoting the use of postpartum contraception since ANC is an important strategy because ovulation can return as early as four weeks after delivery, and women may become pregnant before menstruation returns.¹⁰

The clients hope to get more information about the method chosen. Although the duration of counseling is not a problem, service providers should use time efficiently, more practical in assessing client needs, and avoid giving too much information to irrelevant method. The provider must focus on the method chosen by the client and discuss the method in more depth.¹³

The client's reproductive needs for spacing or limiting pregnancy need to be asked, so that the client is able to decide on the appropriate FP method reproductive needs. Intentions to use contraception that were not asked, caused the selection of method to be incompatible with the purpose of contraceptive use and had an impact on the continuity of contraceptive use.¹³

FP counseling needs to cooperation the partner, and this is reasonable. Some men expect to have a discussion before using contraception.¹⁴ In fact, women who were confident of gaining support from their partners were twice as likely to use contraception.¹⁵ Otherwise, 43% of women stop contraception on the grounds that they are opposed by partners.¹⁶ Therefore, questions about the willingness of partners to work together should not be ignored.

Addition of other health information makes it possible to add. Integrating other health information with FP counseling is an ideal strategy to improve the effectiveness of FP programs, improve cost efficiency, and the possibility of clients accessing additional health services.^{17,18}

Participant felt the need for counseling media to be learned at home to make it easier for clients to remember information obtained from midwives. The women given

leaflets after FP counseling sessions showed there was a significant increase in contraceptive use.¹⁹

FP counseling that is expected integrated with ANC, practical, information was concise, clear, easy to understand, and easy to remember. The expected FP counseling is similar to the Balanced Counseling Strategy (BCS).²⁰ BCS has been proven to improve the quality of FP services, increases contraceptive use and continuity of use.²¹

We concluded that weaknesses were still found in the implementation of FP counseling. FP counseling which is expected to reduce unmet need postpartum is similar to BCS. Therefore, we recommend that considering the use of BCS after adjusting for pregnant women is a wise and strategic choice.

Conflict of Interest: Authors declare that there is no conflict of interest within research, publication paper and funding support.

Ethical Clearance: Research has obtained approval from Medical and Health Research Ethics Committee Faculty of Medicine Universitas Gadjah Mada with number: KE/FK/0971/EC/2017

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References

1. Darroch JE, Audam S, Biddlecom A, Kopplin G, Riley T, Singh S, et al. Adding it up: investing in contraception and maternal and newborn health, 2017. Fact sheet New York: Guttmacher Institute. 2017.
2. Ross JA, Winfrey WL. Contraceptive use, intention to use and unmet need during the extended postpartum period. *International Family Planning Perspectives*. 2001;20-7.
3. Wilopo SA, Setyawan A, Pinandari AW, Prihyugianto T, Juliaan F, Magnani RJ. Levels, trends and correlates of unmet need for family planning among postpartum women in Indonesia: 2007–2015. *BMC women's health*. 2017;17(1):120.
4. Jain AK, Obare F, Rama Rao S, Askew I. Reducing unmet need by supporting women with met need. *International Perspectives on Sexual and Reproductive Health*. 2013;39(3):133.
5. Ahmed S, Ahmed S, McKaig C, Begum N, Mungia J, Norton M, et al. The effect of integrating family

- planning with a maternal and newborn health program on postpartum contraceptive use and optimal birth spacing in rural Bangladesh. *Studies in Family Planning*. 2015;46(3):297-312.
6. Cleland J, Shah IH, Daniele M. Interventions to improve postpartum family planning in low and middle income countries: program implications and research priorities. *Studies in Family Planning*. 2015;46(4):423-41.
 7. Quiterio G, Molina M, Miric M, Vernon R, Rivero-Fuentes ME. Situation analysis of the integration of family planning services in postpartum, postabortion and prevention of mother to child transmission programs in the Dominican Republic. Population Council: *Frontiers in Reproductive Health*. 2008.
 8. Campbell M, Sahin Hodoglugil NN, Potts M. Barriers to fertility regulation: a review of the literature. *Studies in Family Planning*. 2006;37(2):87-98.
 9. Casterline JB, Perez AE, Biddlecom AE. Factors underlying unmet need for family planning in the Philippines. *Studies in Family Planning*. 1997:173-91.
 10. Cleland J, Harbison S, Shah IH. Unmet need for contraception: issues and challenges. *Studies in Family Planning*. 2014;45(2):105-22.
 11. Machiyama K, Cleland J. Unmet need for family planning in Ghana: the shifting contributions of lack of access and attitudinal resistance. *Studies in Family Planning*. 2014;45(2):203-26.
 12. Do M, Hotchkiss D. Relationships between antenatal and postnatal care and post-partum modern contraceptive use: evidence from population surveys in Kenya and Zambia. *BMC health services research*. 2013;13(1):6.
 13. León FR, Monge R, Zumarán A, García I, Ríos A. Length of counseling sessions and the amount of relevant information exchanged: a study in Peruvian clinics. *International Family Planning Perspectives*. 2001:28-46.
 14. Adeniran A, Fawole A, Adesina K, Aboyeji A, Ezeoke G. Maternal near-miss in a great grandmultipara following unsafe abortion: A focus on the uncommon contributing factors. *IMTU Medical Journal*. 2014;5(1):11-4.
 15. Kraft JM, Harvey SM, Hatfield-Timajchy K, Beckman L, Farr SL, Jamieson DJ, et al. Pregnancy motivations and contraceptive use: hers, his, or theirs? *Women's Health Issues*. 2010;20(4):234-41.
 16. Muhindo R, Okonya JN, Groves S, Chenault M. Predictors of contraceptive adherence among women seeking family planning services at Reproductive Health Uganda, Mityana Branch. *International Journal of Population Research*. 2015;2015.
 17. White HL, Meglioli A, Chowdhury R, Nuccio O. Integrating cervical cancer screening and preventive treatment with family planning and HIV related services. *International Journal of Gynecology & Obstetrics*. 2017;138:41-6.
 18. Hewett PC, Nalubamba M, Bozzani F, Digitale J, Vu L, Yam E, et al. Randomized evaluation and cost-effectiveness of HIV and sexual and reproductive health service referral and linkage models in Zambia. *BMC Public Health*. 2016;16(1):785.
 19. Saeed GA, Fakhar S, Rahim F, Tabassum S. Change in trend of contraceptive uptake effect of educational leaflets and counseling. *Contraception*. 2008;77(5):377-81.
 20. León FR, Brambila C, de la Cruz M, Colindres JG, Morales C, Vásquez B. Providers' compliance with the balanced counseling strategy in Guatemala. *Studies in Family Planning*. 2005;36(2):117-26.
 21. León FR, Brambila C, de la Cruz M, Bratt J, Colin-dres JG, Vásquez B, et al. Testing balanced counseling to improve provider-client interaction in Guatemala's MOH clinics. *FRONTIERS Final Report*. 2003.

Outbreak of Diarrhea in Pondok Duta Elementary School, Depok, 2018

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Abstract

Introduction: Diarrhea is an endemic disease in Indonesia. Diarrhea in Pondok Duta Elementary School, Depok was determined as an outbreak in 2018. The purpose of this study is to define the factor associated with diarrheal incidence and provide a recommendation for the outbreak prevention in the future.

Method: This study is used retrospective cohort design, Chi square test andCox regression Proportional Hazard Regression Model.

Results: 335 students(50,2%) were reported diarrhea in October 2018. Bivariate analysis showed that diarrhea was significantly associated with snack behaviour (RR=1.58,95% CI=1.32-1.89,p=0.000), drinking refilled water (RR=1.3,95%CI=1.11-1.52,p=0.003), use of water from old well (RR=1.24,95%CI=1.06-1.45,p=0.010) and cutting nail (RR=1.21,95% CI=1.02-1.44,p=0.038). In final cox regression model, diarrhea was significantly associated with snack behavior (RR=1.70,95%CI=1.34-2.17,p=0.000)and use of water from anew well (RR=0.70,95%CI=0.53-0.93,p=0.010).Coliform and E.Coli were detected in the refilled water samples.

Discussion: There was a great risk of infectious diarrhea among the students for two weeks. Snack behavior was the strongest factor in students diarrhea. Use of water from a new well was considered to be protective against the incidence of diarrhea. Improvement in providing healthy food at the canteen including maintaining the strict food hygiene, sanitation regulation and practices were essential. This recommendation needs to be followed up by the school administrators and local authorities.

Keywords: Diarrhea, outbreak, elementary school, water, snack, hygiene, sanitation

Introduction

Diarrhea is an endemic disease in Indonesia. Diarrhea causes 15-34% of mortality in Indonesia¹. In 2015, there were 18 times diarrheal outbreaks in 18 districts/cities, with 1.213 people and 30 mortality (CFR 2.47%)². In 2018, the prevalence of diarrhea in Indonesia was 8% and in West Java was 8.6%³. Diarrhea cases found and handled in Depok, 2017 were 33,583 cases (69.6%)⁴. Pondok Duta Elementary School as a place of research was due to diarrhea cases being designated as outbreak in 2018.

Method

Design and Subject: This investigation was conducted using a retrospective cohort design. The

investigation was conducted from October 14th-18th 2018 in Pondok Duta Elementary School. The number of samples were 677 students. The definition of diarrhea used was the condition of a student defecating with liquid consistency even in the form of water and a frequency of three times or more in one day⁵.

Data of outbreak consisted of socio-demographic characteristics, illness status, clinical symptoms, onset, and individual behavior for the past two weeks before the investigation.

Environmental Assessment and Laboratory Test: Environmental assessment in school included examination of water from the old well and new well, septic tanks, hygiene of food in the canteen and hygiene of refilled water. Testing of water samples was done to

see biological, physical and chemical contamination. Testing of food from canteen and fecal samples from patient was conducted to confirm the presence of microorganism.

Statistical analysis: All data were imported and analyzed using the Stat a application. The univariate analysis was done to describe case distribution based on characteristic of person, place and time. Bivariate analysis was conducted to determine associations between all risk factors and diarrheal incidence using *Chi-Square* tests. Multivariate analysis was done by using Cox Proportional Hazard Regression Model.

Result

Surveillance data showed an increase of diarrheal cases from late September until mid-October 2018. Within this period, 335 cases of diarrhea were reported. The peak of the curve occurred on October 10th 2018 with 56 cases (Figure 1). Our investigation found that the attack rate of diarrhea was 50.2%. Most predominant symptom was abdominal pain (Table 1).

Further bivariate analysis showed that the incidence of diarrhea was significantly associated with snack behavior in the canteen, drinking of refilled water, use of water from old well, and cutting nail. In the final Cox regression model, snack behavior in the canteen was the strongest risk factors of diarrhea. Use of water from a new well was considered to be protective factor against diarrhea (Table 2).

The foods or drinks for students were brought from home, catering or school canteens. Observation of canteen, snacks were in the form of packaged or ready-to-eat or drink that must be mixed. Canteen used

drinking water from the gallon water. Cookware was washed using water from the new well.

Refilled water from school was taken from a vendor. In early October, the school took an initiative to replace vendor because there was dirt in the gallons of refilled water.

Sources of clean water for students were from the old well that had been used more than 25 years and a new well that has been used for two years. Clean water is used for the purposes of ablution, hand washing, and toilet. On October 9th, students complained that the tap water of ablution produced smelling water. The old well had not been used and the distortion of the water has been diverted using water from a new well.

The samples of clean water were taken directly from both wells. Food samples were taken from the canteen. A refilled water sample was taken from an previous vendor. Stool samples were taken from patients who were still sick.

The septic tank was ±8 meters from the old well and ±25 meters from the new well. The soap for washing hands was often not available.

Laboratory results of water from old well showed E.coli were still below the threshold value of clean water. Chemical and physical parameters of water from the old well were still in normal value but pH of water was below normal value. Laboratory results of refilled water and water from new well showed total coli form and E.coli. *Vibrio cholera* and *Salmonella* were not found. The results of biological culture (food and stool samples), E.coli, *Vibrio cholera* and *Salmonella* were not found (Table 3).

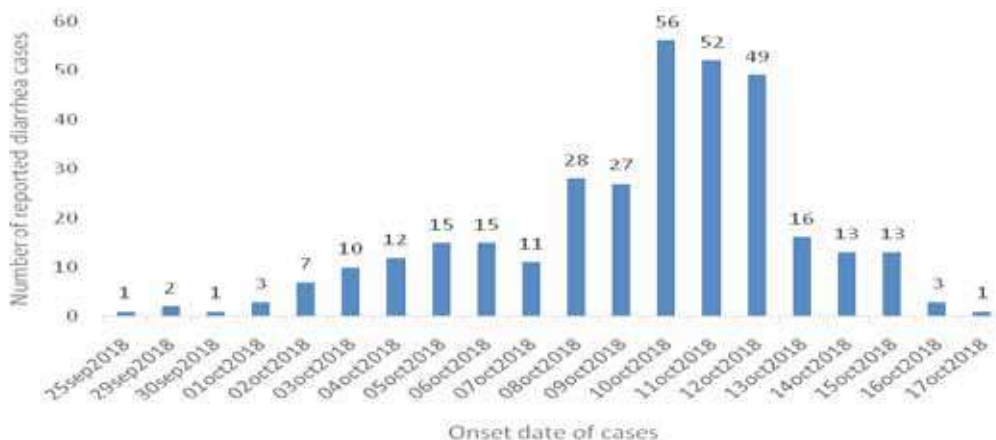


Figure 1. The Epidemic Curve of Reported Diarrhoea

Table 1: Population Characteristic of Outbreak Respondens

	Overall (n=667)	%
Age–median (years)	9	
mean	8.9	
min-max	5 - 12	
Boy	312	46.8
Students with diarrhea		
School grade I	38	41.8
School grade II	51	51.0
School grade III	42	37.5
School grade IV	67	58.8
School grade V	85	64.9
School grade VI	52	43.7
Total	335	50.2
Other symptoms :		
Feces smell bad	44	13.1
Nausea/vomiting	129	38.5
Abdominal pain	234	69.9
Fever	87	26.0
Headache	120	35.8

Table 2.Risk Factor Associated with Diarrhea using Bivariate and Multivariate Analysis

Variable	Diarrhea (%)	RR	Bivariate Analysis		Multivariate Analysis		
			95%CI	p-value	RR	95%CI	p-value
Snack behavior in canteens							
Yes	239 (58.6)	1.58	1.32 – 1.89	0.000	1.70	1.34 - 2.17	0.000
No.	96 (37,1)						
Eating food from catering							
Yes	62 (55.9)	1.14	0.94 – 1.38	0.194			
No.	273 (49.1)						
Drinking of refilled water							
Yes	249 (47.2)	1.3	1.11 - 1.52	0.003			
No.	86 (61.4)						
Use of water from the old well							
Yes	103 (58.5)	1.24	1.06 – 1.45	0.010			
No.	232 (47.3)						
Use of water from the new well							
Yes	64 (43.0)	0.82	0.67 - 1.01	0.044	0.70	0.53 – 0.93	0.010
No.	271 (52.3)						
Not washing hands with soap before eating at school							
Yes	166 (52.4)	1.08	0.93 - 1.26	0.293			
No.	169 (48.3)						
Not washing hands with soap after defecating							
Yes	7 (43.8)	0.87	0.50 – 1.52	0.600			
No.	328 (50.4)						

Variable	Diarrhea (%)	RR	Bivariate Analysis		Multivariate Analysis		
			95%CI	p-value	RR	95%CI	p-value
Borrowing food tools							
Yes	29 (49.2)	0.98	0.74 – 1.28	0.863			
No.	306 (50.3)						
Cutting nail							
Yes	78 (58.2)	1.21	1.02 - 1.44	0.038			
No.	257 (48.2)						
Biting nail							
Yes	51 (49.5)	0.80	0.80 - 1.21	0.875			
No.	284 (50.4)						

Table 3: Laboratory result of Water

Water from Old Well (11th October 2018)				
A. Physics				
No Parameter Result Standard^{14,25} Unit				
1	Smell	Negative	Negative	
2	Amount of solid	232	1500	mg/l
3	Turbidity	0	25	NTU
4	Taste	Normal	Normal	
5	Color	0	50	PtCo
B. Chemistry				
Anorganic				
1	Iron (Fe)	<0.016	1.0	mg/l
2	Fluorida	0.263	1.5	mg/l
3	CaCO ₃	57.42	500	mg/l
4	Clorida	54	600	mg/l
5	Nitrat	0.627	1.0	mg/l
6	Nitrit	0.001	1.0	mg/l
7	pH	6.25	6.5–8.5	pH
8	Zinc	<0.008	15	mg/l
Organic				
1	Detergent	0.216	0.5	mg/l
2	Organic	<1	10.00	mg/l
C. Microbiology				
1	Coliform	11	50	CFU/100ml
2	E.Coli	0	0	CFU/100ml
Refilled Water (18th October 2018)				
1	Coliform	<1.1	0	CFU/100ml
2	E.Coli	<1.1	0	CFU/100ml
Water from New Well (18th October 2018)				
1	Coliform	1	50	CFU/100ml
2	E.Coli	<1	0	CFU/100ml

Discussion

Snack behavior was the strongest factor in students diarrhea. It's like the studies of Dyna, Lambu, Nita and Almanfaluth, there were association of snack with diarrhea in Pekanbaru ($p = 0.01$)⁶, Banjarbaru ($p < 0.05$)⁷, Mraggen ($p = 0.06$)⁸ and Banyumas ($p = 0.002$)⁹.

Contaminated food is defined as food which if consumed by humans will cause disease; foods that contain pathogenic microorganisms cause disease; foods that have decreased in quality from standards; foods that have experienced physical deviations that exceed the limits of quality standards, include irregularities in aspects of color, texture, smell and forms¹⁰. The selection of food ingredients is usually not guaranteed quality, besides the method of storing food is not done properly so as to cause contamination from bacteria and viruses¹¹. Colonies of microorganism were not found in biological cultures. It could be caused by volume and various of food samples were limited and the students got diarrhea had antibiotic treatment before.

Drinking refilled water was the factor of students diarrhea too. It's like studies of Yulviana and Ayuningrum, there were association of refilled water with diarrhea in Birobuli ($p < 0.05$)¹² and East Java (OR 4.41; $p = 0.042$)¹³. Coliform and E.coli should not be found in drinking water¹⁴. This can be caused by lack of sanitation hygiene in the process or transportation. The result of Lipinwati study showed there were 38,10% samples of refilled water contained fecal coliform, and 64,29% samples contained non-fecal coliform¹⁵.

The preference of refilled water vendors must consider the legal aspects such as distribution permit and the protocol of quality inspection. The presence of microorganism prove the existence of contamination in the process of supplying drinking water. Hygiene and sanitation in the process of refilled water need to be improved and evaluated. Laboratory examination of refilled water parameters must be done routinely to ensure the quality of government standard.

Like the studies of Putra and Bumulo in Karangnyar (OR=3.232,95% CI=1,294-8,074, $p = 0.018$)¹⁶, and Gorontalo (OR= 1.61,95% CI=1,15-2.26, $p < 0.05$)¹⁷, clean water supply was the factor of students diarrhea.

The distance of 10 meters between septic tanks and wells has become common knowledge in community. The reason is water from well is not contaminated with septic tank water by pathogenic bacteria that can interfere

with health¹⁸. The old well as a source of clean water has the risk of diarrhea due to the distance less 10 meter from the septic tank. Indonesian National Standard (SNI) 03-2916-1992, the horizontal distance of the well upstream from groundwater flow or source of septic tank is more than 11 meters, while the well distance for communal septic tank to housing is more than 50 meter¹⁹.

Septic tanks are dirt and rarely sucked can seep into the surrounding soil and groundwater. Pipe systems are susceptible to contamination due to leakage and negative pressure caused by irregular supply²⁰. Septic tanks should be given a layer of cement, becoming waterproof so as not to contaminate the surrounding soil. The well excavated must be coated until the cement is at least 3 meters deep to prevent bacterial contamination. Drainage of sediments in reservoirs is also needed to reduce soil deposits contaminated with pathogenic bacteria from septic tanks¹⁹.

pH of this water was lower than the standard. Pure water is neutral, with it's pH at 25 ° C set as 7.0. There is no relationship between pH in drinking water and its effect on health. The pH of stomach fluid is with a mean of approximately 2.0. There is a range of commonly encountered foods that are also of low pH. A direct relationship between human health and the pH of drinking water is impossible to ascertain, because pH is so closely associated with other aspects of water quality; acids is weak and usually very dilute²¹.

The use of water from a new well for all bathrooms and ablution faucets must be maintained because it is considered to be protective against the incidence of diarrhea. However, clean water from both wells must not be consumed because it contains small amount of coliform and E.coli.

There were significantly association of cutting nail with students diarrhea. Sutanto and Nita studies, cutting nail was the factor of students diarrhea in Sukoharjo ($p = 0,004$)²² and Mraggen ($p = 0.02$)⁸. Nails can be a nesting place for germs and where germs breed. Biting nails can cause microorganisms move into the mouth and into the digestive tract which will cause various digestive problems such as diarrhea²². It is recommended that each student cuts his nail every week to prevent diarrhea²³.

We can see that the basic problems triggering the outbreak was about hygiene and sanitation. Food hygiene is a way of handling food ingredients to prevent damage and food poisoning. Kitchen hygiene is a

requirement for kitchen buildings to prevent rodents, insects, and cockroaches from entering the kitchen area. Individual hygiene is a way to maintain personal hygiene and performance requirements of a processor and food waiter. Equipment sanitation is to choose cleaning materials and sanitary materials, selection of cleaning tools, and equipment cleaning techniques. Room sanitation and furniture are preparing cleaning materials and sanitary materials, cleaning and sanitizing techniques, and cleaning schedules¹⁰. No hand washing, less clean and unhygienic snacks, can increase the incidence of diarrhea by 52%. This supports the results of the study that has been done²⁴.

The results of this investigation certainly cannot be fully prevented from various limitations in such way that it may affect the validity and precision of the study. These limitations were information bias. In this study, data collection using a questionnaire was very subjective, so the correctness of the data was very dependent on the honesty of the respondents and the sensitivity of the interviewers at the time of observation.

Conclusion

We concluded that risk factors significantly affected diarrhea in this outbreak were snack behavior in the canteen, drinking refill water, use of water from the old well and cutting nail. Use of water from a new well was considered to be protective against the incidence of diarrhea.

Recomendation: Improvement in providing healthy food at the canteen including maintaining the strict food hygiene, sanitation regulation and practices were essential and necessary to be followed up by the school administrators and local authorities.

Conflict of Interest: There is no conflict of interest.

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Ethical Clearance: Ethical approval number 124/UN2.F10/PPM.00.02/2019 from The Research and Community Engagement Ethical Committee Faculty of Public Health Universitas Indonesia

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References

1. Wardhani D. Faktor-faktor Yang Berhubungan dengan Frekuensi Kejadian Diare pada Bayi Umur 7-12 Bulan di Wilayah Kerja Puskesmas Kedungmundu Kecamatan Tembalang Kota Semarang. *J Kesehat Masy*.2012;1(2):945–54.
2. Kemkes RI. Profil Kesehatan Indonesia tahun 2015.2016.
3. Kemkes RI. Riset Kesehatan Dasar tahun 2018.2019.
4. Dinkes Kota Depok. Profil Kesehatan Kota Depok tahun 2017.2018.
5. Depkes RI. Buku Saku Petugas Kesehatan Lintas Diare. Jakarta;2011.
6. Dyna F, Putri VD, Indrawati D. Hubungan Perilaku Konsumsi Jajanan pada Pedagang Kaki Lima dengan Kejadian Diare. *Endurance*.2018;3(3):524–30.
7. Aditya PH, Djallaluddin MSN. Hubungan Perilaku Jajan dengan Kejadian Diare pada Anak Sekolah Dasar di Kelurahan Cempaka Kec Cempaka Banjarbaru. *Berk Kedokt*. 2013;9(1):81–6.
8. Ayu N. Hubungan Antara Personal Hygiene dengan Kejadian Diare pada Siswa SDN Batusari 5 Mraggen tahun 2016 [Internet].2016[cited 2019 May1]. Available from: http://eprints.dinus.ac.id/20323/2/jurnal_18694.pdf
9. Almanfaluth M, Budi M. Hubungan Antara Konsumsi Jajanan Kaki Lima terhadap Penyakit Diare pada Anak Sekolah Dasar. *Medisains*.2015;XIII(3):58–65.
10. Kemendikbud RI. Sanitasi, Hygiene dan Keselamatan Kerja Bidang Makanan 1.2013.
11. Fatmawati, Arbianingsih M. Faktor yang Mempengaruhi Kejadian Diare Anak Usia 3-6 Tahun di TK Raudhatul Athfal Alauddin Makassar. *J Islam Nurs*.2015;1(1):21–32.
12. Yulviana N. Hubungan Tingkat Kejadian Diare dengan Konsumsi Air Minum Isi Ulang di Wilayah Kerja Puskesmas Birobuli tahun 2015 [Internet]. PSPD;2017[cited 2019 May1]. Available from: http://lib.fkik.untad.ac.id/index.php?p=show_detail&id=2217&keywords=
13. Ayuningrum VSM. Analisis Faktor Sanitasi dan Sumber Air Minum yang Mempengaruhi Insiden Diare Pada Balita di Jawa Timur dengan Regresi Logistik Biner. *Sains dan Seni ITS*.2016;Volume 4(2):223–8.

14. Kemkes RI. Peraturan Menteri Kesehatan No. 492/ Menkes/PER/IV/2010 tentang Persyaratan Kualitas Air Minum.
15. Lipinwati, Darmawan A, Kusdiyah E, Karolina ME. Uji Kualitas Air Minum Isi Ulang di Kota Jambi. *JMJ*.2013;2(2):2–6.
16. Putra A, Rahardjo M, Joko T. Hubungan Sanitasi Dasar dan Personal Hygiene dengan Kejadian Diare pada Balita di Wilayah Kerja Puskesmas Tasikmadu Kabupaten Karanganyar. *Kesehat Masy*.2017;5(1):422–9.
17. Bumulo S. Hubungan Sarana Penyediaan Air Bersih dan Jenis Jamban Keluarga dengan Kejadian Diare pada Anak Balita di Wilayah Kerja Puskesmas Pilolodaa Kecamatan Kota Barat Kota Gorontalo tahun 2012.2012[cited 2019 May1];Available from:<https://media.neliti.com/media/publications/37224-ID-hubungan-sarana-penyediaan-air-bersih-dan-jenis-jamban-keluarga-dengan-kejadian.pdf>
18. Pokja AMPL. Mengatur Jarak Sumur dan Septic Tank Rumah Tangga-Pokja AMPL: Air Minum dan Penyehatan Lingkungan [Internet]. *Pikiran Rakyat*.2007[cited 2019 May1].Available from:<http://www.ampl.or.id/digilib/read/mengatur-jarak-sumur-dan-septic-tank-rumah-tangga/22213>
19. Kesmas. Syarat Jarak Aman antara Septic Tank dengan Sumur Gali dan Faktor yang Mempengaruhinya [Internet].2016[cited 2019 May1].Available from: <http://www.indonesian-publichealth.com/jarak-septic-tank/>
20. Unicef Indonesia. Air Bersih, Sanitasi & Kebersihan [Internet]. Ringkasan Kajian. 2012[cited 2019 May1].Available from:https://www.unicef.org/indonesia/id/A8_-_B_Ringkasan_Kajian_Air_Bersih.pdf
21. WHO. pH in Drinking-water Revised background document for development of WHO Guidelines for Drinking-water Quality [Internet].2007[cited 2019 May1].Available from: https://www.who.int/water_sanitation_health/dwq/chemicals/ph_revised_2007_clean_version.pdf
22. Sutanto. Hubungan Perilaku Higiene dengan Kejadian Diare pada Siswa SD Negeri 01 Trangsan Kecamatan Gatak Kabupaten Sukoharjo. Muhammadiyah Surakarta; 2017.
23. Nurjannah A. Personal Hygiene Siswa Sekolah Dasar Negeri Jatinangor. *Students e-Journal* [Internet].2012[cited 2019 May1];1(1):31. Available from: <http://jurnal.unpad.ac.id/ejournal/article/view/725/771>
24. Purnamasari P, Megatsari H. Determinan yang Berhubungan dengan Tindakan Kebersihan Diri Santriwati di Pondok Pesantren X Jombang. *J Promkes*. 2015;3(2):146–58.
25. Kemkes RI. Peraturan Menteri Kesehatan Republik Indonesia Nomor 32 Tahun 2017 Tentang Standar Baku Mutu Kesehatan Lingkungan dan Persyaratan Kesehatan Air Untuk Keperluan Higiene Sanitasi,Kolam Renang,Solus PerAqua dan Pemandian Umum.

The Effect of Metabolic Syndrome on Systolic Function of Left Ventricle Using Echocardiographic Examination

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Abstract

Objective: Metabolic syndrome may cause bad prognosis on diastolic or systolic function of the left ventricle. Thus, this research aimed to recognize the possible effect of metabolic syndrome on systolic and diastolic function of left ventricle using ECHO.

Study Design: Prospective case-control study.

Place and duration of study: Soad Kafafi Hospital, Egypt, from May 2016 to March 2018.

Methodology: This research included forty patients with metabolic syndrome (18 male, 22 female, mean age=54.13±6.33 years) and forty control matching age and sex volunteers without history of metabolic syndrome disorder (15 male, 25 female, mean age=52.20±5.27). MS was defined according to ATP-NCEP III criteria. Waist circumference will be measured to all participants at the start of study inclusion. Height and weight was measured to calculate Body mass index using standardized formula. Participants underwent laboratory investigations and complete echocardiography. Left ventricular function of the heart was assessed using Echocardiographic examination.

Results: There was a statistical significant difference regarding Left atrial (LA) diameter, Inter ventricular septum and posterior wall thickness in metabolic syndrome patients than normal control persons. The incidence of diastolic dysfunction was significantly higher in metabolic syndrome group compared to control.

Conclusion: MS may cause LV diastolic dysfunction although systolic function was preserved.

Keywords: -metabolic syndrome, diastolic dysfunction, diabetes, hypertension, left ventricular function.

I Introduction

Metabolic syndrome is defined as a group of interacted risk factors which include truncal obesity, type II diabetes mellitus (DM), hypertension, high triglyceride level and low high density lipoprotein level^[1]. The component of metabolic syndrome may be the cause development of cardiovascular disease (CVD)^[2]. Its prevalence is further growing in both males and females due to a life style characterized by high calorie consumption and low physical activity^[3,4]. Plandevall et al. recommend routine waist circumference measurement to determine metabolic syndrome and its related diabetes and coronary heart disorders^[5].

Interestingly it was found that metabolic syndrome components (diabetes, obesity, and hypertension) develop before the development of cardiovascular disease^[6]. Previous studies demonstrated that heart failure may occur as a result of diastolic dysfunction although ejection fraction was normal^[7]. The mechanisms by which Left Ventricular diastolic dysfunction developed to heart failure were not completely identified. Some proposed mechanisms are that metabolic syndrome may alter function and geometry of the left ventricle which may result in coronary heart disease. Some studies have shown that LV dysfunction independently to metabolic syndrome components. However, some studies have shown relation between hypertension as a component

of metabolic syndrome and increased left ventricular mass in MS patients. Further studies might conduct to define different mechanisms for the development of cardiovascular disease as a result of metabolic syndrome^[8].

Methodology

This research included forty patients with metabolic syndrome (18 male, 22 female, mean age=54.13±6.33 years) and forty control matching age and sex volunteers without history of metabolic syndrome disorder (15 male, 25 female, mean age=52.20±5.27). Patients were recruited from the outpatient department at soad-kafafi hospital. Diagnosis of metabolic syndrome was performed according to IDF criteria. According to this criterion MS diagnosed with waist circumference ≥80 cm for women or ≥90 cm for men plus abnormal two parameters of the following: High density lipoprotein cholesterol ≥50 mg/dL for women or ≥40 mg/dL for men; triglyceride levels ≥150 mg/dL and random blood glucose levels ≥100 mg/dL, blood pressure ≥130/85 mmHg.

At inclusion medical history of all subjects was taken then echocardiographic examination was done for all subjects included in the study. Blood pressure was measured by available sphygmomanometer. Height and weight was measured to calculate Body mass index using standardized formula. Complete lipid profile test, random blood sugar, liver and renal function test and

urinalysis using standard operating procedures.

The study approved by ethical committee of Soaad-Kafafi hospital. The exclusion criteria include; Patients suffer from MI, cor pulmonale, atrial fibrillation, cardiomyopathy, valvular heart disease,atrioventricular block hypothyroidism and renal failure.

Echocardiographic examination was done with available machine (GE Vingmed, Horten, Norway) with a 1.5 or 3.2 MHZ phased array transducer. Patients were lying in the left lateral position and breathing gently. A comprehensive echocardiographic study following standardized protocols was carried for all subjects^[9]. Participants are asked to perform passive expiration the whole cardiac movement.

Statistical analysis: Statistical package SPSS version 21 was used for entered of statistical data. Data was summarized using number and percentage for qualitated variables,mean and SD for quantitative variables which are normally distributed while median and interquirtile range formula were used for quantitative variables which are not normally distributed. Independent sample t-test was used for quantitative variables which are normally distributed while non-parametrical Mann-Whitney Test was used for quantitative variables which are not normally distributed. P value<0.05was considered statistically significant. Normality was checked by Shapiro test.

Results

Table 1: Clinical characteristics of the study groups.

Variables	Metabolic Syndrome	Control	P-Value
Age	54.13±6.33 ^a	52.20±5.27 ^a	.143*
BMI	36.22 ± 7.53 ^a	25.55±4.96 ^a	<.001*
WC (cm)	119.65±14.36 ^a	83.03 ± 7.24 ^a	<.001*
SBP	142.50 (130:160) ^b	114.50 (110.00:120.00) ^b	<.001**
DBP	90.00 (80.00:95.00) ^b	76.00 (75.00:80.00) ^b	<.001**
RBS	97.00 (83.00: 143.00) ^b	87.00 (81.00:90.00) ^b	.003**
TG	146.50 (120.00:210.75) ^b	131.00 (113.00:144.75) ^b	.003**
HDL	43.68±8.47 ^a	53.10 ±6.56 ^a	<.001*

BMI: Body mass index; WC; waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; RBS: random blood sugar; HDL: high density lipoprotein cholesterol.

Indicates a significant p-value (p < 0.05). mean ± standard deviation (^a), median (IQR) (^b), P value by independent sample t-test (*); P value by Mann-Whitney Test (**).

Table 2: Sex distribution among control and metabolic syndrome groups

Sex	Metabolic Syndrome		Control		P-Value
	N	%	N	%	
Female	22	55.0	25	62.5	0.496
Male	18	45.0	15	37.5	

Both gender and age were not significantly different among the two studied groups (Table 1a & b). Regarding clinical parameters, the result shown that both body mass index and waist circumference were found to be significantly higher in patients with metabolic syndrome group compared to normal control group. The prevalence of hypertension was found to be significantly higher in group I (metabolic syndrome group) compared to group II (normal control group) (Table 1a). Among laboratory investigations, triglyceride level and random blood sugar were statistically significant higher in metabolic syndrome group compared to control group. However, HDL-cholesterol level was found to be significantly higher in control group compared to metabolic syndrome group compared to (Table 1a).

Table 3: Comparison of standard echo cardiographic parameters between metabolic syndrome group and normal control group

Variables	Metabolic Syndrome Group	Control	P-value
LVED(mm)	47.58±5.08a	46.48±4.96a	.330*
LVES(mm)	29.90±4.83a	28.33±4.03a	.118*
EF%	68.58±8.48a	67.68±5.50a	.575*
FS%	37.30±6.26a	38.58±8.67a	.453*
LA(mm)	38.53±3.83a	27.98±3.77a	<0.001*
AO(mm)	29.83±4.90a	28.23±4.69a	.140*
IVS	10.00 (10.00:11.00)b	9.00 (9.00:10.00)b	.002**
PW	11.00 (10.00:12.00)b	9.00 (9.00:10.00)b	<0.001**

LVED: left ventricular end-diastole; LVES: left ventricular end-systole; EF%: ejection fraction; FS: fractional shortening; LA: left atrium; AO: Aortic root dimension, IVS: Interventricular septum; pw: Posterior Wall thickness.

Mean ± standard deviation (a), median (IQR) (b), P value by independent sample t-test (*); P value by Mann-Whitney Test (**).

LVED, LVES, and LV ejection fraction LV fractional shortening were shown to be within normal ranges and no statistically significant difference was detected between both studied groups regarding the previously mentioned ECHO features (Table 2). Additionally, AO was found to be normal within the two groups with no significant difference (Table 2). However, Left atrial anteroposterior diameter, posterior wall thickness and Inter ventricular septum and were found to be statistically significant higher in metabolic syndrome group compared to normal control group (Table 2).

Table 4: Effect of controlled and uncontrolled hypertension on diastolic dysfunction of the left ventricle

Diastolic Dysfunction	Hypertension						P-Value
	Absent		Controlled		Not Controlled		
	N	%	N	%	N	%	
Present	1	16.7	0	0.0	14	87.5	<0.001
Absent	5	83.3	18	100	2	12.5	

Uncontrolled hypertensive patients show echocardiographic features of diastolic dysfunction which was found to be significantly higher compared to controlled hypertensive patients and normotensive patients.

Table 5: Effect of controlled and uncontrolled diabetes on diastolic dysfunction of the left ventricle

Diastolic Dysfunction	Diabetes						P-Value
	Absent		Controlled		Not Controlled		
	N	%	N	%	N	%	
Present	6	30	1	10	8	80	0.003
Absent	14	70	9	90	2	20	

Uncontrolled diabetic patients show echocardiographic features of diastolic dysfunction which was found to be significantly higher compared to controlled diabetic patients and patients with no diabetes.

Table 6: Effect of controlled and uncontrolled dyslipidemia on diastolic dysfunction of the left ventricle

Diastolic Dysfunction	Dyslipidemia						P-Value
	Absent		Controlled		Not Controlled		
	N	%	N	%	N	%	
Present	5	37.5	3	23.1	7	53.8	.281
Absent	9	64.3	10	76.9	6	46.2	

This table shows that there is no difference in the frequency of diastolic dysfunction among the three studied groups.

Discussion

The term metabolic syndrome (MS) represents a clustering of components including truncal obesity, hypertension, diabetes mellitus and dyslipidemia. Each component of metabolic syndrome may be considered as important risk factors for the development of cardiovascular disease [10]. Previous literatures study the impact of both insulin resistance and obesity on left ventricular function; however, there is lack of studies that show the impact of MS on left ventricular function. Furthermore, some studies demonstrated that individuals with idiopathic dilated cardiomyopathy were diagnosed with insulin resistance; these studies concluded that MS may cause coronary heart disease [11]. Thus, the present study was conducted to evaluate the impact of metabolic syndrome on left ventricular performance using ECHO.

In the current study, all components of metabolic syndrome were found to be significantly higher in patients with metabolic syndrome compared to normal control group. The analysis of traditional echocardiographic parameters showed that both ejection fraction and fractional shortening which represents left ventricular systolic function were not different among MS patients and normal control group. The major finding of the current study was that metabolic syndrome causes diastolic dysfunction as assessed by standard

echocardiographic measurements. Previous studies have demonstrated the effect of metabolic syndrome on the function of left ventricle, but consensus is still lacking. A study by [12] has examined the impact of metabolic syndrome on diastolic function of left ventricle in American Indians using ECHO. They noticed altered of both left ventricular relaxation and of left ventricular diastolic function which is consistent with the current study. Also they concluded that American Indians with the metabolic syndrome had greater posterior wall thickness, left atrial diameter and diastolic dysfunction which are consistent with the current study [12]. In the present study, left atrial diameter of metabolic syndrome group was increased compared to control group, which corresponds to results from other literature [13],[14]. Have shown that left ventricular diastolic function was impaired in MS patients; however ejection fraction and fractional shortening (left ventricular systolic function) is preserved which corresponds to the findings of the present study. [15] Also have shown that only left ventricular diastolic function altered in patients with MS although systolic function is preserved. In contrast, [16] some studies demonstrated that metabolic syndrome is associated with global left ventricular dysfunction (diastolic and systolic) in subjects with MS but no CVD. Previous studies have demonstrated that diastolic function observed in the current study may be as a result of

hypertension. Arterial Stiffness, caused by hypertension may be results in cardiovascular abnormalities ^[17]. In contrast, another study demonstrated that hypertension and obesity were not associated with left ventricular diastolic dysfunction.

Watcher et al., demonstrated that left ventricular diastolic dysfunction occurs at a higher percentage in diabetic patients (80.6%) when compared with patients with no diabetes (69.2%). Furthermore, diabetes cause serious effect on the left ventricular diastolic function^[18]. In the current study the incidence of diastolic dysfunction rise significantly. The rate of Prevalence of diastolic dysfunction was found to be significantly higher among uncontrolled diabetic patients (80%) compared to patients under glycemic control (10%) and patients with no diabetes (30%). Both studies are comparable. Control of glycemia by drug or life style modification in diabetic patients can help in maintaining normal diastolic function. According to the Strong Heart Study there was a relation between degrees of glycemic control and diastolic function ^[19]. However, in the present study glycemic control markers were excluded from the research.

The potential limitations of the present study are a small sample size and lack of randomization.

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References

1. Grundy SM, Brewer Jr. HB, Cleeman JI, Smith Jr. SC, Lenfant, C, National Heart, Lung, and Blood Institute, American Heart Association, Definition of metabolic syndrome: Report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issue related to definition, *Circulation*. 2004; 433:438-109.
2. Reinhard W, Holmer, SR, Fischer, M, et al. Association of the metabolic syndrome with early coronary disease in families with frequent myocardial infarction. *Am J Cardiol*. 2006; 97:964-7.
3. Ford ES, Li Cand Zhao G. Prevalence and correlates of metabolic syndrome based on a harmonious definition among adults in the US. *J. Diabetes* 2010; 2(3): 180–193.
4. Friend A, Craig L, and Turner S. The prevalence of metabolic syndrome in children: a systematic review of the literature. *Metab. Syndr. Relat. Disord*. 2013; 11(2): 71–80.
5. Plandevall M, Singal B, Williams L, Brotons C, Guyer H, Sadurni J, Falces C, Serrano-Rios M, Gabriel R, Shaw JE, Zimmet PZ. and Haffner S. A single factor underlies the metabolic syndrome. *Diabetes Care*. 2006; 29(1): 113-122.
6. Alexander, CM, Landsman, PB, Teutsch, SM and Haffner, SM. NCEP-defined metabolic syndrome, diabetes, and prevalence of coronary heart disease among NHANES III participants age 50 years and older. *Diabetes*. 2007; 52(5):1210–1214.
7. Kane GC, Karon BL, Mahoney, DW, Redfield, MM, Roger VL, Burnett JC, Jacobsen S.J., Rodeheffer R.J. Progression of left ventricular diastolic dysfunction and risk of heart failure. *JAMA*. 2011; 306:856e863.
8. Ford ES. Risks for all-cause mortality, cardiovascular disease, and diabetes associated with the metabolic syndrome: a summary of the evidence. *Diabetes Care*. 2006; 28:1769e1778.
9. Alberti KG, et al. Metabolic syndrome—a new world-wide definition. A Consensus Statement from the International Diabetes Federation. *Diabet Med* 2001; 23(5):469–4800.
10. Kenchaiah S, Evans JC, Levy D, Wilson PW, Benjamin EJ, Larson MG, et al. Obesity and the risk of heart failure, *N. Engl. J. Med*. 2002; 305–313:347.
11. Witteles RM, Fowler MB. Insulin-resistant cardiomyopathy clinical evidence, mechanisms, and treatment options. *J Am Coll Cardiol* 2008; 51(2):93–102.
12. Chinali M, Devereux RB, Howard BV, Roman MJ, Bella JN, Liu JE, et al. Comparison of cardiac structure and function in American Indians with and without metabolic syndrome (the Strong Heart Study). *Am J Cardiol* 2004; 93(1):40–4.
13. Azevedo, A, Bettencourt, p, Almeida, PB, et al. Increasing number of components of the metabolic syndrome and cardiac structural and functional abnormalities – cross-sectional study of the general population. *BMC Cardiovascular Disorders* 2007; 7: 17.

14. Grandi AM, Maresca AM, Giudici E, Laurita E, Marchesi C, Solbiati F. et al. Metabolic syndrome and morphofunctional characteristics of the left ventricle in clinically hypertensive non diabetic subjects, *Am. J. Hypertens.* 2006; 19: 199–205.
15. Masugata H, Senda S, Goda F, Yoshihara Y, Yoshikawa K, Fujita N, et al. Left ventricular diastolic dysfunction as assessed by echocardiography in metabolic syndrome, *Hypertens. Res.* 2006; 29: 897–903.
16. Wong CY, O'Moore-Sullivan T, Fang ZY, Haluska B, Leano R. and Marwick, TH. Myocardial and vascular dysfunction and exercise capacity in the metabolic syndrome, *Am. J. Cardiol.* 2005; 96:1686–1691.
17. Peterson LR, Waggoner AD, Schechtman, KB, Meyer T, Gropler RJ, Barzilai B, Davila-Roman, VG. Alterations in left ventricular structure and function in young healthy obese women: Assessment by echocardiography and tissue Doppler imaging. *J Am Coll Cardiol.* 2004; 43:1399–1404.
18. Wachter R, Lüers C, Kleta S, Griebel K, Herrmann-Lingen C, Binder L, et al. Impact of diabetes on left ventricular diastolic function in patients with arterial hypertension. *Eur J Heart Fail* 2007; 9:469-76.
19. Liu JE, Palmieri V, Roman MJ, Bella JN, Fabsitz R, Howard B.V. et al. The impact of diabetes on left ventricular filling pattern in normotensive and hypertensive adults: the Strong Heart Study. *J Am Coll Cardiol.* 2001; 37: 1943–9.

A Comparative Study of Vitamin D Levels and Some Biochemical Parameters between Healthy and Breast Cancer in Iraqi Females

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Abstract

Breast cancer is one of the most widespread cancers, depending on World Health Organization, cancer calculated for approximately 7.6 million incidences in 2008, who ever expected elevation in incidence is about 13.1 million in 2030. So that the current research investigates vitamin D role in the occurrence of this disease and explains if vitamin D has a positive effect on the incidence of disease, as well as measuring parathyroid hormone and estrogen levels. Three groups were included in this analysis: control healthy women, benign and malignant breast tumor women. All cases that were selected at the beginning of the disease diagnosis. According to statistical values vitamin D showed highly significant ($P < 0.001$) decrease in benign (3.74 ± 2.33) ng/ml and malignant (4.38 ± 3.12) ng/ml tumor patients compared with healthy group (24.96 ± 7.24) ng/ml. Also a high significant increase was shown for PTH values in benign (208.37 ± 132.5) pg/ml and malignant (133.9 ± 60.02) pg/ml tumor patients compared with healthy group (67.04 ± 25.6) pg/ml. Furthermore, results revealed non-significant difference in estrogen levels between benign group (54.11 ± 22.93) pg/ml, and control group (64.85 ± 22.18) pg/ml, while there were a significant difference in levels of estrogen between control and malignant tumor groups (52.4 ± 18.09) pg/ml.

As a results, we found that all patients had sever vitamin D deficiency compared with healthy group, as well as high levels of parathyroid hormone as evidence of vitamin D deficiency, while estrogen levels were within normal levels.

We concluded that all patient groups were suffering from vitamin D deficiency and elevation in parathyroid hormone that gives evidence of the role of vitamin D as anti-cancer agent.

Keywords: Breast cancer, Estrogen, Parathyroid hormone, Vitamin D.

Introduction

Breast cancer (BC) is one of the most widespread cancers around the world and it is the second main reason of death after lung cancer among women⁽¹⁾. Many reports demonstrated reverse correlation between vitamin D concentration and occurrence of 15 types of cancers, including breast, lung, kidney, colorectal, and pancreatic cancer⁽²⁾.

Vitamin D is synthesized in human by more than one step. The first step start when UVB (290-315nm) reaches the skin and stimulates conversion of

7-dehydrocholesterol to pre-vitamin D₃⁽³⁾, approximately 90% of vitamin D comes from endogenous production under the skin, which transported to the liver to produce 25-hydroxyvitamin this step induced hydroxylation by vitamin D-25-hydroxylase enzyme encoded by (CYP2R1)⁽⁴⁾ then undergoes another hydroxylation step in the kidney to yield 1,25-dihydroxyvitamin D (1,25(OH)₂D) by the 25(OH)D-1 α -hydroxylase enzyme which encoded by (CYP27B1), (1,25-dihydroxyvitamin D₃)⁽⁵⁾. The active form of vitamin D, has a short half-life of about 15 hours, while 25-hydroxyvitamin D₃ has a half-life of about 15 days⁽⁶⁾. The active form of vitamin D,

1,25(OH)₂D, plays many important biological function such as modulation of immune responses, impact on hormone excretion, regulate of cellular proliferation and differentiation. Also, anticancer actions for example anti-proliferation, anti-inflammation, induces apoptosis, prompting of differentiation, inhibition of metastasis, and angiogenesis for different malignant cells⁽⁷⁾.

However, VDR signaling has been noticed to impact on the expression of more than 200 genes⁽⁸⁾. Therefore the levels of 1,25(OH)₂D is regulated tightly by phosphorus, calcium and parathyroid hormone (PTH)⁽⁹⁾.

In recent years an anti-cancer mechanism of vitamin D was discovered, so the influences of vitamin D that restrain of mammary tumors are mediated through estrogen pathway by reduce systematization of intracellular estrogen receptors (ER) ⁽¹⁰⁾. Many studies recorded hypo-vitamin D among patients with breast cancer contrasted with healthy group ⁽¹¹⁾.

Aim of the Study: The present study aimed to analyze vitamin D laboratory test results obtained from healthy and breast cancer Iraqi females, in addition to evaluation of estrogen and parathyroid hormone and their relationship with active form of vitamin D.

Materials and Method

Study Groups: All blood samples were collected from Al-Eluia Hospital for Woman Care, Oncology Teaching Hospital and Amel Hospital for Tumors in the period from October 2018 to April 2019. This analysis includes healthy group and breast tumor cases. Samples were divided as three groups (control G1, benign tumor G2 and malignant tumor G3), each groups comprised of 30 blood specimens of Iraqi females in premenopausal stage at age ranged between 32 to 45 years.

Blood Sampling: Five milliliters of blood were withdrawn from healthy and patients subsequently put in gel tube and left to coagulate at room temperature then centrifuge at 3000 rpm for 5 min. After that the serum collected was divided into five sections and put in eppendorf tubes and stored at -20 °C in order to be used for vitamin D, PTH and estradiol (E2) levels measurement by ELISA technique.

Parameters Measurement: Evaluations of direct 25(OH) vitamin D and E2 were achieved by Sequential Competitive Method, while determination of PTH was achieved by Sandwich equilibrium Method.

Statistical Analysis: The results were obtained as a mean ± SD (standard deviation). P-value of <0.001 and <0.05 expressed as a highly significant and significant respectively, as well as Pearson's correlation coefficient was utilized to determine the correlation between two continuous variables.

Results

In our study, we enrolled 90 participants. The median age of the patients at diagnosis ranged between (32-45) years old. The study demonstrated a contributory relationship between vitamin D deficiency and breast cancer occurrence, however the results revealed very low concentration of vitamin D in breast cancer women group compared with healthy women group that suggests inverse association between decrease level of vitamin D and increase risk of breast cancer with many different mechanisms as many recent research suggested. The results of vitamin D, PTH and E2 in G1 healthy group, G2 benign tumor and G3 malignant tumor are shown in table (1) that revealed a highly significant (P<0.001) decrease in vitamin D levels in benign (3.74±2.33)ng/ml and malignant(4.38±3.12)ng/ml tumor patients, respectively compared with healthy group(24.96±7.24)ng/ml, while there is a non-significant difference (p>0.05) between G2 and G3.

Also a high significant increase (P<0.001) was shown for PTH values in benign (208.37±132.5) pg/ml and malignant (133.9±60.02)pg/ml tumor patients compared with healthy group (67.04±25.6) pg/ml, respectively. Also, there was a significant difference in PTH levels between benign and malignant groups.

Furthermore, results revealed non-significant difference in E2 levels between benign group (54.11±22.93) pg/ml, and control group (64.85±22.18) pg/ml, while there were a significant difference in levels of estrogen between control and malignant tumor groups (52.4±18.09) pg/ml, as well as a non-significant difference between G2 and G3 groups.

Table 1: Comparison among vitamin D, PTH and E2 levels in control, benign and malignant groups

Parameters	Control(G1) Mean ± SD	Benign(G2) Mean ± SD	Malignant(G3) Mean ± SD	P-Value G1 vs. G2	P-Value G1 vs. G3	P-Value G2 vs. G3
Vit. D	24.96 ± 7.24	3.74 ± 2.33	4.38 ± 3.12	H.S	H.S	N.S
PTH	67.04 ± 25.6	208.37±132.5	133.9 ± 60.02	H.S	H.S	S.
E2	64.85±22.18	54.11 ±22.93	52.4 ±18. 09	N.S	S	N. S

H.S. Highly significant, S. Significant, N.S. Non-significant

In addition to that mentioned have been demonstrated in table (2) highly significant negative correlation between vitamin D and other parameters which include PTH and E2 in benign group that explained in figures 1 and 2. While in malignant patients we demonstrated a highly significant positive correlation distributed of vitamin D with PTH otherwise the study appeared a highly significant negative correlation between vitamin D and E2 were showed in table (2) and figures 3 and 4.

Table (2): Illustrates the correlation between PTH and E2 in benign and malignant groups.

Parameters	Benign group		Malignant group	
	R	P-value	R	P-value
PTH	-0.09	H.S	0.16	H.S
E2	-0.05	H.S	-0.08	H.S

H.S. Highly significant

The following figures explain the correlation between vitamin D, E2 and PTH in benign and malignant groups.

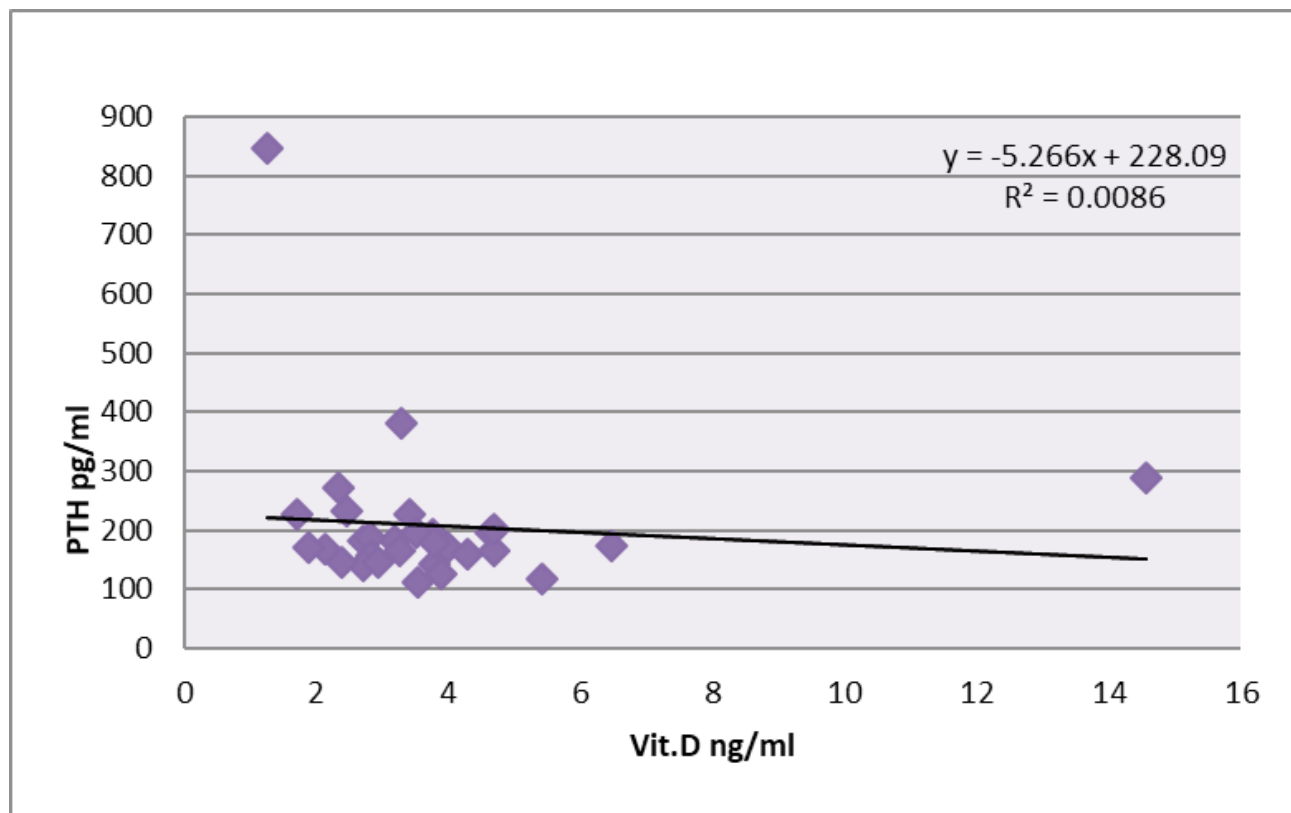
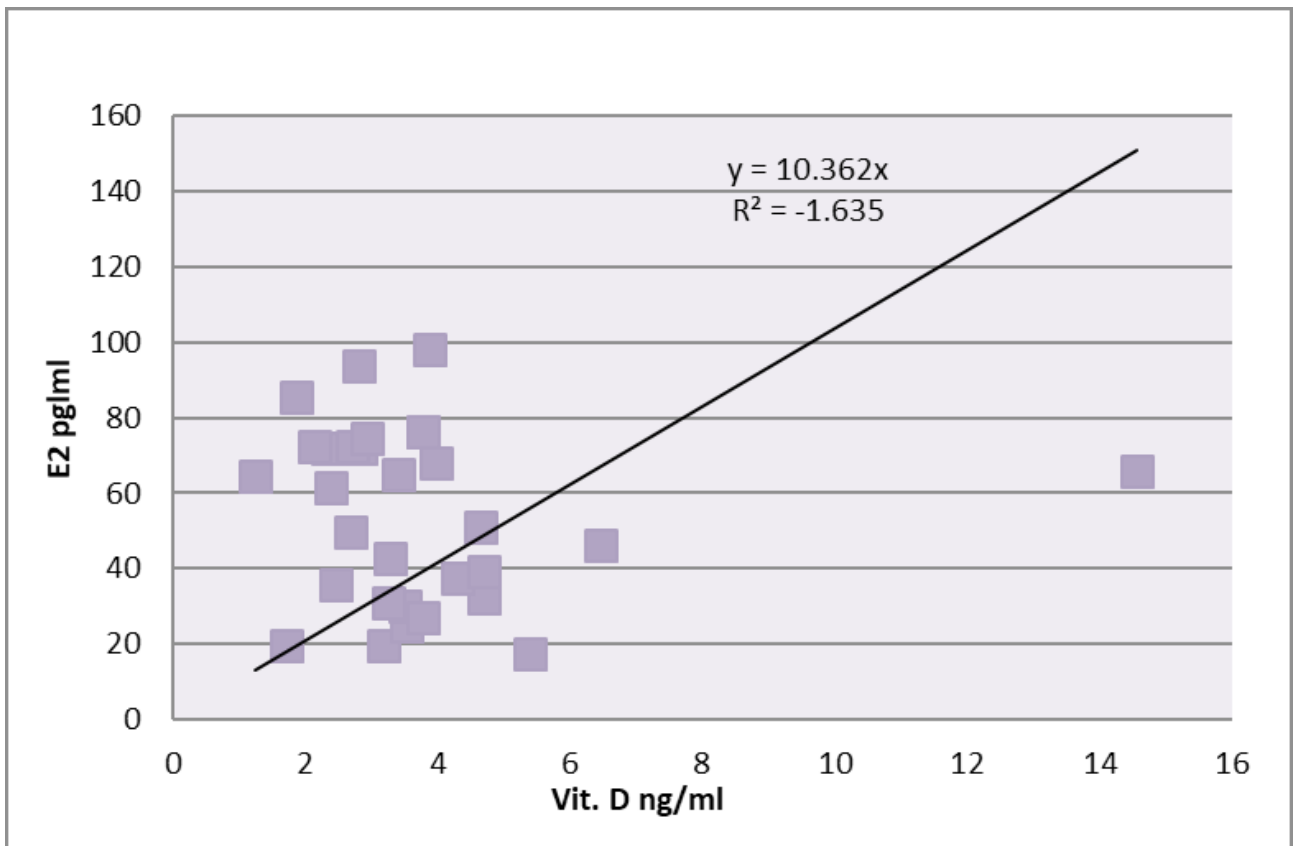


Figure (1): Vitamin D vs. PTH in benign patients



Figure(2): Vitamin D vs. E2 in benign patients

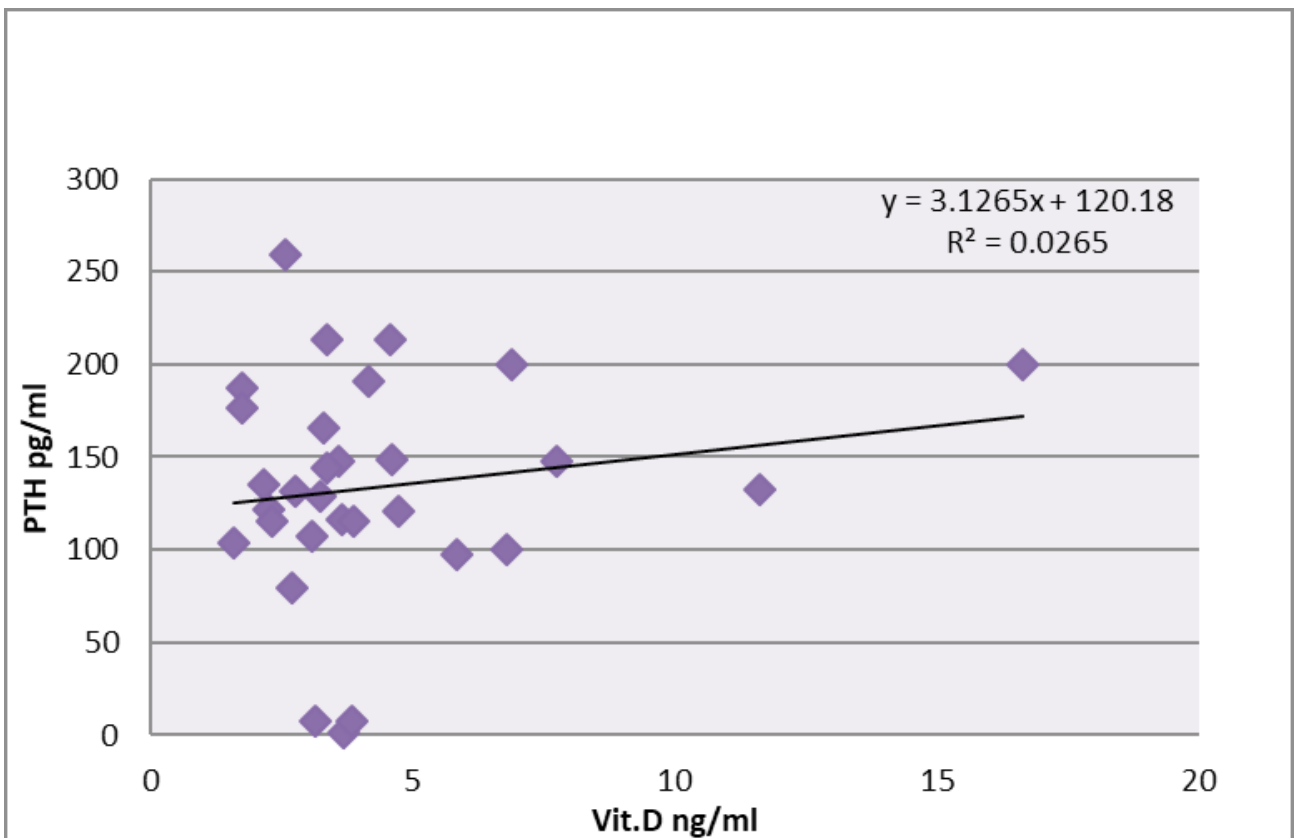


Figure (3): Vitamin D vs. PTH in malignant patients

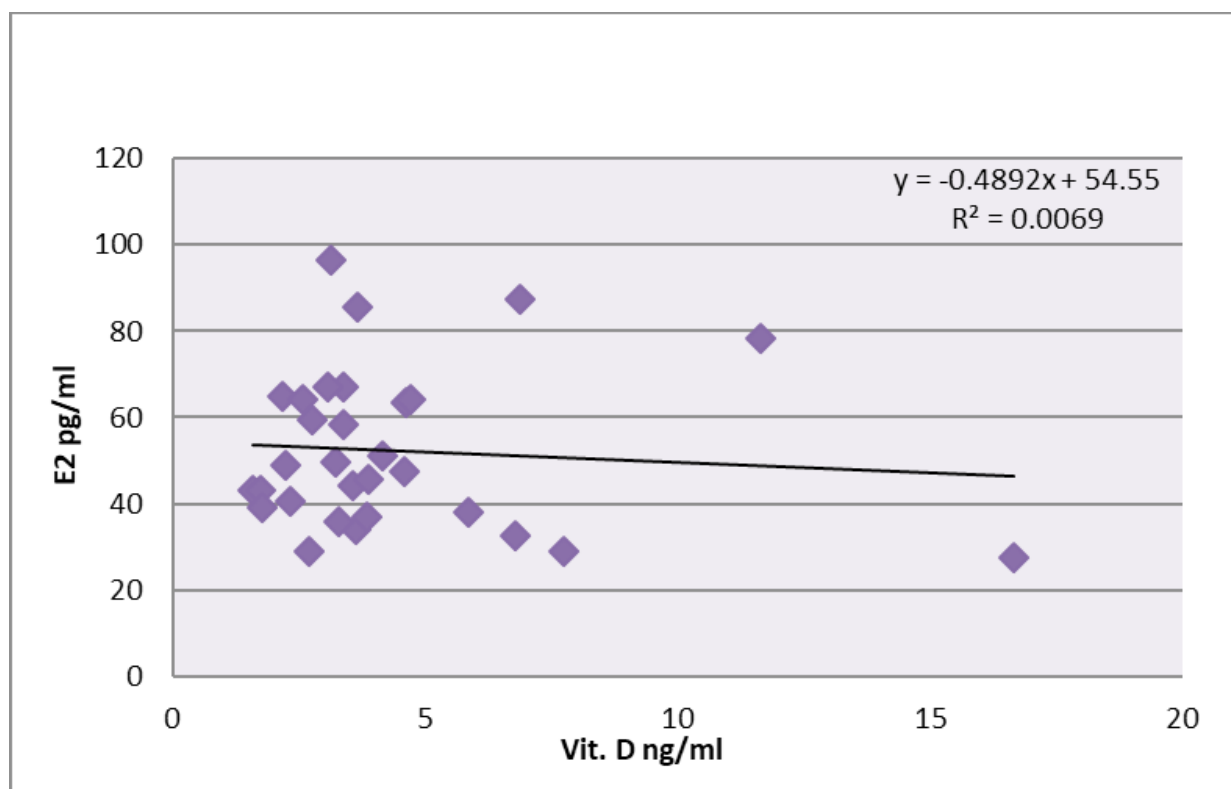


Figure (4): Vitamin D vs. E2 in malignant patients

Discussion

The present study demonstrated a contributory relationship of vitamin D depletion in relation to breast cancer occurrence, however the results of vitamin D levels for the pool of women with breast benign and malignant tumors were very low compared with the group of healthy women that suggests increase risk of breast cancer with various mechanisms. According to some sources the normal values of vitamin D ranged (30-100) ng/mL considered as sufficient⁽¹²⁾. The decrease in vitamin D levels is divided into three sections; levels of 25(OH)D below (<10 ng/ml) that represents severe deficiency, mild deficiency (10-25 ng/ml) and sufficiency > 30ng/ml, the decline is considered acceptable to a society suffering from a lack of vitamin D levels for men and women according to local studies. Another research that agrees with our study found that 90% or more of people with breast cancer have vitamin D deficiency⁽¹³⁾. Since the lack of vitamin D is linked to the disease in more than one course. Firstly, the natural levels of vitamin D regulate more than 200 genes⁽¹⁴⁾. The role of 1,25(OH)2D3 is to regulate some genes involved in cell cycle organization and apoptosis such as p21-activated kinase (PAK1), p53(TP53) insulin-like growth factor⁽¹⁴⁾.

On the other side vitamin D has a role through its effect on estrogen receptor, Estrogen has been found to play a vital role in breast cancer inducing the chest cell to occur uncontrolled division and thus tumor where the low level of vitamin D consider positive effect by increase of estrogen receptor therefore vitamin D has an estrogenic effect on the spilt of chest cell to form tumor⁽¹⁵⁾. The proposed third effect of vitamin D is by influencing on the aromatase enzyme, where 1,25(OH)2D3 decreases expression of aromatase enzyme (CYP19), which catalyzed estrogen synthesis⁽¹⁶⁾. Although there are other factors that contribute to increase positive gene expression of this enzyme such as fatty tissue, which is a source of estrogen, the higher of fatty tissue increase the Nα F and IL-6 thus lead to increased conversion of testosterone to estrogen⁽¹⁶⁾. Either the fourth effect of vitamin D by its effect on generation of reactive oxygen species, mitochondrial disruption and eliminate cytochrome C⁽¹⁷⁾.

Finally another research proposed a mechanism comprising of angiogenesis is process of generation new blood vessels from existing vasculature and is a crucial step which causes progression, and metastasis of tumors⁽³⁾.

According to our results, the estrogen levels were within normal limits. The genetic expression of the enzyme aromatase that converts androgens into estrogen, which occurs as a result of a decrease in vitamin D levels, has been excluded because the levels of estrogen were within normal limits; Estrogen plays a role through estrogen receptors, promoted cell proliferation and initiates mutations that occur as a function of errors during DNA replication⁽¹⁸⁾. A second mechanism of estrogen role in breast cancer can be explained by direct effect by formation of oxygen free radicals which have role in the genetic changes in cell chest⁽¹⁹⁾.

Almost 5–10% of patients are suffering from genetic changes related to breast cancer⁽²⁰⁾. According to a previous study more than 75% of breast tumors occur through estrogen receptors (ER), suggesting that the vast majority of breast cancers are hormone-dependent and grow in response to the hormone estrogen⁽²¹⁾.

On the other hand, some studies indicate carcinogenic effect and tumor stimulation of parathyroid hormone. Other previous cohort studies agreed with our results that found an association between higher levels of parathyroid hormone and breast cancer risk⁽²²⁾. Increase risk of breast cancer in women with hyperparathyroidism⁽²³⁾. One of the conditions of hyperparathyroidism types is the expansion of one or more of the parathyroid glands which cause excessive hormone production called primary hyperparathyroidism the second condition that leads to high levels of parathyroid hormone is called secondary hyperparathyroidism⁽²⁴⁾. It is well established that there is an inverse relationship between serum 25-hydroxyvitamin D (25-OHD) and serum PTH⁽²⁵⁾. Decrease in vitamin D levels causes rise in parathyroid hormone levels. Therefore, high levels of parathyroid hormone stimulate excretion of calcium (Ca^{2+}) from bones into the bloodstream to fill lack of blood calcium levels (hypercalcemia), and increase the risk breast cancer incidence. Some evidence study found that high extra cellular calcium levels have a similar effect of estrogen “estrogen like” effect in vitro⁽²⁶⁾; so all cases of patients with the incidence of benign tumor and malignant where in pre-menopause ages⁽²⁷⁾.

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References

1. World Health Organization. Cancer fact sheet N_297”. 2015. Retrieved 10 October 2015.
2. A. L. Johnson, G. M. Zinser and S. E. Waltz, “Loss of vitamin D receptor signaling from the mammary epithelium or adipose tissue alters pubertal glandular development”, *Am J Physiol Endocrinol Metab*, 2014; 307: E674-685.
3. E. Wintermeyer, C. Ihle, S. Ehnert, U. Stöckle, G. Ochs, P. De Zwart et al., “Crucial role of vitamin D in the musculoskeletal system,” *Nutrients*, 2016; 8(6): 319.
4. D. Bellavia, V. Costa, A. De Luca, M. Maglio, S. Pagani, M. Fini, et al., “Vitamin D level between calcium-phosphorus homeostasis and immune system: new perspective in osteoporosis,” *Current Osteoporosis Reports*, 2016; 1–12.
5. C. J. Narvaez, D. Matthews, E. LaPorta, K. M. Simmons, S. Beaudin and J. Welsh, “The impact of vitamin D in breast cancer: genomics, pathways, metabolism”, *Front Physiol*, 2014; 5: 213. doi:10.3389/fphys.2014.00213.
6. G. Jones, D.E. Prosser and M. Kaufmann, “Cytochrome P450-mediated metabolism of vitamin D”, *J. Lipid Res.*, 2014; 55(1): 13–31.
7. D. Enko, G. Kriegshäuser, R. Stolba, E. Worf and G. Halwachs-Baumann, “Method evaluation study of a new generation of vitamin D assays”, *Biochem Med (Zagreb)*, 2015; 25: 203–212.
8. M. H. Lucky and S. Baig, “The Vitamin D Receptor (VDR) Gene Polymorphisms FokI In Obese Pakistanis– a Preliminary Report”, *Int J Adv Biol Biom Res*, 2015; 3(3): 257-262.
9. J. Li, M. E. Byrne, E. Chang, Y. Jiang, S. S. Donkin, K. K. Buhman et al., “1 α ,25-Dihydroxyvitamin D3 hydroxylase in adipocytes”, *J. Steroid Biochem. Mol. Biol.*, 2008; 112(1–3): 122–126.
10. J. Welsh, “Vitamin D and breast cancer: insights from animal models”, *Am J Clin Nutr*, 2004; 80 Suppl(6): 1721Se4S.
11. L. Yin, N. Grandi, E. Raum, U. Haug, V. Arndt and H. Brenner, “Meta-analysis: serum vitamin D and breast cancer risk”, *Eur J Cancer*, 2010; 46: 2196-205.
12. S. S. Maeda, V. Z. Borba, M. B. Camargo, J.L. Borges, F. Bandeira, M. Lazaretti-Castro et al., “Recommendations of the Brazilian Society of

- Endocrinology and Metabolism (SBEM) for the diagnosis and treatment of hypovitaminosis D”, *Arquivos Brasileiros de Endocrinologia e Metabologia*, 2014; 58(5): 411–433.
13. N. Y. Sofi, M. Jain, U. Kapil, V. Seenu, V. K. Kamal and R. M. Pandey, “Nutritional risk factors and status of serum 25(OH)D levels in patients with breast cancer: a case control study in India”, *J Steroid Biochem Mol Biol*, 2016; Sep 26.
 14. X. Zhang and S. M. Ho, “Epigenetics meets endocrinology”, *J Mol Endocrinol*, 2011; 46(1): R11–32.
 15. N. Gjorevski and C.M. Nelson, “Integrated morphodynamicsignalling of the mammary gland”, *Nat Rev Mol Cell Biol*, 2011; 12: 581-593.
 16. A. Purohit, A. Singh, M. W. Ghilchik, O. Serlupi-Crescenzi and M. J. Reed, “Inhibition of IL-6+IL-6 soluble receptor-stimulated aromatase activity by the IL-6 antagonist, Sant 7, in breast tissue derived fibroblasts”, *Br J Cancer*, 2003; 88: 630–635.
 17. P. Martinez-Miguel, J. M. Valdivielso, D. Medrano-Andres, P. Roman-Garcia, J.L. Cano-Penalver, M. Rodriguez-Puyol et al., “The active form of vitamin D, calcitriol, induces a complex dual upregulation of endothelin and nitric oxide in cultured endothelial cells”, *Am J Physiol Endocrinol Metab*, 2014; 307: E1085–E1096.
 18. C. R. Jefcoate, J. G. Liehr, R. J. Santen, T. R. Sutter, J. D. Yager, W. Yue, et al., “Tissue-specific synthesis and oxidative metabolism of estrogens”, *Journal of the National Cancer Institute Monographs*, 2000; 27, 95–112.
 19. J. D. Yager and N. E. Davidson, “Estrogen carcinogenesis in breast cancer”, *New Engl J Med*, 2006; 354: 270–82.
 20. M. Sundquist, S. Thorstenson, L. Brudin, S. Wingren and B. Nordenskjöld, “Incidence and prognosis in early onset breast cancer”, *Breast*, 2002; 11: 30–35.
 21. F. C. Geyer, D.N. Rodrigues, B. Weigelt and J.S. Reis-Filho, “Molecular classification of estrogen receptor-positive/luminal breast cancers”, *Adv AnatPathol*, 2012; 19(1): 39-53.
 22. A. Tosovic, C. Becker, A. G. Bondeson, L. Bondeson, U. B. Ericsson, J. Malm et al., “Prospectively measured thyroid hormones and thyroid peroxidase antibodies in relation to breast cancer risk”. *International Journal of Cancer*, 2012; 2133: 2126–2133.
 23. A. G. Angelousi, V. K. Anagnostou, M. K. Stamatakos, G. A. Georgiopoulos and K. C. Kontzoglou, “Mechanisms in endocrinology: primary HT and risk for breast cancer: a systematic review and meta-analysis”. *European Journal of Endocrinology*, 2012; 166: 373–381.
 24. S. Bañón, M. Rosillo, A. Gómez, M. J. Pérez-Elias, S. Moreno, and J. L. Casado, “Effect of a monthly dose of calcidiol in improving vitamin D deficiency and secondary hyperparathyroidism in HIV-infected patients”, *Endocrine*, 2015; 49(2): 528–537.
 25. J. Blaine, M. Chonchol and M. Levi, “Renal control of calcium, phosphate, and magnesium homeostasis”, *Clinical Journal of the American Society of Nephrology*, 2015; 10(7): 1257–72.
 26. F. Journe, J. C. Dumon, N. Kheddoumi, J. Fox, I. Laios, G. Leclercq, et al., Extracellular calcium downregulates estrogen receptor alpha and increases its transcriptional activity through calcium sensing receptor in breast cancer cells. *Bone* 2004; 35: 479-88.
 27. M. Almquist, J. Manjer, L. Bondeson and A. G. Bondeson, “Serum calcium and breast cancer risk: results from a prospective cohort study of 7,847women”, *Cancer Causes Control*, 2007; 18: 595– 602.

The Role of Mean Arterial Pressure (MAP), Roll Over Test (ROT), and Body mass Index (BMI) in Preeclampsia Screening in Indonesia

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Abstract

Objective: To evaluate the role of MAP, ROT, and BMI in preeclampsia screening in low resources setting.

Method and Material: This is a retrospective study conducted on 1011 pregnant women who had an antenatal care at Public Health Center in Indonesia. Data taken from public health medical report. The sample groups were 45 preeclampsia patients who have had complete screening of MAP, ROT and BMI. The control groups were normal pregnant women who attained same inclusion criteria.

Results: The preeclampsia group had positive MAP and obesity result respectively 95.6% and 40% of patients, but in control group only had 40% and 11.1% of patient have positive MAP and obesity respectively. Statistical test illustrates a significant association between MAP and BMI screening with the incidence of preeclampsia ($p = 0.0001$, OR = 32.250 and $p = 0.002$, OR = 5.333). Whereas positive ROT showed in 40% PE groups and 57.8% control group. There is no association between ROT screening and the incidence of preeclampsia ($p = 0.092$).

Conclusion: MAP and BMI can be used as baseline screening tools of preeclampsia in low resources setting. But ROT is not associated with the incidence of preeclampsia.

Keywords: Preeclampsia Screening, MAP, ROT, BMI.

Introduction

Preeclampsia (PE) is a complex medical disorder, who is responsible for neonatal and maternal deaths worldwide. It also becomes the biggest cause of high Maternal Mortality Rate (MMR) in Surabaya Indonesia from 2013-2017¹. Accurate prediction and aggressive prevention allowed to elude this pregnancy complication. Effective screening to predict PE in the first trimester

of pregnancy is important to identify women who are at risk of developing PE so that early enough prevention treatment could start to prevent or reduce the frequency of its occurrence.

Preeclampsia screening vary from clinical to biomolecular level depend on the resources availability. In low and middle income countries where resources are limited, variations of the first-trimester combined test can be considered but difficult to reached. The baseline test which is possible to do are combine of maternal risk factors with Mean Arterial Pressure (MAP) and Roll over Test (ROT). In the absence of other biomarker(s), risk calculation can still be done but the detection rates will be reduced .

MAP and ROT are a method to describe hemodynamic conditions in patients with preeclampsia. ROT is not a perfect predictor, but it still have advantages

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to use in populations with high PIH associated maternal and perinatal mortality, mostly in low resources setting². It has been used in many countries but some literature shows that ROT is not related to the incidence of preeclampsia³. The purpose of this study is to determine the effectiveness of preeclampsia screening (MAP, ROT, and BMI) to the incidence of preeclampsia in Indonesia.

Material and Method

This is a retrospective study conducted on 1011 pregnant women who performed an antenatal care at Sidotopo Wetan Public Health Center (*Puskesmas Sidotopo Wetan*), Surabaya, Indonesia from October 2017 to October 2018. Et Data taken from public health

medical report. The sample groups were 45 preeclampsia patient during that period time who fulfilled inclusion criteria: patients in the first and second trimesters who have had complete screening of MAP, ROT and BMI. The control groups were normal pregnant women who attained same inclusion criteria. It was taken by consecutive sampling. Positive result noted if MAP is > 90 mmHg. ROT classified as positive result if there were different of diastolic pressure between supine and lateral position more than 15 mmHg³. The values on BMI screening classified as obesity if the result >30. The samples were traced retrospectively to see the MAP, ROT and BMI screening history and demographic data.

Finding:

Table 1. Demographic Characteristics

Age (Year)	PE group	Control group	Total
	n (%)	n (%)	n (%)
< 20	0 (0)	3 (6.7)	3 (3.3)
20-35	37 (82)	38 (84.4)	75 (83.3)
> 35	8 (18)	4 (8.9)	12 (13.3)
Parity			
Primi	9 (20)	13 (28.9)	22 (24.4)
Multips	36 (80)	32 (71.1)	68 (75.6)
Risk Factor			
Anemia	3 (6.7)	0 (0)	3 (3.3)
Gestational Diabetes	5 (11.1)	2 (4.4)	7 (7.8)
History of Preeclampsia	1 (2.2)	0 (0)	1 (1.1)
Obesity	16 (35.6)	5 (11.1)	21 (23.3)
Tuberculosis	2 (4.4)	0 (0)	2 (2.22)
HbsAg (+)	1 (2.2)	0 (0)	1 (1.1)
History of IUFD	1 (2.2)	0 (0)	1 (1.1)
Under Nutrition	1 (2.2)	6 (13.3)	7 (7.8)

Baseline demographics of study participants are presented in Table 1. Most pregnant women in both groups are in reproductive ages. It also worked on parity data, which is multiples showed have larger number than

nultips. Obesity has the highest rank in PE risk factor in this study. It counts a percentage of 35.6% obesity cases. Followed by Gestational diabetes and anemia.

Table 2. MAP, ROT, BMI and the Incidence of Preeclampsia

Screening	PE group	Control Group	Total	P	OR
	n (%)	n (%)	n (%)		
MAP (-)	2 (4.4)	27 (60)	29 (32.2)	0.0001	32.250
MAP (+)	43 (95.6)	18 (40)	61 (67.8)		
ROT (-)	27 (60)	19 (42.2)	46 (51.1)	0,092	-
ROT (+)	18 (40)	26 (57.8)	44 (48.9)		
Obesity (-)	27 (60)	40 (88.9)	67 (74.4)	0,002	5.333
Obesity (+)	18 (40)	5 (11.1)	23 (25.6)		

The MAP test in this study pointed out that 95.6% preeclampsia samples have a value of positive MAP, while only 40% samples of control groups have a positive MAP. This study in accordance with another study by Gasse et al in 2017, which is showed that first-trimester MAP is a strong predictor of gestational hypertension and preeclampsia in nulliparous women⁴.

Table 2 also showed that 60% preeclampsia patients have negative ROT screening and are inversely proportional to control group that most of them have positive ROT screening with p value 0.092 which means that there is no association between ROT measurement and the incidence of preeclampsia.

The results of BMI measurement and the incidence of preeclampsia in this study showed that 40% preeclampsia patient are obese but only 11.1% control group patient recorded obese. Statistical analysis noted p value 0.002 which could be explained that there is a relationship between BMI and the incidence of preeclampsia.

Discussion

Baseline data in this study discordant with the theory of preeclampsia and other study which is reproductive ages and multips are low risk group to have hypertension in pregnancy. It could be explained that reproductive age in this study has preeclampsia risk factor ie gestational diabetes, obesity, history of preeclampsia and infection. Another study from Indonesia also pictured that more than 50% patients who experienced preeclampsia are between 20 to 35 years old⁵.Parous women without prior history of PE have lower risk of PE; however, this protective effect will change when they have different conception partner⁶.

MAP test showed strong relationship with

incidence of preeclampsia in this study, it revealed odd ratio 32.25. This data inline with Poon study in 2008 which reported first study on MAP measurement using validated automated blood pressure devices according to a standardized protocol and maternal variables in 11+0 to 13+6 weeks pregnancy can predict PE. Maternal blood pressure was measured in 5590 singleton pregnant women. the detection rates for PE, at 10% false positive rate, were 38% and 63%, respectively for MAP alone and in combination with maternal history⁷.

MAP is a reflection of hemodynamic perfusion pressure from vital organs. Another follow-up study on MAP measurement of more than 9000 pregnancies at 11–13 weeks of gestation compared the screening using systolic blood pressure, diastolic blood pressure, and MAP. MAP performed best as a marker, with an increasing of detection rate for early onset PE from 47% (based on maternal factors alone) to 76% (based on MAP and combination of maternal factors) at 10% false positive rate⁸. MAP screening in first-trimester is a strong predictor of gestational hypertension and preeclampsia^{9,10}.

The value of roll-over test has advantages in its simplicity. It requires simple equipment and no special skill. ROT is performed by positioning the patient in a lateral state and then a blood pressure measurement is made until there is no change in blood pressure. Then, the tension is measured in the supine position and the tension results are recorded again.

Some study showed roll-over test are highly variable among different investigators and also inconsistent reproducibility in the same patient. Literature review reveals sensitivities varying between 0 to 93% and specificities between 54–91% and false positive results up to 90%. Walia et all study in 2015 also reported roll-over test performed at 24 weeks had negative in all

study cases. So, it is clear that ROT has no role as early predictive in preeclampsia³.

The relationship between preeclampsia and obesity has been greatly studied. Obesity prevalence has increased over 25 years it is similar to preeclampsia prevalence. This study showed obesity has correlation with incidence of PE. It revealed OR 5.3 in obesity cases compare non obesity cases.

This data support substantial evidence which is show that obesity (BMI ≥ 30 kg/m²) confers a higher risk for PE^{10,11,12}. Obesity also state as meta inflammation, associated with chronic stress and inflammatory response. The inflammatory response was found to increase in obese women and contribute to vascular targets and vascular changes induce endothelial dysfunction and placental ischemia in turn exaggerated maternal inflammatory response and induce preeclampsia^{13,14,15}.

This study in line with FIGO guideline on preeclampsia screening where state that if it is not possible to measure biomarker (PLGF) and/or uterine artery doppler, combination of maternal risk factor and MAP has advantages than maternal risk factor alone. Simple method to measure in Public health will increase awareness, access, affordability, and acceptance prenatal screening of preeclampsia¹⁶.

Conclusion

MAP and BMI can be used as baseline screening tools of preeclampsia in low resources setting with OR = 32.250 and 5.333. But ROT is not associated with the incidence of preeclampsia.

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References

1. Surabaya Health office 5 year report, 2017. Unpublished data
2. Narvaez, M, Weigel, M.M, Felix, A, Jaramilo, L P. The clinical utility of the roll-over test in predicting pregnancy-induced hypertension in a high-risk Andean population. *International Journal of gynecology & Obstetrics*. 1990;vol 31:1; 9-14
3. Walia, D and Gupta. Comparison between roll-over test and placental localization for early prediction of preeclampsia. 2015; DOI: 10.18203/2320-1770.ijrcog20150784
4. Gasse C., Boutin A., Cote M., Chaillet N., Bujold E., and Demers S. First-trimester mean arterial blood pressure and the risk of preeclampsia: The Great Obstetrical Syndromes (GOS) study. *Pregnancy Hypertens*, 2017.;12:178-182. doi: 10.1016
5. Ernawati, ErryGumilar, Kuntoro, JoewonoSoeroso & Gus Dekker. Expectant management of preterm preeclampsia in Indonesia and the role of steroids, *The Journal of Maternal-Fetal & Neonatal Medicine*. 2016;29(11):1736-40.
6. Robillard PY, Hulsey TC, Alexander GR, Keenan A, de Caunes F, Papiernik E. Paternity patterns and risk of preeclampsia in the last pregnancy in multiparae. *J Reprod Immunol*. 1993;24:1-12.
7. Poon, LC., Kameta NA., Valencia C., Nicolaides KH. Mean arterial pressure at 11(+0) to 13(+6) weeks in the prediction of preeclampsia. *Hypertension*. 2008;51(4):1027-33
8. Poon LC, Kametas NA, Valencia C, Chelemen T, Nicolaides KH. Hypertensive disorders in pregnancy: Screening by systolic diastolic and mean arterial pressure at 11-13 weeks. *Hypertens Pregnancy*. 2011;30:93-107
9. Gallo, D., Poon, LC., Fernandez, Wright, D., Nicolaides, KH. Prediction of Preeclampsia by Mean Arterial Pressure at 11-13 and 20-24 Weeks' Gestation. *Fetal Diagnosis Therapy*, 2014;36:28-37
10. Liu L, Hong Z, Zhang L. Associations of prepregnancy body mass index and gestational weight gain with pregnancy outcomes in nulliparous women delivering single live babies. *Sci Rep*. 2015;5:12863.
11. Rahman MM, Abe SK, Kanda M, et al. Maternal body mass index and risk of birth and maternal health outcomes in low and middle income countries: A systematic review and meta-analysis. *Obes Rev*. 2015;16:758-770.
12. Wei Y-M, Yang H-X, Zhu W-W, et al. Risk of adverse pregnancy outcomes stratified for pre-pregnancy body mass index. *J Matern Fetal Neonatal Med*. 2016;29:2205-2209.
13. Gregor MF, Hotamisligil GS. Inflammatory mechanisms in obesity. *Annu Rev Immunol*. 2011;29:415-445.

14. Spradley FT, Palei AC, Granger JP. Immune mechanisms linking obesity and preeclampsia. *Biomolecules*. 2015;5:3142–3176.
15. Reslan, O. M. and Khalil, R. A. Molecular And Vascular Targets In The Pathogenesis And Management Of The Hypertension Associated With Preeclampsia. *Cardiovascular & hematological agents in medicinal chemistry*. 2010; 8(4), pp. 204–26. doi: 10.2174/187152510792481234.
16. Poon. L, Shennan. A, Hyeet. J.A, Kapur. A, Hadar. E, et al. The International Federation of Gynecology and Obstetrics (FIGO) initiative on pre-eclampsia: A pragmatic guide for first-trimester screening and prevention. *Int J Gynecol Obstet*, 2019; 145 (Suppl. 1): 1–33

The Effectiveness of the Cordial Older Family Nursing Model in Order to Improve the Quality of Family Care for Older Persons

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Abstract

Introduction: Older people generally experience an overall functional decline and that may cause high dependence upon their families. The object of this study is to devise The Cordial Older Family Nursing Model in order to improve the quality of family care on them. Material and Method This study used an operational research design that passed through three steps of research.

Findings: The results of this study, were as follows: 1.) Step I: Informational support and coping strategies Acquiring Social Support were the predominant variables of older persons abuse. 2.) Step 2: The results of The Cordial Older Family Nursing Model with module, worksheet, and training curriculum 3.) Step III: There was a significant difference between family support (both informational and instrumental, family strategy, coping criteria and the incidence of elder abuse inter measurement.

Discussion: The cordial older family nursing model testing indicated improvement of mean value of total family support before and after treatment on intervention group which means the capability of family in providing support in elderly care giving were improving. This was carried out during a trimester after the application of the model between interventional and control groups.

Conclusion: The replication of models in cities across Indonesia Continuous training for nurses, health carers, and caregivers while taking care of homebound older adults

Keywords: *The Cordial Older Family Nursing Model, family support, health status of older persons, older persons abuse.*

Introduction

The population of elderly people in the world increases each year. *World Health Organization* (WHO) (2002), stated that the elderly people in Indonesia in the coming 2020 will reach 11.34% or 28,8 million people. Although the percentage of elderly in Indonesia is relatively smaller than the elderly in many countries, yet the real number is actually quite great. This is because of the large population of Indonesia that places the elderly of Indonesia in the fourth place after China, India, and USA^[1].

BPS RI–Susenas 2009, in National Commission on Older Persons/Komisi Nasional Lansia, stated that the average percentage of older persons of the population

in Indonesia was 8.37% hence it could be said that the population of Indonesia could be categorized as elderly structured population. There were 11 provinces in Indonesia with more than 7% older persons in the population, namely Daerah Istimewa Yogyakarta/Special Region of Yogyakarta (14.02%), Central Java (10.99%), East Java (10.92%). BPS RI, in Older Persons Population Profile/Profil Penduduk Lansia compiled by the National Commission on Older Persons/Komisi Nasional Lansia described that West Java was one of the provinces with older persons population because the percentage of its older persons population was 7.95% of its total population amounting as many as 41,902,385 people^[2].

Biological risk occurs with biological change in the elderly due to ageing process. According to Miller's Theory of Consequence health problems in the elderly may occur due to various biological changes in the elderly. Lifestyle risk is health values realized by healthy behaviors^[3]. The elderly as part of a family adopts the believed healthy behaviors in the family. Environmental risk covering social and economy environment occurs due to the elderly's social status change in the society, such as losing main occupation (retiring). Previously working elderly has to adapt to retirement when the previously employed elderly has to adapt to retirement in which income decrease occurs, while medical cost increases due to the increasing health problems^[4].

The family, as the closest social unit to the elderly, is the main support to the elderly. The family is expected to be able to facilitate the elderly in coping and executing the development task, so as to increase the health, comfort, and welfare of the elderly^[5]. Nursing model developed by Sahar verified that *Family Carer's Training Program (FCTP)* has positive impact on the elderly health status through the increasing capability of the family in taking care of the elderly^[6]. The family as service provider at home can affect the elderly's health status. The family will give positive effect when the capability as needs provider is improved by attending *Family Carer's Training Program*. Riasmini focused on a model to make family independent in nursing the elderly. Both models have not specifically given the reference for mistreatment issue on the elderly; nevertheless both have verified the importance of family role in supporting the welfare of the elderly^[7].

Mistreatment might occur when the elder's level of dependency is very high hence nursing provider can show hostile and aggressive behavior which might harm the elderly. Psychopathology theory suggested that people with mental problems, substance addiction, or mentally disabled are abnormal people and do not have the capability to control their behavior^[8]. The theories mentioned earlier explained various factors that might create mistreatment on the elderly. Knowledge about those factors is expected to enable health workers early detect mistreatment and take precautionary efforts so that the elderly living with a family will not experience mistreatment^[9].

Hanson stated that the family functions as social support by seeking and conveying information, emotional support by assisting in emotion control, direct support in providing financial support as well as child and elder care support. The lack of support provided by the family might create mistreatment on the elderly^[10]. Emotional support is a dominant factor on the occurrence of abandonment on the elderly living with a family. Hence various supports which are given by the family can prevent the occurrence of elder mistreatment. Prevention of elder mistreatment's occurrences can increase the health degree of elderly living with families^[11].

Depok as part of West Java province has elderly population of 106,159 consisting of 55,120 male elderly and 51,039 female elderly^[12]. Based on the experience and observation results during supervision in the area of Depok, the family should actually be able to participate in improving the health and welfare of the elderly. An illustration of family support that was not optimal in elderly care was that more than half (55.6%) of the families were not aware of abandonment of the elderly; the family had not yet considered various aspects related to abandonment^[13]. Until the present day, the number of mistreatment in Depok has not been identified. Puskesmas (the Community Health Center) has not had intervention program that is available in the community relating to mistreatment happening to the elderly in the family. Based on the description, the researchers are interested in developing cordial older family nursing model in the efforts to improve the quality of family care on the elderly.

Material and Method

The research was carried out by applying operational research approach. The implementation was carried out in three (3) phases. Phase 1 was to identify the scale of the problem by applying Cross Sectional design with 135 respondents in Kelurahan/Village of Harjamukti area, Kecamatan/District of Cimanggis, Depok city; Phase 2 was to develop a model based on the results found in phase 1, literature studies, and inputs from the experts and; Phase 3 was to validate the model developed in phase 2 by applying *quasi experiment pre-posttest with control* design, Harjamukti village as intervention group with 54 respondents and Mekarsari village as control group with 54 respondents.

Findings:**Table 1: Support, coping strategy, family burden, elderly health status, and family ability in preventing mistreatment after Model implementation between groups (n=108)**

Variable	Intervention (n=54)		Control (n=54)		Value p
	Mean	Median	Mean	Median	
1. Family Support					
- Informational	27.61	28.00	26.28	25.50	0.020
- Appreciation	29.56	31.00	30.74	31.00	0.181
- Emotional	29.87	31.00	30.17	31.00	0.594
- Instrumental	31.46	32.00	27.24	27.00	0.000
- Total	118.50	119.50	114.43	115.00	0.014
2. Family Coping Strategy					
- Acquiring Social Support	29.57	29.00	27.20	27.50	0.015
- Reframming	33.07	33.00	31.07	32.00	0.000
- Passive Appraisal	18.50	18.00	17.28	18.00	0.047
- Seeking Spiritual Support	17.93	18.00	16.33	16.00	0.000
- Mobilizing family to acquire and accept help	20.02	20.00	18.87	20.00	0.001
- Total	119.09	119.00	110.76	110.00	0.000
3. Family Burden	7.78	4.00	10.28	6.00	0.132
4. Elderly Health Status					
- Physical	27.35	28.00	28.48	29.00	0.728
- Mental	21.00	22.50	21.46	22.00	0.219
- Total	48.35	51.50	49.94	50.50	0.747
5. Mistreatment					
- Physical	19.67	20.00	19.07	19.00	0.001
- Financial	15.41	16.00	15.06	15.00	0.006
- Psychological	14.74	15.00	14.09	14.00	0.049
- Abandonment	15.78	16.00	15.22	16.00	0.012
- Total	65.54	66.00	63.44	64.00	0.000

Results of Phase 1 Research are as following: The characteristic of the elderly was most of them are aged between 60-69 years old (51.1%). This indicated that the elderly was categorized as young elderly. They should actually still live actively and be able to be independent in meeting their own basic needs. More than half of the elderly were female (55.6%), almost all of the elderly's income was below the City/County Minimum Wages or UMK (91.9%) and more than half of the elderly were of Betawi ethnic group (57.0%).

Results of Phase 2 Research: Based on the result of phase 1 research, literature study and inputs from experts, a Cordial Older Family Nursing Model was compiled to improve the quality of family nursing on the elderly in phase 2 research. The model developed

referred to the philosophy of the research that is improvement of family support on the elderly, coping strategy, and lowering the burden felt by families hence the occurrence of mistreatment can be minimized and the elderly health status can be optimized.

Results of Phase 3 Research: Phase 3 researches illustrated the effectiveness of Cordial Older Family Nursing Model on the supports, coping strategy, and family burden in nursing the elderly, health status of the elderly, and capability of the family in avoiding mistreatment on the elderly.

Discussion

Results of the cordial older family nursing model testing indicated improvement of mean value of total

family support before and after treatment on intervention group which means the capability of family in providing support in elderly care giving were improving. Statistics test results indicated differences (value of $p=0.000$) in total family support prior to and after the implementation of cordial older family nursing model on intervention group. Based on test on the difference between intervention group and control group a result was drawn that there was a difference ($p=0.014$) in total family support between intervention group and control group after the implementation of cordial older family nursing model. This indicated that cordial older family nursing model was effective in improving total family support in nursing the elderly.

The research carried out by Zulfitri had similar results with this research, i.e. there was a significant relation between family support and the behavior of the elderly in controlling their health in the service area of Melur Pekanbaru Community Health Center (Puskesmas)^[14]. This means by improving family informational support in health related information provision, the elderly health behavior would be improving. Willis (2009), stated that one of the reasons for lack of communication in a family was each of its members was busy with their activities hence they did not have time to listen to each others' wishes and complaints. Such condition was also found in this research. There were families who did not have enough time to listen to the elderly's complaints due to their hectic working hours^[15]. Family counseling is an assistance effort provided to individual family members so as their potential can be developed optimally and the problems resolved based on their eagerness and love for the family. This is in line with the research of Zulfitri which stated that the most dominant family support that was related to the behavior of elderly with hypertension was emotional support^[16].

The results of family instrumental support questionnaires filled in by caregivers stated that most families did not prepare special saving for the elderly needs, this was caused by the priority of family financial management was still put on meeting the family basic needs (food, clothing and housing). In other questionnaire's answer related to instrumental support was that there were families who did not give the elderly a chance of socializing due to financial constraint^[17]. Most of the respondents and families in this research had income that was below Depok city minimum wage (upah minimum kota/UMK). Family income is an important aspect for the family and affects the family

life^[18]. Excellent family income is expected to provide better instrumental support in accordance with the needs of the elderly because the family is the greatest supports source for the elderly.

Widiastuti in her research revealed that a respondent experienced a stress in nursing her spouse who was suffering from Alzheimer. In this case, the respondent dealt with her problem by controlling her emotion first to adapt with existing situation. The coping strategy used by the respondent can be categorized as Reframing coping strategy^[19]. This complied with the result of this research where the family did not always consider problems as an unexpected thing and many families always sought for the blessing in any problems or incidents experienced so they did not cause desperation. The result of chi-square test gave an illustration that elderly with families that did not apply good reframing coping strategy experienced greater mistreatment compared to those with families who applied good reframing coping strategy^[20].

Conclusion

The results of the research showed that:

1. Family informational, instrumental, appreciation, and emotional supports in nursing the elderly have not been optimal. There were relations between appreciation and emotional support to the occurrence of mistreatment on the elderly.
2. Family coping strategy in nursing the elderly that was mostly used was *seeking spiritual support* coping strategy. Families have not implemented the entire existing coping strategies adequately.
3. Most of the families stated that there had not been any burdens in nursing the elderly. There was no relation between caregiver's burdens to the occurrence of mistreatment on the elderly.
4. The health status of the elderly had not been optimal. There was a relation between mental health status to the occurrence of mistreatment on the elderly.
5. The occurrence of mistreatment was found on the elderly in the form of physical, financial, psychological and abandonment mistreatment types
6. Cordial older nursing model was compiled

Conflict of Interest: The researcher declare that there are no conflict interests of this study

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References

1. Komisi NL. Profil penduduk lanjut usia 2009. Jakarta: Komisi Nasional Lanjut Usia;2010
2. Dinas K K D. Laporan kegiatan pelayanan kesehatan lansia di posbindu Kota Depok; 2011.
3. Bratanegara, A. S. Gambaran dukungan keluarga terhadap pemanfaatan posbindu lansia di Kelurahan Karasak Kota Bandung. *eJurnal Mahasiswa Padjajaran Vol.1 No.1.*; 2012.
4. Acierno R, et all.. Prevalance and correlates of emotional, physical, sexual, and financial abuse and potential neglect in the United States: The national elder mistreatment study. *American Journal of Public Health Vol. 100 No. 2.*<https://doi.org/10.2105/ajph.2009.163089>; 2010.
5. Miller, C.A.. Nursing care of older adults: theory and practice. Second edition. Philadelphia: J.B. Lippincott Company;2004
6. Friedman MM, Bowden VR, Jones EG. Family nursing: research, theory and practice. Prentice Hall: Upper Saddle River NJ; 2010.
7. Consedine. The Association of Family Support and Wellbeing in Later Life Depends On Adult Attachment Style..Diakses dari Website The National Center for Biotechnology Information: www.ncbi.nlm.nih.gov/pubmed/19266366; 2009
8. Hanson, S. M. Family health care nursing: an introduction. In. M. H. Hanson, V. Gedaly-Duff, & J. R. Kaakinen (Eds.), *Family health care nursing: theory, practice and research (3rd ed.)* Philadelphia: F.A. Davis; 2005.
9. Hamid. Child-family characteristics and coping patterns of Indonesian families with mentally retarded child. North America: UMI's Dissertation Abstracts database. (1993).
10. Gelles, R.J, and Cornell. Intimate violence in families: Family Studies Text Series no. 2 ed 2. Sage: Newbury Park;2010.
11. Kaakinen, J. R., Gedaly-Duff,V., Coehlo, D.P., & Hanson, S.M.H. *Family health care nursing: theory, practice and research.* 4rd ed. Philadelphia: F.A. Davis Company; 2010.
12. Willis, S. S. *Konseling Keluarga.* Bandung: Alfabeta; 2013.
13. Kim, C.S. Patterns of family support and the quality of life of the elderly. *Social Indicators Research.* Volume 62-63, April 2013, 437-454;2013.
14. Rekawati, E., Laporan Pre Eliminary: Uji Validitas dan Reliabilitas instrumen salah perlakuan (Laporan Penelitian tidak dipublikasikan). Universitas Indonesia, Depok, Indonesia; 2010.
15. Nasution, J.A. Stres dan koping keluarga dalam merawat anggota keluarga yang sakit di wilayah kerja Puskesmas Medan Johor. (Skripsi tidak dipublikasikan). Universitas Sumatra Utara. Medan. Indonesia;2013.
16. WHO. Abuse of the Elderly. Diakses dari Website Resmi WHO: http://www.who.int/violence_injury_prevention.html; 2012.
17. Ramlah. Hubungan pelaksanaan tugas kesehatan dan dukungan keluarga dengan pengabaian lansia di wilayah kerja Puskesmas Kassi-Kassi Makasar (Tesis tidak dipublikasikan). Universitas Indonesia, Depok, Indonesia; 2011.
18. Zulfritri, Reni. Hubungan dukungan keluarga dengan perilaku lanjut usia hipertensi dalam mengontrol kesehatannya di wilayah kerja Puskesmas Melur, Pekanbaru (Tesis tidak dipublikasikan). Universitas Indonesia, Depok, Indonesia; 2016.
19. Riasmini, M. Efektivitas model kelompok keluarga mandiri untuk meningkatkan kualitas hidup lanjut usia di masyarakat wilayah DKI Jakarta. (Disertasi tidak dipublikasikan). Universitas Indonesia, Depok, Indonesia;2013.
20. Sahar, J. Supporting family carers in caring for older people in the community in Indonesia (Tesis tidak dipublikasikan). Queensl and University of Technology, Queensland, Australia;2012.

Early-Onset Neonatal Sepsis in Low-Birth-Weight and Birth-Asphyxia Infants at Haji Hospital Surabaya, Indonesia

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Abstract

Introduction: The incidence of early-onset neonatal sepsis is still high, therefore special attention is needed early detection of risk factors for early management. Many risk factors could affect early-onset neonatal sepsis such as birth-weight and birth-asphyxia.

Aim: This study explored the risk factors for early-onset neonatal sepsis among neonates at Haji Hospital, Surabaya City, Indonesia.

Method: This study was observational analytic with a cross-sectional design. The data used retrospective document review was conducted in NICUs of Haji Hospital, Surabaya City, Indonesia. 1.461 infants were born from January 2018 to December 2018. The data analysis of this study was the Chi-Square Test and Multiple Logistic Regression Test using SPSS for windows v.17.

Result: This study involved 1.461 infants with one hundred seventy-eight suffered of sepsis. The study found out that low-birth-weight and birth-asphyxia were significantly associated with neonatal sepsis ($p < 0.001$). Last, the result of multiple regression analysis showed that early-onset sepsis was influenced by low-birth-weight ($p < 0.001$; RR: 10.405; CI: 6.346 to 17.061) and birth-asphyxia ($p < 0.001$; RR: 17.038; CI: 10.644 to 27.271).

Conclusion: The neonatal sepsis was influenced by low-birth-weight and birth-asphyxia. Based on these results we recommend to focus on the intensive treatment for infants who suffered asphyxia and had low-birth-weight.

Keywords: Neonatal sepsis; low-birth-weight; birth-asphyxia.

Introduction

Infant Mortality Rate (IMR) is an indicator that reflects the state of health in society including Indonesia and is a sensitive benchmark of all management efforts undertaken by the government, especially in the health sector¹. IMR in Indonesia in 2015 was still high at 22.23 per 1,000 live births while in East Java the IMR in 2014 reached 26.66 per 1000 live births². IMR in East Java decreased compared to the previous year but it was not significant, namely in 2013 several 27.5 per 1000 live births. IMR in the city of Surabaya in 2015 amounted to 6.48 per 1000 live births. This figure has increased compared to 2014 which was 5.62 per 100 live births. The United Nations set this indicator on the 2030 Sustainable

Development Goals (SDG's) at point 3, namely in 2015-2030, which is to reduce the infant mortality rate to at least 12 per 1,000 live births.³.

According to WHO in 2016 neonatal deaths account for 45% of child deaths under 5 years. The majority of all neonatal deaths (75%) occur in the first week of life, and between 25% to 45% of neonatal deaths occur within the first 24 hours. Almost all (98%) of five million neonatal deaths occur in developing countries. Neonatal sepsis accounts for nearly 80% of neonatal deaths⁴.

Sepsis was initially defined as a suspicion or proven infection accompanied by clinical conditions of SIRS (Systemic Inflammatory Response Syndrome) but the

definition is now abandoned. As per the consensus regarding the latest sepsis, sepsis is defined as a state of life-threatening organ dysfunction/failure, caused by an unregulated host response to infection. The cause of early onset neonatal sepsis is different from the cause of slow onset neonatorum sepsis. The cause of SNAD is microorganisms that are transmitted vertically from mother to baby, both before and during labor⁵.

As per the consensus regarding the latest sepsis, sepsis is defined as a state of life-threatening organ dysfunction, caused by an unregulated host response to infection. Neonatal sepsis is divided into two namely early-onset neonatal sepsis (age <72 hours) and advanced (age > 72 hours)⁶. Early-onset neonatal sepsis causes high morbidity and mortality in newborns. The incidence of early-onset neonatal sepsis is higher in developing countries (1.8 to 18 per 1000 live births) than in developed countries (1 to 5 per 1000 live births). The case fatality in EONS ranges from 16.7% to 19.4%⁷. The incidence rates of neonatal infection in several referral hospitals in Indonesia is approximately 8.76%–30.29% with the mortality rate is 11.56%–49.9%. The incidence rates of neonatal sepsis in several referrals hospital in Indonesia is 1.5%–3.72% with the mortality rate is 37.09%–80%⁵.

In Haji Hospital Surabaya there was an increase in cases of newborn infections in 2015-2017 to 21.50%. Several factors of mother, babies, and environment are contributed to the infection exposed and non-optimal of NM immunologic response so as the newborn become susceptible to be infection⁸. The objective of this study is to explore the risk factors for early-onset sepsis among neonates at Haji Hospital, Surabaya City, Indonesia.

Material and Method

This study was observational analytic with a cross-sectional design. The data used retrospective document review was conducted in NICUs of Haji Hospital,

Surabaya City, Indonesia. 1.461 infants were born from January 2018 to December 2018. The independent variables of this study were birth-weight and birth-asphyxia. The dependent variable of this study was early-onset sepsis.

This study used SPSS Statistics 17.0 for data analysis. Bivariate analysis was correlated using cross-tabulations and Chi-Square Test with $\alpha=0.05$. A multivariable logistic regression model was created to examine the causal association between independent variables and breast milk production using Multiple Logistic Regression with $\alpha=0.05$. This study was received ethical approval from the Health Research Ethics Committee, Faculty of Medical, Universitas Airlangga.

Findings:

Most of the 928 infants (63.51%) were female while almost half were 533 infants (36.48%) were male. Almost entirely, 1353 babies (92.61%) were born with clear membranes while only a small portion, namely 108 babies (7.39%) were born with turbid green membranes.

Furthermore, almost 1350 babies (92.40%) were born full term and a small part, namely 107 babies (7.30%) were born with a premature period as well as babies born over time (postdate) only a small portion, 4 babies (0.30%). Other data show that almost all 1340 infants (91.72%) had no low birth weight (LBW) while only a small portion, 121 babies (8.28%) were born with LBW.

The data of asphyxia in infants shows that almost all of 1333 infants (92.61%) were born not asphyxia while only a small proportion of 128 infants (8.76%) experienced asphyxia. And it shows that almost all 1420 babies (97.19%) were single born and only a small portion, 41 babies (2.81%) were born twin (multiple)

Based on data which fulfill our inclusion criteria. These are the result.

Table 1. Bivariate analysis between independent variables and early-onset sepsis

Variables	Early-Onset Neonatal Sepsis				Total		p
	EONS		Non-Sepsis		n	%	
	n	%	n	%			
Birth-weight							
Low(< 2500 gram)	76	42.7	45	3.5	121	8.3	< 0.001*
Normal (> 2500 gram)	102	57.3	1238	96.5	1340	91.7	
Asphyxia							
Yes	87	48.9	41	3.2	128	8.8	< 0.001*
No	91	51.1	1242	96.8	1333	91.2	

* Significantly correlate using Chi-Square Test (p < 0.05)

Table 2. Summary of multiple logistic regression

Variables	B	SE	P	RR
Birth-weight				
Low	2.342	0.252	< 0.001*	10.405
Normal (reference group)				
Asphyxia				
Yes	2.835	0.240	< 0.001*	17.038
No (reference group)				

* Significantly associate using Multiple Logistic Regression Test (p < 0.05)

This study involved 1.461 infants with one hundred seventy-eight suffered of sepsis. As shown in **Table 1**, there was a correlation between LWB and neonatal sepsis (p<0.001). Most of infants who had normal weight (96.5%) did not suffer sepsis than infants who had LBW. In contrast, almost half of participants (42.7%) who had LBW were suffer early onset sepsis highly than infants who had normal weight. It could be concluded that the early onset sepsis was more suffered by infants who had low-birth-weight (less than 2500 gram).

Table 1 also shows that there was a correlation between asphyxia and neonatal sepsis (p<0.001). Only 3.2% (n=41) infants who are getting sepsis were infants who had asphyxia. In contrast, almost half of participants (48.9%) who had asphyxia were suffered early onset sepsis highly than normal infants. It could be concluded that the sepsis was more suffered by infants who had asphyxia.

Table 2 shows that the results of multivariate analysis with Multiple Logistic Regression Test (α = 0.05). The result showed that neonatal sepsis was influenced by low-birth-weight (p<0,001; RR: 10.405; CI: 6.346 to 17.061) and birth-asphyxia (p<0.001; RR: 17.038; CI: 10.644 to 27.271)

The infants who had LBW were at risk for getting early onset sepsis 10.405 times greater than infants who had normal weight. Then, infants who suffered asphyxia were at risk for getting early onset sepsis 17.308 times greater than infants who not suffered asphyxia. So that, asphyxia most likely has an influence.

Discussion

Following approval from the institutional ethical committee, almost half of participants (42.7%) who had LBW were suffering early onset sepsis highly than infants who had normal weight. It could be concluded that the early onset sepsis was more suffered by infants who had low-birth-weight (less than 2500 grams).

The results of this study are in line with the results of a research namely LBW has three times the risk of developing sepsis than non LBW^{9,10}. This is in line that infants with sepsis had more low birth weight (85.7%)¹¹. The central regulation of breathing is not perfect, the respiratory muscles and ribs are still weak in LBW infants resulting in less oxygen entering the brain, if oxygen is lacking, anaerobic germs easily develop which causes easy infection. In contrast to research conducted by Rahmawati in Dr. M. Djamil Padang Hospital, the

results showed that there was no statistically significant relationship between birth weight in the form of low and normal categories with the incidence of neonatal sepsis. A significant relationship appears in LBW infants with prematurity where the maturation of their organs (liver, lungs, enzymes, digestion, brain, immune system against infection) is not perfect, so LBW babies often experience complications that end in death^{12,13}.

Then, infants who lived asphyxia were at risk for getting early onset sepsis 17,308 times greater than infants who didn't live asphyxia. So that, asphyxia most likely has an influence to. Neonatal asphyxia facilitates systemic infections. This is due to inhibited leukocyte activity because it requires energy (ATP) for cytoskeletal microfilament contractions. The state of hypoxia will also inhibit the microbicidal activity of polymorphonuclear cells¹⁴. Neonatal asphyxia increased the risk of EONS with a positive blood culture result 4-fold (RO = 4.102; 95% CI 1.04-16.14)^{15,16}.

Neonatal asphyxia was assessed by examining APGAR scores. A low APGAR score increases the risk of EONS. Research conducted by Muhammad et al in 2015 found that Apgar scores <7 in the first minute had a risk of 14.05 times (95% CI 5.487-35.987) for EONS events¹⁷. APGAR scores <7 in the first minute were also reported by Shah et al., which were significant with each OR being 5.7 for EONS events. In general, the first minute APGAR score is associated with Potential Hydrogen (pH) umbilical cord blood and intrapartum depression and is not related to the results, whereas the APGAR score then reflects changes in the baby's condition during resuscitation^{10,18}.

Asphyxia neonatorum is very closely related to health problems of pregnant women, including infections. Babies with asphyxia neonatorum appear unfit and have a history of fetal distress before birth. Neonatal asphyxia facilitates systemic infections. Neonatal asphyxia increases the risk of early onset neonatal sepsis with positive blood cultures. In addition, low birth weight babies, including this risk group. Most problems occur in infants who weigh less than 1500 grams with high mortality and require special medical care and treatment for infants at 2.75 times higher risk of neonatal sepsis^{10,13,16}.

The diagnosis of early onset neonatal sepsis is very important in the management and prognosis of the patient. Delay in diagnosis can potentially threaten the

survival of the baby and worsen the patient's prognosis. The prognosis of neonatal sepsis depends on diagnosis and therapy. The prognosis of neonatal sepsis is good if the diagnosis is made early and the therapy is given appropriately. Mortality rates can increase if clinical manifestations and risk factors for neonatal sepsis are not well identified. Midwives and doctors play an important role in efforts to improve the health of mothers and children, especially in clinical cases^{19,20}.

Conclusion

The neonatal sepsis was influenced by low-birth-weight and birth-asphyxia. Based on its conclusion, it is suggested to Health Service Centre to focus on the intensive treatment for infants who had low-birth-weight and suffered asphyxia. It is also suggested to society, especially for husband, to keep supporting the pregnant-mothers for check their pregnancies regularly.

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References

1. Statistik BP. Badan pusat statistik. Diambil dari <https://www.bps.go.id>. 2017;
2. Kementerian Kesehatan RI. Data dan Informasi: Profil Kesehatan Indonesia. Jakarta Kemenkes RI. 2017;
3. Surabaya DKK. Profil Kesehatan Kota Surabaya Tahun 2015. Surabaya Dinkes Kota Surabaya. 2016;
4. Liu L, Oza S, Hogan D, Perin J, Rudan I, Lawn JE, et al. Global, regional, and national causes of child mortality in 2000–13, with projections to inform post-2015 priorities: an updated systematic analysis. *Lancet*. 2015;385(9966):430–40.
5. Utomo MT. Neonatal sepsis in low birth weight infants in Dr. Soetomo general hospital. *Indones J Trop Infect Dis*. 2010;1(2):86–9.
6. Cunningham M, Eyal FG, Gomella TL. Neonatology: Management, Procedures, On-Call Problems, Diseases, and Drugs. McGraw-Hill Professional; 2009.
7. Jajoo M, Kapoor K, Garg LK, Manchanda V, Mittal SK. To study the incidence and risk factors of early onset neonatal sepsis in an out born neonatal

- intensive care unit of India. *J Clin Neonatol.* 2015;4(2):91.
8. Shah GS, Budhathoki S, Das BK, Mandal RN. Risk factors in early neonatal sepsis. *Kathmandu Univ Med J (KUMJ).* 2006;4(2):187–91.
 9. Wirawan R. Hubungan Antara Bayi Berat Lahir Rendah (Bblr) Dengan Terjadinya Sepsis Neonatorum. Universitas Muhammadiyah Surakarta; 2012.
 10. Simonsen KA, Anderson-Berry AL, Delair SF, Davies HD. Early-onset neonatal sepsis. *Clin Microbiol Rev.* 2014;27(1):21–47.
 11. Carolus W, Rompis J, Wilar R. Hubungan Apgar skor dan berat badan lahir dengan sepsis neonatorum. *e-CliniC.* 2013;1(2).
 12. Putri R. HUBUNGAN SEPSIS NEONATORUM DENGAN BERAT BADAN LAHIR PADA BAYI DI RSUP DR M. DJAMIL PADANG. Universitas Andalas; 2017.
 13. Schuchat A, Zywicki SS, Dinsmoor MJ, Mercer B, Romaguera J, O’Sullivan MJ, et al. Risk factors and opportunities for prevention of early-onset neonatal sepsis: a multicenter case-control study. *Pediatrics.* 2000;105(1):21–6.
 14. Polin RA, Parravicini E, Regan JA. Bacterial sepsis and meningitis. Dalam: Taeusch HW, Ballard RA, Gleason CA, penyunting. *Avery’s diseases of the newborn.* Edisi ke 8. Philadelphia: Elsevier Saunders; 2004.
 15. Stoll BJ, Gordon T, Korones SB, Shankaran S, Tyson JE, Bauer CR, et al. Early-onset sepsis in very low birth weight neonates: a report from the National Institute of Child Health and Human Development Neonatal Research Network. *J Pediatr.* 1996;129(1):72–80.
 16. Stoll BJ, Hansen NI, Higgins RD, Fanaroff AA, Duara S, Goldberg R, et al. Very low birth weight preterm infants with early onset neonatal sepsis: the predominance of gram-negative infections continues in the National Institute of Child Health and Human Development Neonatal Research Network, 2002–2003. *Pediatr Infect Dis J.* 2005;24(7):635–9.
 17. Hayun M, Alasiry E, Daud D, Febriani DB, Madjid D. The risk factors of early onset neonatal sepsis. *Am J Clin Exp Med.* 2015;3(3):78–82.
 18. Ahmadpour-Kacho M, Asnafi N, Javadian M, Hajiahmadi M, Taleghani N. Correlation between umbilical cord pH and Apgar score in high-risk pregnancy. *Iran J Pediatr.* 2010;20(4):401.
 19. Polin RA. Management of neonates with suspected or proven early-onset bacterial sepsis. *Pediatrics.* 2012;129(5):1006–15.
 20. Hornik CP, Fort P, Clark RH, Watt K, Benjamin Jr DK, Smith PB, et al. Early and late onset sepsis in very-low-birth-weight infants from a large group of neonatal intensive care units. *Early Hum Dev.* 2012;88:S69–74.

Comparative Study between Elastic Nail Versus Plates and Screws in the Treatment of Diaphyseal Both Bone Forearm Fracture in Children

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Abstract

Objective: Compare between titanium flexible nail and plate fixation for fracture both radius and ulna regarding the operation time, time of union, functional outcome and complications for each method.

Materials and Method: A prospective comparative study, involved 44 children with displaced fractures of the radius and ulna were reviewed. Group1; (23 patients) underwent closed reduction-intramedullary fixation. Whereas, Group2; (21 patients) underwent open reduction internal fixation with plates. Patients were followed up for 24 weeks.

Results: Both treatments achieved excellent clinical outcomes and union rate, flexible intramedullary nailing showed better cosmeses, shorter operating and discharge times but the disadvantage is radiation exposure.

Conclusion: Both titanium elastic nail and compression plates and screws can be expected to yield excellent results and are proper for treating pediatric forearm shaft fractures. Intramedullary nailing was safe, effective, and easy to do in the management of both-bone forearm shaft fractures in children.

Keywords: Forearm shaft, fracture, titanium elastic nail, plates, scores, Price score system.

Introduction

Pediatric diaphyseal fracture of the radius and ulna commonly referred to as both bone forearm fractures are the third most common fracture in pediatric population, and account for 13 to 14% of all pediatric fracture¹. Most of these fractures treated with non-operative management. Recently, however, there has been a trend toward increased surgical management of these fractures in an effort toward increased functional outcome². The purpose of the operative intervention is to prevent future angular and rotational deformity and maximize functional outcome³. Many epidemiologic studies have

shown that 18% of children will experience a fracture by the age of 9, with children between the ages of 5 and 14 having the highest fracture incidence⁴.

In recent years the proportion of pediatric forearm fractures treated with internal fixation had increased, with a particular rise in the use of intramedullary nailing (IMN). This increase might be driven by improved understanding of the functional implications of mal-union, technological advances, societal expectations or fear of litigation. Traditionally, internal fixation of unstable pediatric forearm fractures had been achieved by open reduction and rigid internal fixation with plate and screws with good results. IMN with Kirschner wires or elastic stable intramedullary nails has become popular due to improved cosmesis, shorter operative time, less soft tissue dissection and ease of removal, with good results reported⁵.

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Open reduction with compression plate and screw fixation offer full stability if performed properly. The

method had been reported as a possible choice in adolescents approaching skeletal maturity. It is also a useful method in cases of re-fracture as the intramedullary canal may be obstructed⁶⁻⁸.

Titanium elastic nails system (TENS), has recently become the primary method of surgery in forearm shaft fractures in children. It has produced results equally good as plate and screw fixation in cases of unstable fractures, with several advantages when compared with plate and screw fixation⁹. In theory, ESIN was based on three-point stabilization by means of opposite tension of two parallel implants in the same intramedullary canal. In the forearm both bones are fixed separately with single nails. Therefore, stability is dependent on the two nails mandatorily orientated with the tips towards each other. In the forearm, the two separate nails in two separate bones together form opposing elastic concavity at the level of the fractures, for this reason both bones should be fixed¹⁰, regardless of opposing reports supporting single bone nailing. ESIN will not fill the medullary canal, in contrast to rigid intramedullary implants. The flexibility of using ESIN facilitates callus formation by enabling minimal movement in the fracture. It is still strong enough to maintain satisfactory alignment¹¹.

The present study aimed to compare titanium elastic nail and plate fixation for treatment of fracture both radius and ulna regarding the operation time, time of union. also, to evaluate the functional outcome and complications for each method.

Method

Study Design: A prospective comparative study between two surgical techniques for the treatment of both forearm bone fracture, the first one was fixation by titanium elastic nail and the second one is fixation by plate and screws.

Study Setting: The study was conducted at the orthopedics department of Erbil teaching hospitals.

Period of the Study: The study was carried out between October 2016 and November 2017

Study Sample: A total of 44 patients were included in the study. A random sampling technique was used by including every other patient in the study.

Inclusion Criteria: Age from 4-14 years old, unstable fracture, failure of conservative treatment, and open fracture (Gustilo type 1).

Exclusion Criteria: Distal metaphyseal fracture, fracture dislocation (Galeazzi and Monteggia fracture), associated arm fracture on the same side, and associated radial neck fracture.

Written consent was obtained from the family of each patient before participation in the study, A semi-formed Questionnaire was constructed by the researcher, the questionnaire includes:

Socio-demographic characteristic of the participants, side and site of injury, mechanism of injury, operative time, time of union, intraoperative complications and any postoperative complications like infection (superficial and deep, insertion site pain, need of nail trimming or removal and loss of reduction) each patient was followed up by 2nd, 6th, and 12th week postoperatively. The duration of the interval between injury and surgery was 1 day to 1 week.

Overall, the number of patients presented to our department with displaced diaphyseal fracture of radius and ulna at that duration was (124) children. Only (44) of them required open reduction and internal fixation.

Patients: Group 1: (23 patients), 17 boys (73.9%) and 6 girls (26.1%), their mean age were $(9.43 \pm 3.23) \pm$ SD years, underwent closed reduction-intramedullary fixation by titanium elastic nail.

Group 2: (21 patients), 14 boys (66.6%) and 7 girls (33.4%), their mean age were $(11.04 \pm 1.82) \pm$ SD years underwent open reduction internal fixation with plates and screws. The patient and method of fixation were chosen randomly.

Statistical Analysis: T-test concerning two means of un-paired group was used to find out if there are significant differences in the duration of the operation of both methods. Pearson Chi-square test was used to see if there was a significant difference in functional outcomes of both methods. The data were analyzed statistically by using statistic package for social science (SPSS) version 18. A p-value < 0.05 considered to be statistically significant.

Results

Table 1 illustrates most of the characteristics of the patients involved in the study. The mean duration of the operation was significantly higher in group 2 compared to group 1, while duration of hospitalization, functional outcomes and time to unite was not statistically different between both groups, as illustrated in table 2.

Table 1: Assessment of demographic and clinical characteristics

Conditions	Titanium Elastic Nail	Plate & Screws	Total
Number	23	21	44
Mechanism of Injury			
Fall on out stretch hand	18 (78.3%)	17 (81.0%)	35(79.54%)
Direct trauma	3(13.0%)	2 (9.5%)	5(11.36%)
Car accident	2 (8.7%)	2 (9.5%)	4(9.09%)
Fracture site			
Right	12(52.2%)	16(76.2%)	28(63.63%)
Left	11 (47.8%)	5 (23.8%)	16(36.36%)
Handedness			
Right	20(97.0%)	19 (90.5%)	39(88.63%)
Left	3 (13.0%)	2 (9.5%)	5(11.36%)
Fracturelevel			
Proximal	4(17.4%)	3(14.3%)	7(15.9%)
Middle	12 (52.2%)	10 (47.6%)	22(50%)
Distal	7 (30.4%)	8 (38.1%)	15(34.1%)
Indication of internal fixation in forearm shaft fractures			
Unstable	7(30.43%)	6(28.57%)	13(29.54%)
Still displaced after manipulation	5(21.73%)	3(14.28%)	8(18.18%)
Re-displaced	4(17.39%)	6(28.57%)	10(22.72%)
Neglected(presented late)	3(13.04%)	4(19.04%)	7(15.90%)
Open(compound) Gustello type 1	2(8.69%)	0	2(4.54%)
Multiple	1(4.34%)	1(4.76%)	2(4.54%)
Segmental	1(4.34%)	0	1(2.27%)
Compartmentsyndrome	0	1(4.76%)	1(2.27%)
Complications	5(33.34%)	10(66.66%)	15(100%)
Edema	2(40%)	4(40%)	6(40%)
Superinfection infection & pin tract infection	2(40%)	3(30%)	5(33.33%)
Deep infection	0	1(10%)	1(6.66%)
Delayed union	1(20%)	1(10%)	2(13.33%)
Compartment syndrome	0	1(10%)	1(6.66%)

Table 2: Assessment of operation characteristics and outcomes

Conditions	Titanium elastic nail	Plate & screws	p-value
Duration of operation	33.4 ± 8.3	47.7± 8.8	<0.001
Duration of hospitalization	1.65±1.11	2.66±0.96	0.150
Functional outcomes			0.750
Excellent	18 (78.26%)	14 (66.66%)	
Good	5 (21.73%)	7 (33.33%)	
Time to union			0.120
3 months	18 (78.26%)	12 (57.14%)	
6 months	5 (21.73%)	9 (42.85%)	

Discussion

The functional outcome following bone pediatric forearm fracture is one of the main considerations for a surgeon to decide between operative and conservative management¹². Most of these fractures can be treated non-operatively with full restoration of forearm function, due to the presence of a tout periosteum, and the very good remodeling capacity of children¹².

This study showed a significantly high proportion (70.45%) of male children with both bone fracture of forearm compared to females (29.55%). This may be because male children are more involved in playful activities like bicycling and this finding correlated with the study by Mohammed et al¹³.

The most common mechanism of injury fell on outstretched hands during playing at school (79.54%), while fracture incidence by car accident was low (9.09%) and this agreed with another study¹⁴.

The indications for open reduction and internal fixation of such fractures were; unstable (29.54%), still displaced after a trial of manipulation (18.18%), re-displaced (22.72%), neglected (15.9%), compound fracture (4.5%), multiple (4.5%), segmental (2.2%), neurovascular injuries and compartment syndrome (2.2%), which is similar to a study by Greenbaum¹⁵.

Concerning the time of operation fixation by titanium flexible nail take a significantly shorter time in comparison to the fixation by plate and screw, this agreed with Kose et al study¹⁶.

There was fewer complications rate in titanium elastic nail than those treated by plate and screws, but it did not reach statistical significance, which was in agreement with other studies like that done by Reinhardt et al¹⁷.

The fracture union complications in the forearm have been shown to be rare in several previous studies¹⁸. Those treated with IM nailing healed within 3 months (78.26%) and (21.73%) healed within six months. By using plate fixation healing within 3 months was (57.14%) and (42.85%) within 6 months, no significant differences between IM nailing and plating in terms of fracture union at 3 and 6 months after surgery.

The functional outcomes were graded according to Price et al. study¹². The result showed in titanium elastic nail group had excellent outcome (78.26%) and (21.74%) had good result, while for group 2 which used

plate and screws in fixation the result showed (66.66%) excellent and (33.33%) good result, there were no fair or poor graded noticed in this study, although there was a little difference in the two groups that's of no statistical significance. Seyfettinoglu et al found that surgical treatment gave excellent and good results in 82% of the patients¹⁹.

Ozkaya et al study recorded that 85.7% had excellent, 14.3% had good results according to Price et al Criteria. The follow-up period in their study was 37 months and the method of treatment was closed reduction and intramedullary nailing. They concluded that intramedullary nailing was safe, effective, and easy to perform in the management of unstable both-bone forearm fractures in children²⁰.

Conclusion

Both techniques have good functional outcome and union rate, flexible intramedullary nailing is a useful method to treat unstable forearm fractures in young children, compression plating is a useful method to treat unstable forearm fractures in late childhood, titanium elastic nail is superior to plate and screws fixation because: the procedure is easier and quicker, skin incisions are smaller, less soft tissue dissection and stripping of the periosteum is avoided, these allow shorter operative time and decrease the risk of prolonged anesthesia, and easier removal without significant complication.

Conflict of Interest: None

Ethical Clearance: Informed written consent was obtained from all the participants in the study, and the study and all its procedures were done in accordance with the Helsinki Declaration of 1975, as revised in 2000. The study was approved by the Iraqi Board of Medical Specializations.

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References

1. Cheng JC, Ng BK, Ying SY, Lam PK. A 10-year study of the changes in the pattern and treatment of 6,493 fractures. *Journal of pediatric orthopedics*. 1999;19(3):344-50
2. Jones K, Weiner DS. The management of forearm fractures in children: a plea for conservatism. *Journal of pediatric orthopedics*. 1999;19(6):811-5

3. Flynn JM, Jones KJ, Garner MR, Goebel J. Eleven years experience in the operative management of pediatric forearm fractures. *Journal of pediatric orthopedics*. 2010;30(4):313-9.<https://doi.org/10.1097/BPO.0b013e3181d98f2c>
4. Landin LA. Epidemiology of children's fractures. *Journal of pediatric orthopedics Part B*. 1997;6(2):79-83.<https://doi.org/10.1097/01202412-199704000-00002>
5. Calder PR, Achan P, Barry M. Diaphyseal forearm fractures in children treated with intramedullary fixation: outcome of K-wire versus elastic stable intramedullary nail. *Injury*. 2003;34(4):278-82.[https://doi.org/10.1016/s0020-1383\(02\)00310-8](https://doi.org/10.1016/s0020-1383(02)00310-8)
6. Goodwin RC, Kuivila TE. Pediatric elbow and forearm fractures requiring surgical treatment. *Hand clinics*. 2002;18(1):135-48.[https://doi.org/10.1016/s0749-0712\(02\)00017-3](https://doi.org/10.1016/s0749-0712(02)00017-3)
7. Herman MJ, Marshall ST. Forearm fractures in children and adolescents: a practical approach. *Hand clinics*. 2006;22(1):55-67.<https://doi.org/10.1016/j.hcl.2005.10.003>
8. Al-Osami MH, Mohammed S, Ali WI, Fawzi HA. The relationship between Hypermobility Syndrome and Systemic Lupus Erythematosus. *Indian Journal of Public Health Research and Development*. 2018;9(12):526-32.<https://doi.org/10.5958/0976-5506.2018.01891.0>
9. Van der Reis WL, Otsuka NY, Moroz P, Mah J. Intramedullary nailing versus plate fixation for unstable forearm fractures in children. *Journal of pediatric orthopedics*. 1998;18(1):9-13
10. Lee S, Nicol RO, Stott NS. Intramedullary fixation for pediatric unstable forearm fractures. *Clinical orthopaedics and related research*. 2002(402):245-50.<https://doi.org/10.1097/00003086-200209000-00024>
11. Huber RI, Keller HW, Huber PM, Rehm KE. Flexible intramedullary nailing as fracture treatment in children. *Journal of pediatric orthopedics*. 1996;16(5):602-5.<https://doi.org/10.1097/00004694-199609000-00011>
12. Price CT, Scott DS, Kurzner ME, Flynn JC. Malunited forearm fractures in children. *Journal of pediatric orthopedics*. 1990;10(6):705-12.<https://doi.org/10.1097/01241398-199011000-00001>
13. Mohammed H, Salloom F, Albagali M, Aljahromy I. Flexible Intramedullary Fixation of Pediatric Forearm Fractures-Report on Twenty-One Patients *Bahrain Med Bull*. 2009;31(1):1-8
14. Wyrsh B, Mencio GA, Green NE. Open reduction and internal fixation of pediatric forearm fractures. *Journal of pediatric orthopedics*. 1996;16(5):644-50.<https://doi.org/10.1097/00004694-199609000-00018>
15. Greenbaum B, Zionts LE, Ebramzadeh E. Open fractures of the forearm in children. *Journal of orthopaedic trauma*. 2001;15(2):111-8.<https://doi.org/10.1097/00005131-200102000-00007>
16. Kose O, Deniz G, Yanik S, Gungor M, Islam NC. Open intramedullary Kirschner wire versus screw and plate fixation for unstable forearm fractures in children. *Journal of orthopaedic surgery (Hong Kong)*. 2008;16(2):165-9.<https://doi.org/10.1177/230949900801600207>
17. Reinhardt KR, Feldman DS, Green DW, Sala DA, Widmann RF, Scher DM. Comparison of intramedullary nailing to plating for both-bone forearm fractures in older children. *Journal of pediatric orthopedics*. 2008;28(4):403-9.<https://doi.org/10.1097/BPO.0b013e31816d71f2>
18. Aboelmagd T, Aboelmagd K, Davies N, El Khouly A. Hybrid Fixation in Pediatric Forearm Fractures, does it Predispose to Non-union? A Case Report and Literature Review. *Journal of orthopaedic case reports*. 2019;9(3):72-4.<https://doi.org/10.13107/jocr.2250-0685.1428>
19. Seyfettinoglu F, Duygun F, Kovalak E, Ersan O, Ates B, Ates Y. [Assessment of surgical and conservative treatment of forearm fractures: results in juveniles]. *Ulusal travma ve acil cerrahi dergisi = Turkish journal of trauma & emergency surgery: TJTES*. 2009;15(4):371-6
20. Ozkaya U, Parmaksizoglu AS, Kabukcuoglu Y, Yeniocak S, Sokucu S. [Surgical management of unstable both-bone forearm fractures in children]. *Acta orthopaedica et traumatologica turcica*. 2008;42(3):188-92.<https://doi.org/10.3944/aott.2008.188>

Humanoid Robot Integration in Rehabilitation of Musculoskeletal Conditions

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Abstract

Robots find numerous applications in medical/health domains and are extensively used in commercial as well as domestic applications to support daily life activities. Human robot (HR) has widened their wings to be used in rehabilitation applications. Interest in robots that provide health care is growing as one of the upcoming fields of next generation. In this study we investigated the Robot-patient performance in physical rehabilitation. A group of musculoskeletal patients diagnosed with pain in muscles or joints or both, aged 20 to 65 years was chosen for the study. The robot was programmed to instruct and guide the patients for physical rehabilitation activities for three trials of 30 minute sessions on different days. The sessions involved interaction with a humanoid robot. Robot was programmed for a set of active exercises with a classified sequences that are time and motion managed. Verbal communication between the robot and patients allowed for re-start, stop, resume and replay functions. The whole performance was filmed and reviewed from the perspectives of the impact on the patient as well as the performance of the robot. The whole process was validated by performing the same procedure on a trial basis with healthy individuals to ensure the setup is operated smoothly. The performance of each variable was evaluated in three successive sessions. Evaluated functions include clarity, therapy sequence, interaction, voice, timing, independency, operation, technical performance and degree of freedom. Results were computed as percentages by an external assessor. Results demonstrated dynamic learning in the 1st and 2nd sessions which showed a remarkable improvement in the 3rd, 4th and 5th sessions. The overall average of the performance for the last 3 sessions was 91+%. Referring to this outcome, it could be concluded that the robot may have the potential to influence the physical therapy imitation. However, to establish the extent of this influence affirmatively, a bigger sample will be needed with a wider variety of patients.

Keywords: *Humanoidrobot, interaction, integration, rehabilitation, musculoskeletal.*

Introduction

Robots are being designed to complement human skill sets, reduce workload and enable professionals to focus on more important activities that have a greater impact on patient care delivery. As this technology advances and becomes more affordable, we can expect more health care institutions to adopt robotics.

Robots are still not a replacement for human interaction. Hospital operations are complex and involve uncertainty. Robots are good for performing repetitive tasks and tracking data, but this technology should only be used to make the clinicians' workflow easier so that they may focus on the most critical part of their jobs, which is caring for patients.

Advanced humanoid robots are employed in a variety of applications in medical/health domains and are also used extensively in commercial establishments as well as in the home support for daily life activities. Beyond the traditional scope, robot can be engaged in the rehabilitation process and it is poised to become one of the most important technological innovations of the 21st century. Literature showed specific uses with elderly patients and some pediatric applications.^{1,2}

In this article, we offer a trial study on the possible uses of robots in rehabilitation, particularly in the management of musculoskeletal conditions.

Human Robot (HR) has widened their wings to be used in rehabilitation. Interest in health care robots is

growing as one of the upcoming fields of next generation in this smart industry, especially as assistive tools in rehabilitation¹. It is believed that humanoid Robot promises excellent experience for CP children to learn motor tasks³. Many studies involving CP children investigated robotic exoskeletons⁴ to replace or support function. There is still a lack of intervention therapy which involves complicated functional tasks.

Some of the robotic technologies were designed to assist the user primarily through social rather than physical interaction⁵. For example, a previous study⁶ has established Kindergarten Assistive Robotics (KAR) as a tool for learning and development for normal children in preschool education. KAR has increased children's motivation and communication during the interaction. Robots have been successfully introduced into physical therapy and rehabilitation of children with disabilities^{7,8}. Thus, KAR is suggested to be applied for CP children. One of the studies involved KAR as a Robotics Agent Coach for CP motor Function (RAC CP FUN)⁹ which is designed to improve their motor functions and activities associated to daily living. Further, another study¹⁰ employed a mobile robot named "Neptune" and used a toy robot named "Cosmobot" and the derived results showed that robot can become a social mediator for learning. The results of a study^{11,12} that used Lego Mind storms robots¹³ for CP children's play activities demonstrated that the children reacted positively toward the robots, while some children increased their attention span and could be better engaged when they used the robots. However, most explored robotic systems earlier were mainly in the form of toys, and not in humanoid form. Thus, this study is designed to use a humanoid robot to instruct patients in physical therapy sessions with musculoskeletal problems. An expert software programmer and a physiotherapist jointly developed the therapy program. Details of the therapy were tailored specifically to meet the needed conditions, interact with the patients, with the mode and specification capable of offering several options.

Methodology

The intended group is a set of musculoskeletal patients diagnosed and referred for P.T clinic. A strengthening exercise was prescribed and endorsed by a licensed physiotherapist specialized in the musculoskeletal disorders, This particular group was for improving the back strength, with age range between 20 to 65 years. Other inclusion criteria were no physical

or mental disability, no hearing and vision deficiency, and a cognitive ability to follow simple commands in English. Signed informed consent was obtained from the participants. Five trials, each of 30 minutes session were performed on different days. The sessions involved interaction with humanoid robot. The experiment protocol was approved by the Occupational Therapy Association Research Board. The robot was programmed for a set of active exercises with a classified sequence managed in time and motion. Verbal communication between the robot and patients allowed re-start, stop, resume and replay functions. The robot was equipped with 4 cameras and programmed to take photos of the patient's face and voice print to enable individual recognition in order to recall the personal therapy program and update the patient information at the end of the session. The whole performance was filmed and reviewed from the perspectives of both the patient and robot. The whole process was validated by performing the same procedure on a trial basis with healthy individuals to ensure the setup is operated smoothly.

Patients were educated about the robot and the study aim. An introduction session was made to familiarize the group (robot, patient, operator and the assessor) with the study methodology. The study was conducted in a simple gym, with the exercise mat laid on the floor for the patients and the NAO was placed on the non-slippery floor. The performance assessment will use met partially met or not met.

NAO has 23 degrees of freedom: 2 degrees of freedom for head, 4 degrees of freedom for each arm, 1 degree of freedom for pelvis, and 5 degrees of freedom for each leg.

Result

The aim of this robotic-patients application is to instruct patients with musculoskeletal problems for several pre-structured and programmed exercises. The overall aim is to measure several factors that govern the robot-patient performance, e.g. clarity, sequence, interaction, voice, timing, independency, operation, technical performance, and degree of freedom. The assessment is expressed by % of excellence for the three times and then the % average is gathered for all patients. The total for each parameter in each session and the total for the five patients for each session is presented. The data in the table below is the grand total for the three sessions for five patients and expressed in %.

Item	Trial sessions		3rd session	4th session	5th session	Average%
	1st session	2nd session				
Clarity	50%	70%	90%	95%	95%	93+
Therapy sequences	30%	60%	90%	90%	100%	93+
Interaction	20%	60%	95%	95%	95%	95
Voice	70%	70%	80%	90%	95%	88+
Timing	40%	60%	100	95%	100%	98+
Independency.	60%	80%	80%	90%	90%	86+
Operation	70%	90%	90%	90%	95%	91+
Technical performance	90%	90%	90%	90%	95%	91+
						Grand 91+

Table 1: The data here is representing the% of performance of each item. The performance of the last three visits are averaged in the last column and the grand average for the overall performance (91+) is also presented. The 1st and 2nd sessions were considered as learning sessions.

Consequently, there are few points to be highlighted and discussed. The data presented represent the external

assessor evaluation of the performance. It is clear that the 1st session is a learning step which shows low levels of performance. Second session showed remarkable improvement and a continuous improvement is recognized in the 3rd session. The overall impression is supporting the fast and reliable interaction integration. The total performance related to the robot therapy assignment is seen as highly satisfactory and manageable with the patient acceptance of the whole process.

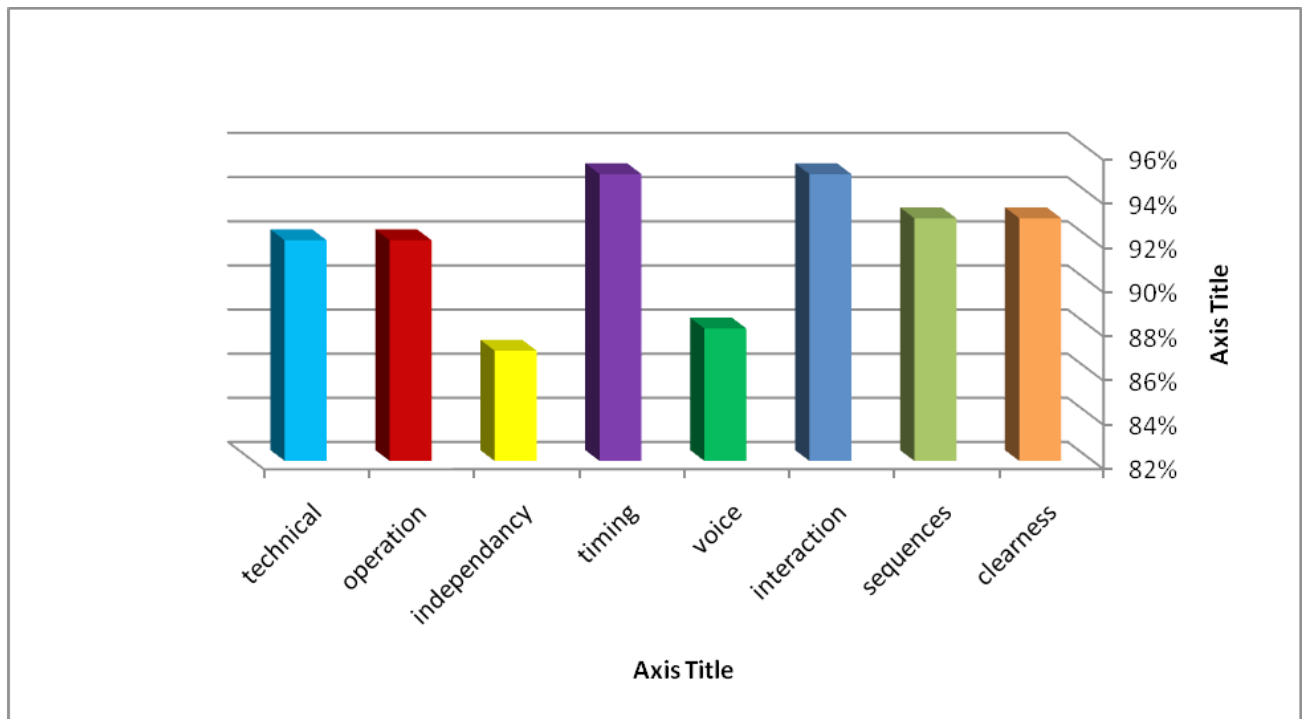


Fig. 1: Shows the representation of various performance parameters. This indicates the average percentage of the last three sessions

Fig 2: A, and B, The robot is oppositely facing the patient to assure face to face communication, both in lying position. The robot NAO asks the patient to imitate each movement. NAO starts to perform the exercise and patient is expected to follow, patients should match the time in a steady sequence and follow and repeat for several times matching the robot command. The robot is watching the patient through the cameras and has the capability to stop, rectify, adjust and resume.



A



B



Fig 3: The instructor checks and makes sure that NAO is ready

Discussion

The set up of this robot rehab program was made to serve patients at the clinic or at home. The overall performance was great, smooth and relatively reliable in this small trial group. This work encourages interest groups to proceed with robot rehab therapy. The available data from this trial study showed the robot-patient performance and the technical performance as well as the operational performance. The imitation of movement simultaneously with the robot confirmed the possibility of independent execution of serial therapy program in the rehab clinic or at home particularly for chronic conditions. The total percentages core of the last three sessions was around 92. However, further optimization of the robot programming and proper prescription of exercise program and careful selection of patients could make the work performance highly efficient. Each of the eight parameters of this study were assessed in five different sessions. These parameters are believed to be the most important factors to govern the implementation. Optimizing them will enable the robot to work independently with the patients at the clinic or at the home and this will enable to personalize this technology and the outcomes^{7,8} are in line with this result.

It is worth saying that the interaction was very successful and the options of stop, resume, restart were

used many times to cater to patients' requests, and this was considered healthy. The clarity of steps and voice level was perfect and the patient's follow-up on sequence was also maintained to a high level. Progressing with time is a notable and clear indicator which means that the patient-robot relation is supporting the level of confidence of the patient as well as the therapist, and this matches earlier reported outcomes¹³. This is an improvement of the technology with a friendly perspective. The overall satisfaction of the patient and the acceptance were high and very promising. The grand total performance of all eight parameters was very high (almost 92%) which substantiates its applicability in the clinical robotic industry in line with the^{16,17,18}.

This article is meant to cover solutions at different stages of applications. Thereafter it is up to the developer to commercially make it ready and available in the market or to look to some alternative or to go for more phases of research and experimentation. The existing data provides examples and pointers to proceed to clinical applications and other major ingredients for the success of these applications as well as the main issues surrounding their adoption for a wide range of everyday physiotherapy use are to be developed further. We have examined how robotics could partially fill in some of the identified gaps in current telehealth-care through internet connectivity since the robot is equipped with 4 Cameras and can recognize individuals by face and by voice tone. Introducing a tele control can pave the way for program modification and alteration based on instantaneous robot-patient interaction and would bring in a possibility of remote sharing with a third party or more in audio-visual mode.

We conclude with a brief glimpse at a couple of emerging developments and promising applications in this field that are expected to play important roles in the future. Readers should note that this paper is intended to be read mainly by non-roboticists, with little or no background in the field. Specifically, the paper is meant to ignite the interests of conventional health informatics and telemedicine/telehealthcare specialists and clinicians, physiotherapists and rehabilitation professionals into such emerging possibilities. It would also be of interest to experts in robotics who are interested in its potential applications, especially about how robotics may help users in the healthcare and social care sectors. This also may facilitate investments and businesses in the long-term to commercialize use of robotics in health sectors, both in health care centers and in homes.

Conclusion/Recommendations

This trial outcome is highly supportive to the use of robot in rehabilitation of patients. More focus may be needed to improve the friendly interaction and flexible sequence between exercises. Logistic support may be included e.g. refreshment time, rest, short breaks may be considered upon patient request.

There is also a need to address some challenges encountered in the set up. The degree of freedom for all joints was of acceptable level except the pelvic rotation. There is a need to improve on the robustness of the pelvic movement.

The issue of the NAO system getting heated up during the performance causing an interruption in the session needs to be investigated and resolved.

Based on this trial, it is recommended that this work be continued with a larger sample and varying conditions to ensure consistent approach and reliable outcomes.

Conflict of Interest: Nil

Source of Funding: Self

Ethical Clearance: Attached

References

1. Tapus A.C. T, and M. Mataric. The Use of Socially Assistive Robots in the Design of Intelligent Cognitive Therapies for People with Dementia. Proceedings of the International Conference on Rehabilitation Robotics (ICORR).2009.
2. Konstantinos P. Michmizos, H. I. K. Assist-as Needed in Lower Extremity Robotic Therapy for Children with Cerebral Palsy. The Fourth IEEE RAS/EMBS International Conference on Biomedical Robotics and Biomechatronics. 2012
3. Marie Fukudome (PY), H.W. A Supportive System Focusing on the Body Coordination for Neurocognitive Rehabilitation. The 21st Annual Conference of the Japanese Neural Network Society. 2011.
4. Montesano, L., Diaz, M., Bhaskar, S. & Minguez, J. Towards an Intelligent Wheelchair System for Users With Cerebral Palsy. Neural Systems and Rehabilitation Engineering, IEEE Transactions on 18, 193-202, doi:10.1109/TNSRE. 2009.2039592. 2010.

5. William Osler S, L. L. a. A, Sigmund Freud and the evolution of ideas concerning cerebral palsy. *Journal of Historical Neuroscience* 2, 255-282.1993.
6. Grigore C, Burdea D.C, Angad Kale, E. Janes William, A. Ross Sandy, R. Jack Engsborg. Robotics and Gaming to improve ankle strength, motor control and function in children with cerebral palsy, *Neural Systems and Rehabilitation Engineering, IEEE Transactions on*, 21 (2012), pp. 165-173
7. Murphy C, Y.-A. M., Decouffle P and Drews. Prevalence of Cerebral Palsy among ten year old children in metropolitan Atlanta, 1985 through 1987 *Journal of Pediatrics* 123: S13-S1.1993.
8. Marie Fukudome (PY), H.W. A Supportive System Focusing on the Body Coordination for Neurocognitive Rehabilitation. The 21st Annual Conference of the Japanese Neural Network Society.2011.
9. Montesano, L., Diaz, M., Bhaskar, S. & Minguéz, J. Towards an Intelligent Wheelchair System for Users With Cerebral Palsy. *Neural Systems and Rehabilitation Engineering, IEEE Transactions on* 18, 193-202, doi:10.1109/TNSRE. 2009.2039592. 2010.
10. Feil-Seifer, D. & Mataric, M.J. in *Rehabilitation Robotics, 2005. ICORR 2005. 9th International Conference on*. 465-468.2005.
11. Keren, G., A. Ben-David, and M. Fridin. Kindergarten Assistive Robotics (KAR) As a Tool for Spatial Cognition Development in Pre-School Education in Intelligent Robots and Systems (IROS), 2012 IEEE/RSJ International Conference. 2012.
12. Amy J. Brisben, A.D. L., Charlotte S. Safos, Jack M. Vice, Corinna E. Lathan. The CosmoBot™ System: “Evaluating its Usability in Therapy Sessions with Children Diagnosed with Cerebral Palsy*” in *Robot and Human Interactive Communication, ROMAN. 2005.*
13. Corinna E. Lathan, S.M. Development of a New Robotic Interface for Telerehabilitation. *Workshop on Universal Accessibility of Ubiquitous Computing; 1; (WUAUC’01).*2001.
14. M. Fridin, S.B.-H., M. Belokopytov. Robotics Agent Coacher for CP motor Function (RAC CP Fun)”. *Workshop on Robotic for Neurology and Rehabilitation. in Workshop on Robotic for Neurology and Rehabilitation.*2011.
15. Pavan Kanajar, I.R., Jartuwat Rajruangrabin, Dan O. Popa, Fillia Makedon in *The 4th International Conference on Pervasive Technologies Related to Assistive Environments (PETRA) 2011.*
16. Schulmeister, J., Wiberg, C., Adams, K., Harbottle, N., & Cook, A. in *Rehabilitation Engineering and Assistive Technology Society of North America (RESNA).*2006.
17. A. Cook, K. Adams, J. Volden, N. Harbottle, C. Harbottle, L.E.G.O. Using robots to estimate cognitive ability in children who have severe physical disabilities *Disability & Rehabilitation: Assistive Technology, 6 (2011), pp. 338-346.*
18. Martin Kocanda, B. M. W. a. D. S. B. Using Lego Mindstorm NXT™ Robotics Kits as a spectrophometric instrument. *International Journal on Smart Sensing and Intelligent Systems* 3, 400-410.2010.

Validity of the Fast Scan for Diagnosis of Intra-Abdominal Injury in Blunt Abdominal Trauma

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Abstract

Objective: To determine the validity of FAST scans in the diagnosis of blunt abdominal trauma in keeping with findings on CT scan and laparotomy.

Methodology: This study was carried out at Department of Accident and Emergency, Minia University Hospital, from August 2017 to August 2019. FAST scan was performed as part of the primary or secondary survey of the trauma patient in the emergency department in all patients with suspected blunt abdominal trauma.

Results: Our study included 150 patients with suspected blunt abdominal trauma who underwent CT abdomen or exploratory laparotomy or both CT abdomen and exploratory laparotomy. The mean age was 32.3±14.4 years. Forty-four patients (29.3%) were hemodynamically unstable and 106 (70.7%) were hemodynamically stable.

Conclusion: FAST scan has good diagnostic accuracy. It can be routinely utilized to triage the blunt abdominal trauma patients for laparotomy, however, a multi-institutional research study in our setup is required to further validate the findings of our study.

Keywords: CT; Abdominal injury; abdominal trauma

Introduction

According to WHO: by the year 2020, trauma will become the first or second leading cause of “loss of productive years of life” for both developed and developing countries⁽¹⁾.

Trauma has been called the neglected disease of modern society, despite its close companionship with man. World over injury is the 7th cause of mortality.

Abdominal injuries require surgery in about 25% of cases. 85% of abdominal traumas are of blunt character⁽²⁾.

Abdominal trauma ranks the third in prevalence after head and chest traumas, with majority of cases being non-penetrating or the so called blunt abdominal trauma (BAT)⁽³⁾.

Major abdominal trauma, both blunt and penetrating, is commonly seen nowadays, being particularly difficult to manage due to the frequent altered mental status of the patients and severity of associated injuries⁽⁴⁾. Early diagnosis and treatment can reduce mortality by up to 50%⁽⁵⁾.

Blunt abdominal trauma (BAT) accounts for about 80% of abdominal injuries seen in patients referred to the emergency departments⁽⁶⁾.

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Ultrasonography can demonstrate variety of post traumatic abdominal organ pathologies including hematomas, contusions, lacerations, and hemoperitoneum⁽⁷⁾.

Ultrasonography (US) is really valuable in the early assessment of a polytrauma, regardless of haemodynamic status; in fact, owing to its high sensitivity in the identification of intra-abdominal free fluid, it has largely replaced peritoneal lavage, becoming the first method used for this purpose, especially in haemodynamically unstable patients⁽⁸⁾.

The need for a prompt diagnostic technique that could be used in the emergency setting led to the introduction of FAST in emergency departments in the 1990's. It is undertaken after the primary survey in order to identify the presence of free fluid in the peritoneal cavity⁽⁹⁾.

FAST has become the common initial screening modality in the majority of trauma centers in the United States and worldwide, and it is included in the Advanced Trauma Life Support program for evaluation of the hypotensive trauma patient.⁽¹⁰⁾

FAST consists of a non-invasive ultrasound examination that can be quickly performed by the patient's bed, aiming to clarify specific clinical issues, regardless of the trauma mechanism that affected the patient⁽¹¹⁾. FAST is a rapid, low-cost examination that can result in valuable prognostic information in patients who are hemodynamically stable or not⁽¹²⁾.

Patients and Method: After approval by hospital ethical committee and taking consent, this cross-sectional study was conducted on 150 patients with blunt abdominal trauma who were admitted to the Minia University Hospital, during the period between August 2017 to August 2019. Patients consists of 111 males and 39 femals, with an age ranged from 6 to 69 years old.

Both patients whom underwent CT scan and patients who were haemodynamically unstable, were concluded in the study. Patients with penetrating abdominal injuries on history and indeterminate (inconclusive) FAST scans due to patient size, subcutaneous emphysema, or limited sonographic windows were excluded.

FAST was performed as part of the primary or secondary survey of the study population in the emergency department. An emergency ultrasound was performed by a radiologist within 1 hour of the patient arriving in the hospital. An ultrasound machine with live 2-D mode (rapid B-mode) and transducer frequencies between 3-6 MHz was used. Optimal depth settings depended on patient body habitus. The four standard views obtained with the patient in supine position were pericardial, perihepatic, perisplenic, and pelvic.

All patients in the study underwent a FAST scan. All of them also underwent either CT or exploratory laparotomy depending on their clinical conditions. FAST examination results, which were recorded as positive or negative and were compared with the findings on CT and/or exploratory laparotomy, which were considered definitive. All exploratory laparotomies were performed by the same surgical team consisting of a surgeon with at least 5-years clinical experience and the trainee as the assistant.

Data Analysis: The data was analyzed using SPSS 12. Categorical variables like gender and true positives were presented as frequencies and percentage. For numerical variables like age, mean \pm standard deviations were presented. The diagnostic accuracy was calculated using the 2 x 2 table.

Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy for the FAST scan will be determined by using the following standard formulas.

- Sensitivity = $TP / (TP + FN) \times 100$
- Specificity = $TN / (FP + TN) \times 100$
- PPV (Positive Predictive Value) = $TP / (TP + FP) \times 100$
- NPV (Negative Predictive Value) = $TN / (FN + TN) \times 100$
- Diagnostic accuracy = $(TP + TN \times 100) / (TP + TN + FP + FN)$

Results

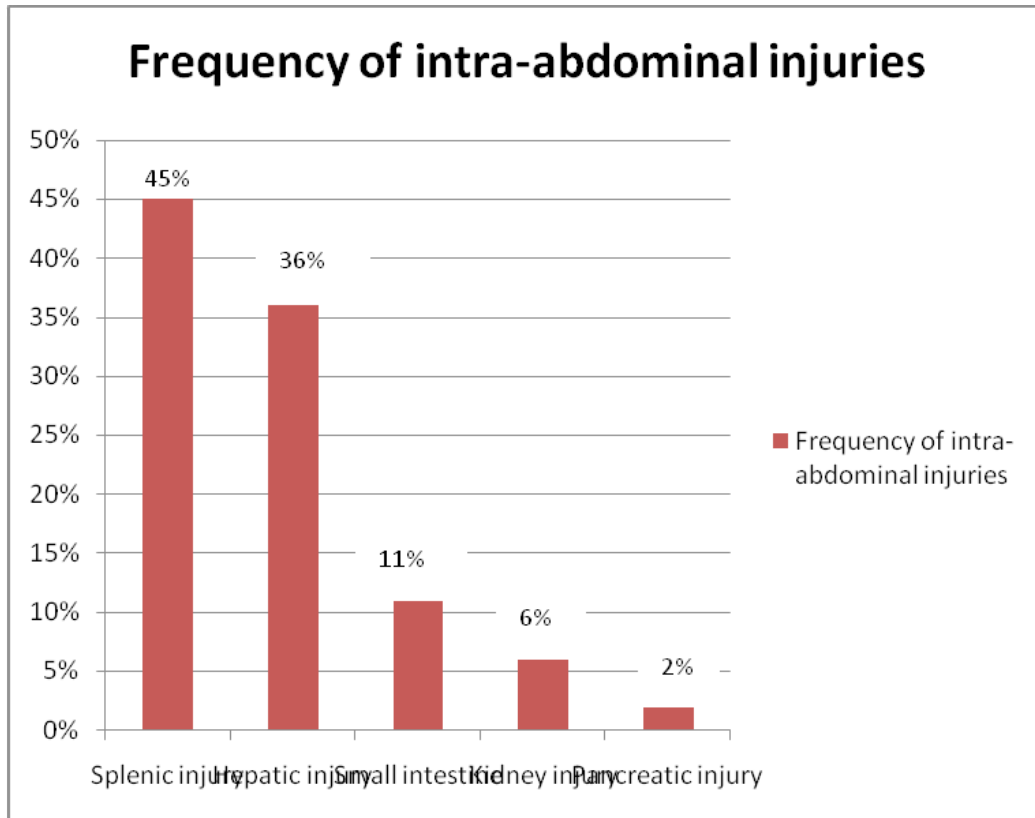


Figure 1: Frequency of intra-abdominal injuries in patients with intra-abdominal injuries.

Our study showed that 40 (45%) of cases with intra-abdominal injuries had splenic injury, 32 (36%) had hepatic injury, 10 (11%) had small intestine injury, 5 (6%) had kidney injury and 2 (2%) had pancreatic injury. Figure 2 exhibits the frequency distribution of intra-abdominal injuries.

Among 72 FAST scan positive in hemodynamically stable patients, 69 had confirmed blunt abdominal trauma on CT scan and 3 had negative CT scan. Among 34 FAST scan negative in hemodynamically stable patients, 4 had confirmed blunt abdominal trauma on CT scan and 30 had negative CT scan. Hence patients with a positive FAST scan had a statistically significant probability of a confirmed blunt trauma on CT scan. $P < 0.0001$. Table 1 illustrates the comparison of FAST Scan and CT Scan Abdomen for stable patients.

Sensitivity of FAST scan in stable patients was calculated as 94.5%, Specificity 90.9%, positive predictive value 95.8%, negative predictive value 88.2% whereas the overall diagnostic accuracy of FAST Scan in stable patients was calculated to be 93.4%. Table 2

gives a comparison of diagnostic accuracy of FAST scan with CT scan in stable patients.

Among 19 FAST scan positive in hemodynamically unstable patients, 15 had confirmed blunt abdominal trauma on exploratory laparotomy and 4 had negative exploratory laparotomy. Among 25 FAST scan negative in hemodynamically unstable patients, 1 had confirmed blunt abdominal trauma on exploratory laparotomy and 24 had negative exploratory laparotomy. Hence patients with a positive FAST scan had a statistically significant probability of a confirmed blunt trauma on exploratory laparotomy. $P < 0.0001$. Table 3 illustrates the comparison of FAST Scan and exploratory laparotomy for unstable patients.

Sensitivity of FAST scan in unstable patients was calculated as 93.7%, Specificity 85.7%, positive predictive value 78.9%, negative predictive value 96% whereas the overall diagnostic accuracy of FAST Scan in unstable patients was calculated to be 88.6%. Table 4 gives a comparison of diagnostic accuracy of FAST scan with laparotomy scan in unstable patients.

Table 1: Chi square test comparing the results of FAST scan and CT Abdomen

			CT Scan Abdomen For stable patients		Total	P value
			Positive	Negative		
FAST scan	Positive	Count	69	3	72	<0.0001
		% of Total	65.1%	2.8%	67.9%	
	Negative	Count	4	30	34	
		% of Total	3.8%	28.3%	32.1%	
Total		Count	73	33	106	
		% of Total	68.9%	31.1%	100%	

Table 2: Diagnostic accuracy of FAST scan in comparison of CT Abdomen

		Stable patients with BAT (as confirmed on CT Abdomen)		
		Positive CT	Negative CT	
FAST	Positive FAST	(TP) 69	(FP) 3	PPV=TP/(TP+ FP) = 69/72= 95.8%
	Negative FAST	(FN) 4	(TN) 30	NPV=TN/(TN+FN) =30/34= 88.2%
		Sensitivity =TP/(TP+FN) =69/73 =94.5%	Specificity =TN/(FP+TN) =30/33 =90.9%	Diagnostic accuracy =TP+TN x 100 TP+TN+FP+FN =69+30x100 =69+30+3+4 = 93.4%

Table 3: Chi square test comparing the results of FAST scan and Laparotomy in unstable patients

			Laparotomy For unstable patients		Total	P value
			Positive	Negative		
FAST scan	Positive	Count	15	4	19	<0.0001
		% of Total	34.1%	9.1%	43.2%	
	Negative	Count	1	24	25	
		% of Total	2.3%	54.5%	56.8%	
Total		Count	16	28	44	
		% of Total	36.4%	63.6%	100%	

Table 4: Diagnostic accuracy of FAST scan in comparison of Laparotomy in unstable patients

		Unstable patients with BAT (as confirmed on Laparotomy)		
		Positive Laparotomy	Negative Laparotomy	
FAST	Positive FAST	(TP) 15	(FP) 4	PPV=TP/(TP+ FP) = 15/19= 78.9%
	Negative FAST	(FN) 1	(TN) 24	NPV=TN/(TN+FN) =24/25= 96%
		Sensitivity =TP/(TP+FN) =15/16 =93.7%	Specificity =TN/(FP+TN) =24/28 =85.7%	Diagnostic accuracy =TP+TN x 100 TP+TN+FP+FN =15+24x100 =15+24+4+1 = 88.6%

Table 5: Diagnostic accuracy of FAST scan in overall patients

		Patients with BAT (as confirmed on CT or laparotomy or both)		
		Positive laparotomy and CT	Negative laparotomy and CT	
FAST	Positive FAST	(TP) 84	(FP) 7	PPV=TP/(TP+ FP) = 84/(84+7) = 92.3%
	Negative FAST	(FN) 5	(TN) 54	NPV=TN/(TN+FN) =54/(54+5) = 91.5%
		Sensitivity =TP/(TP+FN) =84/(84+5) = 94.4%	Specificity =TN/(FP+TN) = 54/(7+54) = 88.5%	Diagnostic accuracy =TP+TN x 100 TP+TN+FP+FN =84+54 X100 = 84+54+7+5 = 91.4%

Discussion

The abdomen is the third most common injured region, in 25% of cases who require surgical interference. Penetrating abdominal trauma is easily diagnosed, while blunt trauma complications can be missed if the clinical signs are not evident⁽⁷⁾.

Focused abdominal sonography for trauma (FAST) is a fast examination method that could demonstrate intraperitoneal fluid. Several studies found this technique to be sensitive (79–100%) and specific (95.6–100%), particularly in hemodynamically unstable patients⁽⁷⁾.

In our study, out of 150 cases; 111 (74%) were males and 39 (26%) were females with a mean age (32.3±14.4) years. The young aged males were the most common victims of blunt abdominal trauma.

There was an increase in incidence of abdominal trauma in males (74%), this is seen to be a similar pattern in other studies as males are more involved in violent and traumatic experiences, involving abdominal injuries.

Ozpek et al implemented a multivariate inquiry of patients with abdominal injuries and the responsible factors affecting mortality and in his study he had (78.9%) being males and (21.1%) being females with a mean age of 36.7 ±16.97 years (3-80 years)⁽¹³⁾. In America census and statistics of 2011 they report that roughly (90%) of patients with invasive trauma are males⁽¹⁴⁾.

In our study, the commonest cause of blunt abdominal trauma was road traffic accidents 112 (74.7%), followed

by fall from height 29 (19.3%) followed by violence 9 (6%).

Our study found FAST to be 94.4% sensitive and 88.5% specific with positive predictive value 92.3%.

Our study found FAST in hemodynamically stable patients to be 94.5% sensitive and 90.9% specific with positive predictive value 95.8%.

While we found FAST in hemodynamically unstable patients to be 93.7% sensitive and 85.7% specific with positive predictive value 78.9%.

A Cochrane systematic review found that the sensitivity for detecting hemoperitoneum in trauma patients was 85-95% and the specificity higher. In blunt trauma studies investigating FAST scanning, outcomes have demonstrated an average specificity of 90-99% and sensitivity of 86-99%. Fleming et al. conducted a retrospective study to compare FAST scan with CT scan or a laparotomy within two days in 100 patients with BAT. The accuracy of FAST in BAT was 59.2%; in these 43.7% were confirmed by CT and 15% by laparotomy. There were 40.8% inaccurate FASTscans, all confirmed by CT. FAST had a specificity of 94.7% (95% CI: 0.75-0.99) and sensitivity of 46.2% (95% CI: 0.33-0.60), positive predictive value of 0.96 (0.81-0.99) and Negative predictive value of 0.39 (0.26-0.54). Fisher’s exact test showed that positive FAST was significantly associated with Intra-abdominal pathology (p= 0.001). Positive FAST results had an accuracy of 75% (95% CI: 57%-87%)⁽¹⁵⁾.

Our study showed that 40 (45%) of cases with intra-abdominal injury had splenic injury, 32 (36%) had hepatic injury, 10 (11%) had small intestine injury, 5 (6%) had Kidney injury and 2 (2%) had pancreatic injury.

Out of total patients of blunt abdominal injury, 90 patients were operated and 60 patients were treated conservatively. Out of these 90 operated patients, most common operative procedure was splenectomy in 35 (38.9%) patients. Second most common operative procedure was repair of liver laceration in 17 (18.9%).

The secondly more commonly injured-organ is liver in all patients with blunt-abdominal injury. Incidence being 21.3% of patients with abdominal trauma. Mechanism of injury: Blunt injury results from direct-blows, compression between the lower rib on the right side and the spine or shearing at fixed point due to deceleration.

In present study, post-operative complications were reported in 10.7% pt. Wound infection was the most common post-operative complication present in 8 cases. Respiratory complication was present in 5 cases, biliary fistula in 2 cases, and pancreatic fistula in one case followed by splenectomy.

Two patients died in the present study, One was due to severe haemorrhage from lower limb compound fracture with liver injury and the other one was due to splenic avulsion. Since out of total patientstwo patients die, mortality rate was about 1.3%.

- Srivastava et al study was 2%.
- Di Vincenti et al study was 23%
- The mortality rate in Davis et al study 13.3%.
- Cox et al study reports a mortality rate of 10%.

Out of total 89 patients of abdominal injury, 76 patients were improved and discharged, 2 patients died, 3 patients escape from the hospital and 8 patients were discharged on personal request.

1 patients escape from the hospital while kept on conservative treatment and another 2 patient escape in post-operative period.

8 patients were discharged on request. They were followed and improved while 3 escaped patient could not be traced due to lack of communication.

Conclusion

- Road traffic accident form the most common mode of injury. Though conservative management is successful in carefully selected patients, operative management remains the main stay of treatment
- Plain x-ray abdomen in erect posture is valuable investigation taken for gastrointestinal injuries.

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References

1. Solanki HJ, Patel HR. A retrospective study of colorectal carcinoma in Central India. *Int Surg J* 2018;5:1763-9.
2. Mehta N, Babu S, Venugopal K. An experience with blunt abdominal trauma: evaluation, management and outcome. *Clinics and Practice* 2014; 4:599.
3. Erfantalab-Avini P, Hafezi-Nejad N, Chardoli M and Rahimi-Movaghar V. Evaluating clinical abdominal scoring system in predicting the necessity of laparotomy in blunt abdominal trauma. *Chinese Journal of Traumatology* 2011; 14(3):156-160.
4. Negoil I, Sorin Paun S, Stoica B, Tanase I, Vartic M, Negoil RI, Hostiuc S, Beuran M. Latest progress of research on acute abdominal injuries. *Journal of Acute Disease* 2016; 5(1): 16–21.
5. Shojaee M, Faridaalae G, Yousefifard M, Yaseri M, Dolatabadi AA, Sabzghabaei A, Malekirastekenari A. New scoring system for intra-abdominal injury diagnosis after blunt trauma. *Chinese Journal of Traumatology* 2014;17(1):19-24.
6. Davoodabadi A, Marzban F, Ghafoor L, Talari HR, Abdolrahim-Kashi E, Akbari H and Mahdian M. Diagnostic Value of Serial Ultrasound in Blunt

- Abdominal Trauma. Arch Trauma Res. 2017 June; 6(2):e44176.
7. Boutros SM, Nassef MA, Abdel-Ghany AF. Blunt abdominal trauma: The role of focused abdominal sonography in assessment of organ injury and reducing the need for CT. Alexandria Journal of Medicine (2016) 52, 35–41.
 8. Miele V, Piccolo CL, Trinci M, Galluzzo M, Ianniello S, Brunese L. Diagnostic imaging of blunt abdominal trauma in pediatric patients. Radiol med (2016) 121:409–430.
 9. Fleming S, Bird R, Ratnasingham K, Sarker S-J, Walsh M, Patel B. Accuracy of FAST scan in blunt abdominal trauma in a major London trauma centre. International Journal of Surgery 10 (2012) 470e474.
 10. Richards JR, McGahan JP . Focused Assessment with Sonography in Trauma (FAST) in 2017: what radiologists can learn. Radiology. 2017; 283(1):30-48.
 11. Savatmongkornkul S, Wongwaisayawan S, Kaewlai R. Focused assessment with sonography for trauma: current perspectives. Open Access Emergency Medicine 2017;9 57–62.
 12. Lane BH (2016). Evidence for cost-effectiveness of ultrasound in evaluation of blunt trauma patients. Emergency Care Journal, 12(2).
 13. Ozpek A., et al. Multivariate analysis of patients with blunt trauma and possible factors affecting mortality. 2015 Nov; 21(6):477-83. Doi: 10.5505/tjtes.2015.43077..
 14. Kochanek K.D., et al. National Vital Statistics Reports. Deaths, Preliminary Data for 2009. Hyattsville, Md: US Department of Health & Human Services; March 16, 2011.
 15. Janjua A, Hussain S, Raza Syed IA, Manzoor A. Validity of The Fast Scan for Diagnosis of Intra-Abdominal Injury in Blunt Abdominal Trauma. Ann. Pak. Inst. Med. Sci. 2017; 13(2):124-129.

Association of Serum Levels of Vitamin D and Interleukin 6 in Type 1 Diabetes in an Egyptian Population

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Abstract

Type 1 diabetes is an inflammatory disease of the pancreatic islets due to interaction of activated T-cells and proinflammatory cytokines in the immune infiltrate. Vitamin D has vital immunomodulatory properties that help in prevention of occurrence of T1DM. IL-6 is a multifunctional cytokine which has role in the pathogenesis of type 1 diabetes. This study was conducted to evaluate levels of vitamin D and IL6 in type 1 diabetic children and their relation to RBS, glycemic control and c-peptide level.

Keywords: Type I diabetes, vitamin D, IL-6, immunomodulatory process.

Introduction

Diabetes mellitus is mainly an error of carbohydrate metabolism associated with hyperglycemia (and disturbance of protein and fat metabolism⁽¹⁾). Type 1 diabetes (T1DM) defined as a complete or near-complete insulin deficiency due to an immune-mediated selective destruction of the insulin producing-cells in the islets of Langerhans. Type 1 diabetes can be considered an inflammatory disease of the pancreatic islets in which a process of programmed cell death (apoptosis) is elicited in the-cells by interaction of activated T-cells and proinflammatory cytokines in the immune infiltrate⁽²⁾

Vitamin D has vital immunomodulatory properties that help in prevention of occurrence of T1DM animal models⁽³⁾. It activates human macrophages, antigen-presenting cell maturation and inhibits dendritic cell differentiation as well as affects cytokine production by interacting with most immune cells^(4,5), one of these cytokines is interleukin 6 (IL-6).

IL-6, a multifunctional cytokine is secreted by T cells and macrophages to stimulate immune response during inflammation and infection. Numerous epidemiological, genetic, rodent, and human in vivo and in vitro studies have investigated the putative role of action/lack of action of IL-6 in the pathogenesis underlying obesity, insulin resistance, cell destruction, type 1 diabetes, and type 2 diabetes⁽⁶⁾. These studies suggest both protective and pathogenetic actions of IL-6 in diabetes. In this review, we briefly evaluate vitamin D level and IL-6 level among T1DM patients and investigate the association between concentration of vit D and IL6 in relation to FBG, C-peptide, glucose control among type 1 diabetic patients.

Subjects and Method

This study was conducted on 105 children, divided into 2 groups, control group 35 apparently healthy children selected from outpatient pediatric clinic. Another 70 children with T1DM (**according to ADA criteria 2019**) were selected from pediatric endocrinology clinic (**Maternity and Children Minia university hospital, Minia, Egypt**). Both groups were matched in age and sex. About 8 ml of venous blood was collected from each patient by sterile venipuncture under complete aseptic conditions. This sample was divided as follows: Two ml in sterile ethylene diamine tetra acetic acid (EDTA) containing tube for HbA1c and six ml into one plain tube. Blood was left to clot

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in the incubator then centrifuged. The expressed serum was used for measurement of serum levels of RBG, C-peptide, 25(OH) vitamin D and IL-6. Vitamin D was determined by detecting the level of 25 OH vitamin D using ELFA technique (Enzyme linked fluorescent Assay) by (MiniVidas, Biomerieux, France), IL-6 was determined by enzyme linked immunosorbent assay (EIA) (Human IL6 EIA Bioassay technology laboratory, China).

Results

Comparison between studied groups regarding laboratory data: Laboratory data of type 1 diabetic children found that statistically significant elevation in IL-6 level among T1D patients when compared to healthy subjects. The mean \pm SD of IL6 was 10.9 ± 1.5 in control group, 165.1 ± 111.4 in diabetic group. Regarding serum vitamin D level the study subjects were categorized into three subsets based on their detected vitamin D: Study subjects with vitamin D levels <20 ng/ml were labeled as having deficiency”, subjects with vitamin D levels between 21-29 ng/ml were classified as having “vitamin D insufficiency” and the ones with vitamin D levels 30-100 ng/ml were considered as having “vitamin D sufficiency”. Vitamin D deficiency was found in 87.1% in diabetic patients and 14.3% in control group, there was significant difference between both groups. 11.4% of diabetic patient had insufficient level of vitamin D and 14.3% of control group were sufficient, only 1.4% of diabetic patients had sufficient vitamin D level while 71.4% of control group had sufficient level (table1) (figure 1),(figure 2).

Correlation between Vitamin D and different parameters in type 1 diabetic patients: There was moderate positive correlation between vitamin D level and c-peptide level, while there was strong negative correlation between vitamin D with both RBS and HbA1c (Table 2).

Correlation between IL 6 and different parameters in type 1 diabetic patients: There was strong positive correlation between IL6 with both RBS and HbA1c while there was strong negative correlation between IL6 and c-peptide level. There was moderate negative correlation between IL6 and vitamin D (Table 3).

Discussion: T1DM is a T-cell mediated disease that completely destroys the body’s ability to synthesize and secrete insulin (7), (8) Vitamin D plays an immune-

modulatory effects in T1DM prevention(9) by decreasing the proinflammatory cytokines expression involved in T1DM pathogenesis, thus making pancreatic β cells less liable to inflammation with subsequent reduction in T-cell recruitment and infiltration so suppression of the autoimmune process(10).

Serum vitamin D level in our study among T1DM revealed that 98.5% of cases have abnormally low vitamin D status (vitamin D deficiency and insufficiency). This was in line with a study done in Egypt⁽¹¹⁾, which found that most of diabetic patients had vitamin D insufficiency. Also, another study done among Egyptian children with T1DM by Abd-Allah et al⁽¹²⁾ reported that 75% of T1DM exhibited vitamin D deficiency or insufficiency. Liu et al⁽¹³⁾ in their meta-analysis study suggested that low vitamin D level is associated with T1DM children. Also, Rasoulet al,⁽¹⁴⁾ reported significant frequency of vitamin D insufficiency and deficiency among T1DM children and concluded that serum vitamin D status is a major contributor in T1DM prevalence among Kuwaiti children. However some studies disagree with our study as a study done in Pakistan⁽¹⁵⁾ that showed non-significant difference between diabetic and control group regarding vit D. Another research conducted in Chile by Garcia, et al., R(2007) found no difference in 25 (OH) D level in type 1DM and healthy control⁽¹⁶⁾. Contrary to some reports⁽¹⁷⁾. The findings of the current study revealed more significant decreased vitamin D levels among those having higher RBS and HbA1c level. Additionally, C-peptide level was more significantly lower in T1DM children with lower serum level of vit. D. These findings can be explained that the vitamin D has strong role in improving β -cell function, inhibiting β -cell apoptosis and increasing β -cell replication thus influencing insulin secretion and increasing insulin sensitivity thus improving glycemic control⁽¹⁸⁾. Similar results were obtained in study done by Ahmed et al (2019) who reported inverse correlation between serum 25(OH)D and HbA1c in T1DM patients with poor glycemic control among diabetic patients having vitamin D deficiency⁽¹⁹⁾.

Regarding IL-6, current study showed significantly increased serum level of IL-6 among T1DM children, these results were consistent with meta-analysis done by (Chen yietal)(2016) where level of IL-6 among diabetic patients were significantly higher than control subjects⁽²⁰⁾, another study done among Egyptian T1DM children⁽²¹⁾ revealed serum IL-6 concentrations were significantly higher in diabetic children however other

studies reported no difference⁽²²⁾ or even decreased⁽²³⁾ IL-6 level in type 1 diabetic patients. Observed positive correlation between IL-6 with both RBS level and HbA1c in T1DM patients in our study agrees with several studies^{(24),(25)} this can be explained by the fact, that persistent hyperglycemia contributes to the formation of advanced glycation end products which has important role in the development of chronic inflammation.

However study done among Egyptian type1 diabetic children shows no correlation between HbA1c and IL6⁽²¹⁾ Regarding correlation between Vit. D level and IL-6 our study revealed moderate negative correlation which may indicate an association with vitamin D deficiency and inflammatory state, represented by elevated circulating IL-6, these results agrees with study done by Shih et al 2014⁽²⁶⁾

Table (1): Comparison between studied groups regarding laboratory data:

p value	Control No=35	Cases N=70	Variable
0.001*	70-122 92.1±14.1	200-580 323.1±79.5	Blood glucose Range (mg/dl) Mean± SD
0.001*	4-5.4 4.6±0.3	7.5-14.1 10.6±1.8	HbA ₁ C Range (%) Mean± SD
0.001*	1.1-3 2.1±0.5	0.006-0.45 0.24±0.14	C-peptide Range (ng/ml) Mean± SD
0.001*	8-14 10.9±1.5	46.8-455 165.1±111.4	IL6 Range (pg/ml) Mean± SD
0.001*	25(71.4%) 5(14.3%) 5(14.3%)	1(1.4%) 8(11.4%) 61(87.1%)	Vitamin D Sufficient (30-100 ng/ml) Insufficient (21-29 ng/ml) Deficient(< 20ng/ml)

Table (2): Correlation between Vitamin D and different parameters in type 1 diabetic patients

	Vitamin D	
	R	P
RBS	-0.75	0.001*
C-Peptide	0.56	0.001*
HbA ₁ c	-0.82	0.001*

Table (3): Correlation between IL-6 and different parameters in type 1 diabetic patients cases

	IL-6	
	R	P
RBS	0.89	0.001*
C-Peptide	-0.82	0.001*
HbA ₁ c	0.90	0.001*
Vitamin D	-0.71	0.001*

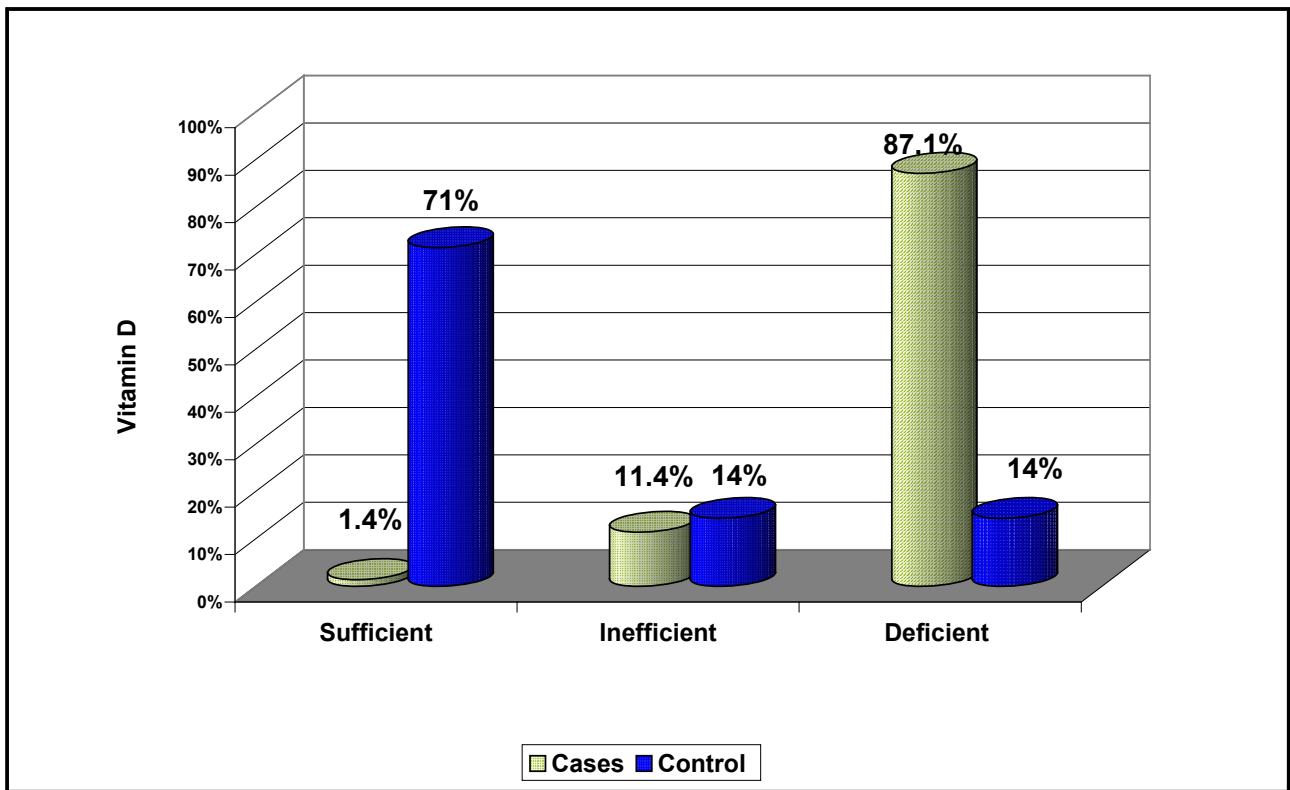


Figure (1): Vitamin D level in diabetic patients and control group

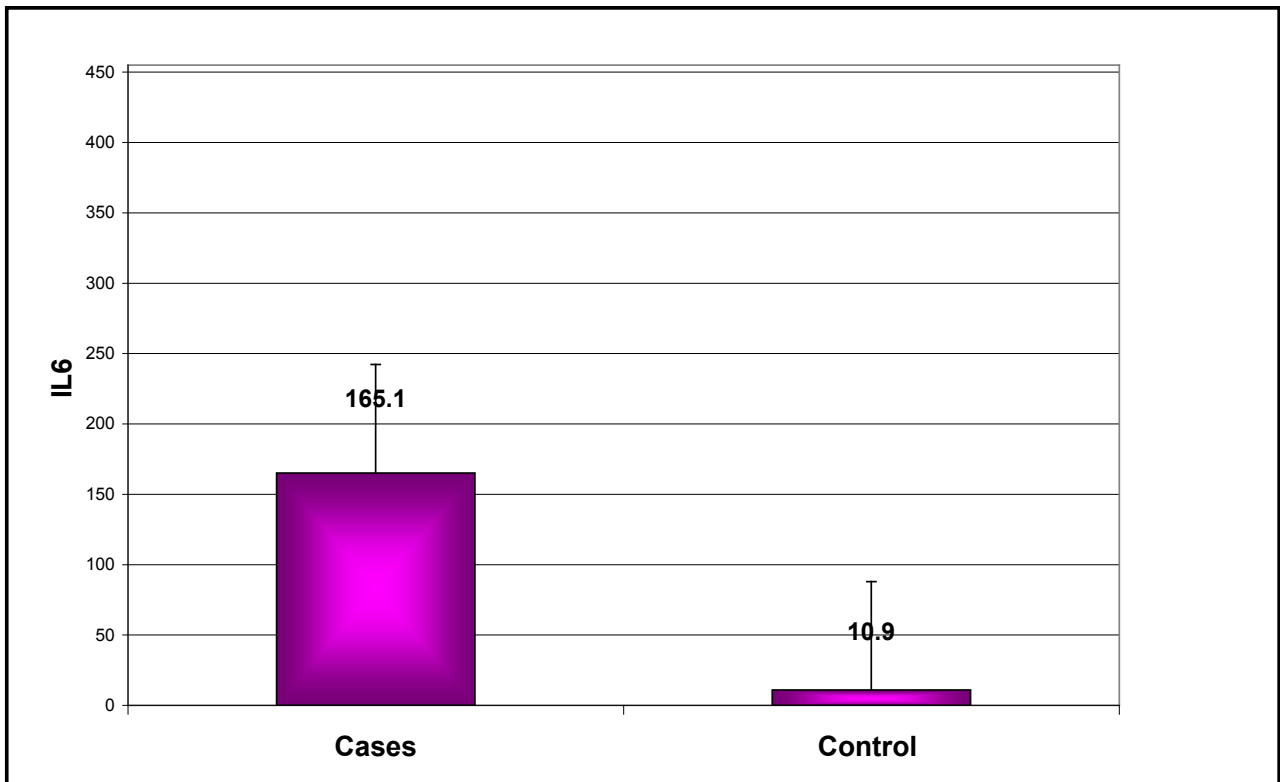


Figure (2): IL6 level in diabetic patients and control group.

Conclusion

The current study support the important role of vitamin D level in type I diabetes and its different level of deficiency with the level of RBG and HbA_{1c}. Also, our study show the correlation between IL-6 with both RBS level and HbA_{1c} in T1DM patients. This suggest the role of IL-6 as inflammatory marker in T1DM.

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References

- Hussain, M.J, Maher, J. Warnock, J. Cytokine over production in healthy first degree relative of patients with IDDM. *Diabetologia* 1998; 41: 343.
- Eizirik DL, Mandrup-Poulsen T: A choice of death: the signal-transduction of immune-mediated beta-cell apoptosis. *Diabetologia* 2001; 44:2115–2133.
- J. N. Yaochite, C. Caliari-Oliveira, M. R. Davanso et al., “Dynamic changes of the Th17/Tc17 and regulatory T cell populations interfere in the experimental autoimmune diabetes pathogenesis,” *Immunobiology*, 2013vol. 218, pp. 338–352.
- L. Yang, J. Ma, X. Zhang, Y. Fan, and L. Wang, “Protective role of the vitamin D receptor,” *Cellular Immunology*, 2012 vol. 279, pp. 160–166.
- A. Busta, B. Alfonso, and L. Poretzky, “Type 1 Diabetes-Complications, Pathogenesis, and Alternative Treatments,” in *Role of Vitamin D in the Pathogenesis and Therapy of Type 1 Diabetes Mellitus*, C.-P. Liu, Ed., INTECH Open Access Publisher, China, 2011.
- Kamimura D, Ishihara K, Hirano T: IL-6 signal transduction and its physiological roles: the signal orchestration model. *Rev PhysiolBiochemPharmacol* 2003 149:1–38.
- Cnop MN, Welsh JC, Jonas A, et al. Mechanisms of pancreatic beta-cell death in type 1 and type 2 diabetes: many differences, few similarities. *Diabetes*. 2005;54:97-107.
- American Diabetes A. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2014;37:81-90.
- Van Etten E, Mathieu C. Immunoregulation by 1,25-dihydroxyvitamin D3: basic concepts. *J Steroid Biochem Mol Biol*. 2005;97:93–101
- Elsayed AM, Mohamed GA. Vitamin D deficiency and its correlation to hemoglobin A1C in adolescent and young adult type 1 diabetes mellitus patients. *Aamj*. 2016;14:76–80.
- Ahmed El-Abd Ahmed, Hala M Sakhr, Mohammed H Hassan, Mostafa I El-Amir, and Hesham H Ameen. Vitamin D receptor rs7975232, rs731236 and rs1544410 single nucleotide polymorphisms, and 25-hydroxyvitamin D levels in Egyptian children with type 1 diabetes mellitus: effect of vitamin D co-therapy, *Diabetes MetabSyndrObes*. 2019; 12: 703–716.
- Abd-Allah SH, Pasha HF, Hagrass HA, et al. Vitamin d status and vitamin D receptor gene polymorphisms and susceptibility to type 1 diabetes in Egyptian children. *Gene*. 2014;536:430–434.
- Liu C, Lu M, Xia X, et al. Correlation of serum vitamin d level with type 1 diabetes mellitus in children: a meta-analysis. *Nutr Hosp*. 2015;32(4):1591–1594.
- Rasoul MA, Al-Mahdi M, Al-Kandari H, et al. Low serum vitamin-D status is associated with high prevalence and early onset of type-1 diabetes mellitus in Kuwaiti children. *BMC Pediatr*. 2016;16:95.
- Nasreen M, Lone KP¹, Khaliq S, Khaliq S². Serum vitamin D levels and gene polymorphisms (FokI and ApaI) in children with type I diabetes and healthy controls. *J Pak Med Assoc*. 2016 Oct;66(10):1215-1220.
- García D, Angel B, Carrasco E, Albala C, Santos JL, Pérez-Bravo F. VDR polymorphisms influence the immune response in type 1 diabetic children from Santiago, Chile. *Diab Res Clin Prac* 2007; 77: 134-40.
- Algebra K, Bokhari S, Khan M. Glycemic changes after vitamin D supplementation in patients with type 1 diabetes mellitus and vitamin D deficiency. *Ann Saudi Med* 2010; 30: 454–458.
- Takiishi T, Gysemans C, Bouillon R, Mathieu C. Vitamin D and diabetes. *Endocrinol Metab Clin North Am*. 2010;39(2):419-46.
- Ahmed El-Abd Ahmed, Hala M Sakhr, Mohammed H Hassan, Mostafa I El-Amir, and Hesham H Ameen. Vitamin D receptor rs7975232, rs731236 and rs1544410 single nucleotide polymorphisms,

- and 25-hydroxyvitamin D levels in Egyptian children with type 1 diabetes mellitus: effect of vitamin D co-therapy *Diabetes MetabSyndrObes.* 2019; 12: 703–716.
20. Yin-LingChen^{ac1} Yong-ChaoQiao^{b1} Yan-HongPan^{ac} YanXu^b Yong-ChengHuang^a Yin-HuiWang^{ac} Li-JunGeng^{ac} Hai-LuZhao^{abc} Xiao-XiZhang^{ac} Correlation between serum interleukin-6 level and type 1 diabetes mellitus: A systematic review and meta-analysis *Cytokine* 2017 Volume 94, 2017, Pages 14-20.
 21. Azza A.A, Mohga S. A, Wafaa GH. SH, Karam AM, Enas R.A, Tarek AS. H, Salwa MEEvaluation of some Inflammatory Cytokines in Children with Type1 Diabetes Mellitus *Journal of American Science*, 2010;6(11).
 21. Kulseng B, Skjak-Braek G, Folling I, Espevik T. TNF production from peripheral blood mononuclear cells in diabetic patients after stimulation with alginate and lipopolysaccharide. *Scandinavian Journal of Immunology.* 1996;43(3):335–340.
 22. Geerlings SE, Brouwer EC, Van Kessel KC, Gaastra W, Stolk RP, Hoepelman AI. Cytokine secretion is impaired in women with diabetes mellitus. *European Journal of Clinical Investigation.* 2000;30 (11):995–1001.
 23. Targher G, Zenari L, Bertolini L, Muggeo M, Zoppini G. Elevated levels of interleukin-6 in young adults with type 1 diabetes without clinical evidence of microvascular and macrovascular complications. *Diabetes Care.* 2001; 24(5):956–957.
 24. Ikhlas K. Hammed, Nada F.Rashid, Baydaa A. Abed.Serum Interleukin-6 level in children with type 1 diabetes mellitus *Fac Med Baghdad* 2012; Vol. 54.
 25. Wegner M, Araszkievicz A, Piorunska-Stolzmann M, Wierusz-Wysocka B, Zozulinska-Ziolkiewicz D. Association Between IL-6 Concentration and Diabetes-Related Variables in DM1 Patients with and without Microvascular Complications, Inflammation. 2013,36(3):723-8.
 26. Shih EM¹, Mittelman S¹ Pitukcheewanont P, Azen CG, MonzaviR.Effects of vitamin D repletion on glycemic control and inflammatory cytokines in adolescents with type 1 diabetes.*Pediatr Diabetes.* 2016;17(1):36-43.

Cost Reduction Using the Time Driven Activity-Based Costing Method for Chemotherapy Treatment Costs for Breast Cancer Patients in the Era of National Health Insurance (JKN) at Airlangga University Hospital

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Abstract

Breast Cancer is one of the leading cause of death in Indonesia after cervical cancer. Indonesian Breast Cancer patients should get managed well in order to make efficient and sufficient treatment without reducing the quality. The National Health Insurance well known as *Jaminan Kesehatan Nasional* (JKN) supporting Breast Cancer treatment via BPJS stands for *Badan Penyelenggara Jaminan Sosial* (Indonesian Government Insurance Coverage). Generally, the payment method in BPJS are divided based on INA CBG's and outside INA CBG's which the payment depends on hospital class. INA CBG'S packages including consultation, accommodation, medical, medical treatment (operation and non-operation). Packages outside of INA CBG'S include anticancer drugs, health aids, chronic drugs, ambulances and CAPD. This package encourages hospitals to be able to make efficiencies so it is not going to make financial loss for Hospital. The research goal is giving best treatment to Breast Cancer patient without financial loss for the hospital. Measurement Used Time Driven Activity Based Costing. Moreover The Benefit of this research are (1). Reducing cost (direct and indirect) without decreasing patients quality treatment. (2). Reducing patient treatment time at the hospital since the patient get direct doctors' therapy. To date The Results of this research are (1). Day care treatment can be compressed into two days and (2) Reducing length of stay.

Keywords: *The National Health Insurance Coverage (JKN), Hospital Cost Reduction, Time Driven Activity Based Costing, Chemotherapy Unit.*

Introduction

Health financing plays important role in the implementation of the Indonesian Government Insurance Coverage (JKN). Health financing at a healthcare facility are obtained by health insurance providers payment for health services provided for Indonesian citizens which are aimed in promoting quality improvement, encouraging patient-oriented services, promoting efficiency by not rewarding providers whom do over-treatment, under-treatment or adverse events and encourage team services. With the right financing system is expected to achieve the above aims.

The implementation of Indonesian Government Insurance Coverage or JKN begins in 2014 via the

Indonesian Health Ministry. The JKN program is organized by the Social Security Administering Agency (BPJS) based on Indonesian Law number (UU) no 24 year 2011. The purpose of JKN is to help financing the health of Indonesian citizens. The implementation is when citizens using JKN is done on one stage to other stages higher as an example: from Health Facility 1 (Faskes 1) to the higher Health Facility, when the disease can't be treated by Health Facility 1 (Faskes 1). Rates applicable to patients using JKN are arranged with the pattern of payment based on Indonesian Case Based Group (INA-CBG's). The payment package is based on grouping the type of disease called the Casemix System. Casemix is a disease grouping which integrate the treatment cost with the type of disease in the hospital.

Catastrophic disease is a disease which its therapy requires special skills, uses sophisticated medical equipment and or requires lifelong healthcare. As a result, catastrophic disease needs higher health claims. The catastrophic diseases at the household level include renal failure, cardiovascular disease (which requires either invasive or noninvasive operation), cancer, and blood disorders, thalassemia and hemophilia¹. Catastrophic disease is a chronic and degenerative disease. Called chronically because the disease is latent that takes a long time to manifest, often unconscious, and takes a long time for healing or takes a lifetime to control it. Called degenerative because the disease more often occurs with age. Since it is needed higher claim led to the emergence of the terminology of catastrophic disease.

According to World Health Organization (WHO), cardiovascular disease is the leading cause of death worldwide. In 2012 an estimated 17.5 million people die because of cardiovascular disease (7.4 million of them are caused by coronary heart disease and 6.7 million deaths caused by stroke. Over one per third of deaths from cardiovascular disease occur in low-and middle-income countries. Meanwhile, cancer is also a major challenge of morbidity and mortality worldwide, with an estimated 14 million new cases and 8.2 million cancer deaths in the same year. In Indonesia, the RISKESDAS report shows that the prevalence of chronic renal failure, stroke, coronary heart disease and cancer increases with age and the highest increase occurs in the ≥ 75 age group². While based on gender, cancer patients, diabetes mellitus, heart failure and coronary heart disease more commonly found in women³.

World Nation Against Cancer (UICC) data shows that the incidence of cancer will increase sharply by 200-300% over the next decade, and 60-70% of these cancers will be present in developing countries, including Indonesia. Viewed from the economic side, data from the Ministry of Health shows that state spending on cancer includes the highest expenditure of the country along with cardiovascular disease and hemodialysis. The country's expenditure on cancer in 2012 amounted to 144.7 billion rupiah, and in 2014 the Social Security Administering Agency (BPJS) spent 905 billion rupiah on cancer. High expenditures are among others due to workload and treatment modalities that need to be issued to cancer patients, especially when treatment is done at local and advanced stage. On the other hand, UICC claims the danger of this cancer is 43% can be prevented

with a clean and healthy lifestyle, and one third can be cured if found at an early stage with appropriate treatment.

Given the high rates of cancer incidence and the magnitude of state expenditure for medical expenses, especially since some are already in an advanced stage, then cancer prevention and cancer discovery activities in the early stages are very important. In the level of health services, from primary care, it should be done healthy life promotion activities to avoid cancer, and early detection, as also presented in this guide. Healthy lifestyle tested according to World Health Organization (WHO) and UICC criteria are actually summarized in CERDIK, i.e. C (routine health check), E (awake smoke), R (physical exercise), D (balanced diet) I (adequate rest), and K (Manage stress). Early detection can be done on several types of cancer, such as cervical cancer, breast, rectal, and cancer in children. By performing early detection, it is expected to change the trend of disease discovery from advanced or advanced local stage, into an early stage. In the treatment of cancer treatment, which now has been divided into primary, secondary, and tertiary referral system, it is expected that every health services facility can perform in accordance with their respective functions and roles, so that cancer treatment can be done quickly, accurately and no long-term oncology handling queue.

In the era of JKN patient service, chemotherapy must be managed well arranged in such a way that the service remains efficiency without reducing the quality of service. The method of payment for BPJS services is generally divided into payments according to the CBG'S INA package and outside the CBG'S INA package, which rate is in accordance with the hospital class. Here is a package of chemotherapy services for cancer in Type B Hospital. This CBG'S INA package includes consultation, accommodation, medical, medication, medical (operative and non-operative) activities. Packages outside of INA CBG'S include anticancer drugs, health aids, chronic drugs, ambulances and CAPD. Method of payment by system This package encourages hospitals to be able to make efficiencies in order not to make high loss to hospital. Health financing is an important part in the implementation of the JKN. Health financing at a health facility is obtained by payment by health insurance providers for health services provided to participants, aimed at promoting quality improvement, encouraging patient-oriented services, promoting efficiency by not rewarding providers who

over-treat, under-treat or adverse events and encourage team services. By the right financing system is expected to achieve those aims.

Hospital as a health facility is required to perform efficiency in order not to make financial lost, so the accuracy of cost calculation is very important for the continuation of the hospital. Airlangga University Hospital is a B class education hospital in Surabaya and it is necessary to make a proper cost calculation because the number of patients at the hospital are increasing every year. In order to count hospital unit cost, there is a method of determining the basis of an activity designed to overcome the distortion in traditional cost accounting called the Time Driven Activity Based Costing. Hospitals that serve patients using BPJS are required to perform efficiency. So the solution to the problem is to use Time Driven Activity Based Costing.

Method

This type of research is quantitative descriptive. Quantitative descriptive research in this study is to analyze and interpret the meaning contained in the documentation and interview data that has been collected⁴. The quantitative descriptive approach in this study was used to explain the savings in the cost of chemotherapy treatments for the treatment of breast cancer patients in the JKN era. The subjects in this study of Airlangga University Hospital. The object of this study is the cost incurred or unit costs on chemotherapy measures at the Airlangga University Hospital on breast cancer to see if it can be done cost reduction in the JKN period.

The data use in this research are primary and secondary data. Data then analyzed by using time driven activity based costing. Primary data is data obtained directly from sources related to research subjects, namely conducting interviews with the finance department to obtain data on unit costs related to chemotherapy for breast cancer patients, in addition to conducting interviews with nurses and doctors who are doing chemotherapy treatment for breast cancer patients. Researchers also conducted direct observations of the chemotherapy action space to find out the length

of the preliminary observation to breast cancer patients until the chemotherapy action was completed and how much it would take to carry out a series of chemotherapy treatment measures.

Finding and Discussion

Time Driven Activity Based Costing

The basic Hospital can use Time Driven Activity Based Costing because it is included in one criterion to provide value added services to consumers⁵, among others:

1. Producing and stocking a greater variety of products
2. Customizing products and services to individual customer preferences
3. Supporting more order-entry and order tracking channels
4. Producing and delivering in smaller order sizes
5. Delivering directly to customers end use locations, often in expedited and narrow time time
6. Providing specialized technical application support

Time Driven Activity Based Costing is a simpler, more powerful path to profitability⁶. The Time Driven Activity Based Costing model requires for each groups of resources only two parameters estimates⁷:

1. The cost rate of supplying resource capacity
2. The consumption of resource capacity (typically unit times) by the activities performed by the resource's products, services and customer

Time-driven ABC starts by identifying the various groups of resources performing activities. For example, customer administration resources include the front-line employees who receive and respond to customer-related requests, their supervisors, and the support resources they require to perform their functions—space, computers, telecommunications, furniture, and, potentially, resources in other support departments (Information technology, human resources, technology, etc.).

Table 1. Normal Cost of Breast Cancer Chemotherapy Treatment

No	Categories	Unit	Amount	Price per Unit	Amount
1	Reg	Act	1	15.000idr	15.000idr
2	Room rent	Day	2	400.000idr	800.000idr
3	Medical equipment rental	Day	2	150.000idr	300.000idr
4	Handling	Day	2	150.000idr	300.000idr
5	Nursing services	Day	2	250.000idr	500.000idr
6	Consumables	Pcs	2	30.150idr	60.300idr
7	Infusion instal	Medical treat	2	75.000idr	150.000idr
8	Infusion app	Medical treat	2	15.000idr	30.000idr
9	Pharmacy	Pcs	2	40.000idr	80.000idr
10	Class 1	Pcs	2	90.000idr	180.000idr
11	Electricity	Pcs	2	1.220idr	2.440idr
12	Cleaning	Pcs	2	1.186idr	2.372idr
13	Maintenance care	Pcs	2	751idr	1.502idr
14	Medical proc	Pcs	2	5.982idr	11.964idr
15	Linen	Pcs	2	5.000idr	10.000idr
16	Depresiasion	Pcs	2	10.748idr	21.496idr
17	Drug	Pcs	2	384.547idr	769.094idr
18	Lab & Radiology	Package	2	109.000idr	218.000idr
19	Doctor	Medical treat	2	1.218.000idr	2.436.000idr
20	Hospital Contribution		2	61.016 idr	122.032 idr
	Total			3.012.600 idr	6.010.200 idr

Source: AUH data processing, Total amount is about: 6.010.200 idr

Table 2. BPJS Claim of Airlangga University Hospital

No	Categories	Unit	Amount	Price per Unit	Amount
1	Reg	Act	1	15.000idr	15.000idr
2	Room rent	Day	1	400.000idr	400.000idr
3	Medical equipment rental	Day	1	150.000idr	150.000idr
4	Handling	Day	1	150.000idr	150.000idr
5	Nursing services	Day	1	250.000idr	250.000idr
6	Consumables	Pcs	1	30.150idr	30.150idr
7	Infusion instal	Medical treat	1	75.000idr	75.000idr
8	Infusion app	Medical treat	1	15.000idr	15.000idr
9	Pharmacy	Pcs	1	40.000idr	40.000idr
10	Class 1	Pcs	1	90.000idr	90.000idr
11	Electricity	Pcs	1	1.220idr	1.220idr
12	Cleaning	Pcs	1	1.186idr	1.186idr
13	Maintenance care	Pcs	1	751idr	751idr
14	Medical proc	Pcs	1	5.982idr	5.982idr
15	Linen	Pcs	1	5.000idr	5.000idr
16	Depresiasion	Pcs	1	10.748idr	10.748idr
17	Drug	Pcs	1	384.547idr	384.547idr
18	Lab & Radiology	Package	1	109.000idr	109.000idr
19	Doctor	Medical treat	1	1.218.000idr	1.218.000idr
20.	Hospital contribution			61.016 idr	61.016 idr
	Total			3.012.600 idr	3.012.600 idr

Source: AUH data processing, Total amount is about: 3.012.600 idr

Comparison between Normal Claim and Airlangga University Hospital Claim is 6.010.200 idr: 3.012.600 idr (2 : 1). To date Airlangga University Hospital can save 3.012.600 idr as of BPJS claim and can get benefit 61.016 idr

1. Activities :

- Diagnosing : 150
- Preparing : 150
- Intervening : 150
- Recovering : 150

2. Capacity Cost Rate

= Cost capacity supplied/Practical capacity of resources supplied

Cost capacity supplied

= 50 patients/months x 3.012.600 idr

= 150.000.000 idr x 3 (quarterly)

= 450.000.000 idr

Practical capacity cost rate = 22 days/month x 6.5 hours x 60 minutes

= 8580 per month x 3 (quarterly)

= 25.000 minutes per quarter x 20 employee

= 500.000 minutes

Capacity cost rate

= 450.000.000 idr/500.000 minutes

= 900 idr/minutes

Unit Time Estimate

1. Activities:

- Diagnosing : 60 minutes
- Preparing : 120 minutes
- Intervening : 240 minutes
- Recovering : 360 minutes

Table 3. Activity Performed Cost Driver Rate

No	Activity	Unit Time	Cost Driver Rate @900/minutes
1	Diagnosing	60	54.000 idr
2	Preparing	120	108.000 idr
3	Intervening	240	216.000 idr
4	Recovering	360	324.000 idr

Then apply these cost driver to the three different activity performed.

Table 4. Activity Performed and Total Cost

No	Activity	Unit Time	Quantity	Total Minutes	Total Cost
1	Diagnosing	60	150	9.000	8.100.000 idr
2	Preparing	120	150	18.000	18.200.000 idr
3	Intervening	240	150	36.000	32.400.000 idr
4	Recovering	360	150	54.000	48.600.000 idr
5	Used capacity		150	117.000	107.300.000 idr
6	Unused capacity			383.000	342.700.000 idr
	Total			500.000	450.000.000 idr

The analysis found that only 23.4% of the practical capacity (117.000/500.000) of the resources supplied during the period was used for the productive work : hence only 23,4% of the total expenses of 450.000.000 idr are assigned to customers for this period. By specifying the unit times to perform each instance of the

activity, the organization gets a valid signal about the cost and the underlying efficiency as well as the as the quantity (383.000 hours) and cost (342.700.000) of the unused capacity in the resources supplied to perform the activity. In Indonesia, the determination of unit cost in each service is not easy if considering the tariff for BPJS

patient services in accordance with PMK No. 50 of 2014 the rate of health services in hospitals is determined based on the density between BPJS Health and the Association of Health facilities based on the standard tariff of INA-CBG's⁸. Hospitals in the JKN era must really consider the cost of treatment claims by calculating unit costs more carefully so that the implementation and planning of costs to national health insurance patients can be well served.

In Indonesia, determining unit costs in each service is not easy when considering the rates for BPJS patient services in accordance with PMK No. 50 of 2014 the rate of health services in hospitals is set based on the density between the Health BPJS and the Association of Health facilities based on the INA-CBG'S tariff standard. Hospitals in the JKN era must really consider the cost of treatment claims by doing a more careful unit cost calculation so that the implementation and planning of costs to national health insurance patients can be well served.

Conclusion

Based on unit cost counting that has been done by Airlangga University Hospital, if the patient is on private treatment, the treatment that they follow as: 1) diagnosing, 2) laboratory checking, 3) radiology checking, 4) diagnosing, 5) preparing, 6) intervening, and 8) recovering with the total cost spend 6 million IDR. While on BPJS and based on INA CBGs then the treatment as follow: 1) laboratory checking, 2) radiology checking, 3) diagnosing, 4) preparing, 5) intervening, and 6) Recovering with total cost spend 3 million IDR.

For all those treatments then Airlangga University Hospital still having hospital margin 61.000 IDR. Time Driven ABC can be used on medical treatment which one of them is the determinant factor the unit cost. By using 23.4% from the source, so the hospital can save 76.6% of the time Comparison Normal Claim and Airlangga University Hospital Claim. 6,000,000 idr: 3,000,000 idr is equal to 2: 1, so far Airlangga University Hospital can

save 3,000,000 idr according to BPJS claims and can get 61,016 idr benefits.

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References

1. Wihandika RC, Suciati N. Retinal blood vessel segmentation with optic disc pixels exclusion. *International Journal of Image, Graphics and Signal Processing*. 2013 Jun 1;5(7):26.
2. RI KK. Laporan hasil riset kesehatan dasar (Riskesdas) 2013. Jakarta: Kementerian Kesehatan RI DinKes Jateng. 2013.
3. Suharsimi Arikunto. *Research Procedure*. Rineka cipta. Jakarta. Indonesia. 2010.
4. Richard Kaplan. *Time driven activity based costing*. Harvard business school. USA. 2009
5. Richard Kaplan. *How to solve the cost crisis in health care*. Harvard business review, reprint R11098. USA. 2011
6. Luthfita A, Nazaruddin I. *Metode Activity Based Costing Dalam Penentuan Unit Cost Eksisi Fibroadenoma Mammae*. *Jurnal Medicoeticoilegal dan Manajemen Rumah Sakit*. 2016 Jul;5(2):1.
7. Minister of health regulation, Republic of Indonesia. Law number 59 of 2014 concerning standard tariffs in national health insurance. Indonesia. 2014
8. Minister of health regulation, Republic of Indonesia. Law number 27 of 2014. Minister of health of the republic of indonesia. National health insurance program. Indonesia. 2014

Association of Sleep Quality with Fatigue among Cancer Patient who Took Chemotherapy in Jend. Ahmad Yani Hospital Metro City 2018

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Abstract

Cancer requires various treatment modalities based on realistic goals that can be achieved for each type of cancer. Chemotherapy has advantages over other therapies because chemotherapy drugs are able to have a systemic effect in damaging cancer cells even though the cancer cells undergo metastases far spread from their original place. Cancer patients during chemotherapy experience sleep disorders and fatigue complaints. This study aims to determine the relationship of sleep quality with fatigue in cancer patients undergoing chemotherapy. The design of this study is quantitative using a cross sectional approach. The method of sample collection is purposive sampling. The study sample was 30 cancer patients who underwent chemotherapy. The measurement of sleep quality uses the Pittsburgh Sleep Quality Index (PSQI) instrument and the measurement of fatigue uses the Brief Fatigue Inventory (BFI) instrument. Chi square test results showed that there was a significant relationship between sleep quality and fatigue (p-value=0.001). Conclusion nursing intervention is needed for the quality of sleep in an effort to overcome fatigue in cancer patients.

Keyword: *Fatigue, sleep disorders, cancer, chemotherapy.*

Introduction

Cancer is one of the causes of world death. Every year there is an increase in the number of cancer sufferers. Based on the international agency for research on cancer (IARC), in 2012 there were 14.67 million new cases of cancer and 8,201 million cancer deaths worldwide.¹ In 2018 an increase in new cases of cancer to 18.08 million with 9.5 million deaths.² The number of new cancer cases in Asia was 6.763 million and 4.499 million deaths from cancer. While the population of cancer patients in Indonesia in 2012 amounted to 2,447 million with 194,500 deaths.¹ Based on 2013 basic health research data (Riskesdas), the prevalence of cancer in Indonesia is 1.4 per 1000 population.³ Increased to 1.8 per 1000 population in 2018.⁴

Cancer is a cell disease, where changes in cell cycle regulation become uncontrolled.⁵ Cancer requires various treatments based on realistic goals that can be achieved for each type of cancer. Cancer treatment aims to cure, inhibit the growth of cancer cells, or eliminate symptoms associated with the cancer process.⁶ Cancer

treatment consists of surgery, radioactivity, biotherapy, and chemotherapy.^{5,7}

Chemotherapy had advantages over other therapies because it was able to have a systemic effect in damaging cancer cells. Although cancer cells spread from their original place. Chemotherapy drugs work to disrupt the reproduction of cancer cells directly or indirectly. So that cancer cells can be controlled and eradicated.⁷ Giving chemotherapy using a combination of drug classes and given in several cycles.⁵

During chemotherapy cancer patients often experience sleep disorders.^{8,9} Some sleep disorders during chemotherapy were often awake at night (49%-56%), inability to sleep within 30 minutes (50%-73%) and woke up early (49%-65%).⁹ Sleep disturbance can be measured using the global Pittsburgh sleep quality index (PSQI) score. The PSQI instrument consists of 19 questions and 7 score components. The seven score components were global PSQI scores ranging from 0-21.^{10,11} A global PSQI score of ≥ 5 indicates poor sleep quality.

Giving chemotherapy can provide fatigue complaints. The National Comprehensive Cancer Network states that about 70% -100% of cancer patients experience Cancer related fatigue (CRF). CRF as a subjective feeling of physical, cognitive, emotional or fatigue related to cancer or cancer treatment. Fatigue that was felt was not comparable with activities that have just been done.¹² Individuals describe fatigue using different words, including fatigue, lack of energy, weakness, lethargy, boredom, being unable to sleep, or having sleep disorders. Fatigue in cancer patients can range from mild to severe.¹³

Fatigue measuring devices in cancer patients can use a variety of instruments. One of them is brief fatigue inventory (BFI). BFI is a specific measurement tool for rapid assessment of the level of fatigue in cancer patients. BFI is a measurement scale for fatigue, in the form of a simple, easy to do assessment.¹⁴ BFI is a short, valid and reliable instrument for assessing fatigue in cancer patients.¹⁵ BFI assesses the level of general fatigue in individuals and fatigue disorders in daily activities in the past 24 hours such as general activity, mood, ability to walk, work activities, relationships with others and enjoy life.¹⁴⁻¹⁶

Method

The design of this study is quantitative using a cross sectional approach. The population in this study were cancer patients undergoing chemotherapy in the chemotherapy service unit at Jend. Ahmad Yani Hospital Metro City. The independent variable of this study was cancer patients and fatigue as the dependent variable. This research was conducted at Jend. Ahmad Yani Hospital Metro City with a sample of 30 respondents who met the inclusion criteria. The inclusion criteria in this study were cancer patients undergoing chemotherapy, experiencing fatigue complaints and experiencing sleep disorders. Data collection tool in this study using the PSQI and BFI questionnaires.

The Pittsburgh Sleep Quality Index (PSQI) was developed by Buysse et al (1989) at the University of Pittsburgh’s Wasren Psychiatric Institute and Clinical, with a Cronbach alpha coefficient of 0.83. Test the validity and reliability of the Indonesian version showed that the Cronbach alpha coefficient is 0.79 and the content validity shows 0.89.¹⁰Based on the global PSQI score can be categorized ≥ 5 shows poor sleep quality and global PSQI score < 5 indicates poor sleep quality.¹¹ The

BFI instrument was developed by Mendoza et al (1999) at MD Anderson Cancer Center, with a cronbach alpha coefficient value of 0.93. Test the convergent validity by comparing the BFI score with the MOS SF-36 subscale (p < 0.001) and the language version reliability test. Indonesia shows that the Indonesian version of Cronbach Alpha is 0.956.¹⁵ Based on the scores obtained, fatigue can be categorized for no fatigue if the scores obtained are 0 (NCCN, 2014), mild fatigue with scores obtained: 1-3, moderate fatigue if scores: 4-6, and severe fatigue if scores are obtained: 7-10.¹⁴ Data collection was carried out by the researchers themselves. The data obtained were analyzed using SPSS version 21 by univariate and bivariate (chi square).

Results

Respondent characteristics data obtained showed that the average age of respondents aged 54.47 years with the youngest age is 28 years old and the oldest age is 77 years old. Univariate analysis of variable data on sex, cancer type, sleep quality, and fatigue based on frequency distribution, can be described as follows:

Table 1. Distribution of respondent characteristics based on the, cancer type, sleep quality and fatigue in Jend. Ahmad Yani Hospital Metro.

Characteristics	Frequency (n=30)	%
Sex		
Male	11	36.7
Female	19	63.3
Cancer type		
Breast cancer	11	36.7
Lung cancer	2	6.7
Colorectal cancer	8	26.7
Lymphoma	4	13.3
Bladder cancer	1	3.3
Nasopharyngeal cancer	4	13.3
Sleep quality		
Good	3	10
Poor	27	90
Fatigue		
Mild	7	23.3
Moderate	23	76.7
Severe	0	0

Table 1 showed that female sex (63.3%) was more than male (36.7%). The most dominant type of cancer was breast cancer (36.7%). The client’s sleep quality showed that the majority of the client’s sleep quality was poor (90%). Whereas variable fatigue showed that

the majority of clients experience moderate fatigue (76.7%) The results of the analysis of the relationship of sleep quality with fatigue in cancer patients undergoing chemotherapy, were described in table 2 below.

Table 2. Relationship between sleep quality and fatigue in cancer patients who took chemotherapy in Jend. Ahmad Yani Hospital Metro

Characteristics	Fatigue				OR (95%CI)	p value
	Mild		Moderate			
	n	%	n	%		
Sleep quality						
Good	3	10.0	0	0.0	0.15 (0.06-0.36)	0.001
Poor	4	13.3	23	76.7		
Total	7	23.3	23	76.7		

Table 2 showed that respondents with good sleep quality a small portion experienced mild fatigue (10.0%) and respondents with poor sleep quality mostly experienced moderate fatigue (76.7%). Chi square test results found that there was a relationship between sleep quality with fatigue (p-value = 0.001). From the analysis results obtained OR value = 0.15, meaning that good sleep quality provides a protective effect against fatigue of 85.0%.

Discussions

This study identifies the relationship of sleep quality with fatigue in cancer patients who took chemotherapy. Chi squared analysis results obtained the results of a relationship between sleep quality with fatigue (p value = 0.001). This is relevant to the results of previous studies which state that there is a relationship between sleep disorders and fatigue in cancer patients during chemotherapy (p value <0.01).¹⁷

The sleep-wake cycle and sleep stages are the result of interactions among the nervous system, sleep-on neurons and sleep-on neurons rapid eye movement. The defense system involves a system of reticular activity (RAS) in the brain stem and special neurons in the hypothalamus. Neurons secrete hypocretin neurotransmitter autonomously, continuously and keep conscious and alert. Sleep on neurons located in the hypothalamus induce slow wave sleep (NREM sleep). REM sleep-on neurons are the centers of REM sleep located in the brain stem.⁷ A person can go through 4-6 sleep cycles when sleeping.¹⁸ Changes in the wake-up sleep cycle that the patient feels during chemotherapy can cause complaints of fatigue.^{13,17,19,20,21} Savard et al

(2009) state that the cancer patient’s sleep-wake cycle is disrupted during the first week of each chemotherapy cycle (week of chemotherapy administration), and it gets worse each cycle of treatment.²⁰

Based on the results of data analysis showed that the majority of respondents have poor sleep quality. Poor sleep quality of respondents can be known from the total Pittsburgh Sleep Quality Index (PSQI) score. The total PSQI score is an accumulation of seven assessment components consisting of the subject’s sleep quality, sleep latency, sleep duration, efficiency of sleep habits, disturbance during sleep, use of sleeping pills and dysfunction during the day.

Subjective sleep quality is a person’s view of the quality of sleep. In the component of sleep quality, most respondents stated poor sleep quality. Sleep latency is the amount of time needed to fall asleep after lying in bed and or after the sleep light is turned off.^{10,11} In the sleep latency component, respondents need > 30 minutes to fall asleep. Prolongation of sleep latency will affect sleep both in quality and quantity. A normal conscience is needed to start sleeping for about 20 minutes.²²

Sleep duration is the amount of sleep time measured from starting to sleep at night until waking up in the morning.^{10,11} In the sleep duration component, respondents stated that the duration of sleep was <5 hours. Signs of insufficient sleep were not enough time to sleep and too much time awake. There were several factors that affect sleep, including physical symptoms (eg pain, physical discomfort); emotional stress, and environmental influences (eg lighting, noise, room temperature).¹⁸

Sleep efficiency is the amount of sleep in the period of time filled with sleep and is the ratio between the amount of sleep time and the amount of time spent in bed.^{10,11} In the component of sleep efficiency the respondent is <65%. While disturbance during sleep is a disorder that causes a person to not be able to sleep or wake up during sleep at night. In this component most respondents stated that experiencing sleep disturbances in the form of waking up at night and difficult to go back to sleep. Sleep disturbance contributes to energy loss or fatigue. Quality sleep functions to store energy. During sleep skeletal muscles relax progressively and there is no contraction of chemical energy storage muscles for cellular processes.¹⁸ Quality REM sleep maintained mental and mood.⁷

Based on the results of univariate analysis showed that the average age of respondents was 54.47 years. This showed that the respondents were included in the elderly. Based on previous research that older people experience sleep problems such as waking up early, having trouble sleeping at night, often waking up at night and having trouble falling asleep at night.²²

Conclusions

The results of this study indicated that there was a relationship between sleep quality and fatigue in cancer patients who took chemotherapy (p value = 0.001). And good sleep quality provides a protective effect against fatigue of 85.0%. Based on the results of this study, nurses need to provide independent nursing interventions by enhancing a supportive environment for sleep, providing comfort measures such as providing backmassage, aromatherapy to improve sleep quality and reduce complaints of fatigue in cancer patients undergoing chemotherapy.

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Conflict of Interest: Nil.

References

1. Interational Agency for Research on Cancer (IARC)/ WHO. GLOBOCAN 2012: Estimated cancer incidence, mortality, and prevalence worldwide in 2012.
2. Global cancer observatory (GCO).Interational Agency forResearchonCancer (IARC), 2019.
3. Ministry of Health RI. Riset Kesehatan Dasar (RISKESDAS). Jakarta: National Institute of Health Research and Development RI, 2013.
4. Ministry of Health RI. Riset Kesehatan Dasar (RISKESDAS). Jakarta: National Institute of Health Research and Development RI, 2018.
5. Desen, Wan. Clinical oncology Textbook. Jakarta: FKUI publishing house, 2011.
6. Smeltzer, S.C & Bare, Brenda.G.Medical-surgical nursing textbooks Brunner & Suddarth. Jakarta: EGC, 2008.
7. Black, J.M & Hawk. J. H. Surgical Medical Nursing: Clinical Management for Expected Results. Singapore : Elsevier, 2014.
8. Palesh et al. Prevalence, demographics, and psychological associations of sleep disruption in patients with cancer: University of Rochest Cancer Center-Community Clinical Oncology Program. Journal of Clinical Oncology 2010, 28 (2). Doi: 10.1200/JCO.2009.22.5011.
9. Palesh, O., Peppone, L., Innominato, P. F., Janelins, M., Jeong, M., Sprod, L., Savard, J., Mustian, K. Prevalence, putative mechanisms, and current management of sleep problems during chemotherapy for cancer. Nature and Science of Sleep 2012, 4, 151–162. doi: 10.2147/NSS.S18895
10. Alim, I.Z. Test validity and reliability of the instrument pittsburgh sleep quality index Indonesia language version. Thesis. Specialist Doctor Education Program in the Field of Mental Medicine. University of Indonesia, 2015.
11. Liu, L., Rissling, M., Neikrug, A., Fiorentino, L., Natarajan, L., Faierman, M., & Ancoli-Israel, S. Fatigue and circadian activity rhythms in breast cancer patients before and after chemotherapy: a controlled study. Fatigue: biomedicine, health &

- behavior 2013, 1(1-2), 12-26.doi:10.1080/21641846.2012.741782
12. Mendoza, et al. The rapid assessment of fatigue severity in cancer patients: Use of the brief fatigue inventory. *Cancer* 1999, 85 (5).1186-119.
 13. Miaskowski, C. & Aouizerat, B. A. Contribution of sleep disturbance to cancer fatigue. In Redline, Sand N.A. Berger, N.A (eds.), *Impact of Sleep and Sleep Disturbances on Obesity and Cancer, Energy Balance and Cancer*. Business Media New York 2014. doi: 10.1007/978-1-4614-9527-7_9
 14. National Comprehensive Cancer Network (NCCN). NCCN clinical practice guide-lines in oncology: cancer-related fatigue IV, 2012. Available at : [http:// www.nccn.org/professionals/physician_gls/PDF/fatigue](http://www.nccn.org/professionals/physician_gls/PDF/fatigue)
 15. National Comprehensive Cancer Network (NCCN). NCCN clinical practice guidelines in oncology (NCCN Guidenlines), 2014: cancer-related fatigue I.2014.NCCN.org
 16. Karagozoglu, S. & Kahve, E. Effects of back massage on chemotherapy related fatigue and anxiety: Supportive care and therapeutic touch in cancer nursing. *Applied Nursing Research*, 2013; 26 (4):210–217.doi.org/10.1016/j.apnr.2013.07.002
 17. Liu, L., Rissling, M., Neikrug, A., Fiorentino, L., Natarajan, L., Faierman, M., & Ancoli-Israel, S. Fatigue and circadian activity rhythms in breast cancer patients before and after chemotherapy: a controlled study. *Fatigue: biomedicine, health & behavior*, 2013, 1(1-2), 12-26.doi:10.1080/21641846.2012.741782
 18. Potter, P.A., & Perry, A.G. *Fundamental nursing textbooks*. Jakarta: EGC, 2006
 19. Payne, J.K. Altered circadian rhythms and cancer- related fatigue outcomes. *Integrative Cancer Therapies*, 2011,10(3): 221-233. doi: 10.1177/153473541039258
 20. Savard, J., Liu, L., Natarajan, L., Rissling, M.B., Neikrug, A.B., He, F., Ancoli-Israel, S. Breast cancer patients have progressively impaired sleep-wake activity rhythms during chemotherapy. *Sleep*, 2009,32(9),1-6.
 21. Wang, X.S. Pathophysiology of cancer-related fatigue. *Clinical Journal of Oncology Nursing*, 2008, 12(5), 11-12. Doi: 10.1188/08.CJON.S2.11-20
 22. Budhrani, P. H., Lengacher, C.A., Kip, K., Toftagen, C., & Jim, H. An integrative review of subjective and objective measures of sleep disturbances in breast cancer survivors. *Clinical journal of oncology nursing*, 2015, 19(2).

Post-Traumatic Growth with Police Officer: System Review (Focused on Korean and Foreign Studies)

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Abstract

Purpose: The purpose of this study was to analyze literature related to post-traumatic growth with police officer. **Method:** Systematic review of studies published were conducted through a variety of databases such as Ovid-Embase, Ovid-Medline, The cochrane library, Pubmed, RISS. The research terms included Police officers, Police, Trauma, Posttraumatic growth, Growth. **Results:** All studies were correlation analysis. In the Korean researches, PTG was positively correlated with self-esteem, problem focused coping, emotion focused coping, social support, self-disclosure and deliberate rumination. In the foreign researches, PTG was correlated with thriving, resilience, events involving threat, personal relationship stress, trauma severity, life stress, and gratitude. Demographic variables such as Female, White were also associated with PTG. **Conclusion:** To improve post-traumatic growth of police officers, strategies to increase stress coping, social support, are needed. Strategies to decrease stress, trauma and PTSD symptoms should be developed.

Keywords: *Police officers, Police, Post-traumatic, Growth, Review literature as topic.*

Introduction

The increases in crime and violence in Korea may have a great impact on the life and safety of police officers, and according to the statistics of the National Police Agency, of 9,552 on-duty-injured people for the last five years, the assaulted injuries, traffic accidents, and negligent accidents accounted for 97% of the total number of on-duty-injured people.¹ Particularly, these traumatic events will be directly linked not only to the police officers' lives but also to the protection for the lives of the people. In DSM-IV (1994) of the American Psychiatric Association, the trauma cases were extended to direct or indirect experiences that may threaten physical well-being, including life threats, serious injuries, striking events and so on.² The experiences of various traumatic events, such as witnessing of the murder scene, usage of guns, and violence during the suppression process, which should be undergone on duty, cause the anxiety, pain, and trauma to the relevant event. These various traumatic experiences lead to Posttraumatic Stress Disorder (PTSD).

Accordingly, in the meantime, the studies on post-traumatic stress have been actively conducted, which have focused on negative physical and psychological

experiences and symptoms, accompanied by traumatic events, such as depression, anxiety.³ However, not all people will be led to the post-traumatic stress after experiencing traumatic events, and even if they experience the same trauma, most people will overcome it well, sometimes experiencing physical and mental growth.⁴ In other words, they may experience positive psychological changes that would be perceived after the traumatic event or crisis, and such changes are called as the posttraumatic growth (PTG).⁵ The positive psychological change, mentioned here, may mean a genuine positive change that transcends the psychological functioning level and the self-awareness level of life – simply beyond physical and psychological functioning levels prior to trauma.⁶ Further, rather than the focus on the physical and pathological symptoms which have been induced by the event itself, mentioned in PTSD, the posttraumatic growth implies a more comprehensive concept focusing on the psychological and subjective response, the individual internal-strengths and adaptive aspects, which would be experienced in the event experiences.⁷

These positive changes had been diversely interpreted by each scholar, which had been used in various terms,

such as discovery of benefits, stress-related growth, etc., by the 1990s, but Calhoun and Tedeschi suggested the terminology of 'Posttraumatic Growth', different from their concept.^{8,9} Examining the research trend on the posttraumatic growth in the meantime, the initial studies on posttraumatic growth have been performed in the field of psychology, but in recent years, the research has been actively conducted in nursing, medicine, etc., as the interest in prevention of diseases and health promotion increases.³ In most precedent studies, the studies concentrating on the posttraumatic growth for specific disease subjects including cancer patients, women experiencing physical violence, the subjects who have experienced war have been conducted. However, the posttraumatic growth studies for high-risk occupational groups experiencing various traumatic events, like police officers, fire-fighting officers, and prison officers, are in very short.

Thus, this study is going to search for and then, systemically investigate various variables related to the posttraumatic growth of police officers.

Study Method

Selection of Searching Database: In terms of searching, the literature search started from 1996, when the posttraumatic growth was developed and the term of the original author began to be used, and all the literature associated with the related keywords and the like were searched by January 2018 based on the search date. In order to conduct the systematic literature review of this study, researcher collected studies focusing on the posttraumatic growth aimed at police officers. In this study, Pubmed, Ovid-medline, Ovid-Embase and The cochrane library were used as the overseas database and RISS (Korean/English) as the Korean one. The research objects included Police officers, Police, Trauma, Posttraumatic growth, and Growth. In addition, the literature search was limited to articles providing abstract and full text.

Literature Screening and Quality Assessment: Based on the literature search strategy, all literature retrieved by each database was merged and then, the duplicate literature was removed. After the elimination of duplicate literature, the studies that did not satisfy the core questions of this study were excluded through the titles and abstracts of the primary study. The primary study, which was unclear to judge whether it might be selected or excluded or which fully met the selection

criteria, based on the title and abstract, was judged by securing the full text.

As all the primary studies included in the literature review of this study are the study analyzing correlations, the quality evaluation on the literature was conducted by utilizing the 'Quality Assessment and Validity Tool for Correlational Studies' which was used in the existing study of Wong and Cummings.¹⁰

Results

Based on the literature search criteria of this study, the total number of retrieved literature was 2683 units, and of these, 420 duplicate literature units were excluded. Among 2263 theses by excluding 420 theses, 351 theses related to PTSD and 407 literature units were left by excluding 505 literature units which were not related to the subject, after reviewing abstract, titles and contents. Of them, in the posttraumatic growth, by excluding 322 theses which were studied on the samples not related to police officers of the subject of this study, 8 review theses, 18 qualitative research theses, 23 experimental theses, 4 non-English theses, and lastly, 11 literature units which were retrieved as the poster-presented literature, the final 24 theses were selected. 24 literature units were systematically analyzed by 2 researchers, and if the exclusion was not identical, they discussed it until they reached the agreement.

Discussion

In this study, with respect to the correlations between variables related to posttraumatic growth of police officers, it was found in Korean studies that self-esteem, problem-centered coping, emotion-centered coping, self-exposure, social support, and intentional rumination had a significant correlation with posttraumatic growth. These results are in agreement with the study²¹ that the higher self-esteem becomes, the higher posttraumatic growth is, and since self-esteem correlates with positive cognition control strategies, it is considered that it has the significant correlation with posttraumatic growth, as a factor of protection and internal growth to control negative emotions in the process of accepting events after experiencing traumatic events. In other correlation studies, problem-centered coping and emotional-centered coping also showed a significant correlation with posttraumatic growth of police officers. This suggests that the adaptive mechanisms and responses will vary depending on the stress coping strategies used by individuals, even if they may experience the same

trauma. In the precedent study²², they stated that if the negative emotions, such as trauma and stress, was controlled well, and the emotion-centered coping was well exerted after the traumatic experience, so that problem-centered coping, one of the active coping strategies, was utilized more, it would be in charge of the responses for well-understanding of their own psychological emotions and expression of their emotions. Therefore, the stress coping strategies, such as problem-centered coping and emotional-centered coping, after traumatic events, will be served as important variables to induce the posttraumatic growth. Self-exposures were also established to have a significant correlation with posttraumatic growth, and in the precedent study¹⁵, it was said that those who actively engaged in self-disclosure were more likely to participate in cognitive processes related to growth than those who did not. It was confirmed that self-exposure was statistically related to posttraumatic growth as an important factor of psychological recovery in the growth of trauma experience. In the precedent studies^{15,16,17}, social support and intentional relativity also showed a significant correlation with posttraumatic emotions. In precedent research²³, when social support was well supported after experiencing the traumatic event, it was considered to be an important factor in well coping with stress situations and functioning for the psychological adjustment in adverse situations, which was regarded as an important parameter to induce posttraumatic growth after experiencing the traumatic event. Finally, intentional rumination was found to have a significant correlation with posttraumatic growth, which was considered as an important parameter to promote posttraumatic growth to by thinking carefully about the cast through that event and discovering the positive meanings or benefits from that case, rather than that the trauma experience was not just regarded as a negative event²³. As a result of precedent studies of such Korean studies, the valuables significantly correlated with posttraumatic growth was found to be self-esteem, problem-centered coping, emotion-centered coping, self-exposure, social support, and intentional rumination. By getting out of these phases to explore the relations with valuables, the future research will provide the baseline data for developing programs to promote a positive and healthy direction and posttraumatic growth of police officers, and be helpful as an important factor in conducting a more realistic and multifaceted research. In overseas theses, as the posttraumatic growth-related variables, prosperity and resilience, appreciation, traumatic event threatening the personal life, stress induced from human relations,

severity of trauma, PTSD symptoms, relationship stress, working stress, and depression were identified. It suggested that in overseas studies, Positive variables, such as prosperity and resilience, and negative variables, like stress and trauma, were found to be more variously related to posttraumatic growth than in domestic ones, as a variable related to posttraumatic growth of police officers. Prosperity and resilience were found to be significantly correlated with posttraumatic growth in the precedent theses. In the positive psychology, the constructively adaptive ability, well-being, and individual strengths focused on the prosperity of humans, and in the self-formation and prosperity theory, Frederikson²⁴ argued that the positive emotions, such as prosperity, would undergo a process to promote posttraumatic growth. In addition, referring to resilience as one of coping abilities when confronting a crisis after generally experiencing a traumatic event, he stated that this had a static correlation with posttraumatic growth causing less psychological trauma in crisis. Finally, the appreciation, as a positive variable, corresponded to the study results²⁵ suggesting that the higher the appreciation tendency, the higher the posttraumatic growth.

Conclusion

The purpose of this study was to investigate and explore the precedent literature on posttraumatic growth aimed at police officers, to establish the variables related to the posttraumatic growth of Korean and abroad police officers, and at the same time, to provide baseline data for the development of programs that can promote posttraumatic growth. In the present study, as a result of investigating the literature that have been created since 1996 when the term of posttraumatic growth was firstly used, in the Korean theses, self-esteem, problem-centered coping, emotion-centered coping, self-exposure, social support, and intentional rumination were identified and in overseas theses, prosperity and resilience, appreciation, stress caused by traumatic events threatening the individual live and human relationships, severity of trauma and PTSD symptoms, relation stress, work stress, and depression were confirmed.

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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References

1. Korean national police agency. 2015 Police Statistical Yearbook. [cited 2016 November 23]. Available from <http://www.police.go.kr/portal/main/2015>.
2. American Psychiatric Association. 4th ed. Diagnostic and statistical manual of mental disorders. Washington, DC: Author; 1994.
3. Calhoun, LG, Tedeschi, RG. The post-traumatic growth inventory: Measuring the positive legacy of trauma. *Journal of Traumatic Stress*. 1996;9(3):455-471.
4. Choi SM. Exploration of posttraumatic growth variables [Doctoral dissertation]. Korea University; 2008.
5. Calhoun, LG, Tedeschi, RG. Posttraumatic growth: Future directions. In *Posttraumatic growth: Positive changes in the aftermath of crisis* 1998:215-238. Mahwah, NJ: Lawrence Erlbaum Associates Publishers.
6. Maercker, A, Zoellner, T. The janus face of self-perceived growth: Toward two-component model of post-traumatic growth. *Psychological Inquiry*. 2004;15:41-48.
7. Calhoun, LG, Tedeschi RG. The foundation of posttraumatic growth: An expanded framework. In: Calhoun LG & Tedeschi RG, editors. *Handbook of posttraumatic growth: Research and practice*. Mahwah, NY: Lawrence Erlbaum Association; 2006;1-23.
8. Jeon, YJ, Bae, JK. The Effects of Self-Disclosure, Social Support and Intentional Rumination on Posttraumatic Growth. *Journal of Human Understanding and Counseling* . 2013; 34(2): 215-228.
9. Calhoun, LG, Tedeschi, RG. The Foundations of Post-traumatic Growth; New Considerations. *Psychological injury*, 2004;15(1):93-102.
10. Wong, CA, Cummings, GG. The relationship between nursing leadership and patient outcomes: A systematic review. *Journal of Nursing Management*, 2007;15:508-521. <http://dx.doi.org/10.1111/j.1365-2834.2007.00723.x>.
11. Norlander, T, Schedvin, HV, Archer, T. Thriving as a function of affective personality: relation to personality factors, coping strategies and stress. *Anxiety, Stress & Coping*, 2005;18(2):105-116.
12. Song, SH, Lee, HS, Park, JH, Kim, KH. Validity and Reliability of the Korean Version of the Posttraumatic Growth Inventory. *Korean Journal of health psychology*, 2009;14(1):193-214.
13. Han, SW, Choi, ES. The Effects of Self-esteem and Problem Focused Coping on Post-traumatic Growth among Police Officers. *Korean Journal of Occupational Health Nursing*, 2016;25(3):141-147.
14. Han, SW, Kim, HS. Factors Influencing Post-Traumatic Growth with police officer. *Crisis and Emergency Management. Theory and Praxis*, 2015;11(3):189-205.
15. Jeon, YJ, Bae, JK. The effects of self-disclosure, social support and intentional rumination on posttraumatic growth. *Journal of Human Understanding and Counseling*. 2013;34(2):215-28.
16. Jung, YK. A Study on the Structural Relationship of Influential Factors for Post-traumatic Growth of Police Officers [Doctoral thesis]. Seoul: Dongguk University; 2015.
17. Jung, YK, Choi, ER. A study on influential factors of post traumatic growth in Korea Police Officers: Focus on police officers in the metropolitan cities. *Korean Police Studies Association*, 2014;48(0):243-76.
18. Chopko, BA, Palmieri, PA, Adams, RE. Associations between police stress and alcohol use: Implications for practice. *Journal of Loss and Trauma*, 2013;18(5):482-497. <http://dx.doi.org/10.1080/15325024.2012.719340>.
19. Chopko, BA, Palmieri, PA, Adams, RE. Relationships among traumatic experiences, PTSD, and posttraumatic growth for police officers: A path analysis. *Psychological Trauma: Theory, Research, Practice, and Policy*, 2017;10(2):183-189. <http://dx.doi.org/10.1037/tra0000261>
20. McCanlies, EC, Mnatsakanova, A, Andrew, ME, Burchfiel, CM, Violanti, JM. Positive psychological factors are associated with lower PTSD symptoms among police officers: post Hurricane Katrina. *Stress and Health*, 2014;30(5):405-415. <http://dx.doi.org/10.1002/smi.2615>.
21. Carver, Charles S, Scheier, Michael F, Weintraub, Jagdish K., et al. Assessing coping strategies: A theoretically based approach. *Journal of Personality and Social Psychology*, 1989;56(2):267-283.

22. Smyth, JM., Hockemeyer, JR., Tulloch, H. Expressive writing and post-traumatic stress disorder: Effects on trauma symptoms mood states, and cortisol reactivity. *British Journal of Health Psychology*, 2008;13: 85-93.
23. Yu HJ. A study of the structural relationship between variables that influence posttraumatic growth [Doctoral dissertation]. Pusan National University;2012.
24. Fredrickson, BL. The role of positive emotions in positive psychology: The broaden and build theory of positive emotions. *American Psychologist*, 2001;56: 218-226.
25. Kim, E, Kim, JK..The Effect of Grateful Disposition on The Posttraumatic Growth - The Mediating Effect of Social Support and Ego resilience. *The Korean Psychological Association*, 2015;8: 261-261.

Quality of Life among Sample of Children and Teenagers with Type 1 Diabetes Mellitus in Holy City of Karbala/Iraq 2019

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Abstract

Background: Type 1 Diabetes mellitus (T1DM) is one of the most widely seen chronic disease in child hood and its prevalence rate till age of 18 is approximately one in every 300 and its late complications responsible for reduced life expectancy and major health costs.

Aims: To assess the quality of life (QOL) among children and teenagers with T1DM and its determinants and to compare their QOL to that of healthy peers.

Subjects and Method: A case-control study was carried out in Al Imam Hussain Medical City in Holy Kerbala / Iraq. The sample size included 164 diabetic child as case group and 330 healthy child as a control group. The participants were selected by consecutive convenience sampling technique; the information were collected by using specific questionnaire through direct interview with the participants. The study was performed during the period from 1st of December 2018 to 31th of August 2019.

Results: There were a significant difference in each domain and in all quality of life between the study groups; In addition to that there was a significant association between QOL of diabetic children and certain variables like gender, birth order, number of siblings and paternal education. The study also concluded a negative correlation between the age of the child and QOL there is no significant association between QOL and residence or economic state.

Conclusion: Iraqi children and teenagers with T1DM who live in Kerbala governorate and aged between 5-18 year had poorer QOL than healthy peers. The QOL is associated in all or some domains with certain factors and not associated with others.

Keywords: *Quality of life, Children, adolescents, Type I diabetes mellitus.*

Introduction

Type 1 Diabetes Mellitus is a heterogeneous disorder that usually develops during adolescence and childhood, this disease characterized by a deficit of insulin production secondary to destruction of pancreatic B-cells⁽¹⁾.

Type 1 diabetes mellitus is one of the most widely seen chronic disease in child hood, numbers do not present for the real total population with T1DM, but estimates mention that they may represent 5% of the total diabetes burden⁽²⁾, its prevalence rate approximately 0.25% furthermore the incidence of T1DM continues to increase in most studied populations by 3-5% per year⁽³⁾.

The main aims of diabetes care are to fulfill optimal glycemic control in order to delay or prevent complications and preserve normal development. Most of guidelines on diabetes care focus on the medical aspects of management and winking other issues which are of great importance to the patient⁽⁴⁾

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Diabetes is highly demanding disease approximately affects every day life so the patient expected to hold out much of the responsibilities for making decisions which may affect his entire health⁽⁵⁾.

The most essential feature of measuring the QOL is to capture the individual's subjective assessment of their QOL and not what others imagine it to be. Progressively it has been acknowledged that it is an important health outcome measure in pediatric medicine⁽⁶⁾.

When the child has poor glycemic control and has a lot of episodes of ketoacidosis this can have a serious effect on growth and development⁽⁷⁾. For adolescents, the metabolic control of patients with T1DM often worsens during the pubertal years because this stage is the time of rapid physical, emotional and psychological growth⁽⁸⁾. Regarding the physical changes, the most important one is the growth hormone that cause a lean body mass to be twice in the first 2 to 5 years of puberty⁽⁹⁾.

The studies regarding QOL and T1DM is controversial, some showed that QOL of T1DM patient is lower than that of healthy peer. others showed that there is no difference in QOL between diabetic child and healthy one.

Subjects and Method

A case-control study was carried out in Al Imam Hussain Medical City in Holy Kerbala / Iraq, the study was performed during the period from 1st of December 2018 to 31th of August 2019. The sample included 164 diabetic child for case group and 330 healthy child for control group. Consecutive convenience sampling technique was used. The cases were collected from Al Hassan center which is the only specialized center for diabetes and endocrine glands in holy city, these cases are matched for sex, age, residence and school level to control group which was collected from the consultancy clinics like the clinic of ophthalmology, dermatology and the clinic of ear, nose and throat (ENT).

Inclusion criteria and the exclusion criteria:

Inclusion criteria are: the diabetic type 1 cases and the control are aged between 5-18 years while the exclusion criteria are: Any diabetic case with other chronic disease like comorbid autoimmune disease, any hemoglobinopathy or other chronic condition like

asthma, heart disease, epilepsy and who was mentally retarded, Cases diagnosed with T1DM since less than one year, Control group with any chronic diseases. The diabetic and control groups with a history of recent physical trauma or surgery.

The Questionnaire: The questionnaire consists of three parts: the first part is related to demographic information, the second part is related to the disease like duration of disease, history of DM in immediate family (parents or siblings) and last HbA1c within the last month the forth part is pediatric quality of life inventory; version 4.0 generic core scale.

The Pediatric Quality of Life Inventory TM; was originally developed in the English language by Varni et al, the generic module evaluates four dimensions: Physical functioning (8 items), emotional functioning (5 items), social functioning (5 items) and school functioning (5 items), for a total of 23 items using a five-point Likert scale The responses ranged from never, almost never, sometimes, often and almost always. Items are reversed scored and linearly transformed to a 0-100 scale 0=100, 1=75, 2=50, 3=25, 4=0⁽¹⁰⁾.

PedsQL 4.0 Cut-Off Point Scores: One standard deviation below the population mean (control mean) was explored as a meaningful cut-off point score for an at-risk status for impaired QOL relative to the population sample⁽¹¹⁾

Ethical consideration:

- The study obtained approval from kerbala health directorate and from al immamhussian medical city.
- Verbal consents were obtained from all participants.

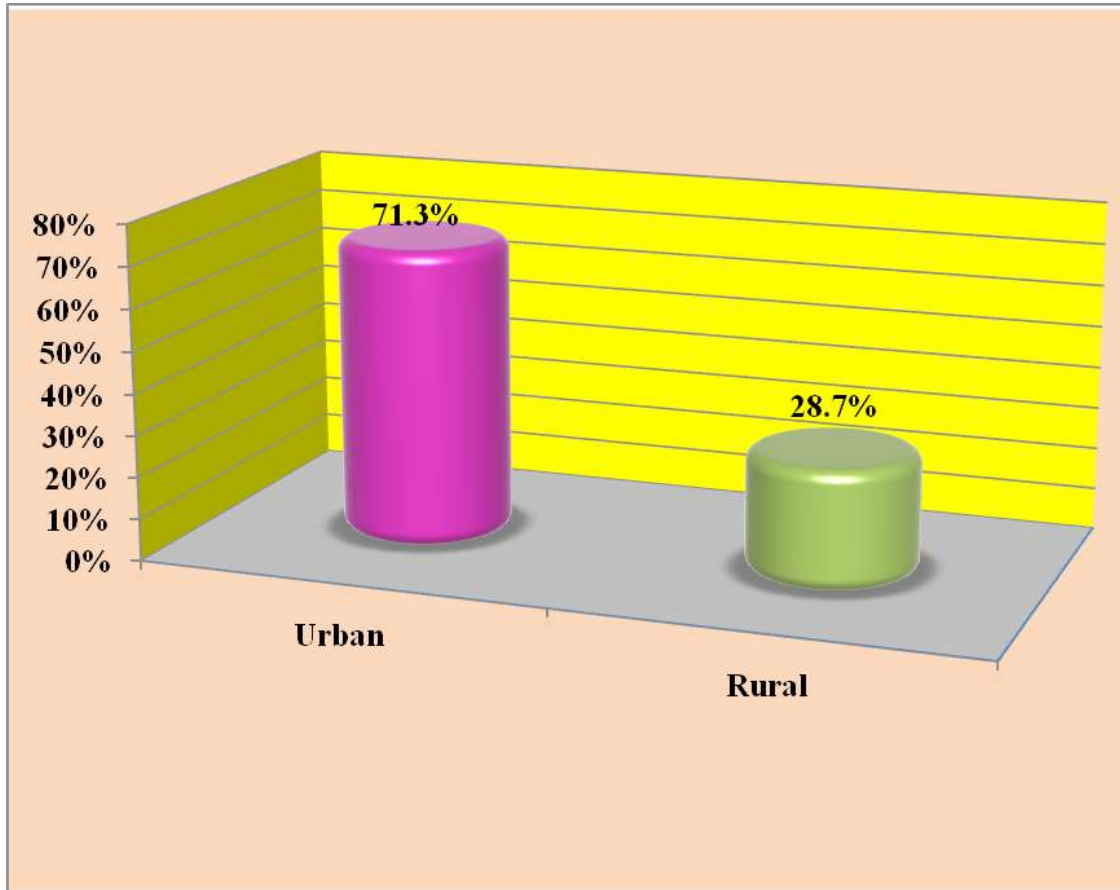
Statistical analysis: Data analysis was done using statistical package for social sciences version 24.

T-test and F test (ANOVA) was used to determine the mean differences between groups, P value of ≤ 0.05 was considered as statistically significant.

Results

Distribution of diabetic children according to residence. Figure 1 shows that the majority of diabetic children were part of urban households which represented 71.3%.

Figure 1: Distribution of diabetic children according to residence



Distribution of diabetic children according to crowding index: Figure 2 shows that socio economic status measured by level of crowding index which is good (9.1%), intermediate (61.6%) and poor (29.3%).

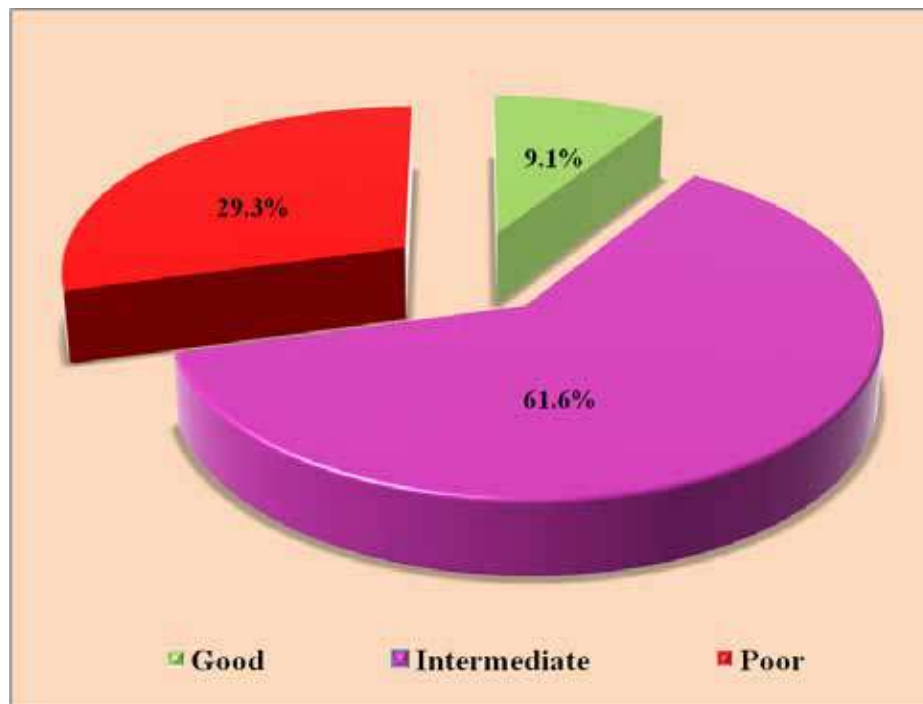


Figure 2 Distribution of diabetic children according to crowding index.

Table 1. shows that t test was conducted to show a mean differences of quality of life domains in case and control group.

There is a significant mean differences in all domains and total score according to study groups.

Table 1: Mean difference of quality of life between study groups

Study variable	Study group	N	Mean ± SD	t-test	P-value
Physical functioning	Case	164	75.72±19.22	-9.760	<0.001*
	Control	330	91.20±9.28		
Emotional functioning	Case	164	66.13±18.54	-12.347	<0.001*
	Control	330	85.59±11.29		
Social functioning	Case	164	90.09±12.68	-2.908	0.004*
	Control	330	93.30±8.79		
School functioning	Case	138	80.72±15.58	-4.505	<0.001*
	Control	272	87.38±10.69		
Total score	Case	164	74.97±15.81	-7.655	<0.001*
	Control	330	85.52±11.10		

Distribution of quality of life cut-off point in four domains: Table 2 shows the quality of life cut-off point according to four domains and total score the cut-off points are 81.92,74.3,84.51,76.69 and 74.42 respectively.

Table 2: Distribution of quality of life cut-off point in four domains in diabetic children.

Variable	Quality of life cut-off point	Number(%)
Physical functioning	<81.92(at risk)	76(46.3%)
	≥81.92(HRQOL)	88(53.7%)
Emotional functioning	<74.3(at risk)	100(61.0%)
	≥74.3(HRQOL)	64(39.0%)
Social functioning	<84.51(at risk)	30(18.3%)
	≥84.51(HRQOL)	134(81.7%)
School functioning	<76.69(at risk)	52(37.7)
	≥76.69(HRQOL)	86(62.3)
Total score	<74.42(at risk)	68(41.5%)
	≥74.42(HRQOL)	96(58.5%)

Mean difference of quality of life according to diabetic children’s socio demographic factors: Table 3 shows that t and F test was conducted to show a mean difference of quality of life domains and total score according to some sociodemographic factors of diabetic children.

Table 3: Mean difference of quality of life according to diabetic children's socio demographic factors

Socio demographic Factors	Number	Quality of life				
		Physical functioning Mean±SD	Emotional functioning Mean±SD	Social functioning Mean±SD	School functioning Mean±SD	Total score Mean±SD
Gender						
Male	70	79.06±16.83	68.43±15.47	91.00±11.15	79.67 ±15.23	76.69±13.33
Female	94	73.24±20.56	64.41±20.45	89.41±13.73	81.54±15.90	73.68±17.38
Total	164					
T test		1.992	1.431	0.791	-0.698	1.255
P value		0.048*	0.154	0.430	0.486	0.211
Birth order						
First	47	74.87±18.44	66.49±19.50	89.47±13.23	79.76±18.11	75.52±15.68
Middle	83	73.95±20.28	64.70±18.28	90.48±12.89	80.43±15.26	74.24±16.59
Last	33	82.29±16.10	70.45±16.45	91.21±9.44	83.00±12.16	76.72±13.85
Only born	1	46.88	25.00	50.00	85.00	51.72
Total	164					
F test		2.360	2.473	3.650	0.260	0.932
P value		0.074	0.064	0.014*	0.854	0.427
Number of siblings						
0	1	46.88	25.00	50.00	85.00	51.72
1	14	82.14±15.9	64.64±18.02	91.07 ±8.36	84.62 ±14.06	79.1±13.97
2-3	75	76.42±17.77	68±19.06	89.47±13.59	78.97±16.96	76.37±15.25
≥4	74	74.2±20.92	65.07±17.7	91.08±11.65	81.88±14.22	73.08±16.47
Total	164					
F test		1.471	2.043	3.75	0.679	1.607
P value		0.224	0.11	0.012*	0.566	0.19

Correlation between quality of life and age in diabetic children: Table 4 shows that correlation test is conducted between age of diabetic child each one with the four domains of quality of life.

Table 4: Correlation between quality of life and age in diabetic children

Variable	Study group	N	Mean ± SD	R	P –value
Age (Year) (Mean± SD) 12.11±3.004	Physical functioning	164	75.72±19.22	-0.213	0.006*
	Emotional functioning	164	66.13±18.54	-0.156	0.046*
	Social functioning	164	90.09±12.68	-0.059	0.450
	School functioning	138	80.72±15.58	-0.064	0.455
	Total score	164	74.97±15.81	-0.117	0.135

Discussion

The current study proved the negative impact of T1DM on all domains of QOL for diabetic children so their quality of life was impaired when compared it to their healthy peers. This probably due to the facts that the high number and complexity of different tasks involved in managing T1DM place a hard burden on the children, or because in Iraq the main technique in administration of insulin is by using daily insulin injections while other countries introduced insulin pump as one of treatment options which proved in many studies its role in improving the QOL as it is considered beneficial by children and parents alike as they experienced more

treatment flexibility and comfort than with daily insulin injections^(12,13), The current study found large percentage of risky patients in those whom have impaired QOL from diabetic children.

our finding regarding QOL is consistent with many studies like of, Kalyva et al., Abdul rasoul et al, Arabiat et al, Sabri et al, Rivera et al, Samardizic et al and Gadallah et al^(6,15-20) at the same time our results are different from other studies like of laffel et al, Emmanouil et al, Rozemarijn et al, Mills et al, and Murillo et al.⁽²¹⁻²⁵⁾.

This study showed that female gender was not impacted in all domains except in physical functioning

which is inconsistent with many studies that conclude female have impaired QOL when compared to male like the study of Hoey et al, Albuhaireen et al, Murillo et al, Kalyva et al, Frøisland et al, Abdul rasoul et al^(6,14,24-27). A lower physical activity among girls in comparison to boys can be explained according to our culture by weaker utilization of this activity due to the poor support given from school and parents with little encouragement to girls to participate in community sports, our result regarding the gender similar to what has been concluded by Chen et al⁽²⁸⁾. Other studies showed no difference in QOL between male and female as reported by Jawad et al, Samardzic et al, Emmanouil et al^(5,17,21).

The negative correlation of the QOL with the age which found in this study may be due to the following: the role of developmental changes that occur at school-age children whom grow in to adolescence, the individual differences in caloric intake related to growth spurts and participation in sports, and adolescent mood swings, menses in female adolescents all these contribute to the lower score of physical and emotional QOL. Our result regarding this correlation is in line with the result of Jawad et al, Murillo et al^(5,24) and not in line with result of Özyazıcıoğlu et al and Abdul rasoul et al^(2,6). There are other studies which said that there is no association between them at all as Samardzic et al, Emmanouil et al and Gadallah et al^(16,17,21).

It is found that there is no association between QOL with both residence and the economic state that is because in Iraq even a child who comes from low-income households or rural region he is able to access the recommended treatment by receiving it from the official primary health centers.

Conclusions

The current study concluded that Iraqi children and teenagers with T1DM who live in Kerbala governorate and aged between 5-18 year had poorer QOL than healthy peers.

Source of Funding: Self.

Conflict of Interest: Nil.

References

1. Almahfoodh D, Alabbod M, Alali A, Mansour A. Epidemiology of type 1 diabetes mellitus in Basrah, Southern Iraq: a retrospective study. *diabetes research and clinical practice*. 2017;133:104-8.
2. Özyazıcıoğlu N, Avdal EÜ, Sağlam H. A determination of the quality of life of children and adolescents with type 1 diabetes and their parents. *International Journal of Nursing Sciences*. 2017;4(2):94-8.
3. Shukir S, Kareema A, Rozhan T. Physical Problems among Children and Adolescents Complain of Diabetes Type I in Erbil City. *.kufa Journal for Nursing sciences*. 2016;6(3):60-9.
4. Kalra S, Jena BN, Yeravdekar R. Emotional and Psychological Needs of People with Diabetes. *Indian journal of endocrinology and metabolism*. 2018;22(5):696-704
5. Jawad KAA-D. Health - Related Quality of Life of diabetic Adolescents in Iraq: A preliminary Report. *IRAQI JOURNAL OF COMMUNITY MEDICINE* 2006;19(1):23-5.
6. Abdul-Rasoul M, AlOtaibi F, Abdulla A, Rahme Z, AlShawaf F. Quality of life of children and adolescents with type 1 diabetes in Kuwait. *Medical Principles and Practice*. 2013;22(4):379-84.
7. NEWS a. How Does Type 1 Diabetes Affect A Child's Growth And Development? [cited 2019 16 march]. Available from: <https://abcnews.go.com/Health/DiabetesLivingWith/story?id=3813567>.
8. Hamilton J, Daneman D. Deteriorating diabetes control during adolescence: physiological or psychosocial? *Journal of pediatric endocrinology & metabolism : JPEM*. 2002;15(2):115-26
9. Council TD. How Does Puberty Affect Diabetes 2018 [cited 2019 16 march]. Available from: <https://www.thediabetescouncil.com/how-does-puberty-affect-diabetes/10>.
10. Varni JW, Seid M, Rode CA. The PedsQL™: measurement model for the pediatric quality of life inventory. *Medical care*. 1999;126-39.
11. Varni JW, Burwinkle TM, Seid M, Skarr D. The PedsQL™* 4.0 as a pediatric population health measure: feasibility, reliability, and validity. *Ambulatory pediatrics*. 2003;3(6):329-41
12. Nuboer R, Borsboom GJJM, Zoethout JA, Koot HM, Bruining J. Effects of insulin pump vs. injection treatment on quality of life and impact of disease in children with type 1 diabetes mellitus in a randomized, prospective comparison. *Pediatric Diabetes*. 2008;9(4pt1):291-6
13. Baş V, Bideci A, Yeşilkaya E, Soysal A, Çamurdan O, Cinaz P. Evaluation of factors affecting quality

- of life in children with type 1 diabetes mellitus. *J Diabetes Metab.* 2011;2(8):154-8.
14. Kalyva E, Malakonaki E, Eiser C, Mamoulakis D. Health-related quality of life (HRQoL) of children with type 1 diabetes mellitus (T1DM): self and parental perceptions. *Pediatric diabetes.* 2011;12(1):34-40.
 15. Sabri Y, Sharkawy A, Farrag S, El Boraie H. Quality of life and self-esteem of children and adolescents with diabetes type 1. *Egyptian Journal of Psychiatry.* 2014;35(3):173-.
 16. Gadallah MA, Ismail TA-AM, Aty NSA. Health related quality of life among children with Type I diabetes, Assiut city, Egypt. *Journal of Nursing Education and Practice.* 2017;7(10):73.
 17. Samardzic M, Tahirovic H, Popovic N, Popovic-Samardzic M. Health-related quality of life in children and adolescents with type 1 diabetes mellitus from Montenegro: relationship to metabolic control. *Journal of Pediatric Endocrinology and Metabolism.* 2016;29(6):663-8.
 18. Arabiat DH, Al Jabery MA. Health related quality of life in paediatric chronic health conditions: A comparative study among children and adolescents in Jordan. *Health.* 2013;5(11):19.
 19. Rivera C, Mamondi V, Fueyo J, Jouglard EF, Pogany L, Sanchez M, et al. Health-related quality of life in children with and without chronic conditions. A multicenter study. *Arch Argent Pediatr.* 2015;113(5):404-10.
 20. Laffel LM, Connell A, Vangsness L, Goebel-Fabbri A, Mansfield A, Anderson BJ. General quality of life in youth with type 1 diabetes: relationship to patient management and diabetes-specific family conflict. *Diabetes care.* 2003;26(11):3067-73.
 21. Emmanouilidou E, Galli-Tsinopoulou A, Karavatos A, Nousia-Arvanitakis S. Quality of life of children and adolescents with diabetes of Northern Greek origin. *Hippokratia.* 2008;12(3):168.
 22. Kamp Rvd. Quality of Life in Children with Ttype 1 Diabetes Mellitatesareview. 2012.
 23. Mills SA, Hofman PL, Jiang Y, Anderson YC. Health-related quality of life of Taranaki children with type 1 Diabetes. *NZ Med J.* 2015;128:25-32.
 24. Murillo M, Bel J, Pérez J, Corripio R, Carreras G, Herrero X, et al. Health-related quality of life (HRQOL) and its associated factors in children with Type 1 Diabetes Mellitus (T1DM). *BMC pediatrics.* 2017;17(1):16.
 25. Frøisland DH, Graue M, Markestad T, Skriverhaug T, Wentzel-Larsen T, Dahl-Jørgensen K. Health-related quality of life among Norwegian children and adolescents with type 1 diabetes on intensive insulin treatment: a population-based study. *Acta paediatrica.* 2013;102(9):889-95
 26. AlBuhairan F, Nasim M, Al Otaibi A, Shaheen NA, Al Jaser S, Al Alwan I. Health related quality of life and family impact of type 1 diabetes among adolescents in Saudi Arabia. *Diabetes research and clinical practice.* 2016;114:173-9.
 27. Hoey H, Aanstoot H-J, Chiarelli F, Daneman D, Danne T, Dorchy H, et al. Good metabolic control is associated with better quality of life in 2,101 adolescents with type 1 diabetes. *Diabetes care.* 2001;24(11):1923-8
 28. Chen X, Origasa H, Ichida F, Kamibeppu K, Varni JW. Reliability and validity of the Pediatric Quality of Life Inventory™ (PedsQL™) Short Form 15 generic core scales in Japan. *Quality of Life Research.* 2007;16(7):1239-49.

The Factors Associated with Incomplete Vaccination among Children below 4 Years in Holy Karbala/Iraq

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Abstract

Background: Vaccines has an essential role for the prevention of infectious diseases. It has an important role in promoting child survival, several reasons are related to incomplete vaccination of children.

Objectives: To find out the reasons related to incomplete vaccination among children under five years in Karbala city.

Method: A cross sectional study, convenient sample of 400 children was approached who attended primary health care centers in urban and rural areas in Karbala city. Data collection done between the first of March to 30th of June, 2019 through direct interview using a questionnaire adapted from similar researches. Statistical Package for the Social Sciences (SPSS) program version 24 was used for data analysis and P value of a level < 0.05 considered significant.

Results: The most (22.2%) reported reason for incomplete vaccination that are related to the health centers was unavailability of vaccine.

Child sickness (33.5%) and fear of adverse effects (31.5%) were the most reported reasons for incomplete vaccination that are related to the family and child.

Conclusions: Unavailability of vaccine, child sickness and fear of adverse effect were the most reported reasons for incomplete vaccination.

Keywords: *Immunization, incomplete vaccination, reasons.*

Introduction

Childhood immunization is the induction of immunity throughout vaccination⁽¹⁾. Human beings have profited from immunization for more than two centuries⁽²⁾. Immunization is a core constitute of the human right and recognized as an individual, community and governmental responsibility⁽³⁾. Vaccines are so special as it's: promote health, have an

expansive reach, have rapid impact and save lives and costs⁽⁴⁾. Clinical studies are conducted to assess the safety and efficacy of a vaccine before it can be brought to market⁽⁵⁾. The chance of any adverse response is almost one in a million dosages given, they proceed to be observed carefully even after consent⁽⁶⁾. False thoughts and rumors with no scientific background about their possible negative response may prevent people from being vaccinated, with the consequent risks for the health of the population⁽⁷⁾. In 1985, the Expanded Program of Immunization was established nationwide⁽⁸⁾. It is necessary to understanding factors that affect the immunization coverage to increase routine immunization coverage rates⁽⁹⁾. Factors that commonly influence vaccination programme performance are either health-system-related (e.g. quality of services, distance,

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security, waiting time, reliability of vaccination session schedule) or user-related (e.g. family characteristics, parental attitudes and knowledge)⁽¹⁰⁾. Family characteristics include: poor-income status, residence in rural areas, extremes of maternal age, high parity, low maternal education level, larger families, residence in the area for < 1 year, mother working outside the home, lack of knowledge about vaccine-preventable diseases, transportation difficulties, lack of health insurance and presence of disease among the children⁽¹¹⁾. Factors like low education, age, poor access to health facilities, single parent, inadequate antenatal care, ethnicity and no belief in vaccination associated with low immunization uptake around the world⁽¹²⁾. In Iraq, few studies had done to assess the factors that affect vaccination coverage⁽¹³⁻¹⁵⁾, Some studies had done to assess the awareness towards childhood vaccination⁽¹⁶⁻¹⁸⁾.

Subjects and Method

Study design, setting and time: A cross sectional study was carried out at 4 primary health care centers (PHCCs) in urban and rural areas in Karbala city from the first of March to 30th of June, 2019.

Study population and Sampling technique: The study included a sample of 400 children born from 1/ 1/ 2016 and above according to the time of introduction of the new vaccination schedule who attended PHCCs for vaccination, health problems or accompanied by their caregivers and agree to participate in this study. The sample was selected conveniently from four PHCCs, which were selected by simple random technique. Two randomly selected from the urban areas (Al Mulhaq and Al Nidal) and Two PHCCs were selected from the rural areas (Aon bin abdulla and Husseiniya PHCC).

Inclusion Criteria:

- Children born from 1/ 1/ 2016 and above according to the time of introduction of the new vaccination schedule in Iraq.
- Children resident in Karbala.

Exclusion criteria:

- Completely vaccinated children.
- Internally displaced children.
- Children from other cities rather than Karbala.

- Very ill and mentally retarded caregiver.

The questionnaire included the following data:

- Demographic factors of the child, which included:
(Age, gender, sequence in the family, place of birth, family size, house ownership and residence)
- Socio-demographic factors of the caregiver:
(Marital status, mother age, mother's educational status, mother's occupational status, father age, father's educational and occupational status)

Other related factors: Walking time to reach healthcare center, means of reaching healthcare center, source of the information on vaccination in general, presence of immunization card.

Causes for incomplete vaccination among children: The last part of the questionnaire contained the possible reasons incomplete vaccination among children which included the followings:

Causes related to health center: Unavailability of vaccine, absence of vaccinator, poor health staff motivation, inconvenient time of immunization, long waiting time, child illness –not given vaccine by vaccinator and others (specify).

Causes related to the family and child: Unaware of need for immunization, unaware of need to return for subsequent dose, no belief in immunization schedule, fear of adverse effects, rumors about vaccine such as vaccine causes diseases, the belief that vaccination campaigns are adequate, child sickness(child ill – not taken to health center), busy mother, mother forgetfulness, family problems including illness of mother, and others (specify).

Under vaccinated child (or child with an incomplete vaccination schedule): “Child aged <5 years lacking one or more of the vaccines in the national schedule, including boosters”⁽¹⁹⁾.

Operational definitions for vaccinated children should be provided by age and vaccine and should include vaccine boosters. New vaccines that have been recently introduced in the country should also be considered⁽¹⁹⁾.

Table 1: Basic national vaccination schedule by age that must be given to the children to be completely

Age	Basic Schedule
From birth to one month	BCG + OPV0 + Hep B1
2-3 months	BCG + OPV0 + OPV1+ pneumococcal1 + rotavirus 1+ Hexa 1 (DTaP ₁ -IPV ₁ -Hib ₁ -HepB ₁)
4-5months	BCG + OPV0 + OPV1+ OPV2+ pneumococcal1+ pneumococcal2 + rotavirus 1+ rotavirus 2+ Hexa 2 (DTaP ₂ -IPV ₂ -Hib ₂ -HepB ₂)
6-12 months	BCG + OPV0 + OPV1+ OPV2+ OPV3+ pneumococcal1+ pneumococcal2+ pneumococcal3+ rotavirus 1+ rotavirus 2+ Hexa 3 (DTaP ₃ -IPV ₃ -Hib ₃ -HepB ₃) + measles
12-23months	BCG + OPV0 + OPV1+ OPV2+ OPV3+ pneumococcal1+ pneumococcal2 + pneumococcal3+ rotavirus 1+ rotavirus 2+ measles+ MMR
18-23 months	All vaccines + Boosters doses
Measles→ 12 months MMR→24 months Boosters →24months	

Ethical Consideration:

1. Study protocol was approved by the ethical committee in collage of medicine/Kerbala University.
2. Written agreement was obtained from Karbala health directorate with facilitation letter to the PHCCs where the study was conducted.
3. Verbal consents were obtained from the mothers prior to interviewing after explaining the objectives of the study to them.

Results

Distribution of variables of children with incomplete vaccination: The mean age of children was 18.49±10.77 ranging from (3-41) months. In terms of gender, females outweigh males (females accounted for 53.0%, while males accounted for 47.0%). Over half (52.5%) have a third birth order or more, the other half (19.8% and 28.2%) are either first or second in birth order. 88.2% of the children were born in maternity hospitals and 87.5% have vaccination card present.

Table 2: Distribution of variables of children with incomplete vaccination

Variables	Mean±SD	Range
Current age (Month)	18.49±10.77	(3-41)
Gender		
Male	188	47.0%
Female	212	53.0%
Total	400	100.0%
Birth Order		
First	79	19.8%
Second	113	28.2%
Third or more	208	52.0%
Total	400	100.0%
Place of Birth		
Maternity hospital	353	88.2%
Home	47	11.8%
Total	400	100.0%
Presence of Immunization Card		
Yes	350	87.5%
No	50	12.5%
Total	400	100.0%

Distribution of source of information on vaccination: Figure 1 shows that (97.3%) of the source of information regarding vaccination comes from health

centers, the other sources of information are (family, television and internet) in a percentage of (2.3%, 0.2% and 0.2%) respectively.

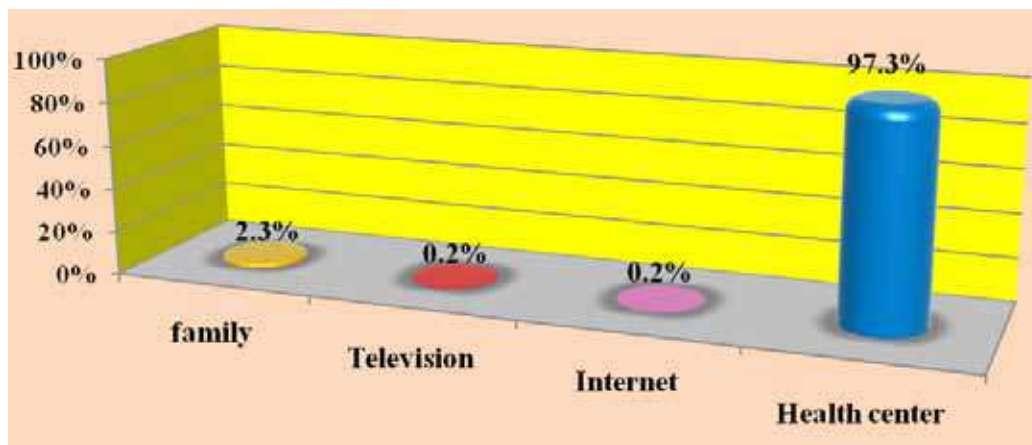


Figure 1: Distribution of source of information on vaccination.

Distribution of incompletely vaccinated children by type of missed vaccines: In the first week of life, the percentage of missed vaccines was low: 5% for BCG, 5% for oral polio vaccine (zero doses) and 1% for Hepatitis B vaccine (first dose). Other missed vaccines are shown in table 3

Table 3: Distribution of incompletely vaccinated children by type of missed vaccines

Vaccine Type	Number	Percent
One week after birth		
BCG	20	5%
Oral polio vaccine (zero dose)	21	5%
Hepatitis B vaccine(first dose)	4	1%
Two months		
Oral polio vaccine (first dose)	131	30%
Rota vaccine (first dose)	278	69%
Pneumococcal vaccine (first dose)	146	36%
Hexa vaccine (first dose)	130	32%
Four months		
Oral polio vaccine (second dose)	189	47%
Rota vaccine (second dose)	366	91%
Pneumococcal vaccine (second dose)	205	50%
Hexa vaccine (second dose)	190	47%
Six months		
Oral polio vaccine (third dose)	207	60%
Pneumococcal vaccine (third dose)	223	64%
Hexa vaccine (third dose)	207	60%
Nine months		
Measles	256	88%
Fifteen months		
MMR* vaccine(first dose)	131	83%
Eighteen months		
Oral polio vaccine (first booster dose)	14	90%
Penta vaccine (first booster dose)	14	90%

*MMR Measles, Mumps and Rubella. * children may missed more than one vaccine

Reasons for incomplete vaccination that are related to the health center: Figure 2 shows that (22.2%) didn't vaccinate their children because the vaccination is not available in health centers. Other related reasons are shown in figure 2.

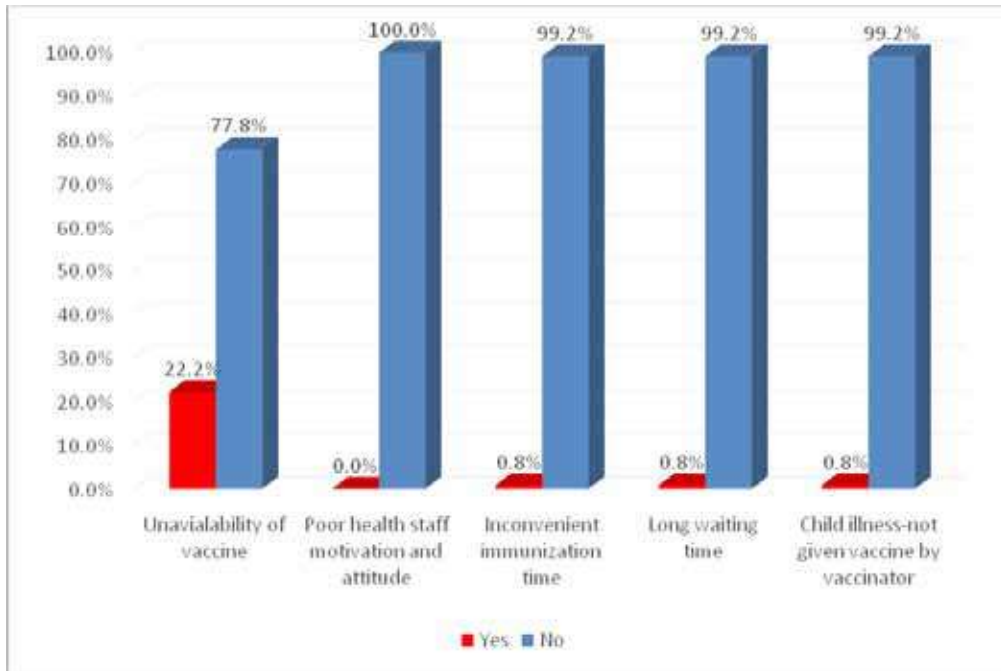


Figure 2: Reasons for incomplete vaccination that are related to the health center.

Reasons for incomplete vaccination that are related to the family and child: Figure 3 shows that being not aware of the need for vaccination was (6.0%), although being not aware of the need for subsequent vaccination was not cited at all as a reason for incomplete vaccination, other related reasons are shown in figure 3.

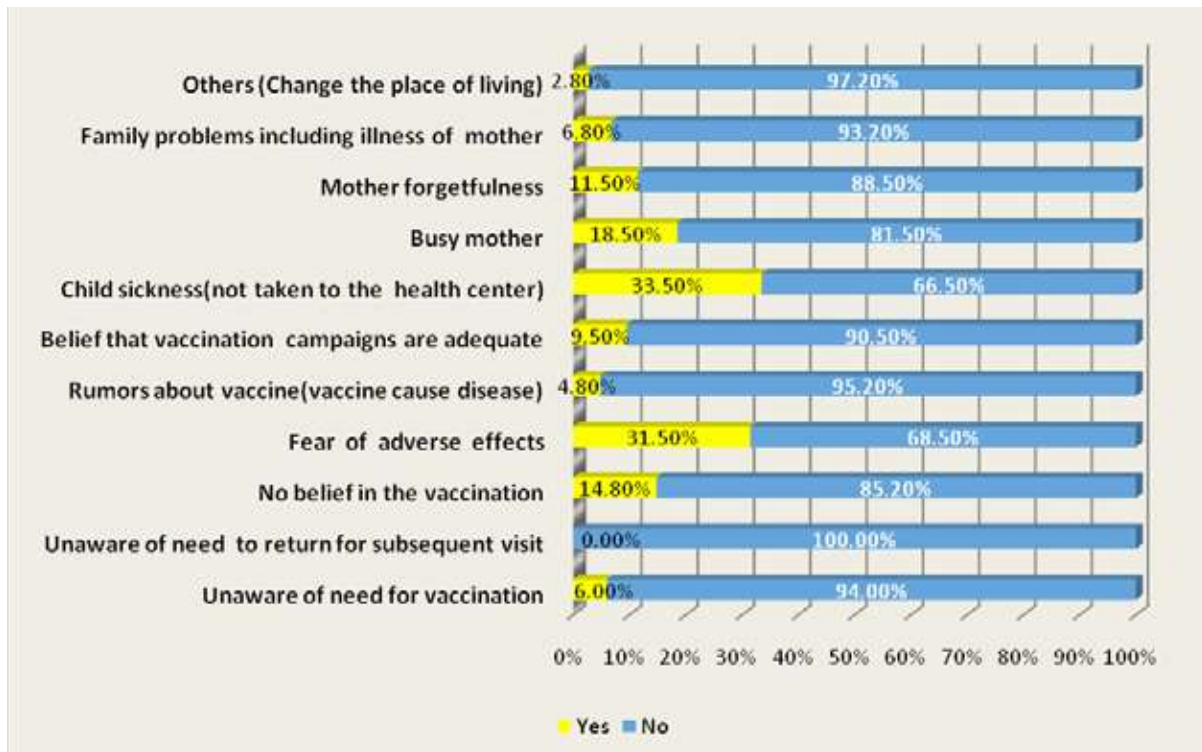


Figure 3: Reasons for incomplete vaccination that are related to the family and child.

Discussion

Vaccination is a very effective way for preventing certain infectious diseases. Routine immunization programs protect most of the world's children from a number of infectious diseases that previously claimed millions of lives each year⁽²⁰⁾.

The prevalence of incomplete vaccination is a main public health issue because it continues to sustain a high spread of vaccine-preventable diseases in some countries⁽²¹⁾.

Regarding to birth order, most (52.5%) of incompletely vaccinated children in this study had a third birth order or more rather than first (19.8%) or second order (28.2%), While in other studies birth order has no effect on vaccination status⁽²²⁻²⁴⁾. This might be attributed to increase family size that made the parent busy and forget the vaccination schedule.

Regarding to the source of information towards vaccination, it was shown that 97.3% come from health centers. In another study done in Ethiopia, It showed that the major (88%) sources of information were health workers and health extension workers⁽²⁵⁾. Another study done in Baquba city showed that most (87.2%) of the information about vaccination comes from physicians or health care workers⁽¹⁸⁾.

The percentage missed vaccines in this study were more when the child get older in age i.e the percentages of missed vaccines At age 18 months and more [Oral polio vaccine (first booster dose)(90%) and Penta vaccine (first booster dose)] were more than that in the first week of life [BCG (5%), Oral polio vaccine(5%) (zero dose), hepatitis B vaccine (1%) (First dose)] except for Rota doses (start high percentage from the beginning) as the permitted period for Rota is too short(Children should receive all doses of rotavirus vaccine before they turn 3 months old (child aged 91 days and more will be prohibited from the vaccine)⁽²⁶⁾.

This variation may be related to the country's policy in Iraq that birth certificate is not permitted until the child takes BCG vaccine, HBV1 and OPV0 vaccines are taken at the same time. Then when the child get older, there will be a several reasons (it will be mentioned later) for missing vaccination schedule.

In addition, there was a concept that the first week vaccines is the crucial one and the parents or caregivers must brought their neonate to gain that vaccines in a

timely manner.

Vaccination coverage start high in percentage in the first week schedule then declines gradually as the child proceed in age as reported in the studies done in Iraq⁽¹³⁻¹⁵⁾.

According to the reasons for incomplete vaccination that are related to the health centers, the mostly mentioned reason was unavailability of vaccine (22.2%).

In a study done by Al Lela et al. 2013 in Iraq, It was found that lack of vaccine was considered to be a barrier for vaccination by the greatest proportion 42.4% of the participants⁽²⁷⁾. Absence of vaccinators or vaccines was the found as the second most (17.7%) common cause for incomplete vaccination in the study done in Pakistan by Riaz et al. 2018⁽²⁸⁾.

According to the reasons for incomplete vaccination that are related to the family and child: child sickness (33.5%) and fear of adverse effects (31.5%) were the most reported reasons for incomplete vaccination. In a study done by Kadhum 2015 in Baquba city, the most reported barriers for immunization were child illness(58.8%) followed by lack of mother knowledge concerning the place and date of vaccination(23.5%)⁽¹⁸⁾.

Conclusion

- Unavailability of vaccine was the most reported reason for incomplete vaccination that are related to the health centers.
- Child sickness and fear of adverse effect were the most reported reason for incomplete vaccination that are related to the family and child.

Source of Funding: Self.

Conflict of Interest: Nil.

References

1. Lujain Anwer Al-Kazrajy THH. Immunization Status of Internally Displaced Iraqi Children During 2017. *Family Medicine & Medical Science Research*. 2017.
2. Stern AM, Markel H. The History Of Vaccines And Immunization: Familiar Patterns, New Challenges. *Health Affairs*. 2005;24(3):611-21.
3. World Health Organization. Sixty-Fifth World Health Assembly Accessed March. 19, 2019

- [Available from: http://apps.who.int/gb/ebwha/pdf_files/WHA65-REC1/A65_REC1-en.pdf
4. World Health Organization. Importance Of Immunization Programmes Accessed Feb. 19, 2019 [Available from: <https://vaccine-safety-training.org/Importance-of-immunization-programmes.html>
 5. Kimmel SR. Vaccine adverse events: separating myth from reality. *American family physician*. 2002;66(11):2113-20.
 6. Centers for Disease Control and Prevention. Epidemiology and prevention of vaccine-preventable diseases. Washington DC Public Health Foundation. 2015;2:20-2.
 7. Dominguez A, Astray J, Castilla J, Godoy P, Tuells J, Barrabeig I. [False beliefs about vaccines]. *Atencionprimaria*. 2019;51(1):40-6.
 8. Lafta R, Hussain A. Trend of vaccine preventable diseases in Iraq in time of conflict. *Pan African Medical Journal*. 2018;31(130).
 9. Noh J-W, Kim Y-m, Akram N, Yoo K-B, Park J, Cheon J, et al. Factors affecting complete and timely childhood immunization coverage in Sindh, Pakistan; A secondary analysis of cross-sectional survey data. *PloS one*. 2018;13(10):e0206766.
 10. Kagoné M, Yé M, Nébié E, Sie A, Schoeps A, Becher H, et al. Vaccination coverage and factors associated with adherence to the vaccination schedule in young children of a rural area in Burkina Faso. 2017;10(1):1399749.
 11. Oliveira MFSd, Martinez EZ, Rocha JSY. Factors associated with vaccination coverage in children < 5 years in Angola. *Revista de saude publica*. 2014;48:906-15.
 12. Chidiebere ODI, Uchenna E, Kenechi O. Maternal sociodemographic factors that influence full child immunisation uptake in Nigeria. *South African Journal of Child Health*. 2014;8(4):138-42.
 13. Al-Lami F, Loai SF. Proportion and Determinants of Incomplete Vaccination among Children Aged Less than Two Years in Baghdad City. *Iraqi Academic Scientific Journal* 2010;9(2):169-73.
 14. Kholod Dhaher Al S. Causes of Delay in Age Appropriate Vaccination. *Iraqi Academic Scientific Journal* 2006;5(3):298-301.
 15. Lamia Dhia A, Lena Mustafa A. Incomplete Vaccination among Children below Two Years in a sample of urban Primary Health Care Centers at Al-Karkh Baghdad City. *IRAQI JOURNAL OF COMMUNITY MEDICINE* 2016;29(3):139-45.
 16. Essam JALZ. The Awareness about NIDs Program in a Rural Area of Al-Nahrawan District of Baghdad. *Iraqi Academic Scientific Journal* 2006;5(3):325-9.
 17. Kafia Hashim K, Sana Hassan A, Khalat Karwan F. Knowledge of Mothers Who Attending HacıQadir Antenatal Clinical Center Regarding Immunization kufa *Journal for Nursing sciences* 2016;6(2):41-6.
 18. Kadhum SA. Assessment of Mother's knowledge Concerning Child Immunization in Primary Health Care Centers in Baquba City. *Diyala Journal of Medicine*. 2015;9(2):25-33.
 19. Pan American Health Organization, World Health Organization. Methodology For The Evaluation Of Missed Opportunities For Vaccination. Washington: PAHO, WHO; 2013.
 20. Gualu T, Dilie A. Vaccination Coverage and Associated Factors among Children Aged 12–23 Months in Debre Markos Town, Amhara Regional State, Ethiopia. *Advances in Public Health*. 2017;2017.
 21. Landoh DE, Ouro-Kavalah F, Yaya I, Kahn A-L, Wasswa P, Lacle A, et al. Predictors of incomplete immunization coverage among one to five years old children in Togo. *BMC public health*. 2016;16:968.
 22. Odutola A, Afolabi MO, Ogundare EO, Lowe-Jallow YN, Worwui A, Okebe J, et al. Risk factors for delay in age-appropriate vaccinations among Gambian children. 2015;15(1):346.
 23. Vinodkumar Mugada SC, Divya Sai Kaja, Satya Gopala Krishna Machara. Knowledge towards childhood immunization among mothers & reasons for incomplete immunization. *Journal of Applied Pharmaceutical Science*. 2017;7(10):157-61.
 24. Boulton ML, Carlson BF, Power LE, Wagner AL. Socioeconomic factors associated with full childhood vaccination in Bangladesh, 2014. *International Journal of Infectious Diseases*. 2018;69:35-40.
 25. Bogale T. Assessment of Incomplete Vaccination and Associated Risk Factors among Children Under one Year at Guder Hospital, West Shoa Zone, Oromia Regional State, Ethiopia. *Journal of Health, Medicine and Nursin*. 2017;45.
 26. U.S. Agency for International Development and MOH Iraq. Extended Program of Immunization

- Staff Manual 2014 [Available from: <http://phd.iq/LionImages/PDFStore/brnamj%20almwsaa%20lthsun.pdf>
27. Al Lela O, Bahari M, Al Abbassi M, Salih M, Basher A. Iraqi parents' views of barriers to childhood immunization. 2013.
28. Riaz A, Husain S, Yousafzai MT, Nisar I, Shaheen F, Mahesar W, et al. Reasons for non-vaccination and incomplete vaccinations among children in Pakistan. *Vaccine*. 2018;36(35):5288-93.

Chipping Resistance of Nanosilica Treated Zirconia Cores Veneered with Porcelain after Thermocycling and Cycling Loading

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Abstract

Aim: This study was conducted to evaluate the effect of nanosilica surface coating of pre-sintered zirconia on chipping of veneered zirconia crowns after thermocycling and cyclic loading.

Method: Twenty zirconia cores were subjected to nanosilica slurry treatment before sintering then veneered and fired to produce crowns. The crowns were cemented by resin cement on their epoxy dies and 10 crowns were subjected to 10000 thermocycles and 10000 cyclic loading. All crowns were loaded till chipping of veneer layer then the chipped surfaces were examined by SEM/EDX.

Results: Crowns which were subjected to thermocycling and cyclic loading gave lower chipping resistance than the non-aged crowns.

Conclusions: Treatment of zirconia cores with nanosilica before sintering and after thermal and mechanical aging didn't increase the chipping resistance of the veneer layer.

Keywords: Nanosilica, Zirconia, Chipping, Veneer.

Introduction

Yttria-stabilized tetragonal zirconia polycrystal (Y-TZP) became the most ceramic material used for production of fixed partial dentures. The successful outcome of Y-TZP has been associated with the intrinsic material toughening mechanism that occurs through phase transformation from tetragonal to monoclinic crystalline form^[1,2].

Due to the relative opacity, zirconia substructure needs to be veneered for better esthetic performance. Veneering porcelains are used to coat the surface of zirconia to enhance the natural appearance of prosthesis. Porcelain-veneered zirconia restorations are subjected to failure by the fracture of the veneering layers which dominant clinically observed failure mode and it is called chipping^[3].

Studies proved that nano silica had performed greatly in many branches of dentistry^[4,5]. Modifying zirconia surface in its pre-sintered stage is an effective

technique to change the properties of zirconia based dental restorations^[6].

Many previous studies documented that thermal and mechanical aging for the prediction of restorations durability is recommended as they simulate oral conditions in thermal and mechanical fluctuations with less period of time and they have great effect on the chipping resistance^[2,7,8].

Hypothesis: The treatment of zirconia core surface with nanosilica before sintering may increase the chipping resistance of the veneer layer.

Aim of the study: To evaluate the effect of nanosilica surface coating of pre-sintered zirconia on chipping of veneered zirconia crowns after thermocycling and cyclic loading.

Method

A model acrylic tooth (Typodont, Columbia)

simulating mandibular first molar was prepared after imbedding vertically in a cylindrical Teflon mold with self-cured acrylic resin (Trayresin™, Dentsply sirona, USA) to obtain a full anatomy ceramic crown preparation having the dimensions of 1.5mm Axial walls reduction, 2mm occlusal surface reduction and 1mm gingival margins reduction using a high speed hand piece (NSK, Tokyo, Japan), size 010,012 tapered diamond stones with flat end and size 012 flame shaped stone (Dentsply, sirona, UK). The angle of convergence was 6°-8° and all line angles were rounded to prevent stress concentration.

Twenty silicon impressions (Speedex®, Coltène/Whaledent AGAltstätten, Switzerland) were recorded for the prepared acrylic tooth by using double mix 2 steps technique (heavy and light). Impressions were poured by epoxy resin die material (Kemapoxy 150, CMB international, Egypt) and the resulted dies dimensions were measured by a digital caliper (APT, china). Dies with dimensions exceed the range of error ± 0.1 mm were discarded.

Each die was coated with a thin layer of optical reflection spray (Occlutec Spray, Renfert Dental Corp, USA) and optical impressions were recorded using a scanning machine (Ceramill map400, Amn Girschbach, Austria). Twenty zirconia cores (Ceramill zirconia, Amn Girschbach, Austria) were designed and milled by the aid of computerized milling machine (Ceramill map400, Amn Girschbach, Austria) with a uniform thickness of 1mm and with cuspal inclination of 30°. Milled cores were air dried with oil free air for 1 minute.

Nanosilica slurry was prepared by mixing the nanosilica powder of average size 40 wt% (Jiangsu, Mainland, China) with ethyl alcohol (Elahram, Cairo, Egypt) by ratio 4:1 wt%. The slurry was applied to the outer surface of zirconia cores with porcelain brushes size 4 and 6 (Koli, Bredent, Germany). Surface treated zirconia cores were sintered in a sintering furnace (Ceramill therm, Amn Girschbach, Austria) following the manufacturer instructions.

A full-contour wax pattern with cuspal inclination 30° was built up onto one of the copings to mimic the final veneer layer dimensions; silicon impression was recorded for the pattern. This silicon key provided a uniform thickness and shape of the veneer layer for all specimens. Veneering porcelain (GC® Initial, Illinois, America) was sequentially built up by the same technician following the manufacturer's instructions

with the help of the silicon key, followed by firing according to manufacturer instructions. The thickness of the crowns was measured with a digital caliper to ensure uniformity among all specimens.

Fired crowns were cemented to their corresponding dies using resin cement (Rely™ x ultimate 3M Deuschl and, Germany). The cement was mixed and applied to the fitting surface of the crowns according to manufacturer instructions. The crowns were seated firmly and 1 kg weight was applied to the occlusal surface for 3 minutes to ensure equal pressure for cementation of all specimens. That was followed by light curing (LED blue phase, Ivoclar Vivadent, Germany) from each side for 10 seconds. The specimens were left undisturbed for 15 minutes and were stored in distilled water for 24 hours.

The specimens were divided into 2 groups (n=10). Group I was the control and group II was subjected to thermocycling and cyclic loading before chipping resistance test. Thermocycling was done in thermocycling machine (Robota automated thermal cycle; Bilge, Turkey). Thermocycling was performed for 10000 cycles intermittently with a 300 cycles per day in a water bath; dwell times were 25 seconds in low temperature point of 5C° and the high temperature point was 55 C° with the lag time of 10 seconds.

The thermocycled crowns were stored in distilled water for 24 hours and then they were transferred to chewing simulator (Robota, ad-tech technology, Germany) to receive 10000 successive compression loads with 200N. All specimens were stored in distilled water for 24 hours.

For chipping resistance test each cemented crown was fixed in the lower jaw of the universal testing machine (Instron, 3345L8741, Assembled Canton, USA). Compressive load was applied directly to the central fossa of crowns by a steel ball (5mm in diameter) with rate of loading 0.5mm/min. A piece of polyethylene sheet was placed between the ball and the crown in order to properly distribute the load.

The area of loading was calculated by the help of articulating paper (Zogear, China) to determine the points of loading between cusps and the steel ball. As the cuspal inclinations were tangential to the steel ball in certain points so the line between two opposing points is the diameter of the formed circle. 3D CAD design software (Solid works 2015)^[9] was used to help in drawing the circle and calculating the area (Figure 1,2,3);

so by knowing the diameter of the drawn circle; the area could be calculated through the following equation:

$$A = \pi r^2$$

Load was applied until chipping of the veneer layer took place. The load at chipping for each specimen was recorded and the compressive chipping stresses were calculated using the following equation:

$$\text{Chipping stress (MPa)} = \frac{\text{Load at chipping (N)}}{\text{Stress area (mm}^2\text{)}}$$

Fractured surfaces were coated with gold by gold sputtering machine (JEOL, JFC-1100E, Fine coat, USA.) then examined by scanning electron microscope (SEM) (JSM-IT200, JEOL Ltd, Tokyo, Japan) and elemental analysis was performed by using energy dispersive x ray spectroscopy (EDX) in order to reveal the presence or absence of silica and its percentage.

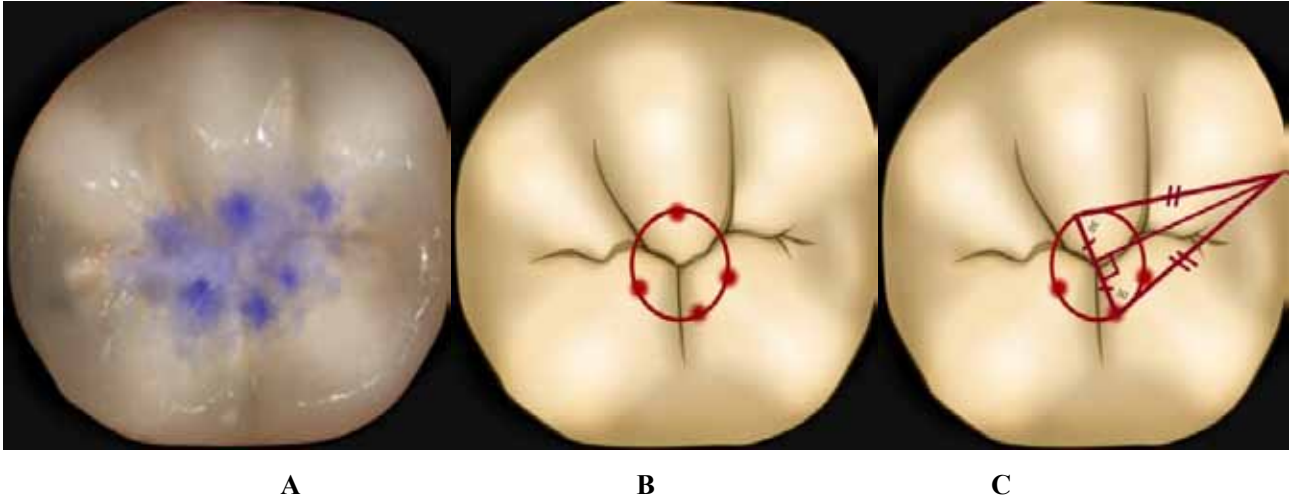


Fig. 1: Carbon paper marks show loading points of steel ball on the crown (A). Diagram defines the loading points (B). Method of calculation of area of loading (C).

Results

- I. **Chipping Resistance:** There was a significant difference between both groups in chipping resistance (p value was <0.05). Group I showed higher mean of chipping load which was 1300.404±340.361N with chipping stress of 413.877MPa. Group II mean of chipping load was 820.913±396.200N with chipping stress of 261.270MPa.

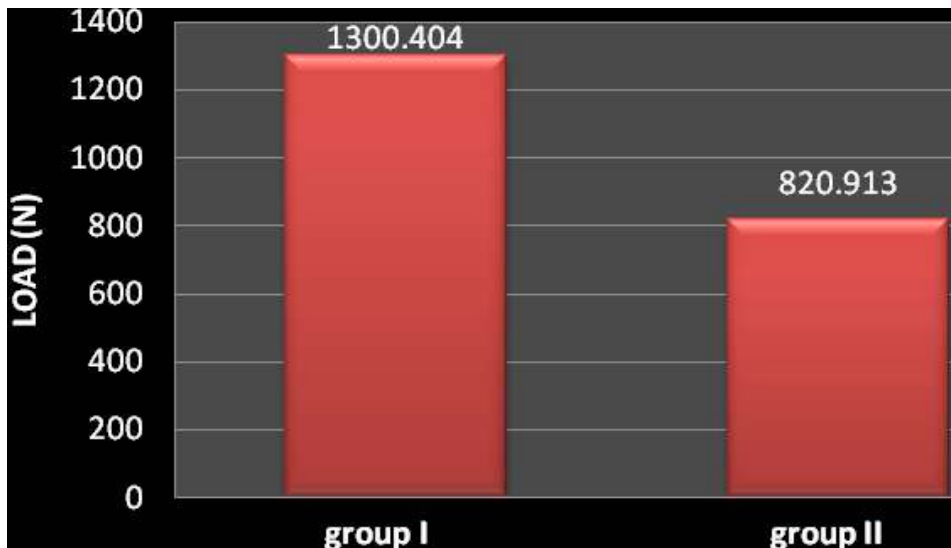


Fig. 2: Means of load at chipping of both groups.

II. SEM and EDX Results: Scanning electron microscope examination and EDX analysis showed that the mode of failure was mainly mixed (70% of specimens) in group I in which there was areas of zirconia not covered with nanosilica in EDX analysis. The failure was mainly adhesive (70% of specimens) in group II in which the zirconia surface was completely covered with nanosilica revealing that the fracture was between nanosilica layer and veneer layer (Figure 3, 4).

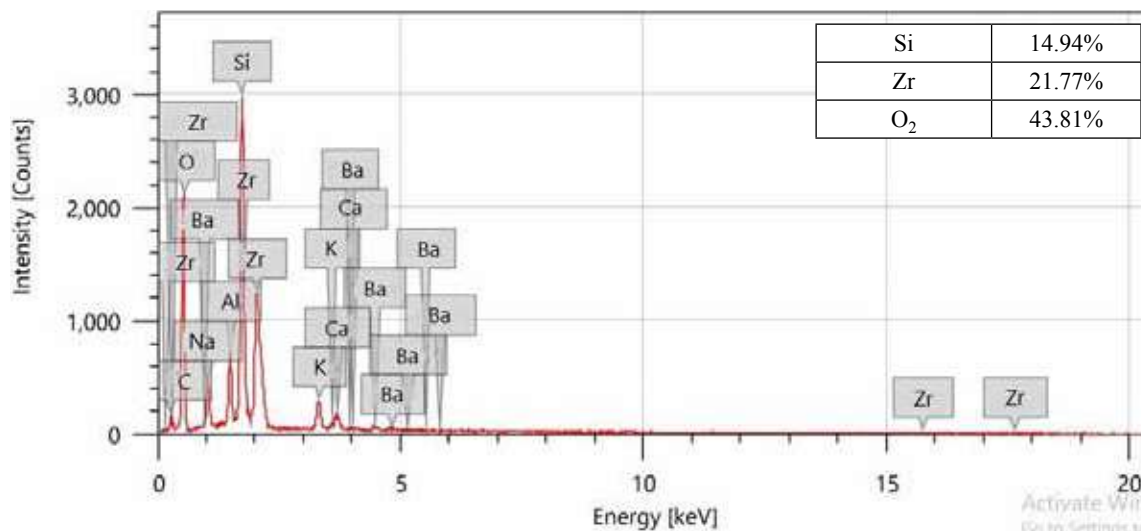


Fig.3: EDX analysis of zirconia surface of group I(Mixed mode of failure).

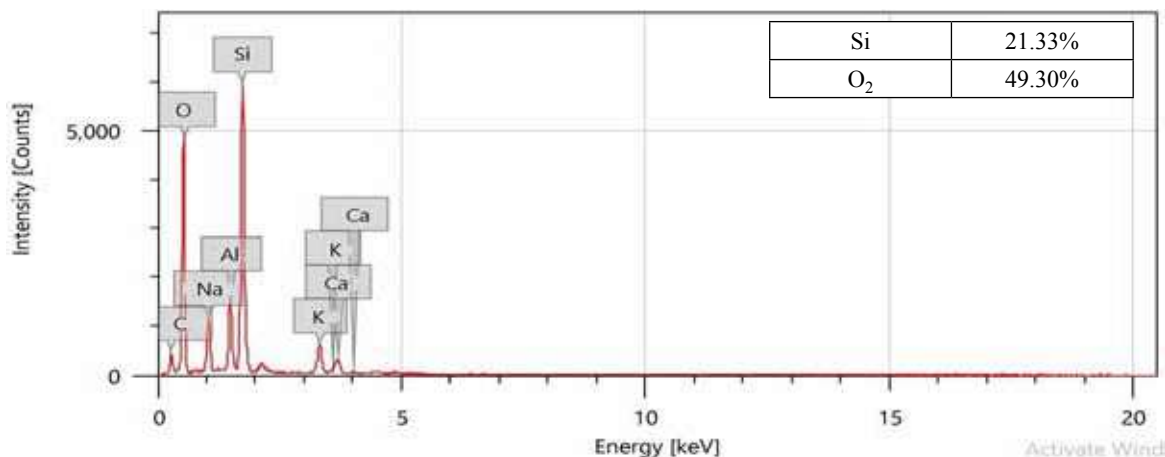


Fig.4: EDX analysis of zirconia surface of group II (adhesive mode of failure).

Scanning electronmicrographs of chipped zirconia showed areas of detachment in the mixed mode of failure and empty holes on the chipped veneers surface. In the adhesive mode of failure there were no empty holes (Figure 5).

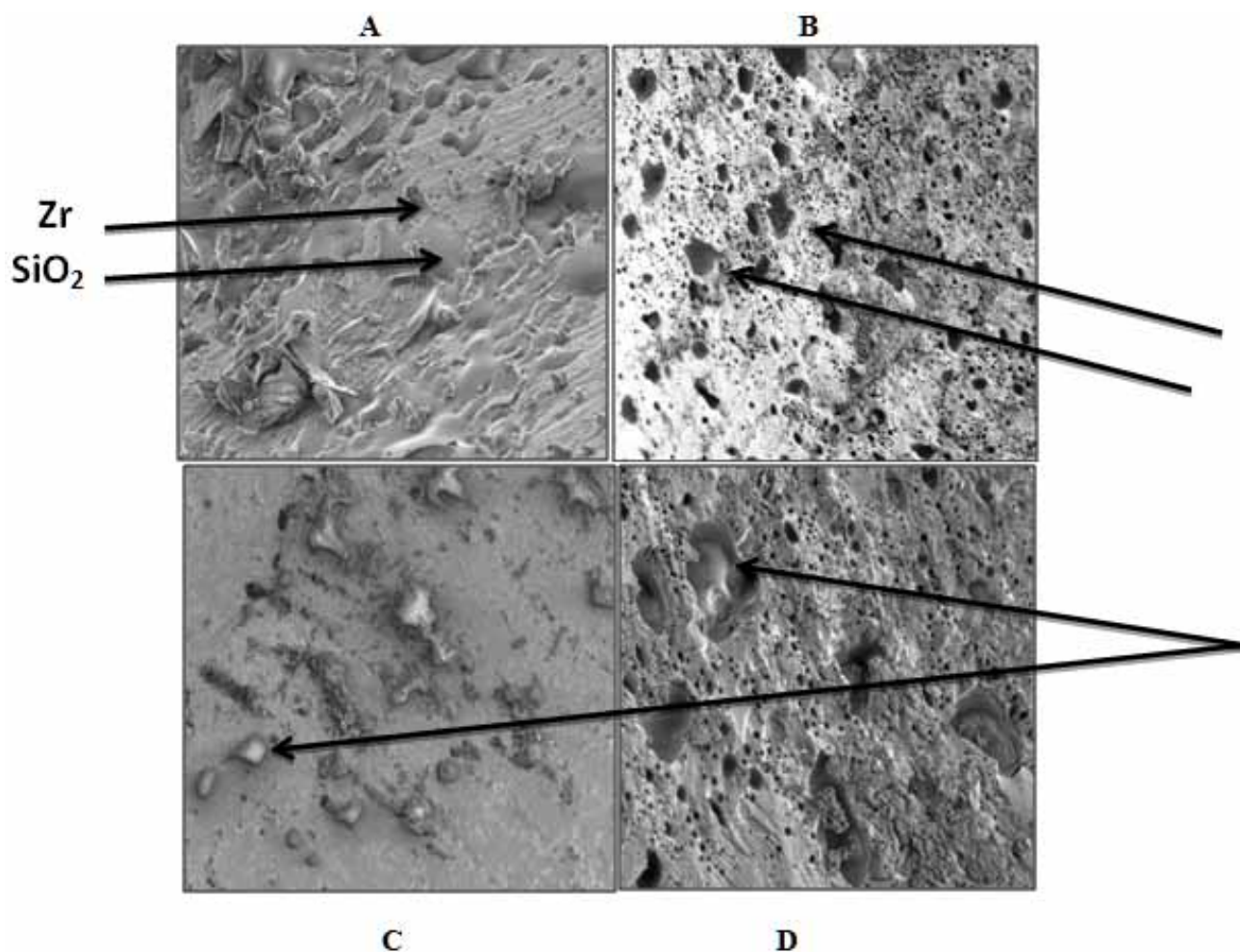


Fig.5: SEM (800X) micrographs show the surface topography of zirconia core of group I (A); arrows refer to elevations. The opposing porcelain veneer surface of the same sample (B) after chipping; arrows refer to empty holes (Mixed mode of failure). The surface topography of zirconia core of group II (C) and the opposing porcelain veneer surface of the same sample (D) after chipping; arrows refer to silica rich areas (adhesive mode of failure).

Discussion

The incidence of veneering porcelain fracture when a zirconia core is used became a major complication that has been reported in the dental literatures. The cause of veneer chipping is complex material factors, including differences in coefficient of thermal expansion between veneer and core, likely create residual stresses which enhance veneer chipping^[10-12]. Evaluation and comparing chipping resistance of veneered zirconia crowns had been conducted in several previous studies^[2,10].

This study was conducted to evaluate the chipping resistance of nanosilica treated zirconia-porcelain interface after thermocycling and cycling loading.

According to ISO 11405, the use of 500 thermal cycles between 5°C and 55°C is considered to be suitable to simulate short-term aging of dental materials^[13]. In addition, *Gale and Darvell*^[14] supposed that 10,000 cycles might represent approximately 1 year of *in vivo* functioning, with 20 to 50 cycles considered equivalent to a single day.

There is a large variation between number of cycles and the vertical loading applied in aging studies in the literature. Combining both thermocycling and cyclic loading is more clinically relevant protocol and might give prediction of longer time service^[2,15,16].

The resulted load which cause chipping of veneers of group I was comparable to the results of previous

studies with slight non-significant difference. This may be attributed to different techniques of veneering, different core design or thickness and different testing methodology^[17-19].

Group II showed lower chipping resistance than previous studies; however it is important to consider that both groups showed higher loads than the maximum chewing forces reported in literature of previous studies. Studied showed that the average maximum biting force of healthy and young adults is approximately from 400-700N^[20,21]. Therefore, the results indicated that the load at chipping of both tested groups in this study may withstand the clinical services without failure.

Mode of failure in group II was mainly adhesive failure between silica and veneer. As stated by many researchers^[22-24] that chipping mainly occurred due to difference in coefficient of thermal expansion which lead to unfavorable thermal stresses at the interface between silica and porcelain veneer layer. However, the SEM and the EDX results indicate the strong bond between the silica coat and zirconia.

The difference in coefficient of thermal expansion between silica and porcelain may be the cause of veneer chipping and lower chipping resistance than the control. This may draw a tension to the possibility of using a veneering ceramic compatible with the nanosilica coat.

Conclusions

Within the limitations of this study it was concluded that:

1. The treatment of pre-sintered of zirconia cores with nanosilica before sintering without aging lead to high chipping resistance.
2. Aging decreased this resistance to chipping but it is still within acceptable limits of human maximum biting force.

Recommendation:

1. Nanosilica layer thickness, particle size and shape play great role and should be subjected for further research.
2. The results of this study did not support the hypothesis but revealed that surface treatment of pre-sintered zirconia with nanosilica is a potential cause increasing chipping resistance if the composition of the veneering ceramics is modified to be compatible

with the coefficient of thermal expansion of the nanosilica.

Ethical Clearance: Was taken from Faculty of Dentistry, Minia University.

Source of Funding: Was self-funding.

Conflict of Interest: Nil.

References

1. Bona A, Pecho O, Alessandretti R. Zirconia as a dental biomaterial. *Materials*. 2015;8(8):4978-91.
2. Alsarani M, Souza G, Rizkalla A, El-Mowafy O. Influence of crown design and material on chipping-resistance of all-ceramic molar crowns: An in vitro study. *Dental and medical problems*. 2018;55(1):35-42.
3. Benetti P, Pelogia F, Valandro LF, Bottino MA, Della Bona A. The effect of porcelain thickness and surface liner application on the fracture behavior of a ceramic system. *Dental materials*. 2011;27(9):948-53.
4. Priyadarsini S, Mukherjee S, Mishra M. Nanoparticles used in dentistry: A review. *Journal of oral biology and craniofacial research*. 2018;8(1):58-67.
5. Golpayegani MV, Sohrabi A, Biria M, Ansari G. Remineralization effect of topical NovaMin versus sodium fluoride (1.1%) on caries-like lesions in permanent teeth. *Journal of dentistry (Tehran, Iran)*. 2012;9(1):68.
6. Skienhe H, Habchi R, Ounsi H, Ferrari M, Salameh Z. Structural and Morphological Evaluation of Presintered Zirconia following Different Surface Treatments. *The journal of contemporary dental practice*. 2018;19(2):156-65.
7. Blatz MB, Bergler M, Ozer F, Holst S, Phark J-H, Chiche GJ. Bond strength of different veneering ceramics to zirconia and their susceptibility to thermocycling. *American journal of dentistry*. 2010;23(4):213-6.
8. Bhowmick S, Meléndez-Martínez JJ, Zhang Y, Lawn BR. Design maps for failure of all-ceramic layer structures in concentrated cyclic loading. *Acta materialia*. 2007;55(7):2479-88.
9. Corporation DSS. 175 Wyman Street, Waltham, Mass. 02451 USA: a Dassault Systèmes S.A. company; 2015.

10. Shahin AMA-W, Ahed Mohammed. Masri, Radi M. Zirconia-Based Restorations: Literature Review. *International Journal of Medical Research Professionals* 2017;3(2):253-60.
11. Larsson C, Wennerberg A. The clinical success of zirconia-based crowns: a systematic review. *International Journal of Prosthodontics*. 2014;27(1):253-60.
12. Sailer I, Gottner J, Känel S, Franz Hämmerle CH. Randomized controlled clinical trial of zirconia-ceramic and metal-ceramic posterior fixed dental prostheses: a 3-year follow-up. *International Journal of Prosthodontics*. 2009;22(6):553-60.
13. Standardization IOF. Testing of adhesion to tooth structure. 3rd ed. Geneva.: International Organization for Standardization; 2015.
14. Gale M, Darvell B. Thermal cycling procedures for laboratory testing of dental restorations. *Journal of dentistry*. 1999;27(2):89-99.
15. Kelly JR. Clinically relevant approach to failure testing of all-ceramic restorations. *The Journal of prosthetic dentistry*. 1999;81(6):652-61.
16. Wiskott HW, Nicholls JI, Belser UC, Wiskott H, Nicholls J, Belser U. Stress fatigue: Basic principles and prosthodontic implications. *International Journal of Prosthodontics*. 1995;8(2):105-16.
17. Vigolo P, Mutinelli S. Evaluation of zirconium-oxide-based ceramic single-unit posterior fixed dental prostheses (FDPs) generated with two CAD/CAM systems compared to porcelain-fused-to-metal single-unit posterior FDPs: a 5-year clinical prospective study. *Journal of Prosthodontics: Implant, Esthetic and Reconstructive Dentistry*. 2012;21(4):265-9.
18. Sorrentino R, De Simone G, Tetè S, Russo S, Zarone F. Five-year prospective clinical study of posterior three-unit zirconia-based fixed dental prostheses. *Clinical oral investigations*. 2012;16(3):977-85.
19. Örtorp A, Kihl ML, Carlsson GE. A 5-year retrospective study of survival of zirconia single crowns fitted in a private clinical setting. *Journal of Dentistry*. 2012;40(6):527-30.
20. Gibbs CH, Anusavice KJ, Young HM, Jones JS, Esquivel-Upshaw JF. Maximum clenching force of patients with moderate loss of posterior tooth support: a pilot study. *The Journal of prosthetic dentistry*. 2002;88(5):498-502.
21. Ferrario VF, Sforza C, Zanotti G, Tartaglia GM. Maximal bite forces in healthy young adults as predicted by surface electromyography. *Journal of dentistry*. 2004;32(6):451-7.
22. Özkurt Z, Kazazoglu E, Ünal A. In vitro evaluation of shear bond strength of veneering ceramics to zirconia. *Dental materials journal*. 2010;29(2):138-46.
23. Hermann I, Bhowmick S, Lawn BR. Role of core support material in veneer failure of brittle layer structures. *Journal of Biomedical Materials Research Part B: Applied Biomaterials*. 2007;82(1):115-21.
24. Sui T, Dragnevski K, Neo TK, editors. Mechanisms of failure in porcelain-veneered sintered zirconia restorations. *ICF13*; 2013.

Assessment of Fracture Force of CAD-CAM-fabricated Occlusal Veneer Restorations with Different Thicknesses

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Abstract

Purpose: To evaluate the fracture force of occlusal veneer restorations using ceramic material (Lithium di-silicate) and hybrid ceramic (VITA Enamic) Computer Aided Design/Computer Aided Manufacturer (CAD/CAM) material at different thicknesses after thermocycling.

Material and Method: Thirty CAD/CAM occlusal veneer restorations were fabricated from group E (IPS e.max CAD), V (VITA Enamic) and divided into subgroups according to thickness 0.3, 0.6, 1 mm. The occlusal veneers were luted to epoxy dies (n=5). The specimens were subjected to thermocycling test then they were subjected to load until fracture using a computer controlled materials testing machine. Data were tabulated and statistically analyzed using Two-ways analysis of variance (ANOVA).

Results: There was no significant difference in the fracture force between the two materials regardless the thickness. The fracture force increases with the increase of the thickness.

Conclusion: VITA Enamic hybrid ceramic material is closer to IPS e.max CAD ceramic material in the fracture force. With the increase of thickness, it leads to increase of fracture force.

Clinical Implication: Within the limitation of this in-vitro study, hybrid ceramic (VITA ENAMIC) and IPS e.max CAD are clinically applicable as occlusal veneer restoration with thickness 0.6 mm and more.

Keywords: Hybrid ceramics, Fracture force, CAD/CAM.

Introduction

Ceramics are the materials of choice as long term functional indirect restorations, due to their properties esthetic, biocompatibility and high strength. Nowadays dental technologies such as CAD/CAM are in continuous evolution offering both, the dentist and the patient. All ceramic restorations are cemented by using resin cement as they provide low solubility and they have high bond strength and better esthetic. Due to high bond strength of resin to tooth structure and complicated bonding between ceramic and tooth structure, resin was added to ceramic material to make a new compound structure called hybrid ceramics. Resin bonding is required for clinical success of indirect restorations at long time. With the use of CAD/CAM indirect restorations, there is a need for successful bonding for new hybrid ceramic materials.⁽¹⁶⁾ All ceramic materials are superior to composite in its physical and mechanical properties.

The hypothesis of this study, that there is a significant difference between all ceramic and hybrid ceramic occlusal veneer restorations; the fracture force of all ceramic is better than hybrid ceramic.

Materials and Method

The materials were used are: IPS e.max CAD ceramic blocks; low translucency, shade A2 and size C14 (Ivoclar Vivadent/ Italy), VITA ENAMIC Innovative ceramic blocks; low translucency, shade 2M2 and size C14 (VITA Zahnfabrik spitalgasse 3 D-79713 Bad Säckingen Germany), and RelyX™ Ultimate adhesive dual cured resin cement (3MESPE, Seefeld, Germany).

Sample Size Calculation for Fracture Force Test: A sample size of 15 samples in each group was determined to provide 80% power for independent samples T test at the level of 0.05 significance using G

Power 3.19.2 software. So we made our study on 15 samples for each material (5 samples for each thickness). (Figure 1).

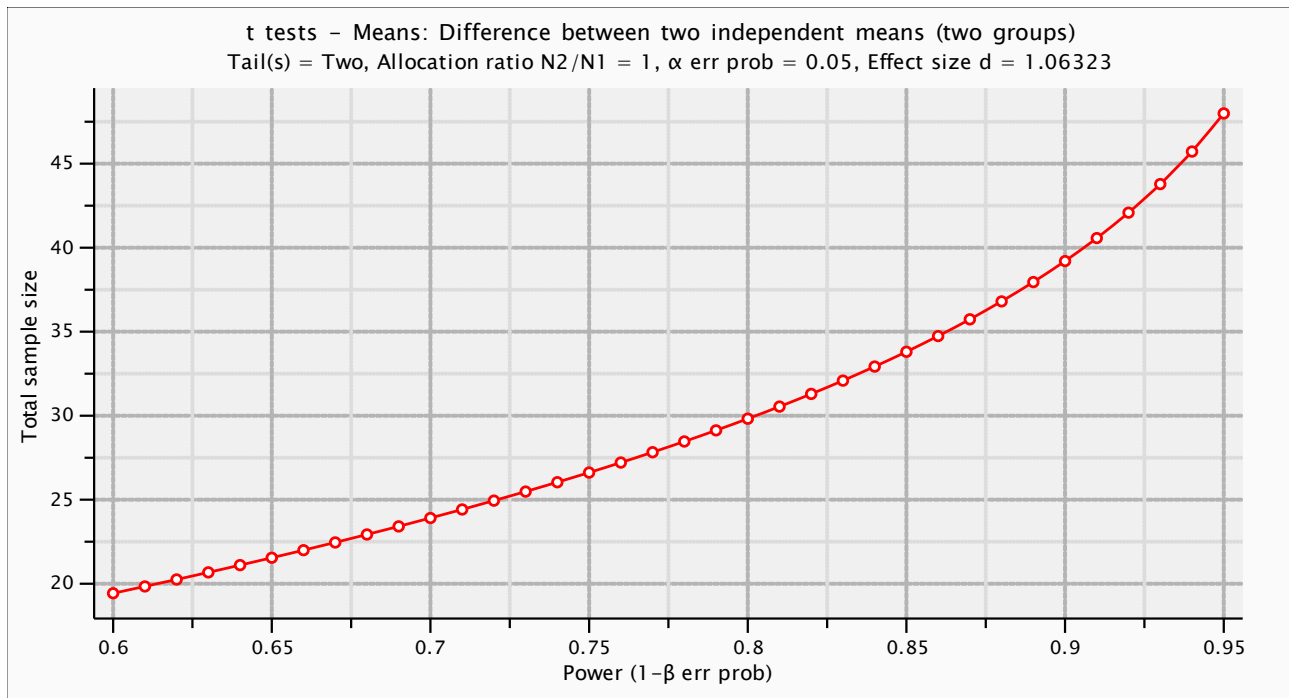


Figure 1:

Maxillary molar teeth with occlusal dimension average size (6mm x 5mm) were collected from the outpatient clinics of faculty of Dentistry Minia University. Teeth were freshly extracted, free from caries, restorations and fracture. The teeth were ultrasonically cleaned (Coltene Whaledent, Biosonic UC50 Ultrasonic, USA) of any surface debris then they were ready for use for samples construction.

Proper powder/ liquid ratio of self-curing acrylic resin (cold cure acrylic resin, Acrostone, Egypt) was mixed according to the manufacturer’s instructions. As it reached the dough stage, it was poured into customade split Teflon mold with (2.5cm diameter x 2.5cm height). The roots of the tooth were inserted into the center of the mold till 2 mm apical to the cement enamel junction. With the use of customade paralleling device (Egypt), to centralize the tooth in the mold. The excess of the acrylic resin was rapidly removed with metallic wax carver (Miltex. Stainless steel. pakistan). After complete polymerization of acrylic resin, the split Teflon mold was removed. The samples were subjected to uniform occlusal reduction with diamond cutting tools (Komet Dental. Gabr. B raseler GmbH & Co.KG Trophagener Weg 25.32657 Lemgo. Germany.)

to produce a uniform preparation. Before preparation, condensation silicone rubber base (Speedix putty Ivoclar Vivadent, Liechtenstein) indices were made for tooth to aid in standardization of preparation thickness Silicone indices made by hand mixing of putty paste with catalyst according to manufacturer’s instructions and loaded into a custom made metallic perforated tray. After impression setting, the index was removed⁽¹²⁾.

The molar teeth were prepared manually using diamond cutting stones size 14 with high speed handpiece (W & H Dental Work, Burmoos, Austria) under water cooling. The occlusal surface reduction was 0.3 & 0.6 & 1.0 mm at the central fossa⁽¹⁹⁾.

The preparations resulted were flat occlusal reduction without finish line (butt joint preparation). The three different preparation thicknesses were checked using a digital caliper (Miltex, stainless steel, Pakistan) with the silicon guide on the preparation. Epoxy resin dies construction; by the use of custom made perforated tray that has an internal diameter of 20 mm and 25 mm height⁽²⁴⁾.

Thirty impressions of prepared teeth were made using condensation silicone rubber base impression

material (Speedix, Ivoclar VivaDent, Liechtenstein) by hand mixing according to manufacturer's instructions. The impression was loaded into the tray, prepared tooth was embedded in the impression and after setting the tooth was removed. The impression was poured by epoxy resin (kemapoxy 150, CMB, Egypt). The method was repeated to create sixty epoxy dies. One size of epoxy paste and 1.5 size of activator were mixed under vibration (Vibromaster Bego Bremer, GmBA, Germany) for two minutes then it was left ten minutes before pouring to become homogenous mixture. The mixture was poured into the impression and left to set for 48 hours in order to reach complete setting and dimensional stability. The dies were removed from impressions, then was finished by low speed straight hand piece (Sirona Dental systems GmbH Fabrikstra Be 31 64625 Benesheim Germany) and polished by pumice (Dental Lab Pumice, Dentsply, USA) with smooth electronic brush (Miltex. Stainless steel. Pakistan).

Occlusal surfaces were surface roughened by low speed wheel stone (Komet Dental. Gabr. B raseler GmbH & Co.KG Trophagener Weg 25.32657 Lemgo. Germany) and it was ready for occlusal veneers construction (Figure 2).



Figure 2: Epoxy die

Designing, milling and crystallization of occlusal veneers; all occlusal veneers (IPS e.max CAD & VITA ENAMIC) were fabricated according to the direction of manufacturing companies for each fabrication system. Epoxy dies were scanned sequentially with camera system without powder (Cerec Omnicam 4.4.4 by Dentsply Sirona). Designing of all occlusal veneers were carried out using a standard protocol, on the computer software.

The thickness of occlusal veneers was 0.3 mm, 0.6 mm and 1.0 mm.

The integrity of the structure was visually checked before crystallization. The IPS e.max ceramic occlusal veneers were placed into the oven (programat P310

by ivoclar vivadent) for crystallization. At the end, the veneers were removed from the oven when it reached at room temperature. (Figure 3)



Figure 3: Visual veneer in position

Cementation of the occlusal veneers to the corresponding epoxy resin dies; occlusal veneers were etched using hydrofluoric acid gel 9.5% (BISCO-Schaumburg U.S.A) for 60 seconds, for VITA ENAMIC and 90 seconds, for IPS e.max CAD according to manufacturer instructions. After etching, the veneers were washed with water and dried using air spray (dental chair Roson. China). Then, veneers were brushed by silane coupling agent (BISCO-Schaumburg U.S.A) and wait for 30 seconds then it was dried with air syringe according to manufacturer instructions. Epoxy dies were left clean dry; bonding agent (Adper Single Bond 3M ESPE U.S.A) was brushed to the epoxy dies and light cured (Denjoy, China) for 20 seconds.

Rely X-Ultimate dual cured resin cement clicker was used. One click applied on the veneer and applied on the die and loaded by the loading device 6 N load⁹

Under load, the excess was removed then curing of the samples for 40 seconds.

After complete cementation of all occlusal veneers, the samples were ready for the tests. (Figure 4).



Figure 4: Sample after cementation

Thermocycling Procedures: In this study the number of cycles used was 1000 cycles representing nearly 2years clinically. Dwell times were 25s in each water bath (Robota automated thermal cycle; BILGE, Turkey) with a lag time 10s. The low-temperature point was 5°C. The high temperature point was 55°C.

Fracture Force test: According to manufacturer instructions, samples were secured to the lower fixed compartment of testing machine by tightening screws. Fracture test was done by compressive mode of load applied occlusally using a metallic rod with spherical tip (5.6 mm diameter) attached to the upper movable compartment of testing machine (Model 3345; Instron Industrial Product, Norwood, MA, USA) travelling at cross-head speed of 1mm/min. The load at failure manifested by an audible crack and confirmed by a sharp drop at load-deflection curve recorded using computer software (Bluehill Lite Software Instron Instruments). The load required to fracture was recorded in Newton.

Results

There was no significant difference in the fracture force between the two materials regardless the thickness. There was significant difference between different thicknesses regardless the material type. There was no significant difference between the two materials at thickness of 0.3mm. In the group with 0.6 and 1mm thicknesses, there was a significant difference and IPSe.max CAD had higher strength than VITA Enamic. The fracture strength increases with the increase of the thickness in both materials.

1. Fracture Force Measurement:

Table 1: Effect of material, thickness and interaction between both on Fracture force

Fracture force	F	P Value
Material	12.89	0.001*
Thickness	92.98	<0.001*
Material * Thickness	1.49	0.245

Two-ways-ANOVA test, *: Significant level at P value < 0.05

Table 2: Comparison of fracture force between the two materials regardless the thickness

		Material		P value
		E-max N=15	Vita Enamic N=15	
Fracture force	Range	(632.5-2310)	(547.3-1723)	0.272
	Mean ± SD	1329.5±552.9	1096.5±418.3	
	Median	1292.5	1049	

Mann Whitney test for non-parametric quantitative data (expressed as median) between the two groups, Significant level at P value < 0.05

Table 3: Comparison of fracture force between the different thicknesses regardless the Material type

		Thickness			P value
		0.3 mm	0.6 mm	1 mm	
		N=10	N=10	N=10	
Fracture force	Range Mean ± SD	(547.3-846) ^c 706.5±93.3	(820-1393.8) ^b 1147.8±188.1	(1410-2310) ^a 1784.8±309.7	<0.001*

One-way ANOVA test for parametric quantitative data between the three groups followed by post hoc analysis between each two groups, Superscripts with different small letters refer to a significant difference between each two groups, *: Significant level at P value

< 0.05

Discussion

Egbert J S, et al (2015) stated that in case of patient with severely worn dentition, CAD/CAM occlusal veneer restoration made of hybrid ceramic is an alternative

to full coverage restorations. The failure load of teeth restored with full coverage with 1.5- 2.00 mm was to be 771-1183 N⁽³⁾, that is lower than this study (1727-2415). This fracture strength was reported to be higher than human masticatory forces (585-880) **Kikuchi M et al, 1997.**

In accordance to **Chen C, et al (2014)** reported that with increase the thickness of IPS e.max CAD, the fracture resistance increased. There is no change between 0.5 mm and 1.5 mm thickness but sharp increase occurred at 2.0 mm. The normal occlusal load is 100 N-200 N in the molar area and 965 in accidental bite. 1000 N is required for clinical longevity. This requirement was achieved in the test specimens of Chen et al, 2014 and also at 0.5 mm or 1.0 mm thickness.^(4 & 5 & 6).

Stawarczyk B et al (2016) reported that the fatigue resistance of occlusal veneers was increased by CAD/CAM composite in comparison with lithium disilicate ceramics (Schlichting et al., 2011). Results of their study (Stawarczyk) CAD/CAM revealed higher flexural strength than VITA Enamic, but lower than lithium disilicate ceramic.

Hamburger J T, et al (2014): Using a total-etch adhesive system improved the resistance to fracture⁽⁷⁾. Normal occlusal forces are 50-300 N and reaches to 1200 N in case of clenching⁽⁸⁾. E.max CAD showed minimal occlusal thickness 1.5 mm. In the study of **Hamburger J T, et al;** Direct composite restorations give good properties at high occlusal load.

The hypothesis of this study was partially rejected that there was no significant difference between IPS e.max and VITA Enamic materials in fracture force test but there was a significant difference between the two materials at 0.6 mm thickness.

Conclusion

Within the limitation of this study:

1. IPS e.max CAD and VITA Enamic are clinically applicable for occlusal veneer restorations and they are closer to each other in the fracture force.
2. Thickness has great effect on the restoration force, as with increase of the thickness the force increases.
3. Thin thickness as 0.3 has questionable survival in the oral environment. In case of patients with bruxism, it is advised to use restoration thickness not less than 0.5 mm.
4. Occlusal veneer restorations are advised to be used as a conservative approach and accepted force.

References

1. Martin R, Tobias P, Carola K, Michael B and Gerhard H. The in vitro fracture force and marginal adaptation of ceramic crowns fixed on natural

- and artificial teeth. *J Prosthodontics* (2000);p387-391.5p.
2. 68. Rosenstiel S F, Land M F and Fujimoto J. *Contemporary fixed Prosthodontics*. 3rd ed., Mosby, St Louis, USA, 2001.
3. Pallis K, Griggs J A, Woody R D. Fracture resistance of three all-ceramic restorative systems for posterior applications. *J Prosthet Dent* 2004;91:561-9.)
4. Thompson V P, Rekow D E. Dental ceramics and the molar crown testing ground. *Journal of Applied Oral Science: Revista FOB* 2004;12:26-36.
5. Kurtoglu C, Uysal H, Mamedov A. Influence of layer thickness on stress distribution in ceramic-cement dentin multilayer system. *Dental Materials Journal* 2008;27:626-32.
6. Ohlmann B, Gruber R, Eickemeyer G, Rammelsberg P. optimizing preparation design for metal-free composite resin crowns. *Journal of Prosthetic Dentistry* 2008;100:211-9.
7. Al-Wahadni A, David J H, Grey N and Hatamleh M. The fracture resistance of Aluminium Oxide and Lithium Disilicate-based crowns using different luting cements: An in vitro Study. *J Contemp Dent Pract* 2009 March; (10)2:051-058.
8. Magne P, Schlichting L H, Pires H M and Narciso L B. In vitro fatigue resistance of CAD/CAM composite resin and ceramic posterior occlusal veneers. *J Prosthet Dent* 2010;104:149-157.
9. Henrique L S, Pires H M, Narciso L B, Magne P. Novel-design Ultra-thin CAD/CAM composite resin and ceramic occlusal veneers for the treatment of severe dental erosion. *J Prosthet Dent* 2011;105:217-226.
10. Davidowitz G and Kotick P G. The use of CAD/CAM in Dentistry. *Dent Clin N Am* 55 (2011) 559-570.
11. He H L and Swain M. A novel polymer infiltrated ceramic dental material. *Dental materials* 27 (2011) 527-534.
12. (Korkut L, Cotret H S, Kurtulmus H. Marginal, internal fit and microleakage of zirconia infrastructures: An in-vitro study. *Oper Dent* 2011; 36:72-79.)
13. Sorrentino R., De Simone G. and Tetè S. "Five-year prospective clinical study of posterior three-unit zirconia-based fixed dental prostheses" *Clin Oral Invest.* 2012; 16:977-985.)
14. Coldea A, Swain V M and Thiel N. Mechanical

- properties of polymer-infiltrated-ceramic-network. *Dental Materials* 29 (2013) 419-426.
15. Kurbad A and Kurbad S. Anew, hybrid material for minimally invasive restorations in clinical use. *International Journal of computerized Dentistry* Jan 2013, 16 (1):69-79.
 16. Spitznagel A F, Horvath D S, GUESS C P and Blatz B M. Resin bond to indirect composite and new ceramic/polymer materials: A review of the literature. (*J Esthet Dent* 26:382-393. 2014).
 17. Ruse N D and Sadoun M J. Resin-composie blocks for dental CAD/CAM applications. *J Dent Res* 2014.
 18. Hamburger J T, Opdam N J, Bronkhorst E M and Huysmans M C. Indirect restorations for severe tooth wear: fracture risk and layer thickness. *J of Dentistry* 42 (2014) 413-418.
 19. Johnson A C, Versluis A, Tantbirojn D and Ahuja S. The fracture strength of CAD/CAM composite and composite-ceramic occlusal veneers. *J of Prosthodontic research* 58 (2014) 107-114.
 20. Ruse N D and Sadoun M J. Resin-composie blocks for dental CAD/CAM applications. *J Dent Res* 2014.
 21. Della A B, Corazza P H and Zhang Y. Characterization of a polymer-infiltrated ceramic-network material. *Dental Materials* 30 (2014) 564-569.
 22. (Baciu S., Burde A., Grecu A. "Particularities of laboratory procedures for obtaining an aesthetic overlay with Cerec technology" *Inter J Medical Dent.*2014;4:313-317.)
 23. Awada A and Nathanson D. Mechanical properties of resin-ceramic CAD/CAM restorative materials. *J Prosthet Dent* 2015;114:587-593.
 24. Stawarczyk B, Liebermann A, Eichberger M and Guth J. Evaluation of mechanical and optical behavior of current esthetic dental restorative CAD/CAM composite. *J of the mechanical behavior of biomedical materials* 55 (2016) 1-11.

Antibacterial Activity of Sappan Wood (*Caesalpinia Sappan L.*) against *Aggregatibacter Actinomycetemcomitans* and *Porphyromonas Gingivalis*

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Abstract

The aim of this study was to find the Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) of sappan wood ethanol extract (*Caesalpinia sappan L.*) toward the growth of *A. actinomycetemcomitans* and *P. gingivalis*. The randomized posttest only control group design was applied to this study. The sappan wood ethanol extract was conducted with maceration method using 96% ethanol. Diluted to 50%, 25%, 12.5%, 6.25%, 3.125%, 1.56%, 0.78%, and 0.39% concentration. The MIC and MBC values of sappan wood ethanol extract toward *A. actinomycetemcomitans* and *P. gingivalis* was then known via the evaluation for Colony Forming Units (CFUs) in MH medium. The MIC and MBC of sappan wood ethanol extract toward *A. actinomycetemcomitans* and *P. gingivalis* was at 1.56% and 3.125% concentration. The ethanol extract of sappan wood reduces the number of bacterial colonies significantly at $p=0.00$. This study concluded that the growth of *A. actinomycetemcomitans* and *P. gingivalis* can be inhibited by sappan wood ethanol extract (*Caesalpinia sappan L.*) at MIC 1.56% and MBC 3.125% concentration.

Keywords: Sappan Wood Ethanol Extract, MIC, MBC, *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*.

Introduction

Periodontal disease is a chronic inflammatory disease that affects the gum tissue and bone supporting the teeth, which is indicated by gingival inflammation and periodontal pockets (periodontitis) and the second most common dental disease suffered by the world population. Periodontitis is a chronic infectious disease caused by microorganisms. Its key features include periodontal pocket formation, loss of connective tissue attachment, alveolar bone resorption, and gingival inflammation. The studies states that periodontal disease occurs in 20-50% of the entire population, and can

increase the risk of cardiovascular disease by 19%; this risk increases by 44% at the 65 years old.^{1,2,3} It is not yet known for sure of the complications that can happen in patients with untreated caries or periodontal disease. Those conditions can cause pain, distinction, bad appearance, and disruption of everyday activity.^{4,5}

Periodontitis can be treated mechanically, surgically, and with supportive treatment. *Chlorhexidine* is one of the mouthwashes often recommended for supportive treatment to treat periodontal disease because of its antibacterial and antiplaque effect. Extended usage of *chlorhexidine* could lead toward changes in tooth color and dorsal part of the tongue, increasing the buildup of calculus, change the taste perception and drying of the oral mucosa.^{6,7} Antibiotic can be used as a supportive treatment because of its ability to decrease the bacterial growth that still exists after mechanical therapy. But, even so, the inaccurate and extended administration of antibiotic could lead to bacterial resistance, this has created the need for a therapy using natural ingredients with antibacterial effects to be developed.^{8,9}

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Sappan (*Caesalpinia sappan* L.) is a plant from the *Febaceae* family which grows in tropical region and the stem of the plant has been used as traditional medicine since previous times.¹⁰ Sappan wood contains active compounds in the form of flavonoids, which are homoisoflavonoid, brazilin, protosappanin and chalcone, saponin, terpenoid and tannin.¹¹ Brazilin acts as an antibacterial agent to inhibit the synthesis of amino acid and cellular proteins in bacteria. Thus, Brazilin has a high antibacterial efficacy toward *S. mutans*, a caries-triggering bacteria and *P. intermedia*, a negative gram bacteria that causes periodontal diseases.^{12,13} In previous study, sappan wood was proven to be able to inhibit bacterial growth such as *S. typhi*, *K. pneumonia*, *E. coli*, *B. subtilis*, *P. aerogenosa* and *S. aureus*.¹⁴ Sappan wood extract has an antibacterial effect against *E. faecalis*, *S. salivarius*, *S. sanguinis* and *A. viscosus*.¹⁵ The aim of this study was to find the Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) of sappan wood ethanol extract (*Caesalpinia sappan* L.) toward the growth of *A. actinomycetemcomitans* and *P. gingivalis* which caused periodontal infections.

Materials and Method

The bark from sappan wood which has been crushed to a powder was collected by 1650 gram, then macerated twice with 96% ethanol, then inserted to a digital shaker with the speed of 50rpm for 24 hours and then filtered with a cloth filter to obtain filtrate. The filtrate was then evaporated using Rotary Vacuum Evaporator at the temperature of 40°C for 13 hours until a thick extract with 100% concentration was obtained.¹⁶

A colony of bacteria that was taken from the stock using sterile inoculation loop was inserted to the BHIB. After that, the bacterial culture in the BHIB medium was inserted to an anaerobic jar in an anaerobe state and incubated inside an incubator at the temperature of 37°C for 24 hours. Then, the culture's turbidity was observed to be equalized with the 0.5 McFarland standard (1.5×10^8 CFU/ml). Eleven sterile reaction tubes were prepared and labeled with numbers 1-9, (+) for the positive control group and (-) for negative control group. The number 1 sterile tube was filled with 10ml of 100% sappan wood ethanol extract, and, in tube numbers 2-9, the positive control tubes and negative control tubes were filled with 5ml of BHIB medium. Then, 5ml of solution from tube 1 was added into tube 2, thus, half the concentration of sappan wood ethanol extract was obtained by mixing 5ml of BHIB and 5ml

of 100% sappan wood ethanol extract. After that, 5ml of mixture was taken from tube number 2 and inserted in tube number 3 to obtain 25% concentration of ethanol extract. The procedure was repeated until tube number 9 so that a group of sappan wood ethanol extract with 12.5%, 6.25%, 3.125%, 1.56%, 0.78%, and 0.39% was obtained. The positive control tubes contained BHIB medium and bacteria, and the negative control tubes only contained BHIB medium; 0.1ml bacteria was then inserted into tube numbers 1-9 and the positive control tubes. All tubes were incubated at the temperature of 37°C for 24 hours to observe the turbidity after the procedure. Results from the dilution technique were then cultivated in the *Mueller Hinton* medium with streak method to obtain MIC and MBC number.¹⁷ In order to obtain a more accurate result, 0.1 ml of bacteria from each tube, including positive and negative control, was subcultured with spreader method on a *Mueller Hinton* medium to count the number of bacterial colonies that had grown. The calculation of growing colony in each concentration was manually counted three times, each with a different observer.

The data of the bacterial colonies was analyzed statistically using SPSS version 13.0 (IBM, Armonk, New York, USA). We performed Anova to compare CFU between groups concentration and the post hoc analysis was performed using Tukey Honest Significant Difference Test (HSD).

Findings: According to the qualitative phytochemical analysis of the sappan wood ethanol extract, contents of flavonoid, alkaloid, saponin, and terpenoid active substances were discovered to have antibacterial potential (Table 1).

Table 1. Phytochemical Test Result on Sappan Wood Ethanol Extract

Active Substance	Phytochemical Test Result
Flavonoid	+
Tannin	+
Terpenoid	+
Saponin	+
Alkaloid	+

+ it means contains active compounds

Dilution method was carried out in order to find the antibacterial potential of sappan wood ethanol extract, (*Caesalpinia sappan*), hence, its Minimum Inhibitory Concentration (MIC) and Minimum Bacterial Concentration (MBC). This method was done by adding

sappan wood ethanol extract into BHIB, in which after, *A. actinomycetemcomitans* and *P. gingivalis* were inserted to be tested. The result of the dilution method continued with cultivation in each tube with streak method in a *Mueller Hinton* medium to obtain MIC and MBC (Figure 1).

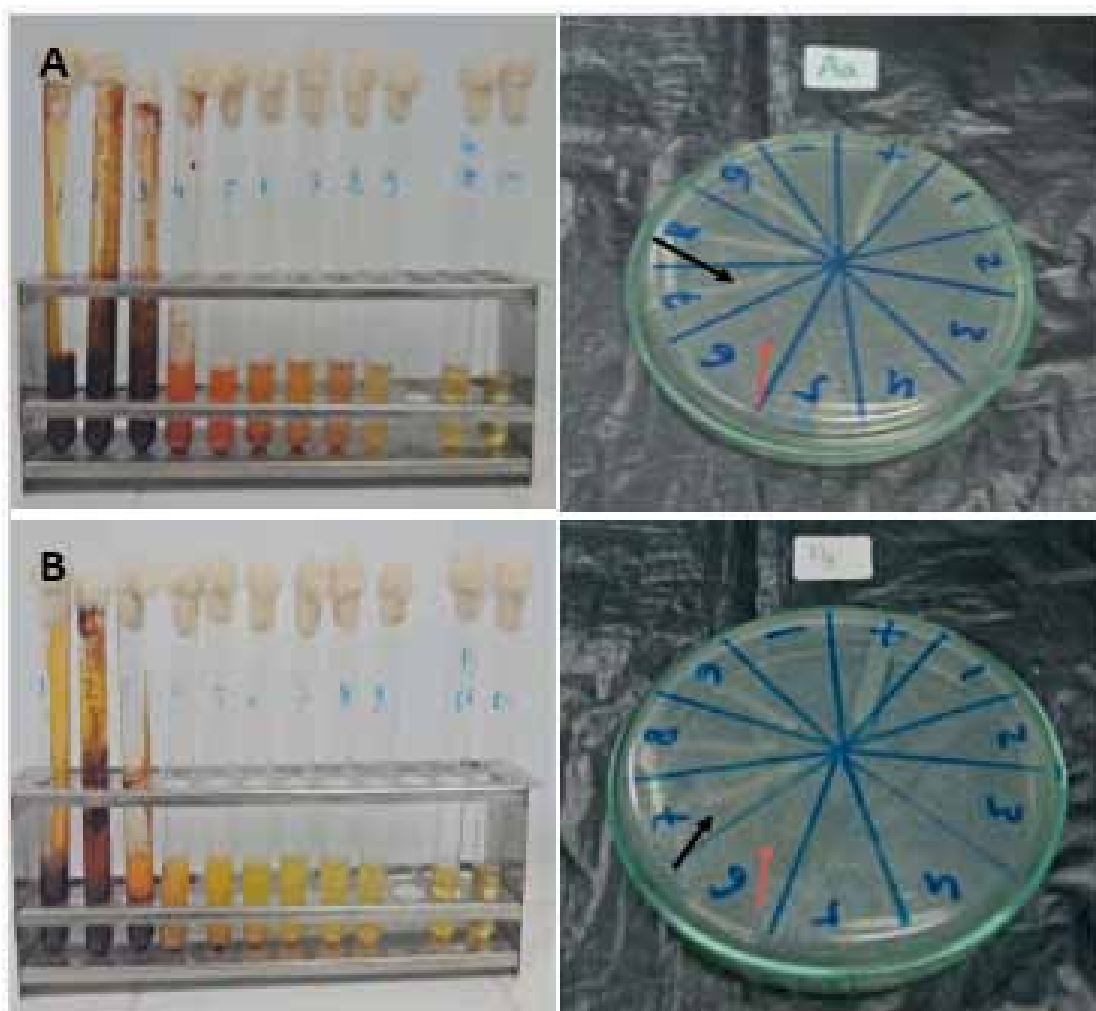


Figure 1. Sappan Wood Ethanol Extract Antibacterial Potential toward *A. Actinomycetemcomitans* bacteria and *P. gingivalis*. Annotation: A. Observation of turbidity with dilution method and B. Observation of bacterial colony on the Mueller Hinton using streak method. Tube Number 1-9 consecutively with 100%, 50%, 25%, 12.5%, 6.25%, 3.125%, 1.56%, 0.78%, and 0.39%. Tube with (+) mark was positive control and (-) mark was negative control. The area indicated by red arrow did not show growth of bacterial colony, area indicated by black arrow showed growth of bacterial colonies.

The cultivation of sappan wood ethanol extract in each concentration which had been administered with bacteria *A. actinomycetemcomitans* and *P. gingivalis* were conducted in *Mueller Hinton* medium with three replications. The result showed that, in the positive control, an average of 139 *A. actinomycetemcomitans* colonies was spotted, meanwhile, in the sappan wood ethanol extract with 100%, 50%, 25%, 12.5%, 6.25%, and 3.125% concentration and negative control, no bacterial colony growth. In 1.56% concentration, an

average of 12.667 colonies. Meanwhile, in each of the 0.78% and 0.39% were 31.67 and 42 colonies. The result from the calculation of *P. gingivalis* colony in positive control averaged at 138,667 colonies, at 100%, 50%, 25%, 12.5%, 6.25% and 3.125% concentration and negative control, there was no growth of *P. gingivalis* colony. The number of colonies on 1.56% concentration was 11,667 colonies and at 0.78% and 0.39% were 32,334 and 49,667 colonies, respectively (Table 2).

Table 2. Average amount of bacterial colony growth

Groups (Concentration)	n (Repetition)	<i>A. actinomycetemcomitans</i> (CFU)	<i>P. gingivalis</i> (CFU)
100%	3	-	-
50%	3	-	-
25%	3	-	-
12.5%	3	-	-
6.25%	3	-	-
3.125%	3	-	-
1.56%	3	12,67 ^a	11,67 ^a
0.78%	3	31,67 ^b	32,33 ^b
0.39%	3	42,0 ^c	49,67 ^c
Positive Control	3	139,0 ^d	138,67 ^d
Negative Control	3	-	-

The values with different superscript letters in a column are significantly different ($p < 0.05$).

Discussion

A. actinomycetemcomitans and *P. gingivalis* have a relationship to pathogenesis of the periodontal tissue. The ultrasonic scaling and laser therapy are efforts to decrease the severity of a disease, thus requiring other modes of therapy.¹⁸ The result of sappan wood study revealed contents of active substances such as flavonoid, saponin, alkaloid, tannin and terpenoid. Flavonoid can disrupt the formation of cell membrane and damage the permeability of bacteria's cell walls and inhibit the function of the cell membrane.^{19,20}

Other study has also revealed that flavonoid can inhibit expression of inflammatory cytokine by lipopolysaccharide,²¹ which are one of the main components from negative gram bacteria virulence, such as *A. actinomycetemcomitans*.²² *Brazilin* was included into the flavonoid group that had the potential as anti-inflammatory, antioxidant and antibacteria.²³ The tannin mechanism can inhibit DNA synthesis in the *A. actinomycetemcomitans* bacteria. Tannin can deactivate cellular adhesion of the *P. gingivalis* which, in turn, inhibits the enzyme that triggers protein transport, rendering it disrupted inside the inner membrane of the microbial cell.²⁴

The effectivity of saponin as antibacterial agent worked by triggering leakage of protein and enzymes inside the cell and reducing the stability of the cell membrane. The active substance, terpenoid, can disrupt the formation process of cell walls and membranes; this caused the stability of the cell walls to be disrupted and killed the bacteria.^{25,26,27} High quantities of alkaloids

were found in various tissues of *C. sappan* twig. Alkaloids and their derivatives are used for analgesic, antispasmodic and antibacterial effects, anticancer activity and anti-inflammatory activity.^{28,29}

The flavonoids, alkaloids, tannins, saponins, and terpenoids are active substances from sappan wood ethanol extract with each of its working mechanisms working in synergy to combat *A. actinomycetemcomitans* and *P. gingivalis* bacteria. Those mechanisms caused a decline in the physiological activity of the bacteria, which caused an inhibition toward the bacteria's growth, and, in turn, killed the bacteria.³⁰

The result showed that 1.56% concentration of sappan wood ethanol extract expressed an inhibitory effect toward the growth of *A. actinomycetemcomitans* bacteria at 90.887% toward the positive control group. This showed MIC value at the concentration of 1.56%, which according to the study conducted by Khan et al. (2016).³¹ The MIC value of sappan wood ethanol extract toward *P. gingivalis* was obtained at 1.56% concentration at 91.587% inhibition rate toward the growth of *P. gingivalis* in positive control group.

Sappan wood ethanol extract was capable of killing *A. actinomycetemcomitans* at 3.125%, as it was observed that bacterial growth was halted at this concentration. The MBC value of sappan wood ethanol extract toward *P. gingivalis* was also at 3.125% because, at the appropriate concentration, there was no longer bacterial colony growth observed. The MBC was defined as the lowest concentration needed for an antimicrobial agent to kill 99.9% of bacteria.

Increased concentration of sappan wood extract provides more active antimicrobial substances. Therefore, giving a higher concentration have a potential in inhibiting microbial growth. There were no differences observed in the sensitivity of the bacteria from sappan wood extract between *A. actinomycetemcomitans* and *P. gingivalis*. This study concluded that the growth of *A. actinomycetemcomitans* and *P. gingivalis* can be inhibited by sappan wood ethanol extract (*Caesalpinia sappan L.*) at MIC 1.56% and MBC 3.125% concentration.

Conflict of Interests: The authors declare that they have no competing interests.

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References

1. Tsuchida S, Satoh M, Takiwaki M, Nomura F. Ubiquitination in Periodontal Disease: A Review. *Int J Mol Sci* 2017; 18:1476
2. Petersen PE and Ogawa H. The global burden of periodontal disease: towards integration with chronic disease prevention and control. *Period* 2000 2012; 60(1):15-39.
3. Chauhan VS, Chauhan RS, Devkar N, Vibhute A, More S. Gingival and periodontal diseases in children and adolescents. *J Dent Allied Sci* 2012;4(5):26-9.
4. Manji F, Dahlen G and Fejerskov O. Caries and periodontitis: Contesting the conventional wisdom on their aetiology. *Caries Res* 2018;52:548–64.
5. Newman MG, Takei H, Klokkevold PR, Carranza FA. Carranza's clinical periodontology 12th Ed. St Louis:Elsevier saunders 2015:47,137,728.
6. Zaugg B, Sahrman P, Roos M, Attin T, Schmidlin PR. Improving scaling and root planing over the past 40 years: a meta-analysis. *Dentistry* 2014;4(3):2-5.
7. Najafi MH, Taheri M, Mokhtari MR, Forouzanfar A, Farazi F, Mirzaee M, et al. Comparative study of 0.2% and 0.12% digluconate chlorhexidine mouth rinses on the level of dental staining and gingival indices. *Dent Res J* 2012;9(3):305-8.
8. Tjekyan S. Pola kuman dan resistensi antibiotik di Pediatric Intensive Care Unit (PICU) RS. Dr. Mohammad Hoesin Palembang Tahun 2013 *J Ked Kes.* 2015;2(2):91-7.
9. Ventola CL. The antibiotic resistance crisis. *Pharm Ther* 2015;40(4):277–83
10. Senthilkumar N, Murugesan S, Banu N, Supriya S, Rajeshkannan C. Biochemical estimation and antimicrobial activities of the extracts of *Caesalpinia sappan* Linn. *Bangladesh J Sci Ind Res* 2011;46(4):429-36.
11. Konan Y, Witabouna KM, Bassirou B, Kagoyire K. Antioxidant activity and total phenolic content of nine plants from Côte d'Ivoire (West Africa). *J Appl Pharm Sci* 2014;4(8):36-41.
12. Pawar CR, Landge AD and Surana SJ. Phytochemical and pharmacological aspects of *Caesalpinia sappan*. *J Pharm Res* 2008;1(2):131-8.
13. Nirmal NP, Rajput MS, Prasad RG, Ahmad M. Brazilin from *Caesalpinia sappan* heartwood and its pharmacological activities: A review. *Asian Pac J Trop Med* 2015;8(6):421-30.
14. Puttipan R, Wanachantararak P, Khongkhunthian S, Okonogi S. Effects of *Caesalpinia sappan* on pathogenic bacteria causing dental caries and gingivitis. *Drug Discov Ther* 2017;11(6):316-22.
15. Keramat H, Moaddabi A and Ranjbari A. In vitro antimicrobial effects of aqueous extracts of *Caesalpinia sappan* Linn derivatives against oral pathogens. *Indian J Sci Res* 2014;7(1):342-7.
16. Agoes G. Natural material technology. Revised ed. Bandung: ITB Press 2009:37,85.
17. Jorgensen JH and Ferraro MJ. Antimicrobial susceptibility testing: A review of general principles and contemporary practices. *Clin Infect Dis* 2009;49:1749–55.
18. Akiyama S, Amano A, Kato T, Takada Y, Kimura KR, Morisaki I. Relationship of periodontal bacteria and *Porphyromonas gingivalis* fimA variations with phenytoin-induced gingival overgrowth. *Oral Dis* 2006;12(1):51-6.
19. Kumar S and Pandey AK. Chemistry and biological activities of flavonoids: an overview. *Sci World J* 2013;162750.
20. Yury ST, Yuri AK, Elena AY, Eugeny NM. Flavonoid–membrane interactions: Involvement

- of flavonoid–metal complexes in raft signaling. *Biochimica et Biophysica Acta (BBA) – Biomembranes* 2014;1838(5):1235-46.
21. Jiang F, Guan H, Liu D, Wu X, Fan M, Han J. Flavonoids from sea buckthorn inhibit the lipopolysaccharide-induced inflammatory response in RAW264.7 macrophages through the MAPK and NF- κ B pathways. *Food Funct.* 2017;8(3):1313-22.
 22. Gutiérrez VG, Kawasaki CP, Arroyo CSR, Maldonado FS. Luteolin inhibits lipopolysaccharide actions on human gingival fibroblasts. *Eur J Pharmacol.* 2006;541(1-2):95-105.
 23. Wang Y, Sun S, and Zhou Y. Extract of the dried heartwood of *Caesalpinia sappan* L. attenuates collagen-induced arthritis. *J Ethnopharm* 2011;136(1):271–8.
 24. Nafisyah AL, Tjahjaningsih W, Kusdarwati R, Abdillah AA. Effect of red algae (*Kappaphycus alvarezii*) on the quality of mackerel (*Rastrelliger* sp.). *J Ilm Perik Kel* 2015;7(1):87-93.
 25. Mujeeb F, Bajpai P, and Pathak N. Phytochemical evaluation, antimicrobial activity, and determination of bioactive components from leaves of *Aegle marmelos*. *Biomed Res Int* 2014;497606.
 26. Berti PL, Nawawi S and Ningsih JR. Antibacterial effect of lemon juice (*Citrus Limon* (L.) Burm. F.) against *porphyromonas gingivalis* dominant in periodontitis (In Vitro). Dissertation. Universitas Muhammadiyah Surakarta. 2015:3-12.
 27. Bello F, Babandi A and Murtala Y. Phytochemicals as Potential Alternatives to Counteract Bacterial Antibiotic Resistance: A Mini-Review. *J Biomed Sci* 2016;1:124-41.
 28. Nilesh PN, Mithun SR, Rangabhatla GSVP, Mehraj A. Brazilin from *Caesalpinia sappan* heartwood and its pharmacological activities: A review. *Asian Pac J Trop Med.* 2015;8(6):421–30.
 29. Senthilkumar N, Murugesan S, Bhanu S, Supriya S, Rajeshkannan C. Biochemical estimation and antimicrobial activities of the extracts of *Caesalpinia Sappan* Linn. *Bangladesh J. Sci. Ind. Res.* 2011;46(4):429-36.
 30. Cushnie T and Lamb AJ. Recent advances in understanding the antibacterial properties of flavonoids. *Int J Antimic Ag* 2011;38(2):99-107.
 31. Khan R, Islam B, Akram M, Shakil S, Ahmad AA, Ali SM, et al. Antimicrobial activity of five herbal extracts against multi drug resistant (MDR) strains of bacteria and fungus of clinical origin. *Mol* 2009;14(2):586-97.

Hormonal Regimens Using for Early Puberty Induction of Iraqi Female Lambs

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Abstract

This study was accompanied by thirty-six female lambs in addition, six rams of proven fertility were used in the present study in a private flock at Samawa/Iraq in breeding season at November 2018. The ages of lambs ranging from 8-12 months and weighing 30 to 35 kg were used in the study. All ewe lambs are Awassi breed. The experimental lambs were divided into three groups randomly each group has twelve lambs. Groups 1, 2 and 3 received intra-vaginal sponges containing 20 mg of fluorogestone acetate FGA (Chronogest, Intervet®) for 14 days, the lambs were given intramuscularly 200 IU (group 1, n= 12), 300 IU (group 2, n=12) and 400 IU (group 3, n= 12) of PMSG (Intervet®, Holland) after removing of intravaginal sponges within 14 h. Estrus was monitored every 6h from 12 to 120 h following injection of PMSG. The lambs were considered in estrus when they were mounted by the rams. The pregnancy of ewes was determined after one month by using of ultrasonography and after 3 months depended to abdominal distention and then waiting until time of parturition. The results showed that all ewe lambs in the group 2 of treatment (T₂) (FGA+300IU PMSG), but only two ewe lambs and one ewe lamb were not appear estrus from group 1 of treatment (T₁) (FGA+200IU PMSG) and group 3 of treatment (T₃) (FGA+400IU PMSG) respectively. The study showed that the estrus response, pregnancy rate and lambing rate were not significantly different between the three treatment groups at (P<0.05). Estrus response in three groups was 83.3%, 100%, 91.6% respectively. Pregnancy rate in three groups were 100%, 83.3%, 90.9% respectively. Lambing rate in three groups were 100% in all groups. The result showed there are no significant differences between the treatment groups in litter size and number of lambs (P<0.05). This study appeared single lambing were 100%, 90%, 100% respectively while twins lambing were zero, 10%, zero respectively and this study did not appear triple lambing.

Keywords: Early puberty, Induction, Lambs, Hormonal Regimes.

Introduction

The studies on puberty in Iraqi sheep are very limited. Puberty is the age when first estrus accompanied by spontaneous ovulation occurs [1]. The onset of puberty in sheep is influenced by genetic and environmental factors such as breed and strain differences. Workers on age at puberty agree that the early age is associated with the time of birth and the nutritional planes [2]. Suppose, for example that the breeding season in a highly seasonal breed is March to June and the earliest age at which puberty is possible in well-fed lambs is 8 months.

The lambs from ewes which conceive in March to May reach to puberty at few months of age, but those

from ewes which do not conceive until June cannot reach puberty until they are 16 months old [3]. First estrus occurs in ewe lambs at 30-50 kg of body weight 50-60% of adult weight [4, 5, 6]. Recently, progesterone or its analogues are generally used to synchronize and induce estrus during the breeding and non-breeding season [7]. Administration of gonadotropins such as human menopausal gonadotropin (hMG) [8], pregnant mare serum gonadotropin (PMSG) [9], follicle stimulating hormone (FSH) and mixed with gonadotropins [10] after stopping progestagens treatment, causes increasing rate of ovulation. [11, 12] demonstrated the positive relationship between the dosage of PMSG (250– 500 IU) and the percentage of ovulation, reproductive performance of

ewe lambs. The treated ewe lambs with PMSG induce follicular growth and increased secretion of estrogens. The purpose of this study were induce early puberty in Iraqi ewe lambs by using progesterone intra-vaginal sponges and different doses of PMSG.

Materials and Method

This study was accompanies on thirty-six female lambs in addition, six rams of proven fertility were used in the present study in a private flock at Samawaprovince inbreeding seasonat September 2018. The ages of lambs ranging from 8-12 months and weighing 30 to 35 kg were used in the study. All ewe lambs are awassi breed. The lambs were grazed daily for 6-8 h on a pasture in addition; these ewes received 1-1.5 kg of mixture feed during the entire period of study. The experimental lambs were divides into three groups randomly each group have twelve lambs. Groups 1, 2 and 3 received intra-vaginal sponges containing 20 mg of fluorogestone acetate FGA (Chronogest, Intervet®) for 14 days, the lambs were given intramuscularly 200 IU (group 1, n= 12), 300 IU (group 2, n=12) and 400 IU (group 3, n= 12) of PMSG (Intervet®, Holland) after removing of intravaginal sponges within 14 h. Estrous was monitored every 6h from 12 to 120 h following injection of PMSG. The lambs were considers in estrous when they were mounts by the rams.

The pregnancy of ewes was determined after one month by using of ultrasonagraphy and after 3 months depended to abdominal distention and then waiting until time of parturition after that recorded number of lambs, the following parameters were records:

1. Estrus response: number of ewes showing estrus/ total ewes treated in each group $\times 100$ [13].

2. Pregnancy rate: number of pregnant ewes/ number of mated ewes in each group $\times 100$.
3. Lambing rate: number of ewes lambing/number of pregnant ewes in each group $\times 100$ [14].
4. Litter size: number of total lambs / number of lambing ewes.

Statistical analysis: Estrus response and reproductive performance were analyzed using the chi-square test (SPSS 10.0.1 software program) was use for all statistical analysis [15]. Differences were considered significant at level of $p < 0.05$.

Results

The results showed that the all ewe lambs in the group 2 of treatment (T_2) (FGA+300IU PMSG), butonly two ewes lambs and one ewe lamb were not appear estrus from group 1 of treatment (T_1)(FGA+200IU PMSG) and group 3 of treatment (T_3) (FGA+400IU PMSG) respectively (Table 1).

The study showed that the estrus response, pregnancy rate and lambing rate were not significantly differences between the three treatments groups, ($P < 0.05$) were presents in. Estrus response in three groups were 83.3%, 100%, 91.6% respectively. (Table 1).

Pregnancy rate in three group were 100%, 83.3%, 90.9% respectively .Lambing rate in three groups were 100% in all groups. The result showed there are no significant differences between the treatments groups in litter size and number of lambs ($P < 0.05$). This study appeared single lambing were 100%, 90%.100% respectively while twins lambing were zero, 10%, zero respectively and this study did not appear triple lambing (Table 2).

Table 1: Reproductive performance of ewe lambs after different dose of PMSG treatments

Treatment Groups	N	Estrus Response%	Pregnancy Rate%	Lambing rate%
(T_1) FGA+ 200 IU PMSG	12	83.3 (10/ 12)	100 (10 /10)	100 (10 /10)
(T_2) FGA + 300 IUPMSG	12	100 (12 /12)	83.3(10/12)	100 (10/10)
(T_3) FGA + 400 IUPMSG	12	91.6 (11 /12)	100 (11/11)	100 (11/11)
Statically analysis		$\chi^2 = 2.182 P > 0.05 = NS$	$\chi^2 = 0.355 P > 0.05 = NS$	$\chi^2 = P > 0.05 = NS$

S= Significant : NS= No significant

Table 2: Litter Size of the Treatment Groups

Treatment Groups	N	Single	Twins	Triples	Total	Litter Size
(T ₁) FGA+ 200 IU PMSG	12	10	-	-	10	1 (10/10)
(T ₂) FGA + 300 IU PMSG	12	9	1	-	11	1.1 (11/10)
(T ₃) FGA + 400 IU PMSG	12	11	-	-	11	1 (11/11)
Statically analysis						$\chi^2 = 2.069$ P >0.05 =NS

S=Significant : NS= No significant

Discussion

In all groups of these study; only two ewes lambs and one ewe lamb were not appear estrus from group 1(FAP+200IU PMSG) and group 3 (FGA+400IU PMSG) respectively. Contrast with group2 (FGA+300IU PMSG) which is all appear estrus, and this results concurrent with [16], that show no advantage to using a higher dose of PMSG in ewes with a natural relatively high fecundity. The result showed no significant differences between these group in litter size and number of lambs ($P < 0.05$) concurrent with [17] which show the differences in conception rates were not evident between the various treatment groups (0, 250, 500 or 750 IU pregnant mare serum PMSG). This study appeared single number of lamb were 100%, 90%.10% respectively while twins were zero, 10%, zero respectively while this study did not appear triple birth comparative with [17] which is show a significantly higher ($P < 0.05$) litter size followed the use of the 750 IU. PMSG dose.

This study in conclusion indicate that primary P4 and PMSG is a beneficial adjunct to the breeding of sheep by AI at progestagens-synchronized estrus and administration of 300 IU PMSG at sponge withdrawal is more effective for increasing the reproductive performance in ewes in breeding season concurrent with [18]. Treatment with PMSG increased the total number of lambs born per ewe lambing from mating at induced estrus compared to that of ewes lambing from a spontaneous estrus [19]. Sixty-four percent of ewes that lambed had twins and was greater than the 36% (5/14) of ewes that had births of singles [19] concurrent with our study that show the percent of twins less than single lambing. Boland and Gordon (1973) reported that increased number of multiple ovulation and higher lambing rate following progestagens-PMSG treatment in anestrus ewes [20]. Results concurrent with [21] that showed that all ewes (100%) in each treatment group with progesterone sponges and PMSG responded to

treatments and exhibited estrus signs reflecting no significant effect of treatments on estrous rate of ewes during the breeding season. Results concurrent with [22] who found that estrous response of Dammar ewes treated with CIDR for 12 days + eCG or 6 days + eCG was 100% for both treatments. Injection of 500 IU of PMSG following the treatment of ewes in the breeding season with vaginal sponges containing 30-40 mg of FGA resulted in 90% and 85% estrus and conception rates, respectively [23]. Pregnancy rates in ewe lamb receiving the same dose of PMSG and MGA were higher than in the controls, but there was not significant effect on estrus rate concurrent with [24].

The pregnancy rate in the present study was higher; the percentages of estrus and conception were 100% was consistent with that reported by some other researchers, whereas the conception rate was higher than the reported one [24]. The different reproductive performance may be associated with using animals of different breeds and age, nutritional factors or type of insemination. In the presented study, the percentages of estrus and pregnancy rates are 100% concurrent with [25].

Conclusion

The purpose of this study was to accelerate the arrival of Iraqi lambs using progesterone vaginal sponges and various doses of PMSG because of the economic importance of these animals and part of the livestock in the region and accelerate puberty means increasing the number of births in a shorter period of normal puberty. The results showed that using (FGA + 300IU PMSG) combination is better for accelerating puberty and the appearance of estrous in all treated lambs compared to using other combinations of treatment. During the study, the pregnancy rate was not related to the quality of treatment used and there were no statistically significant differences between the three treatment groups. Results also showed no statistically significant differences

between treatment groups in litter size and number of lambs.

Conflict of Interest: None

Funding: Self

Ethical Clearance: Not required.

References

1. Bazer FW, Ott TL, Spencer TE. Endocrinology of the transition from recurring estrous cycles to establishment of pregnancy in sub primate mammals. In *Endocrinology of Pregnancy*, 1998. pp.1-34.
2. Ali A, Bin T, Floris B. Advancing puberty of Iraqi Awassi EWE Lambs by using multiply injection of HCG and PMSG. *Collage of Agriculture, university of Baghdad –Iraqi. MSc. Articles*. 2005. pp. 33.
3. Osinowo OA, James IJ, Williams TJ. Controlled breeding of cattle, sheep and goats. Department of Animal physiology, UNAAB. 2008. pp. 34.
4. Juma KH, Alkass JE. Genetic and phenotypic parameters of some economic characteristics in Awassi sheep of Iraq: A review. *Egyptian Journal of Sheep, Goat and Desert Animals Sciences*, 2006. 1(1), 15-29.
5. Driancourt MA, Bodin L, Boomarov O, Thimonier J, Elsen JM. Number of mature follicles ovulating after a challenge of human chorionic gonadotropin in different breeds of sheep at different physiological stages. *Journal of animal science*, 1990. 68(3), 719-724.
6. Hafez ES. Semen evaluation. *Reproduction in farm animals*, 1993. 5, 405-423.
7. Dogan I, Nur Z, Gunay U, Sagirkaya H, Soylu MK, Sonmez C. Estrous synchronization during the natural breeding season in Anatolian black does. *Vet Med-Czech*, 2005. 50(1), 33-38.
8. Evans AC. Ovarian follicle growth and consequences for fertility in sheep. *Animal Reproduction Science*, 2003. 78(3-4), 289-306.
9. Lamrani F, Benyounes A, Sulon J, Khaldi G, Rekik R, Bouraoui B, Tahar A. Effects of repeated use of PMSG on reproductive performances of the Ouled Djellal ewes. *J. Anim. Vet. Adv*, 2008. 2, 22-30.
10. Knights M, Baptiste QS, Dixon AB, Pate JL, Marsh DJ, Inskoop EK, Lewis PE. Effects of dosage of FSH, vehicle and time of treatment on ovulation rate and prolificacy in ewes during the anestrus season. *Small ruminant research*, 2003. 50(1-2), 1-9.
11. Al-Jubouri AJ. Technique of modifying reproductive performance in sheep production: breeding and production. (ed.) Wicham, G.A. and Mc Donald, M.F., New Zealand Institute of Agricultural Science, 1982. pp. 239-236.
12. McNatty KP, Gibb M, Dobson C, Ball K, Coster J, Heath D, Thurley DC. Preovulatory follicular development in sheep treated with PMSG and/or prostaglandin. *Reproduction*, 1982. 65(1), 111-123.
13. Akoz M, Bulbul B, Bozkurt AM, Dere SU. Induction of multiple births in Akkaraman crossbred sheep synchronized with short duration and different doses of progesterone treatment combined with PMSG outside the breeding season. *Bulletin-Veterinary Institute in Pulawy*, 2006. 50(1), 97.
14. Martinez MF, Kastelic JP, Colazo MG, Mapletoft RJ. Effects of estradiol on gonadotrophin release, estrus and ovulation in CIDR-treated beef cattle. *Domestic animal endocrinology*, 2007. 33(1), 77-90.
15. Dogan I, Nur Z, Gunay U, Sagirkaya H, Soylu MK, Sonmez C. Estrous synchronization during the natural breeding season in Anatolian black does. *Vet Med-Czech*, 2005. 50(1), 33-38.
16. Grant VJ. *Maternal personality, evolution and the sex ratio: do mothers control the sex of the infant?* Routledge. 2006.
17. Liu JS, Lu LY, Lu WM, Lin BJ. A survey of DEA applications. *Omega*, 2013. 41(5), 893-902.
18. Abdel-Khalek AE, Khalil WA, El-Saidy BE, Youssif AI. Estrous synchronization in ewes using sponges with PMSG or tam effect with or without progesterone injection. *Animal and Poultry Prod., Mansoura 371 Univ.*, 2014. Vol.5 (4): 173 – 185).
19. Hussein MQ, Kridli RT. Reproductive responses of Awassi ewes treated with either naturally occurring progesterone or synthetic progestagen. *Asian-australasian journal of animal sciences*, 2002. 15(9), 1257-1262.
20. Boland MP, Gordon I. Oestrus and ovulatory response to progesterone-PMSG treatments in anoestrous ewes. *J. Dept. Agric. Fish., Ireland*, 1973. 70, 65-70.

21. Kumar BH, Bramhaiah KV, Srinivas M, Ekambaram B, Dhanalakshmi N. Effect of estrus synchronization by progesterone sponge along with PMSG on estrus response and fertility in Nellore Jodipi ewe lambs. *Theriogenology Insight*, 2016. 6(3), 135.
22. Nasser SO, Wahid H, Aziz AS, Zuki AB, Azam MK. Synchronization method and subsequent eCG treatment out of the breeding season. *Int J Biol Med Res.*, 2012. 3(2): 1485-1489.
23. Timurkan HU, Yildiz HA. Synchronization of oestrus in Hamdani ewes: The use of different PMSG doses. *Bulletin-Veterinary Institute in Pulawy*, 2005. 49(3), 311.
24. Dumitrescu I, Stoica A, Culea C, Ristea P. Induction of oestrus in ewes treated with synthetic hormones. *Anim. Breed Abstr*, 1985. 53, 7605.
25. Miljkovic V, Petrujkic T, Vujosevic J, Mrvos P, Mihajlovksi P, Predojevic M, Naumov N, Tanev D, Stanojevic T, Jovanovic V. Contemporary aspects of physiology of reproduction and artificial insemination in small ruminants. *Vet Glas*, 1989. 43, 875-882.

Evaluation of Angiopoietin One and Angiopoietin Two with Missed Abortion

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Abstract

Missed abortion (MA) is a type of miscarriage, refer to pregnancy in which there is fetal demise without intervention, and also uterine that may expel the product of conception prior to 20 weeks of gestation to assess the role of ANG1 and ANG2 level in early pregnancy and compare these level with healthy pregnancy women, ANG1 play role in new blood vessels maturation and stabilization, the inhibition of endothelial apoptosis and reduction of vascular permeability in stable environment. ANG2 is an antagonist of ANG1 and it known to enhance the plasticity, destabilization and permeability of blood vessels and vascular remodeling site. A prospective cross - study, all women were attended to obstetrics and gynecology outpatient, and this study was carried out from Jan 2019 to July 2019. Sixty Women with missed miscarriage fetus heart negative 6-8 weeks were screened to participate in the present study group, Ages were between 18 – 35 years old, and they were from center and the periphery of Kirkuk city to comparative forty apparently health women with early pregnancy fetus heart positive a control groups. A serum level of ANG1 and ANG2 was measured by ELIZA. The result shows that the mean serum level of Angiopoietin one was significantly decrease in missed miscarriage compared to control women (2.92 ± 2.4 vs. 5.6 ± 3.2 ng/ml) respectively at a $P < 0.05$. And this study showed that there was the significant decrease serum level of angiopoietin two in missed miscarriage patients compared with the control group women (8.12 ± 3.5 vs. 16.81 ± 12.3). This study showed that there were the positive correlations of Angiopoietin one and two with missed miscarriage. It can be conclude that the level of serum Angiopoietin -1 and level of serum angiopoietin -2 in missed abortion decrease and it is can be used as an early and effective biomarker for diagnosis of missed abortion.

Keywords: *Angiopoietin -1, Angiopoietin -2, missed abortion, Biomarker.*

Introduction

Spontaneous abortion in the ending of pregnancy by removal or expulsion of an embryo or fetus before it can survive the uterus; an abortion without intervention is known miscarriage or spontaneous abortion. Spontaneous abortion can be divided into various subtypes: threatened, inevitable, incomplete, complete, and missed abortion.⁽¹⁾ When deliberate step are taken to end the pregnancy it called an induced abortion or less frequently induced miscarriage. Miscarriage also known spontaneous abortion is the intentional expulsion of an embryo or fetus before the 24 week gestation. Missed abortion is defined is a condition with retained products of conception, with no cardiac activity but the uterus is still silent making no attempt to expel the fetus or unrecognized intrauterine death of the embryo

or fetus without expulsion of the product of conception it is constitutes approximately 15% of the clinically diagnosed pregnancies⁽²⁾. Accurate differentiation between normal pregnancy and pregnancy loss in early gestation remains a clinical challenge; it is estimate that approximately 30-40% of implanted pregnancy result in spontaneous abortion during first trimester⁽³⁾. Clinical feature in the typical instance .early pregnancy appearance to be normal .with amenorrhea, nausea, vomiting, growth of uterus and breast change after fetal death there may or may not be vaginal bleeding, abdominal pain, cramping, vaginal spotting .other symptoms denoting missed miscarriage many woman have no symptoms during this period except persistent amenorrhea. No symptoms for missed abortion appear for several weeks and if appear, these vary from spotting

to heavy vaginal bleed and loss of pregnancy symptoms. Signs of missed abortions include loss of fetal heart sounds and closure of cervical⁽⁴⁾. The etiological factors for missed abortion include chromosomal abnormalities, maternal, fetal and embryonic malformations, placental and uterine anomalies, history of recurrent abortions, sexually transmitted diseases, thyroid disease and maternal diabetes.⁽⁵⁾ Complications of missed abortions may include pain, Fever, hemorrhage, retained products of conception, septic shock, bladder, bowel and uterine injuries and perforation⁽⁶⁾. Angiopoietin 1 encodes a 484 amino acid with M.W 57 KD, has ability to form higher order multimers though it super clustering. However not all structure can interact with tyrosine kinase receptor, the receptor can be only be activity at the tetramer level or high⁽⁷⁾. ANG1 act as chemo attractant for endothelial cell while also promoting endothelial cell sprouting and facilitating tissue invasion by nascent blood vessels through activation MMPs⁽⁸⁾. It plays critical role in mediating reciprocal interaction between the surrounding matrix and mesenchyme and inhibits endothelial permeability protein also contribute to blood vessel, maturation and stability and may be involved in early development of the heart⁽⁹⁾. Angiopoietin 2 encodes 466 amino acid polypeptides with molecular weight 75 KDa. ANGPT2 are secreted glycoproteins that play a complex role in angiogenesis and inflammation, ANGPT2 is widely expressed during development, but it is to restricted postnatal to high angiogenic tissue such as placenta, ovaries and uterus.⁽¹⁰⁾ The aim of this study is to estimate the level of angiopoietin 1 and angiopoietin 2 in patient missed abortion. Furthermore, the current study objectives are:

1. To determine the serum angiopoietin one with patient missed abortion.
2. To determine the serum of angiopoietin two with patient missed abortion.
3. To determine the serum angiopoietin one and two with pregnancy women.
4. Find correlation and level angiopoietin one and two with patient with missed abortion and compared with pregnancy women as control group.

Materials and Method

Study Design: A prospective cross-sectional study, hospital based study the protocol of this study was approved by the scientific committee of Tikrit University College of Medicine, the agreement of attendance to

Azadi Teaching Hospital, Kirkuk General Hospital and Kirkuk Department of Obstetrics and Gynecology Center, that approved by Kirkuk Health Directorate, to collect the samples from the patients.

This study was carried out from March 2019 to august 2019. The patients admitted Department of Obstetrics and Gynecology, unit in hospitals Kirkuk City-Iraq. An interview was carried out with these patients using questionnaire form designed by the investigator including their name, age, etc.

Study Population:

Patient and Control: Sixty women with missed abortion were screened to participate in the present study. Men ages were between 18–35 years old, and they were from center and the periphery of Kirkuk city. Sixty–case with missed abortion were considered as study group, while thirty woman normal pregnancies as control group.

Patient sample were inclusion criteria:

1. Woman in the age between 18 -35 years
2. Natural conception
3. History of positive pregnancy test
4. Intrauterine pregnancy
5. First attendance in the pregnancy

Patient sample were Exclusion criteria:

1. Pregnant women who refuse to participate in this study
2. Gestation age less than 6 weeks or more than 8 weeks
3. Multiple gestations
4. Ectopic pregnancy
5. Previous history of infertility
6. History of autoimmune or endocrine diseases (D.M, ALP, POS)
7. Smoker patient
8. Patient with recognizable cause of recurrent missed abortion

Sampling: Five ml of blood sample were taken by vein puncture from each subject enrolled in this study. Blood samples were placed into disposable gel test tubes, after 20 minute blood clotting, centrifuged at 5000 rpm

for 15 minute and the obtained serum were aspirated using mechanical micropipette and transferred into clean test tubes which labeled and stored in deep freeze at -80°C for biochemical measurement of the levels of angiotensin one and angiotensin two were measured.

Result

This study includes ninety pregnant women and in there is first trimester they were divided into two groups:

1. First group represent 60 pregnant women with missed miscarriage were considering studies group F.H (-ve).
2. Second group represent 30 pregnant with normal intrauterine pregnancy .were considered as control group F.H (+ve).

There ages were ranged between 18 -35 years, were investigation for determination Angiotensin one and Angiotensin two in both group.

Serum level of angiotensin one in missed miscarriage and the

Control Group: As show in the table (1), the mean serum level of angiotensin one was significantly decreased in women compared to control women. (2.94 ± 2.4 vs 5.6 ± 3.2 ng/ml) respectively at a $p < 0.05$.

Table 1: The mean and standard deviation of serum Angiotensin one in missed miscarriage and control group

Angiotensin One (ng/mL)	Missed Miscarriage Women	Control Group
No	60	30
Mean	2.94	5.6
SD	2.4	3.2

t.test 4.02 p. value < 0.05 Highly Significant

Serum level of angiotensin two in missed miscarriage and the

Control Group: As show in the table (2), the mean serum level of angiotensin two was significantly decreased in women compared to control women (8.12 ± 3.5 vs 16.81 ± 12.3 ng/mL) respectively at a $p < 0.05$.

Table 2: The mean and standard deviation of serum Angiotensin two in missed miscarriages and control group

Angiotensin two (ng/mL)	Missed Miscarriage Women	Control Group
No	60	30
Mean	8.12	16.81
SD.	3.5	12.3

t.test 3.79 p. value < 0.05 Highly Significant

Correlation between angiotensin one and angiotensin two in missed miscarriage women:

This study showed strong positive correlation between angiotensin one and two with missed miscarriage women figure (1).

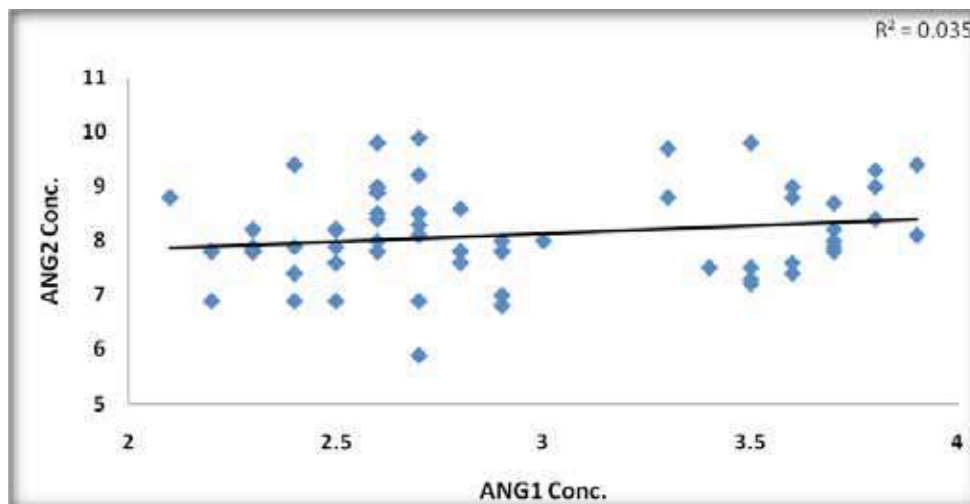


Figure 1: Correlation between angiotensin one and two with missed miscarriage women

Discussion

Serum level of angiotensin II in missed miscarriage and the Control group: This study showed that there was a significantly decrease serum level of Angiotensin II in missed miscarriage compared with that of control group (intrauterine pregnancy) women same gestational age 6–8 weeks.

The result of study was agreement with Daponte *et al*⁽¹¹⁾ their study showed that optimal levels of serum Angiotensin II were around 963.5 pg/ml (793.9–1277.6) in normal pregnancy women with gestation age 6-8 weeks, and 810 pg/ml (595-767.9) in women with missed miscarriage. The current study showed that these value relatively higher level of angiotensin II in normal pregnancy compared with women failed pregnancy, angiotensin II is responsible for vascular growth and maturation of placenta, so decreased levels lead of angiotensin II leads to increase chance of failure of pregnancy because of the defective vascular formation, when the every step of vessels formation is impaired starting from sprouting of vessels to maturation, then the chance of survival of the fetus decrease due to lack of exchange of nutrient and waste product, impaired placental vascular development is related to imbalance in angiogenic factor, as implicated in pathological pregnancy .

Schneuer FJ, Roberts CL, Ashton AW,⁽¹²⁾ studies conducted high level Angiotensin II is mainly expressed in perivascular sertoli cell including pericyte, vascular smooth muscle cells, it binds specifically to the TIE2 receptor on peripheral endothelial membrane through paracrine function, causing phosphorylation of its receptor and subsequent signal transmission.

Serum level of angiotensin II in missed miscarriage and the Control group: This study showed that there was a significantly decrease serum level of Angiotensin II in missed miscarriage compared with that of control group (intrauterine pregnancy) women same gestational age 6–8 weeks.

The hypothesis of this study were compromised fetal growth is the result of compromised placental development and potential markers in maternal blood can detected those pregnancies risk, in view of its control role of angiogenesis we hypothesized that ANG2 maternal blood vessels would be increased at the first trimester when both maternal uterine vascular remodeling and placental branching angiogenesis take place, and level

would be lower than normal in pregnancy destined for abnormal pregnancy.

This study shows its agreement with GevaE, *et al*⁽¹³⁾ for angiotensin II significantly decrease in missed miscarriage patient and recorded high level in normal pregnancy, and this result ANG-2 observed in women at 6-8 weeks gestation may indicate that ANG-2 plays an important role in early placental angiogenesis, particularly in maternal vascular remodeling the lower maternal serum level of ANG -2 observed in women whose fetus subsequently developed IUGR may indicate compromised placental angiogenesis early pregnancy well before any clinical evidence of IUGR.

High level angiotensin II in the normal pregnancy that ANG-2 may also target fetal endothelial cell which also express the TIE-2 receptor thus potentially affecting branching angiogenesis, and affect placental villous vascular change, interestingly TIE-2 is also expressed in endovascular trophoblast invading the uterine spiral arteries suggesting that an interaction between ANG-2 and TIE-2 may play a significant role in trophoblast behavior placental development.

Correlation between angiotensin II and angiotensin II in missed miscarriage women: This study showed strong positive correlation between angiotensin II and angiotensin II with missed miscarriage women. Angiotensin II and angiotensin II -2 are both expressed in the placenta from the very early stage of pregnancy and they mediate number of endothelial and non-endothelial effects that are thought to be pivotal for proper placental development, ANG-2 stimulation an increase in trophoblast synthesis, ANG-1 act as a potent chemotactic factor for trophoblast. ANG-1 expression was restricted to the perivascular stroma of stem villi surrounding large blood vessels, supporting the hypothesis that angiotensin II play a role in maturation and maintenance of the placental vessels in contrast ANG-2 was expressed by the perivascular stroma of all placental villi. Furthermore this study shows that level of ANG-1 and ANG-2 were significantly reduced in missed miscarriage and suggests that this decreased expression may therefore contribute to be reported poor angiogenesis.

Seval *et al*⁽¹⁴⁾ with agreement with study a few previous in situ hybridization studies have described the localization pattern of angiotensin II in the placenta in different stages of pregnancy in very early human

placenta (as early as the 4th week) ANG-1 protein was localized only in the syncytiotrophoblast while ANG-2 was localized primarily in the syncytiotrophoblast and less extent in the cytotrophoblastic layer of placental villi.

Previous study Dunk *et al*⁽¹⁵⁾ demonstrated that ANG-1 and TIE-2 were detected in the trophoblast bilyar of first trimester placenta, where ANG-2 was restricted to cytotrophoblast in same study ANG-1 and ANG-2 were show to be implicated the regulation of trophoblast behavior through different mechanisms and to promote the growth and migration of trophoblast in vivo, which ANG-1 and ANG-2 and TIE-2 localized to the trophoblast, suggestion that the angiotensin may play an autocrine role in the trophoblast function.

Conclusion

Serum angiotensin -1 and angiotensin -2 levels decrease during pregnancy failure. The measurement angiotensin -1 and angiotensin -2 can be used first tool, to support the conformation of diagnosis of missed miscarriage.

Conflict of Interest: None

Funding: self

Ethical Clearance: Not required.

Reference

- Jibril UN, Kayode OS, Umar A, Umar AG, Abubakar IA, Ayoade IM, Blessing NJ. Spontaneous abortion among women admitted into gynaecology wards of three selected hospitals in Maiduguri, Nigeria. *International Journal of Nursing and Midwifery*. 2014 Apr 30;6(2):24-31.
- Wood SL, Brain PH. Medical management of missed abortion: a randomized clinical trial. *Obstetrics & Gynecology*. 2002 Apr 1;99(4):563-6.
- Papioannou GI, Syngelaki A, Poon LC, Ross JA, Nicolaides KH. Normal ranges of embryonic length, embryonic heart rate, gestational sac diameter and yolk sac diameter at 6–10 weeks. *Fetal diagnosis and therapy*. 2010;28(4):207-19.
- National Institutes of Health. US National Library of Medicine, Medline Plus. Failure to Thrive. 2016.
- Bartlett LA, Berg CJ, Shulman HB, Zane SB, Green CA, Whitehead S, Atrash HK. Risk factors for legal induced abortion-related mortality in the United States. *Obstetrics & gynecology*. 2004 Apr 1;103(4):729-37.
- Schorge JO, Williams JW. *Williams gynecology*. McGraw-Hill; 2008.
- Smith AH, Kuliszewski MA, Liao C, Rudenko D, Stewart DJ, Leong-Poi H. Sustained improvement in perfusion and flow reserve after temporally separated delivery of vascular endothelial growth factor and angiotensin-1 plasmid deoxyribonucleic acid. *Journal of the American College of Cardiology*. 2012 Apr 3;59(14):1320-8.
- Burnett A, Gomez I, De Leon DD, Ariaans M, Progas P, Kammerer RA, Velasco G, Marron M, Hellewell P, Ridger V. Angiotensin-1 enhances neutrophil chemotaxis in vitro and migration in vivo through interaction with CD18 and release of CCL4. *Scientific reports*. 2017 May 24;7(1):2332.
- Gutbier B, Neuhauß AK, Reppe K, Ehrler C, Santel A, Kaufmann J, Scholz M, Weissmann N, Morawietz L, Mitchell TJ, Aliberti S. Prognostic and pathogenic role of angiotensin-1 and-2 in pneumonia. *American journal of respiratory and critical care medicine*. 2018 Jul 15;198(2):220-31.
- Fiorimanti MR, Rabaglino MB, Cristofolini AL, Merkis CI. Immunohistochemical determination of Ang-1, Ang-2 and Tie-2 in placentas of sows at 30, 60 and 114 days of gestation and validation through a bioinformatic approach. *Animal reproduction science*. 2018 Aug 1;195:242-50.
- Partridge S, Balayla J, Holcroft CA, Abenheim HA. Inadequate prenatal care utilization and risks of infant mortality and poor birth outcome: a retrospective analysis of 28,729,765 US deliveries over 8 years. *American journal of perinatology*. 2012 Nov;29(10):787-94.
- Daponte A, Deligeoroglou E, Pournaras S, Tsezou A, Garas A, Anastasiadou F, Hadjichristodoulou C, Messinis IE. Angiotensin-1 and angiotensin-2 as serum biomarkers for ectopic pregnancy and missed abortion: A case-control study. *Clinica Chimica Acta*. 2013 Jan 16;415:145-51.
- Schneuer FJ, Roberts CL, Ashton AW, Guilbert C, Tasevski V, Morris JM, et al. Angiotensin-1 and 2 serum concentrations in first trimester of pregnancy *Am J Obstet Gynecol* 2014;210(4):345.e1–e9.
- Geva E, Ginzinger DG, Zaloudek CJ, Moore DH, Byrne A, Jaffe RB. Human placental vascular development: vasculogenic and angiogenic

- (branching and nonbranching) transformation is regulated by vascular endothelial growth factor-A, angiopoietin-1, and angiopoietin-2. *The Journal of Clinical Endocrinology & Metabolism*. 2002 Sep 1;87(9):4213-24.
15. Seval Y, Korgun ET, Demir R. Hofbauer cells in early human placenta: possible implications in vasculogenesis and angiogenesis. *Placenta*. 2007 Aug 1;28(8-9):841-5.
 16. Dunk C, Shams M, Nijjar S, Rhaman M, Qiu Y, Bussolati B, Ahmed A. Angiopoietin-1 and angiopoietin-2 activate trophoblast Tie-2 to promote growth and migration during placental development. *The American journal of pathology*. 2000 Jun 1;156(6):2185-99.

Cellular Phone and Laptop Radiation Effects on Subjective Complaints in Informatics Students

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Abstract

The increasing use of cell phones and laptops in today's modern society has a negative impact on health; one such impact is on informatics students, who struggle with the use of cell phones and computers in their daily activities. This study aimed to determine the relationship between radiation exposure to cell phones and laptops with subjective complaints in the form of sleep quality, headache, dry eye syndrome (DES) and concentration disorders.

The research is analytic observational and cross-sectional approaches. The study used simple random sampling to select 112 respondents, all of which were informatics students of Universitas Sebelas Maret (UNS). The Pearson correlation test results were obtained from cell phone and laptop radiation exposure with sleep quality ($p < 0.05$; $r = 0.192$), headache ($p < 0.05$; $r = 0.510$), dry eye syndrome ($p < 0.05$; $r = 0.1950$) and disturbances concentration ($p < 0.05$; $r = 0.406$).

Keyword: Radiation exposure, sleep quality, headache, dry eye syndrome, disturbances concentration

Introduction

Cell phones and laptops are very essential in today's world, and their use is inevitable. However, for all the benefits associated with their use, they also have downsides. For example, cell phones and laptops are major sources of electromagnetic pollution, which has unpleasant effects on public health. The results in 2015 showed that 54% of the world's total population or 3.996 trillion of the 7.476 trillion people on earth have cell phones, and most users are 18-34 years old⁽¹⁾, while in America, cell phone use is mostly among adolescents aged 8 to 18 years⁽²⁾. In 2015, cell phone use in Indonesia is currently at 56.92% of the total population⁽³⁾. The use of laptops has also become a lifestyle in the community,

especially among students and employees. In 2013, the majority of laptop users in the UK were 14-24-year olds, and they accounted for as much as 70% of the total users⁽⁴⁾. Meanwhile, in Indonesia, the number of laptop users reached stood at 42% of the total population, and consisted mostly of students, entrepreneurs and housewives⁽⁵⁾.

The increasing use of cell phones and laptops has an adverse effect on health. Based on the research in Sweden, young adult cell phone users complained of subjective complaints in the form of stress, depressive symptoms, and decreased sleep quality⁽⁶⁾. The study showed that sleep disturbances were experienced by 19.2% of students and concentration disruption was experienced by 14.5% of the students due to exposure to cell phone radiation⁽⁷⁾ and an effect on the pattern of Electroencephalograph (EEG) and human sleep patterns⁽⁸⁾. Cell phone usage disrupts the pattern of sleep at night and also affects the quality of sleep if one's phone is still turned on⁽⁹⁾. Decreased sleep quality is associated with cellular phone radiation exposure due to metabolic and cardiovascular disorders which have an effect on the occurrence of insomnia and decreased sleep duration⁽¹⁰⁾.

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Exposure to cell phone radiation in the form of electromagnetic waves acutely causes headache, eye disorders, fatigue, and sleep disorders. According to the NIOSH, it is reported that 88% of those who use laptops for at least 3 hours will experience fatigue and dry eye syndrome⁽¹¹⁾. Dry eye syndrome could be in the form of sensitive eye, feeling discomfort when exposed to bright light, the eyes feeling itchy and sandy, eye aches, blurred vision and reduced vision.

The body can recognize cell phone radiation exposure as a carrier of information that disrupts the body's metabolism and biochemical reactions by interfering with the body's physiological processes and which cause an increase in intracellular free radicals, genetic damage, inter-cell communication disorders, leakage in the blood-brain barrier, and the risk of tumor. However, exposure to radiation from cell phones does not directly cause harm to one's health, but rather triggers biochemical responses in cells so that the manifestations of the disorder usually occur for a long time, as carcinogenic and has the potential to cause interference with various organs of the body⁽¹²⁾.

Exposure to electromagnetic radiation from cell phones can cause physical stress where the body responds by secreting hormones from the hypothalamus. Increased hormone secretion in the hypothalamus results in increased levels of glucocorticoid hormones, which increases cortisol levels and causes a decrease in the levels of HMG-CoA reductase. The decrease in the level of HMG-CoA reductase will cause a decrease in the rate of endogenous synthesis of cholesterol. A decrease in endogenous synthesis will cause a decrease in plasma cholesterol levels.

Any physical and psychological stress on the body for just a few minutes can lead to an increase in ACTH secretion. Consequently, there will be an increase in the secretion of glucocorticoids and cortisol. Glucocorticoids play an important role for catecholamines to fully implement the effect of free fatty acid mobilization. Increased secretion of glucocorticoid hormones will also increase the secretion of the hormone epinephrine which can increase the rate of lipolysis in adipose tissues, and norepinephrine, which can increase the use of circulating lipoproteins, so that cholesterol levels in the plasma will decrease. The secretion of cortisol is higher when the body is exposed to stress, both physical and psychological. Cortisol can modulate the immune system because all leukocytes have receptors for cortisol. Increased cortisol

levels will cause a decrease in the levels of HMG-CoA reductase. Decreasing levels of HMG-CoA reductase will cause a decrease in the rate of endogenous synthesis of cholesterol. The decrease in endogenous synthesis will cause a decrease in cholesterol levels in the plasma which results in subjective complaints in humans⁽¹³⁾.

Material and Method

The research is observational analytic with cross-sectional approaches to analyze the relationship between radiation exposure from cell phones and laptops with subjective complaints by students. The study utilized simple random sampling to select 112 UNS informatics students from a population of 155 students. The respondents were adjusted to the inclusion criteria in the form of UNS informatic students who used cell phones and laptops every day, while the exclusion criteria were: 1) Students who consume sleeping pills, antiarrhythmic agents, corticosteroids, diuretics, and theophylline; and 2). Students who consume coffee or soft drinks 6 hours before going to bed.

The independent variable was the duration of exposure to electromagnetic radiation from cell phones and laptops as revealed by a questionnaire, with the results indicating the average duration cell phone and laptop usage each day, expressed in minutes. The questionnaire used scale measurement in ratios.

The dependent variable was subjective complaints in the form of: 1) Sleep quality, measured using the Pittsburgh Sleep Quality Index (PSQI) questionnaire which had 7 main components with a score range 0-21. A score of 0 indicates that sleep quality is getting better, while a score of 21 indicates that sleep quality is very poor. For the sake of statistical analysis, sleep quality was grouped into two, namely good sleep quality (score <5) and poor sleep quality (score > 5)⁽¹⁴⁾; 2) Headache, which was revealed using a questionnaire containing the description/degree of headache with a score range of 0-10, so that the scale of measurement was a ratio; 3) Dry eye syndrome, which was revealed using the Ocular Surface Disease Index (OSDI) questionnaire. OSDI scores were obtained using the formula: total number of scores x 25. OSDI scores were categorized into four, namely: normal (score 0-12), mild (score 13-20), moderate (score 21-32) and severe (score 33-100)⁽¹⁵⁾ and 4) Headache symptoms which was revealed by a questionnaire about headache symptoms that had undergone validation and reliability. Disturbance concentration, which was revealed using the

Grid Concentration Test. Grid Concentration Test scores were categorized into two, namely: normal (score > 10), severe (score 0-10).⁽¹⁶⁾ Pearson correlation test was used to determine the relationship between cell phone and laptop radiation exposure and subjective complaints, at a significance level of 0.05.

Findings:

Table 1: Distribution of repondents’ characteristics

Characteristic	Amount (n)	Percentage (%)
Gender		
Male	50	44.3
Female	62	55.7
Duration of radiation exposure		
High (> 2 hour)	105	93.75
Low (< 2 hour)	7	6.25

Characteristic	Amount (n)	Percentage (%)
Subjective complaint:		
Sleep quality		
Good	42	37.50
Bad	70	62.50
Headache		
Tense muscle headache	78	69.64
Migraine	26	23.22
Cluster	8	7.14
Dry eye syndrome		
Normal	27	24.10
Mild	19	16.96
Moderate	31	27.68
Severe	35	31.26
Concentration disorder		
With	68	60.72
Without	44	39.28

Table 2: Variable correlation test for exposure to cell phone and laptop radiation and subjective complaints

Subjective Complaints Variables	Correlation Coefficient (r)	p Value
Radiation cell phones and laptops exposure with sleep quality	0.192	0.042
Radiation cell phones and laptops exposure with headache	0.510	0.000
Radiation cell phones and laptops exposure with dry eyes syndrome	0.195	0.034
Radiation cell phones and laptops exposure with concentration disturbance	0.406	0.020

Discussion

Based on research data, 93.75% of the research subjects used cell phones and laptops for more than 2 hours per day. This shows that, in terms of cell phone and laptop usage, UNS informatics students are in the high intensity category, in accordance with the research of Saxena; 57% of their respondents use cellphones and laptops for more than two hours each day.⁽¹⁷⁾

The results of the Pearson statistical test showed a significant relationship between exposure to cell phone and laptop radiation and sleep quality in UNS informatics students ($p = 0.042$; $r = 0.192$). The results of other Pearson statistical tests also show a significant relationship between exposure to radiation from cell phones and laptops and interference with concentration among UNS informatics students ($p = 0.020$; $r = 0.406$). This situation is consistent with the research in which there was a positive correlation between cellphone use and deteriorating sleep quality among medical students⁽¹⁶⁾. Exposure to radiation from cell phones

and laptops can disrupt the diurnal rhythm; reduce the production of melatonin hormone in the pineal gland which can reduce sleep onset, thereby reducing sleep; and encourage the secretion of cortisol hormone which can affect the metabolic cycle, the sleep-wake cycle, and of sleep quality in the REM phase.⁽¹⁸⁾

Concentration is defined as a person’s ability to maintain attention in a long period. Attention involves parts of the brain called alerting, orienting, and attention executives.⁽¹⁹⁾ Orienting as a process of directing attention to sources of stimulation involving visual orienting functions. The anatomical structure associated with orienting is the parietal and frontal lobes which produce neurotransmitters acetylcholin and play a role in the process of orienting. The function of acetylcholin is to help communicate between the nerves and muscles of the eye and the process of storing and recalling memories and attention. Physical environment such as radiation exposure can affect the production of acetylcholin so that it can cause interference with concentration in a person.

The results of the Pearson statistical test showed a significant relationship between radiation exposure to cell phones and laptops and headache among UNS informatics students ($p = 0.000$; $r = 0.510$). The resulting headache is related to the occurrence of electrical hypersensitivity resulting from oxidative damage in brain cells. Brain cells will change the electrical activity of the brain, followed by changes in the blood-brain barrier permeability, resulting in the disruption of the active transport of Na^+ and K^+ ions, and the release of Ca^{++} ions by cellular membranes.⁽²⁰⁾ When the cell experiences stress, there is a regulatory disorder so that the Ca^{++} ion undergoes regulation opposite to that of Ca^{++} ions going into the cell and triggering focal ischemics in the brain region, thus causing complaints of headache.⁽²¹⁾ The exposure to radiation for one hour caused a stress response to the cell endothelium in the form of a change in phosphorylation status of certain types of proteins namely Heat shock protein 27 (Hsp 27). This will facilitate the elements of albumin, ions, metal, chemicals and viruses to pass through so that microedema and inflammation occur, thus causing complaints of headache.⁽²²⁾

The results of the Pearson statistical test showed a significant relationship between exposure to radiation from cell phones and laptops and the incidence of dry eye among UNS informatics students ($p = 0.034$; $r = 0.195$). This is consistent which states that dry eye syndrome results from continuous radiation exposure to the eye, resulting in hyperosmolarity in the tear layer, which causes irrigation in the eyeball to be disrupted, thus causing inflammation on the eye surface.^{(21),(23)} The severity of dry eye syndrome can be influenced by different eye distances to the monitor, as well as the brightness level of the monitor and the different light conditions around the location.⁽²⁴⁾ Exposure to cell phone radiation increases the concentration of free radicals such as reactivity oxygen species (ROS) in cells. The high level of ROS results in oxidative stress and injury to the cell, namely Lipid peroxidation in membranes is characterized by increased levels of malondialdehyde (MDA).⁽²¹⁾ Long radiation exposure can cause damage to cell structures, resulting in decreased function and death of cells.⁽²⁵⁾

Conclusion

Exposure to electromagnetic radiation from cell phones and laptops causes subjective complaints such as decreased sleep quality, headache, dry eye syndrome

and impaired concentration among UNS informatics students.

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References

1. Poushter J. Smartphone Ownership and Internet Usage Continues to Climb in Emerging Economies [Internet]. 2016. Available from: www.pewresearch.org
2. Victoria J. Rideout, M.A. Ulla G. Foehr PD and, Donald F. Roberts P. Generation M2 Media in the Lives of 8 to 18 Year Olds. California; 2010.
3. Nurwan, Achmad N, Resmawan. Pemanfaatan Smartphone dan Laptop Pribadi Menuju Smart Teacher dan Smart Society di Desa Monggupo Kecamatan Atinggola Kabupaten Gorontalo Utara. *J Bakti Masy Indones*. 2018;1(1):39–47.
4. Mahdi H Miraz MB and MEH. Impacts of Culture and Socio-Economic Circumstances on Users Behavior and Mobile Broadband Technology Diffusions Trends A Comparison Between The United Kingdom (UK) and Bangladesh. *arXiv*. 2017;1708(02798):473–9.
5. Qomariyah AN. Perilaku Penggunaan Internet pada Kalangan Remaja di Perkotaan. Universitas Airlangga Surabaya; 2009.
6. Thomée S, Härenstam A, Hagberg M. Mobile phone use and stress, sleep disturbances, and symptoms of depression among young adults - a prospective cohort study. *BMC Public Health* [Internet]. 2011;11(1):66. Available from: <http://www.biomedcentral.com/1471-2458/11/66>
7. Manarisip M, Rumampuk JF, Pangemanan DHC. Gambaran gangguan radiasi handphone terhadap kesehatan siswa kelas xi SMK discovery manado. *J Kedokt Komunitas dan Trop*. 2015;3(3):154–9.
8. Vijayalaxmi, Scarfi MR. International and National

- Expert Group Evaluations: Biological / Health Effects of Radiofrequency Fields. *Int J Environ Res Public Health*. 2014;11:9376–408.
9. Schoeni A, Roser K, Rösli M. Symptoms and Cognitive Functions in Adolescents in Relation to Mobile Phone Use during Night. *PLoS One*. 2015;10(7):1–11.
 10. Zhang J, Ma RCW, Kong APS, Physician F, So WY, Li AM, et al. Relationship of Sleep Quantity and Quality with 24-Hour Urinary Catecholamines and Salivary Awakening Cortisol in Healthy Middle-Aged Adults. *Sleep*. 2011;34(2):225–33.
 11. Abdul Rahim Sya'ban IMRR. Faktor-Faktor Yang Berhubungan Dengan Gejala Kelelahan Mata (Asstenopia) Pada Karyawan Pengguna Komputer Pt.Grapari Telkomsel Kota Kendari. In: *Prosiding Seminar Bisnis & Teknologi*. Bandar Lampung: Lembaga Pengembangan Pembelajaran, Penelitian & Pengabdian Kepada Masyarakat IBI Darmajaya; 2014. p. 15–6.
 12. Swamardika IBA. Pengaruh Radiasi Gelombang Elektromagnetik Terhadap Kesehatan Manusia. *Teknologi Elektro*. 2009;8(1).
 13. Ganong WF. *Buku ajar fisiologi kedokteran edisi 22*. Jakarta; 2008. 56 p.
 14. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Quality Index: A New Instrument for Psychiatric Practice and Research. *Psychiatry Res*. 1989;28:213.
 15. Dougherty BE, Nichols JJ, Nichols KK. Rasch Analysis of the Ocular Surface Disease Index (OSDI). *IOVS*. 2011;52(12):8630–5.
 16. Harris, D. V., & Harris, B. L. (1984). *The athlete's guide to sports psychology: Mental skills for physical people (Vol. 1)*. Human Kinetics. 1984;1:1984.
 17. Shrivastava A, Saxena Y. Original Article Effect of mobile usage on serum melatonin levels among medical students. 2014;58(4):395–9.
 18. Mohammed HS, Elsayed AA. Non-thermal continuous and modulated electromagnetic radiation fields effects on sleep EEG of rats q. *J Adv Res [Internet]*. 2013;4(2):181–7. Available from: <http://dx.doi.org/10.1016/j.jare.2012.05.005>
 19. Higgins, E. S., & George, M. S. (2013). *Neuroscience of clinical psychiatry: the pathophysiology of behavior and mental illness*. Lippincott Williams & Wilkins. 2013;2013.
 20. No Title. 2001;52:2001.
 21. No Title. 2007;14:2007.
 22. Leszczynski D, Joenväärä S. Non-thermal activation of the hsp27 / p38MAPK stress pathway by mobile phone radiation in human endothelial cells: Molecular mechanism for cancer- and blood-brain barrier-related effects. *Differentiation*. 2002;70:120–9.
 23. Messmer, E. M. (2015). The pathophysiology, diagnosis, and treatment of dry eye disease. *Deutsches Ärzteblatt International*, 112 (5), 71. 2015;112:2015.
 24. Ranasinghe, P., Wathurapatha, W. S., Perera, Y. S., Lamabadusuriya, D. A., Kulatunga, S., Jayawardana, N., & Katulanda, P. (2016). Computer vision syndrome among computer office workers in a developing country: an evaluation of prevalence and risk factors. 2016;9:2016.
 25. Jafar S, Hossein G, Kamarei M, Aliakbarian H, Sattarahmady N, Sharifzadeh A, et al. *International Journal of Biological Macromolecules* Effects of mobile phone radiofrequency on the structure and function of the normal human hemoglobin. 2009;44:278–85.

The Correlation Analysis between Hypertension Controlling Factors and Blood Pressure in the Elderly Living in Griya Werdha Retirement Home, Surabaya

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Abstract

Background: Hypertension is a condition when the blood pressure in blood vessels increases chronically. Living a healthy life has been shown to reduce blood pressure and reduce the risk of cardiovascular diseases. The reduction of body weight and mental stress, low sodium diet, and increased physical activities can also reduce the risk of hypertension.

Objective: To analyze the hypertension controlling factors of the elderly's blood pressure living in Griya Werdha Retirement Home in Surabaya.

Method: In this study, the method used was descriptive analytical design with cross-sectional approach by using purposive sampling technique. This study involved 18 elderly with the following inclusion criteria: elderly who had systolic blood pressure of more than 120mm Hg and diastolic blood pressure of more than 80 mm Hg. The independent variables in this study were the food diet and body mass index, while the dependent variable was the blood pressure. The collected data was analyzed by using Spearman's Rho correlation test with a significance level $\alpha < 0.05$.

Results: The research results found that the majority of elderly people were 60-75 years old, female, had stayed for more than 12 months and had a history of hypertension of 5 years or more. The analysis results of research variables using the Spearman's Rho correlation test indicated that the p-value for the variables of DASH dietary, body mass index, stress and physical activities were all more than 0.05.

Conclusion: DASH diet, body mass index, stress and physical activities did not have correlation with blood pressure, thus, no variables were associated with controlling hypertension on the elderly living in UPTD Griya Werdha Retirement Home in Surabaya.

Keywords: Hypertension, elderly, diet, lifestyle.

Introduction

Hypertension is a condition when blood pressure in blood vessels increases chronically⁽¹⁾. One in three adults in the USA suffers from hypertension or is treated for hypertension, and their life expectancy is shortened. According to Joint National Committee on Prevention, Detection, Evaluation, and Treatment on High Blood Pressure 8, or JNC 8, one billion people of the world's population, or 1 in 4 adults, suffers from hypertension. The criteria used in determining hypertension refers to the diagnosis criteria for JNC VII 2003, which is the

measurement results of systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg. *The World Health Organization* (WHO) recommends the use of a non-pharmacological approach to treat hypertension⁽²⁾. Living a healthy life has been proven to reduce blood pressure and reduce the risk of cardiovascular diseases. The reduction of body weight and mental stress, low sodium diet, and increased physical activities can also reduce the risk of hypertension⁽³⁾. Most of the elderly population who experience hypertension are at the age of above 60. In 2025, people with hypertension will

reach 1.6 billion⁽⁴⁾. According to the National Basic Health Survey (2013) the prevalence of hypertension in Indonesia based on age groups are as follows: 45.9% at the age of 55-64 years; 57.6% at the age of 65-74; and 63.8% at the age of above 75. Hypertension can lead to heart disease and stroke, heart failure, peripheral vascular diseases, kidney disorders, retinal bleeding and visual impairment⁽⁵⁾. The basic mechanism that causes hypertension is the loss of distensibility and elasticity of large arteries. This stiffness of the arteries can increase progressively based on age. Blood vessels thickening and widening are the main changes that occur in the aging process. The factors that play a role in the stiffness of great arteries in the aging process include collagen, reduced elastin and classification. This study aimed to analyze the hypertension controlling factors of the elderly's blood pressure living in Griya Werdha Retirement Home in Surabaya.

Method

This study utilized descriptive analytical design with cross-sectional approach while the data was collected through purposive sampling technique. The research collected information and identified the factors related to hypertension control in the elderly living in Griya Werdha Retirement Home in Surabaya, which included dietary factors, body mass index, stress, and physical activities. This study involved 18 elderly people who met the inclusion criteria of having systolic blood pressure >120mmHg and diastolic blood pressure >80 mmHg. On the other hand, the exclusion criteria included elderly who had serious hearing loss, aggressive physical behavior and the elderly who were sick during the study. The independent variables in this study included the food

diet and body mass index, while the dependent variable was the blood pressure. The instrument utilized was the DASH from NHLBI diet observation sheet (2015)⁽⁶⁾ to find out the diet of food consumed by the elderly. The diet observation was done through measuring the food intake that had been adjusted with the age and physical activities, while the measurement of salt intake was conducted by measuring the total grams included in the elderly's food by the kitchen attendants. The stress data was collected by using the DASS 42 questionnaire (Lovibond & Lovibond, 1995) which had been modified by adding questions related to stress. The physical activity observation sheet was the modified version from Riskesdas (2013) questionnaire and demographic questionnaire to determine body mass index and general description of the condition of the study respondents. The measurement of blood pressure as the dependent variable used standard operating procedures from Perry & Potter (2005) and JNC 8 (2014) ⁽⁷⁾ which had been modified. The collected data was analyzed by using Spearman's Rho correlation test with a significance level (α) of less than 0.05. From the Spearman's Rho correlation test, the correlation coefficient value was determined. Then, the significance between the two variables was determined by comparing the rho-value with rho's critical value table.

Results

Respondents demographic characteristics:

The respondents' demographic data regarding the demographic characteristics of the 18 respondents in this study based on age, sex, length of stay and history of hypertension can be seen in Table 1 as follows.

Table 1: Respondents' Demographic Characteristics

No.	Respondents Characteristics	Category	F(x)	%
1	Age (Years)	45-59	1	5.5
		60-75	11	66.7
		76-90	5	27.3
		>90	1	5.5
2	Sex	Female	11	61
		Male	7	39
3	Length of stay	0-6 months	1	5.5
		7-12 months	4	22.2
		>12 Months	13	72.3
4	History of hypertension	<5 years	4	22.2
		≥5 Years	14	77.8

Based on Table 1, out of 18 respondents, the demographic characteristics of the respondents suggested that the majority of respondents were the elderly in the range of 60-75 years old, and were female.

The respondents were dominated by those who stayed more than 12 months and those who had hypertension medical history of more than 5 years.

Table 2. The Corellation between Dependent and Independent Variables

Variables	Blood pressure				Total		p-value
	Not match the hypertension treatment target		Match the hypertension treatment target		f(x)	%	
	f(x)	%	f(x)	%			
DASH Diet							
Insufficient	0	0	0	0	0	0	-
Sufficient	7	39	11	61	18	100	
Good	0	0	0	0	0	0	
Body Mass Index							
Overweight	1	5.5	1	5.5	2	11	0.432
Thin	1	5.5	5	27.7	6	33.2	
Normal	5	27.7	5	27.7	10	55.4	
Stress							
Severe stress	1	5.5	0	0	1	5.5	0.633
Heavy stress	0	0	1	5.5	1	5.5	
Moderate stress	0	0	1	5.5	2	11	
Mild stress	1	5.5	0	0	1	5.5	
Normal	5	27.7	9	50	14	77.7	
Physical Activities							
Insufficient	0	0	0	0	0	0	-
Good	7	39	11	61	18	100	

The analysis results of the correlation between the DASH diet and elderly blood pressure indicated that most of the respondents had sufficient DASH diet with blood pressure in accordance with the target of hypertension treatment. Further statistical test results indicated that p-value was undefined. It can be concluded that H1 was rejected, meaning that there was no corellation between the DASH diet and the elderly blood pressure. From the results of the observations on the corellation between body mass index and elderly blood pressure, the researchers found that almost half of the respondents who had normal body mass index range suffered from blood pressure and did not belong to the hypertension treatment target. Mean while, the respondents who were not in the hypertension treatment target, or within the normal range, reached almost half of the respondents. Further statistical test results indicated that the p value amounted to 0.432. There fore, it can be concluded that H1 was rejected, meaning there was no corellation

between body mass index and elderly blood pressure. The analysis results of the corellation between stress and elderly blood pressure suggested that almost half of the respondents who were within the hypertension treatment target had normal stress level. Further statistical test results obtained p value of 0.31. The analysis results of the corellation between physical activities and elderly blood pressure indicated that most of the respondents who belonged to good physical activity criterion suggested from hypertension in accordance with the hypertension treatment target.

Discussion

DASH diet, body mass index, stress and physical activities did not have any corellation with blood pressure. Therefore, there were no dominant factors associated with controlling hypertension and the elderly living in Griya Werdha Retirement Home in Surabaya. Lifestyle modification could be a treatment option for

hypertension for the elderly⁽⁸⁾. In this study, there was an influence by Griya Werdha Retirement Home policy in applying the lifestyle modification for the elderly. The aforementioned lifestyle modification was not all applicable in Griya Werdha because the elderly had already stopped consuming alcohol and quit smoking. Therefore, the results of the hypertension control factors that could be studied were the food diet using the recommended DASH diet, weight control by measuring body mass index, stress control, and physical activities.

In the elderly group, there was a decrease in the elasticity of peripheral blood vessels due to the aging process⁽⁹⁾. The mechanism of increasing blood pressure is induced by sodium, a component in salt, which is excreted through the kidneys. When the kidneys cannot excrete sodium as a result of damage to the nephron, sodium retention will occur⁽¹⁰⁾. Low-salt food intake can be promoted through DASH diet by avoiding the occurrence of adipocyte cell hypertrophy due to lipogenesis processes in white fat tissue. If this situation continues, it will cause narrowing of the arteries causing increase in blood vessels⁽¹¹⁾. High intake of fruits and vegetables can increase the concentration of K^+ in the intracellular fluid which can result in fluid transfer to extra cellular fluid and lower the blood pressure⁽¹²⁾. High fruit and vegetable intake, as a part of healthy diet, has beneficial effects on controlling hypertension⁽¹³⁾. The DASH diet aims to reduce blood pressure by increasing a diet rich in fruits, vegetables, whole grains, low-fat dairy products, nuts, low-salt food and low sugar intake⁽¹⁴⁾. The results of the study regarding the DASH diet could be obtained because the respondents' food consumption was scheduled and had the same diversity for each respondent. Male and female respondents received the same portion.

The correlation between body mass index and blood pressure in elderly hypertension suggested that almost half of the study respondents were in the category of normal body mass index and were included in the hypertension treatment target. The results of the Spearman's Rho statistical test indicated that there was no correlation between body mass index and elderly blood pressure. Overweight and obesity are risk factors for hypertension⁽¹⁵⁾. Obesity is an abnormal or excessive accumulation of fat in adipose tissue, reaching a level that can cause health problems. Obesity is influenced by a number of factors, including food intake, neuroendocrine, genetic, social and lifestyle factors⁽¹⁶⁾. The aging process is experienced by everyone. This

process is not a disease but the process of growth and development that organisms will pass. In this stage, the body will experience various conditions, including muscle atrophy and decreased food appetite. Elderly people who experience muscle atrophy and decreased food appetite will have a constant weight.

Stress with pressure is body response or reaction to events outside the body and responses from within the body. Stress is also related to hypertension because it can activate sympathetic nerves, so that the blood pressure increases intermittently. Stress increases peripheral vascular resistance and cardiac output so it will stimulate sympathetic nerve activity. The responses caused by the body include muscle tension, increased heart rate, and increased blood pressure. These reactions are prepared by the body to react quickly. If not used, it will cause diseases including hypertension. There is a meaningful correlation between stress (based on personality type) and hypertension⁽¹⁷⁾. Impatience, ambition, competitive perfectionism, and irritability contribute a greater risk of developing hypertension. Psychological stress has a correlation with hypertension. This gap can occur because the response of each person is very individual. Individuals who cannot adapt to stressors can cause physical or psychological disorders. Stressors that can be managed properly can have a positive impact on individuals.

The correlation between physical activities and blood pressure in elderly hypertension indicated that all study respondents were in a good range in carrying out activities with blood pressure according to the target of treatment for hypertension. Spearman's Rho statistical test results suggested that there was no correlation between physical activities and elderly blood pressure. Physical activities affect the occurrence of hypertension where people with lack of activities tend to have a higher heart rate, causing the heart muscles work harder and lead to hypertension. Hypertension causes an increase in blood pressure and causes complications such as stroke, coronary heart disease for the heart blood vessels and heart muscles⁽¹⁵⁾. Good and routine physical activities will train the heart muscles and peripheral resistance which can prevent an increase in blood pressure. Regular exercises can stimulate the release of endorphins which cause an euphoria effect and muscle relaxation, stopping the blood pressure from increasing⁽¹⁸⁾. Physical activities result in changes in plasma renin activity level, serum aldosterone concentration, and meaningful converting enzyme angiotensin activities. Therefore, moderate and

heavy physical activities can decrease blood pressure. Physical activities can be carried out for 30 minutes with moderate and heavy intensity⁽¹⁶⁾.

Conclusion

The DASH diet, body mass index, stress and physical activities did not have any correlation with blood pressure. Therefore, no dominant factors were associated with controlling hypertension and the elderly living in Griya Werdha Retirement Home in Surabaya. This research is expected to develop nursing science in controlling hypertension so that the mortality and morbidity rate due to hypertension can decrease.

Ethical Clearance: This study had received ethical approval from the ethical review team through the ethical certificate number 221-KEPK.

Conflict of Interest: The author reports no conflict of interest of this work.

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References

1. Foëx P, Sear JW. Hypertension: Pathophysiology and Treatment. *Contin Educ Anaesthesia, Crit Care Pain*. 2004;4(3):71–5.
2. Wallace JP. Exercise in Hypertension. *Sport Med*. 2006;33(8):585–98.
3. Callaghan DM. Health-Promoting Self-Care Behaviors, Self-Care Self-Efficacy, and Self-Care Agency. *NursSci Quarterly*. 2003;16(3):247–54.
4. Association AH. Expert Consensus Document on Hypertension in the Elderly: A Report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents. *J Am CollCardiol*. 2011;57(20).
5. Organization WH. Physical Activity: in Guide Community Preventive Service. 2010;
6. Chobanian A V, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, *et al*. the Online Version of This Article, Along with Updated Information and Services, Is Located on the World Wide Web At: 2003;
7. Perry, Potter. *Buku Ajar Fundamental Keperawatan*. Jakarta: EGC; 2009.
8. Aronow WS, Fleg JL, Pepine CJ, Artinian NT, Bakris G, Brown AS, *et al*. ACCF/AHA Expert Consensus Document ACCF/AHA 2011 Expert Consensus Document on Hypertension in the Elderly A Report of the American College of Cardiology Foundation Task Force On. 2011;2434–506.
9. Babatsikou F, Zavitsanou A. Epidemiology of Hypertension in the Elderly. 2010;1:24–30.
10. He FJ, Li J, Macgregor GA. Effect of Longer Term Modest Salt Reduction on Blood Pressure: Cochrane Systematic Review and Meta-Analysis of Randomised Trials. *RESEARCH*. 2013;1325(April):1–15.
11. Vindy Destiany, Sulchan M. Asupan Tinggi Natrium Dan Lama Menonton Tv Sebagai Faktor Risiko Hipertensi Obesitik Pada Remaja Awal. *J Nutr Coll*. 2012;1:153–9.
12. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, *et al*. 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults Report from the Panel Members Appointed to the Eighth Joint National Committee (JNC 8). *Clin Rev Spec*. 2014;1097(5):507–20.
13. Wang L, Manson JE, Gaziano JM, Buring JE, Sesso HD. Fruit and Vegetable Intake and the Risk of Hypertension in Middle-aged and Older Women. *Am J Hypertens*. 2013;25(2):180–9.
14. Siervo M, Lara J, Chowdhury S, Ashor A, Oggioni C, Mathers JC. Systematic Review with Meta-Analysis Effects of the Dietary Approach to Stop Hypertension (DASH) Diet on Cardiovascular Risk Factors: A Systematic Review and Meta-Analysis *British Journal of Nutrition*. 2015;1–15.
15. Appel LJ, Brands MW, Daniels SR, Karanja N, Elmer PJ, Sacks FM, *et al*. Dietary Approaches to Prevent and Treat Hypertension A Scientific Statement from the American Heart Association. 2006;296–308.

16. Leon N, Charles S, D AV, Magloire D, Clemence M, Azandjeme C, *et al.* Determinants of Adherence to Recommendations of the Dietary Approach to Stop Hypertension in Adults with Hypertension Treated in A Hospital in Benin. 2015;3(5):213–9.
17. Mokhtari Z, Hosseini S, Miri R, Baghestani AR, Zahedirad M, Rismanchi M, *et al.* Relationship Between Dietary Approaches to Stop Hypertension Score and Alternative Healthy Eating Index Score with Plasma Asymmetrical Dimethylarginine Levels in Patients Referring *for* Coronary Angiography. 2015;
18. Okkinos PEFK, Iannelou ANG, Anolis ATM, Ittaras ANP. Physical Activity in the Prevention and Management of High Blood Pressure. *Hell J Cardiol.* 2009; 50:52–9.

Association of Exon Deletion of MXI1 Gene with Cervical Abnormalities and Cancers Incidence in Some Iraqi Married Women

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Abstract

Cervical cancer is one of the most frequently diagnosed malignancies representing the fourth leading cause of cancer-related death in females' worldwide, with approximately 500,000 new cases diagnosed and 280,000 deaths occurring each year. Mxi1, an antagonist of c-Myc, maps to human chromosome 10q24-q25, a region altered in a substantial fraction of prostate tumors, in prostate cancer, where a high frequency of loss and mutation of the *MXI1* gene has been reported. The aim of present study was to find out the possible association of exon deletion of *MXI1* gene with incidence of cervical abnormalities and cancers in some Iraqi married women. The present study include collection of 120 scraping cervical cells samples from women clinically diagnosed with cervical abnormalities and cancer, and 30 scraping cervical cells samples from apparently healthy women and all these samples were submitted for cytological and histopathological examination. DNA was extracted from all these samples, and then the singleplex PCR was performed with primers targeted the exon1, 2, 3, 4, 5 and 6 of *MXI1* gene. The results of cytological examination showed that 30(25%), 21(17.5%), 15(12.5%), 11(9.16%), 2(1.66%), 1(0.83%), 22(18.33%) and 18(15%) out of 120 scraping cervical cells samples were detected for ASCUS, LSIL, HSIL, SCC, AGUS, cervicitis, and cervicitis with squamous metaplatia, respectively. Also the results of histopathological examination showed that 32(26.66%), 19(15.83%), 17(14.16%), 11(9.16%), 1(0.83%), 22(18.33%) and 18(15%) out of scraping cervical cells samples were detected for CINI, CINII, CINIII, SCC, adenocarcinoma, cervicitis, and cervicitis with squamous metaplatia, respectively. The results of singleplex PCR revealed that the positive singleplex PCR samples were identified by presence of 240, 140, 210, 200, 260, 300 bp amplicons of the exon1, 2, 3, 4, 5 and 6 of *MXI1* gene respectively. The PCR results exhibited that 57(47.5%) out of 120 scraping cervical cells samples were showed deletion in the exon5 represented by 22(38.59%), 11(19.29%), 8(14.03%), 7(12.28%) and 9(15.78%) out of 57 positive deletion samples that were detected for ASCUS, CINI, CINII, CINIII and SCC, respectively. In addition, the results showed that 22(73.33%) out of 30 ASCUS, 11(34.37%) out of 32 CINI, 8(42.1%) out of 19 CINII, 7(41.17%) out of 17 CINIII, and 9(81.81%) out of 11 SCC were had exon5 deletion. Whereas 63(52.5%) out of 120 scraping cervical cells samples were didn't show any deletion in the exon5 of *MXI1* gene.

Conclusion: The exon deletion of *MXI1* gene was clearly associated with the exon5, whereas other exons of *MXI1* gene didn't show any deletion, and the results revealed there was remarkable association between the exon5 deletion and the incidence of precancerous stages include ASCUS, CINI, CINII, CINIII and cancerous stage represented by SCC.

Keywords: Cervical abnormalities, cervical cancer, married women, *MXI1* gene.

Introduction

Cervical cancer is the third most common cancer worldwide and a major fatal malignancy among women,

causing about 275,000 deaths annually worldwide, mostly in developing countries. It can be a preventable disease if identified at its early (precancerous) stages and

treated by ablation^(1,2). Max interactor 1 gene (MXI1) is a transcription factor that belongs to the mad family of Myc antagonists, which encode proteins that are highly homologous to c-Myc. Mxi1 opposes the growth-promoting activity of c-Myc by repressing transcription of c-Myc activated target genes. Mxi1 inhibits the ability of c-Myc to transform cells in vitro, and its expression is associated with cellular differentiation⁽³⁾. The MXI1 gene has been localized to chromosome 10q24-25⁽⁴⁾, a region demonstrating deletions or rearrangements in 60-97% of human glioblastomas and up to 30% of human prostate cancers. Although loss of heterozygosity for MXI1 is seen in a substantial fraction of glioblastoma tumors (64%), no MXI1 coding sequence mutations have been seen in these tumors⁽⁵⁾. Furthermore, a majority of studies have failed to demonstrate MXI1 mutations in prostate tumors⁽⁶⁾. By counteracting c-Myc, MXI1 functions as a growth suppressor, resulting in reduced cell proliferation in vitro^(4,5,7), previously localized the human MXI1 gene to chromosome 10q24-q25. Deletions resulting in loss of alleles in this region of chromosome 10 are observed in 30±50% of human prostate tumors⁽⁸⁾.

Materials and Method

Samples Collection: During the period of study, from beginning of March 2017 to the end of September 2017. 120 scraping cervical cells samples were collected from Iraqi women clinically diagnosed with cervical abnormalities and cancer, and 30 scraping cervical cells samples from apparently healthy women who attended to Baghdad Medical City and Al-Elwiya Maternity

Teaching Hospitals in Baghdad City, Patients’ ages ranged from 20 to 70 years of age. This study was carried out after obtaining the approval from the Institute of Genetic Engineering and Biotechnology for Post Graduate Studies/ Baghdad University and Ministry of Health/ Iraq.

Extraction of DNA: The DNA was extracted from scraping cervical cell samples using DNA-Sorb-A nucleic acid extraction kit (Sacace Biotechnologies/ Italy), according to the manufacturer’s instructions.

Agarose gel electrophoresis: After extraction of DNA carrying out, agarose gel electrophoresis was adopted to confirm the presence and integrity extracted genomic DNA⁽⁹⁾.

Detection of MXI1 gene by using PCR: The PCR was adopted to detect the exons 1, 2, 3, 4, 5 and 6 of MXI1 gene in the extracted DNA of scraping cervical cells from clinically diagnosed women with cervical cancer. To select PCR primers that can give specific amplification for exons 1, 2, 3, 4, 5 and 6 of MXI1 gene. The (MXE1-F/MXE1-R) for exon 1, (MXE2-F/MXE2-R) for exon 2, (MXE4-F/MXE4-R) for exon 4, (MXE5-F/MXE5-R) for exon 5, (MXE6-F/MXE6-R) for exon 6, were used according to⁽¹⁰⁾, the (MXE3-F/MXE3-R) for exon 3 was used according to⁽¹¹⁾. The general properties of these primers were checked by using Oligocalc Oligonucleotide Properties Calculator program, the name and sequence of these primers are listed below in table (1).

Table 1: The name, sequence and product size of PCR primers for exons of MXI1 gene

Name of primer	Sequece of Primer 5’-3’	Size of Product (bp)
MXE1-F	ATGGAGCGGGTGAAGATGAT	240
MXE1-R	GCACTGCCGAAAAAGATTAG	
MXE2-F	GGGTCAATGGATTTGGGTAC	140
MXE2-R	TAAGCGTTCCCAGCTTGCTA	
MXE3-F	GCAACAAAGCATGGCTAATG	210
MXE3-R	TTCACAATGGGCTATACATCTGA	
MXE4-F	TAACCAGACTGTGCTGATTTG	200
MXE4-R	ACCAGAACTGAGGGAATTGTG	
MXE5-F	TGTTTGTACTGGACTATACAC	260
MXE5-R	ATGTTTAGTATTTTCATTAGAGAAG	
MXE6-F	GTTAGTTTTTGAAGGTGCGC	300
MXE6-R	TGTTATGTCATGCTGGGTTC	

The PCR reactions for detection of exons of MXI1 gene were performed in 25 µl volumes containing, amplification of exons of MXI1 gene was carried out with initial denaturation at 94°C for 1 minutes, followed by 35 cycles of denaturation at 94°C for 30 seconds, annealing at 66, 65, 55, 66, 65 and 56°C for F and R primers of exons 1, 2, 3, 4, 5 and 6 respectively for 1 minute, and extension at 72°C for 1 minutes. The thermal cycles were terminated by a final extension for 5 minutes at 72°C⁽¹¹⁾. The PCR products were resolved by electrophoresis. Chi-square test was used to significant compare between percentage (0.05 and 0.01 probability) in this study⁽¹²⁾.

Results

Agarose gel electrophoresis was adopted to confirm the presence and integrity of the extracted DNA. The results of PCR showed that samples of present study gave positive result for PCR of exon 1, 2, 3, 4, and 6 of MXI1 gene products with 240, 140, 210, 200 and 300 bp molecular weight, whereas no amplification was observed with exon5 (260bp) in 57 out of 120 samples and negative control (Figures 1).

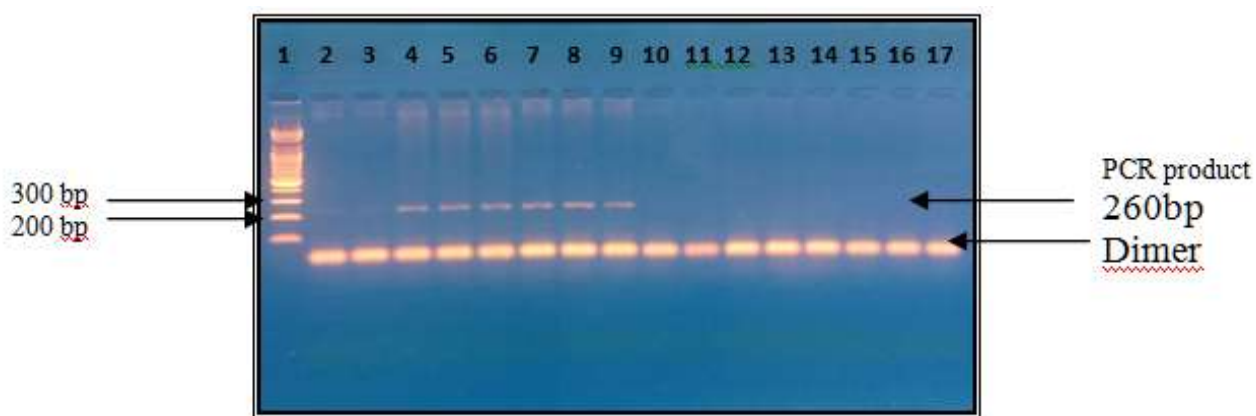


Figure (1): Gel electrophoresis of singplex PCR products of exon 5 of MXI1 gene on 1.5% agarose gel at 10volt/cm for 1 hour. Lane 1: 100 bp DNA ladder, lane 2-17: PCR products of exon 5.

The patient group was divided to eight groups according to cytology examination; i) Atypical squamous cells of undetermined significance (ASCUS) 30 samples, ii) low grade squamous intraepithelial lesion LSIL 21 samples, iii) high grade squamous intraepithelial lesion HSIL 15 samples, iv) squamous cervical cancer 11 samples, v) atypical glandular cells of undetermined significance 2 samples, vi) adenocarcinoma 1 sample, vii) cervicitis 22 samples, and viii) cervicitis with squamous metaplatia 18 samples. The samples were also including 30 specimens (scraping cervical cells) of healthy women used as a control (Table 2).

Table (2): Distribution of samples study according to cytological examination.

Cytological examination	No. of cases	Percentage of cases (%)
ASCUS	30	25.00
LSIL	21	17.50

Cytological examination	No. of cases	Percentage of cases (%)
HSIL	15	12.50
Squamous cervical cancer	11	9.16
AGUS	2	1.66
Adenocarcinoma	1	0.83
Cervicitis	22	18.33
Cervicitis with squamous metaplasia	18	15.00
Total	120	100%
Chi-square value	---	9.074 **
P-value	---	0.0005

** (P<0.01).

ASCUS: Atypical squamous cells of undetermined significance, **LSIL:** Low-grade squamous intraepithelial lesion, **HSIL:** High-grade squamous intraepithelial lesion. **AGUS:** atypical glandular cells of undetermined significance.

Also the results of histopathological examination showed that 32(26.66%), 19(15.83%), 17(14.16%), 11(9.16%), 1(0.83%), 22(18.33%) and 18(15%) out of scraping cervical cells samples were detected for CINI, CINII, CINIII, SCC, adenocarcinoma, cervicitis, and cervicitis with squamous metaplatia, respectively (Table 3).

Table (3): The distribution of sample study according to the histopathological examination.

Histological examination	No. of case	Percentage of case (%)
CIN I	32	26.66
CIN II	19	15.83
CIN III	17	14.16
Squamous cervical cancer	11	9.16
Adenocarcinoma	1	0.83
Cervicitis	22	18.33
Cervicitis with squamous metaplasia	18	15.00
Total	120	100%
Chi-square value	---	9.261 **
P-value	---	0.0003

** (P<0.01), CIN: Cervical intraepithelial neoplasia.

A total of 120 cases of cervical abnormalities were studied, the MXI1 deletion were identified in 57/120 (47.5%) and 63/120 (52.5%) not deleted table (4).

Table (4): Distribution of the study sample according to deletion of exon5 of MXI1.

PCR	Number	Percentage (%)
Positive	57	47.5
Negative	63	52.5
Total	120	100%
Chi-square value	---	2.071 NS
P-value	---	0.0966

NS: Non-Significant.

The PCR results exhibited that 57(47.5%) out of 120 scraping cervical cells samples were showed deletion in the exon5 represented by 22(38.59%), 11(19.29%), 8(14.03%), 7(12.28%) and 9(15.78%) out of 57 positive deletion samples that were detected for ASCUS, CINI, CINII, CINIII and SCC, respectively (Table 5).

Table (5): Correlation samples of study and deletion of exon5 of MXI1 according histopathological examinatin.

Cytology	Number	Percentage (%)
ASC-US	22	38.59
CINI	11	19.29
CINII	8	14.03
CINIII	7	12.28
Squamous cervical cancer	9	15.78
Total	57	100%
Chi-square value	---	6.944 **
P-value	---	0.0078

** (P<0.01).

In addition, the results showed that 22(73.33%) out of 30 ASCUS, 11(34.37%) out of 32 CINI, 8(42.1%) out of 19 CINII, 7(41.17%) out of 17 CINIII, and 9(81.81%) out of 11 SCC were had exon5 deletion.

Discussion

Extension of our study to include *MXII*, located at 10q24-45, identified mutations in 2 cell lines but no detectable change in exon sequences of this gene in bladder tumors. This finding is consistent with *MXII* mapping outside of the critical region of loss on 10q in bladder tumors (13), where mutations in *MXII* do not play a role in urothelial neoplastic progression. These results contrast with observations in prostate cancer, where a high frequency of loss and mutation of the *MXII* gene has been reported (6).

Wang and colleges have found no evidence for loss or mutation of *MXII* in bladder tumors, in contrast to findings in prostate carcinomas (11). We have found deletion in *MXI1* gene in precancerous stages of cervical cancer in Iraqi married women.

Conclusion

Presence of exon deletion in exon5 of *MXI1* gene whereas other 5 exons didn't show any deletion in scraping cervical cell samples that collected from some Iraqi women clinically diagnosed with cervical abnormalities and cancers.

The exon5 deletion was found with high variable percentage in precancerous stages included ASCUS, CINI, CINII, CINIII and cancer stage represented by SCC. whereas the exon5 deletion didn't present in cervicitis and Cervicitis with squamous metaplasia as well as the result revealed high (81.81%) incidence of exon 5 deletion in SCC comparing with other precancerous stage include ASCUS, CINI, CINII, CINIII.

According several points that mention above can be conclude that there is a strong association between the exon5 deletion and the incidence in cervical abnormalities and squamous cervical cancer in marred women which can refer to possible use the exon5 deletion of MXI1 gene as early molecular marker for cervical abnormalities and squamous cervical cancer detection in marred women.

Conflict of Interest: None

Funding: Self

Ethical Clearance: Not required.

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Reference

1. American Cancer Society, Cancer Facts and Figures. Atlanta, Ga: American Cancer Society, 2018. Available online. Last accessed April 27, 2018
2. Lee S, Vigliotti J, Vigliotti V, Jones W. From human papillomavirus (HPV) detection to cervical cancer prevention in clinical practice. *Cancers*, 2014, 6: 2072-2099.
3. O'Hagan R, Schreiber-Agus N, Chen K, David G, Engelman J, Schwab R, Alland L, Thomson C, Ronning D, Sacchettini J, Meltzer P, DePinho R. Gene-target recognition among members of the myc superfamily and implications for oncogenesis. *Nat Genet*, 2000, 24:113±119.
4. Wechsler D, Hawkins A, Li X, Jabs E, Grifm C, Dang C. Localization of the human Mxi1 transcription factor gene (MXI1) to chromosome 10q24-q25. *Genomics*, 1994, 21:669±672.
5. Wechsler D, Shelly C, Petroff C, Dang C. MXI1, a putative tumor suppressor gene, suppresses growth of human glioblastoma cells. *Cancer Res.*, 1997, 57:4905–12.
6. Prichowink E, Grovo L, Deubler D, Zhu X, Stephenson R, Rohr L, Yin X, Brothman A. Commonly occurring loss and mutation of the MXI1 gene in prostate cancer. *Genes Chromosomes Cancer*, 1998, 22: 295–304.
7. Edelhoff S, Ayer D, Zervos A, Steingrimsson E, Jenkins N, Copeland N, Eisenman R, Brent R, Distech C. Mapping of two genes encoding members of a distinct subfamily of MAX interacting proteins: MAD to human chromosome 2 and mouse chromosome 6, and MXI1 to human chromosome 10 and mouse chromosome 19. *Oncogene*, 1994, 9:665±668.
8. Lacombe L, Orlow I, Reuter V, Fair W, Dalbagni G, Zhang Z, Cordon-Cardo C. Microsatellite instability and deletion analysis of chromosome 10 in human prostate cancer. *Int. J. Cancer*, 1996, 69:110±113.
9. Sambrook J. *Molecular Cloning: A Laboratory manual*. Second Edition. (Plainview, New York: Cold Spring Harbor Laboratory Press). 1989.
10. Li X, Wang D, Zhu Y, Guo R, Wang X, Lubomir K, Mukai K, Sasaki H, Yoshida H, Oka T, Machinami R, Shinmura K, Tanaka M, Sugimura H. Mxi1 mutations in human neurofibrosarcomas. *Jpn. J. Cancer Res.*, 1999, 90(7):740-6.
11. Wang D, Rieger-christ K, Latini J, Moinzadeh A, Stoffel J, Pezza J, Saini K, Libertion J, Summerhayes I. Molecular analysis of PTEN and MXI1 in primary bladder carcinoma. *Int. J. Cancer*, 2000, 88: 620–625.
12. SAS. *Statistical Analysis System, User's Guide*. Statistical. Version 9.1th ed. SAS. Inst. Inc. Cary. N.C. USA. 2012.
13. Kagan J, Liu J, Stein J, Wagner S, Babkowski R, Grossman B, Katz R. Cluster of allele losses within a 2.5 cM region of chromosome 10 in high-grade invasive bladder cancer. *Oncogene*, 1998, 16: 909–913.

Curcumin and 6-Shogaol Increase Hemoglobin F Levels by Inhibiting Expression of STAT3 mRNA Gene in K562 Line Cell

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Abstract

One of the approaches for beta-thalassemia therapy is the induction of the Haemoglobin F (Hb F). Curcumin and 6-Shogaol are empirically known to induce HbF, but the signalling cascade has not been widely explained. This study aims to uncover the potential of Curcumin and 6-shogaol in inhibiting the expression of STAT3 mRNA gene. This study uses the K562 erythroleukemic line cell model with an experimental design post-test only with a control group. There are 5 groups, each group has 3 replications, named the control group without treatment, the positive control group with Hydroxyurea treatment (75 μ M), the combination treatment group of Curcumin (2 μ M) and 6-Shogaol (10 μ M), the single curcumin (2 μ M) treatment group and a single 6-Shogaol (10 μ M) treatment group. Test samples were taken in 72-h and 96-h time series, then RNA extraction from the cell line was continued by cDNA synthesis. The expression of STAT3 mRNA gene was measured using the qRT-PCR technique; then, the Hb F level was measured by the ELISA method. Statistical analysis using ANOVA test with significance level $p < 0.05$. In the 72-h time series, there was a significant decrease in STAT3 Gena mRNA expression ($p < 0.05$). The lowest single curcumin group ($p < 0.01$) followed by a single 6-Shogaol group ($p < 0.05$) compared to the untreated control group, while the positive control group with hydroxyurea treatment and the Curcumin and 6-shogaol combination treatment groups are not significant. Hb F levels, there was an increase in 96-h time series ($p < 0.05$) respectively from highest to lowest in the curcumin group ($p < 0.05$), 6-shogaol ($p > 0.05$) compared to the control group, but in the positive control group ($p > 0.05$) and the combination group ($p > 0.05$) it is lower than the control group without any treatment. Curcumin and 6-shogaol increase Hb F levels through inhibition expression of STAT3 mRNA Gene on K562 cells. The results of this study could be the basis for further research in vivo to reveal the signalling pathway in Hb F induction therapy.

Keywords: Curcumin, 6-shogaol, STAT3 Gena mRNA, Hemoglobin F, K562 cells.

Introduction

β -Thalassemia is a group of heterogeneous recessive autosomal hereditary genetic diseases associated with

point mutation or small deletion resulting in the absence or reduction of β -globin chain protein synthesis, resulting in haemoglobin deficiency. There are alternative therapies that can be developed to overcome the severity of this disease by inducing Fetal Haemoglobin (Hb F). The globin- γ chain, which is similar to the globin- β chain, is produced during pregnancy when it joins with globin- α chain, is to form Fetal Hemoglobin ($\alpha_2\gamma_2$). Hence, one of the potential current therapeutic approaches to haematological disorders, including β -thalassemia, is the stimulation of induction of fetal haemoglobin production⁽¹⁻⁴⁾.

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One of the transcription factors that play a role in the production of Hemoglobin F is the phosphorylated STAT3 protein. This protein, which is the dominant-negative regulator, which acts in the 5'-untranslated globin- γ promoter region bound to A γ STAT3, thus inhibiting the expression of globin- γ -dependent concentrations⁽⁵⁾. Therefore, it is necessary to have a potential inhibitor to STAT3 in the framework of globin- γ induction. Curcumin is a STAT3 inhibitor in the SH2 domain. Inhibition of the SH2 domain, not only disrupts activation but also dimerization of transcription factors⁽⁶⁾. Other active compounds of herbal ingredients that have molecular targets related to the regulation of Hemoglobin F are Shogaol. 6-shogaol is the most potent inhibitor of STAT3 activation when compared to analogues such as 6-gingerol, 8-gingerol and 10-gingerol⁽⁷⁾. The purpose of this study was to uncover the potential of Curcumin and 6-shogaol on the expression of STAT3 mRNA as one of the induction signals for Hemoglobin F.

Material and Method

Provision of Curcumin and 6-shogaol and Hydroxyurea: Curcumin (BioBasic, Canada) with > 95% of purity, 6-shogaol (Fortopchem, China) with >98% purity and Hydroxyurea (HU) (Sigma-Aldrich, USA) with approx >98% of purity. Curcumin, HU and 6-shogaol are dissolved in 100% dimethyl sulfoxide (DMSO) to reaches the final concentration of curcumin 271,000 μ M, 6-Shogaol 361,000 μ M, and HU 1,315,000 μ M as a stock solution, then stored at -20°C.

K562 cell culture: Erythroleukemia K562 cells obtained from CANCER CHEMOPREVENTION RESEARCH CENTER (CCRC) Faculty of Pharmacy in the University of Gadjah Mada was cultured with RPMI 1640 supplementary media (without phenol red) with 10% Fetal Bovine Serum (FBS) and 50 U/ml - 50 μ g/ml penicillin-streptomycin (pen-strep). Culture was maintained under atmospheric humidity with 95% air/5% CO₂ at 37°C with cell densities between 2 x 10⁴ to 1 x 10⁵ cells/ml.

Cytotoxic test with MTT method assay 24 hours, 48 hours and 72 hours: Cytotoxic tests were performed to obtain IC₅₀ values following the protocol of CCRC Faculty of Pharmacy in the University of Gadjah Mada. The results of the IC₅₀ values of each sample were taken from 24 hours, 48 hours and 72 hours incubation. The IC₅₀ values obtained were 60 μ M curcumin, 6 μ M 40 μ M shogaol and 300 μ M HU, respectively.

Combination Test: K562 cells were distributed into 96 wells as much as 100 μ L and incubated for 24 hours. Enter the Curcumin and 6-shogaol concentration series into the wells of 50 μ L with five series of concentrations each consisting of 1/2 IC₅₀, 1/4 IC₅₀, 1/8 IC₅₀, 1/16 IC₅₀ and 1/32 IC₅₀. Incubation for 24 hours. Cells were counted by using a haemocytometer so that the number of living and dead cells in each well was obtained. The highest number of living cells is an indicator of the best combination dose, named Curcumin 2 μ M, 6-shogaol 10 μ M, and for HU it is determined by treatment of 75 μ M (1/4 IC₅₀).

ELISA test to measure Hb F levels: K562 cells that have been given the appropriate treatment in their groups are then carried out protein extraction by the procedure of the M-PER Kit (Thermo Scientific, USA). The lysate obtained was used for examination of Hb F levels measured by the Human HbF Cat ELISA kit. No: EH3213 (Fine Test, China) according to the manufacturer's instructions.

Analysis of STAT3 Gena mRNA expression: Total K562 RNA cells were extracted at different times depending on the treatment, using # RB100 (Geneaid, Taiwan), 1 μ g of total RNA from each sample was carried out reverse transcripts to cDNA using the cDNA Synthesis Kit (Toyobo, Japan). Real-time PCR is done by machine (ABs) using the SensiFAST SYBR Lo-ROX Kit (Bioline, Germany). The relative mRNA levels of the target gene are normalized to the mean of the internal control gene, β -Actin.

Primary mRNA with STAT3, forward: 5'-ATC ACG CCT TCT ACA GAC TGC-3', reverse: 5'-CAT CCT GGA TCT CTA CCA CT-3'. β -ACTIN forward: 5'-ACG GCC AGG TCA TCA CCA TTG-3', reverse: 5'-GGC GTA CAG GTC TTT GCG GAT-3 TT'. The STAT3 gene expression between treated and untreated samples was calculated as 2^{- $\Delta\Delta$ Ct} relatively to the reference gene, β -actin.

Statistic analysis: Data is displayed in mean \pm SD and statistical analysis using one way ANOVA test followed by post hoc LSD. The test results are considered significant if p < 0.05 and 95% confidence intervals.

Findings: In this study, the impact of Curcumin, 6-shogaol and their combination on the interpretation of STAT3 mRNA expression were measured by the qRT-PCR method, and the results can be seen in Figure 1.

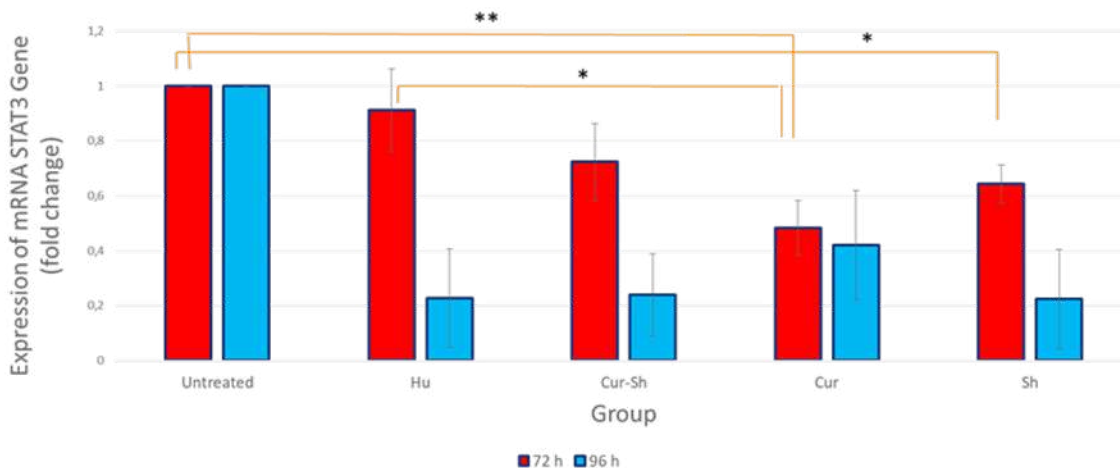


Figure 1: Differences in fold changes of STAT3 mRNA between groups after incubation of Curcumin (Cur), 6-Shogaol (Sh) and Hydroxyurea (Hu) on serial K562 cells for 72 and 96 h. Curcumin showed the strongest expression followed by 6-Shogaol compared with the control group without treatment (* $p < 0.05$, ** $p < 0.01$).

The results showed a decrease in STAT3 mRNA expression in all treatment groups in both the 72-h and 96-h time series compared to the untreated group. In the 72-h time series, the results are significantly different $p < 0.05$. Then followed by post hoc LSD test, in the Curcumin treatment group, the lowest expression of STAT3 mRNA gene was 0.48 ± 0.1 ($p = 0.008$) which was significant compared to the control group without treatment. Next, in the 6-Shogaol treatment group, the expression of STAT3 mRNA gene (0.64 ± 0.07 , $p = 0.045$) was significant compared to the control group without treatment. In the combination group of Curcumin with 6-shogaol, the expression of STAT3 mRNA gene (0.72 ± 0.14) was lower than the positive control group but higher than the curcumin and 6-shogaol group. In the 96-h time series, the results did not have significantly different ($p = 0.098$) between the treatment group and the control group without treatment. So, in the 96-h time series, there was a decrease in STAT3 mRNA expression, which was not significantly different.

The effect of Curcumin and 6-shogaol on haemoglobin F levels measured by the ELISA method can be seen from Figure 2. The results show that in a 96-h time series, Hb F levels were the highest in the curcumin group (1.6 ± 0.15 ; $p = 0.015$), then followed by the 6-shogaol group (1.11 ± 0.29). In the positive control group hydroxyurea and the combination of Curcumin + 6-shogaol, Hb F levels were consecutively (0.85 ± 0.16), (0.41 ± 0.01) lower than those in the untreated control group. The combination group of Curcumin with 6-shogaol was the group with the lowest Hb F level compared with the treatment group and the control group without treatment ($p < 0.05$). In the 72-h time series, the Hb F level of all treatment groups was lower than the control group without treatment. Based on the one way ANOVA test, the 72-h treatment did not differ significantly ($p > 0.05$), but in the 96-h treatment, there was a significant difference ($p < 0.05$). So, in the 96-h time series, the highest Hb F level occurred in the curcumin group, and the lowest Hb F level occurred in the combination group of Curcumin with 6-shogaol.

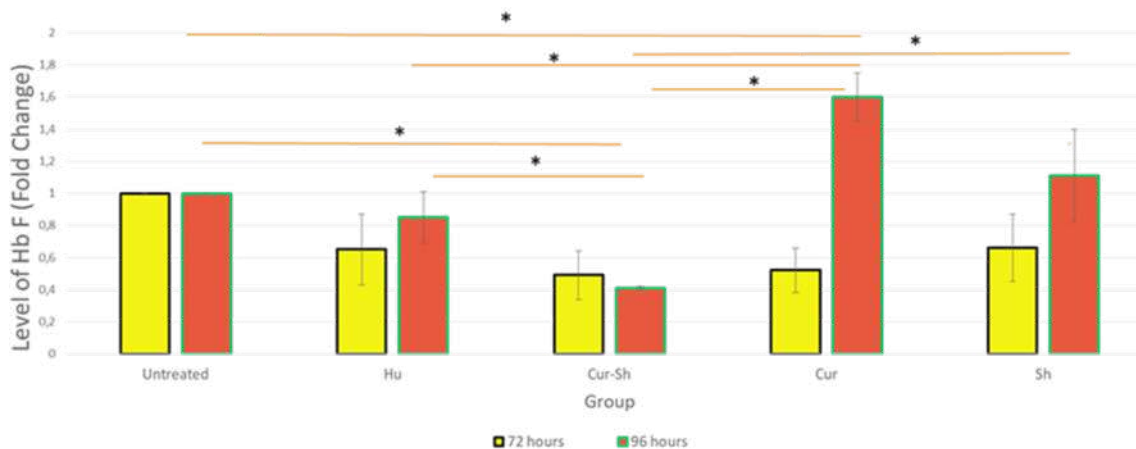


Figure 2: Differences in fold changes of HbF levels between groups after incubation of Curcumin (Cur), 6-Shogaol (Sh) and Hydroxyurea (Hu) on 72 and 96 h serial K562 cells. In the 96-h time series, Curcumin showed the highest effect on changes in HbF levels followed by 6-Shogaol compared to the control group without treatment (* p <0.0).

Reduced hexahydro-bisdemethoxycurcumin (HHBDMC) reduced curcuminoids were most effective in inducing gamma-globin mRNA (3.6 ± 0.4 fold) and Hb F (2.0 ± 0.4 fold) in erythroid primary precursor cells for seven days⁽⁸⁾. Curcumin works to reduce the expression of STAT3 genes so, the decrease in STAT3 gene expression will increase the production of Hb F. The role of 6-shogaol in Hb F induction through the activation of the p-p38 MAPK signal⁽⁹⁾ whereas p38 MAPK is reduced by two weeks of curcumin activation⁽¹⁰⁾.

Discussion and Conclusion

In beta-thalassemia patients there is an imbalance in the number of globin- α /globin- β chains, due to the lack or absence of globin- β synthesis, resulting in precipitation of free globin- α chains in erythroid precursors which results in the maturation and damage of erythrocyte cells, causing prolonged anaemia⁽¹¹⁾. Therefore the best choice for the treatment of thalassemia patients is reactivation/induction of globin- γ , so that replaces globin- β to join globin- α to form fetal haemoglobin and ultimately there is no excess free globin- α chains⁽¹²⁾. Individuals with elevated Hb F levels (> 8.6%) show a reduction in symptoms and increase patient life expectancy; hence, the induction of Hb F has the potential as a therapy in beta-thalassemia patients. Of the current therapeutic options, Hb F induction through pharmacological agents is the most feasible therapeutic choice⁽⁸⁾.

Other transcription factors that play a role in the production of haemoglobin F are the phosphorylated STAT3 protein. Therefore, it is necessary to have a potential inhibitor to STAT3 in the framework of gamma-globin induction. Pharmacological inhibitors targeting STAT3 can be done in 5 ways, namely inhibition of STAT3 DNA-binding domain, abrogation of the STAT3 N-terminal domain, suppression of the STAT3 SH2 domain, inhibition of the STAT3-importin interaction, and/or blockage of upstream kinase activity⁽¹³⁾.

The active compounds of the following herb, Curcumin, have broad molecular targets related to various molecular and biochemical cascades interacting directly on the target protein and epigenetic modulation of the target genes. Curcumin, as an epigenetic agent, functionally in modulating multiple biological processes, occurs at low concentrations. Curcumin plays a role in the expression of genes through direct interaction with transcription factors such as nuclear factor kappa-light-chain-enhancer of activated B cells (NF- κ B), epigenetic modulation through inhibition of DNA methyltransferase I (DNMT1), histone acetyltransferase (HAT), histone deacetylase complex (HDAC)⁽¹⁴⁾. Various molecular targets of Curcumin include inflammation, kinase activity (MAPK, PKA, JAK), transcription factors (CREB, STAT3, PPAR γ), enzyme activity (COX-2, INOS, MMP), and others (VEGF, adiponectin, ROS)⁽¹⁵⁻¹⁶⁾. The 6-Shogaol are other active compounds of herbal ingredients that have molecular targets related to the

regulation of Hemoglobin F. The 6-shogaol suppresses the expression of the products governed by STAT3. It was also reported that 6-shogaol caused the activation of JNK, p38 and ERK, as well as downregulating the expression of p38 MAPK, NF- κ B and COX-2 ⁽¹⁷⁾. Therefore, 6-shogaol can play a role in the induction of Hemoglobin F.

Hydroxyurea (100 μ M) has a link between the regulator of globin- γ expression (MYB, BCL11A and KLF-1) with specific miRNA, and reveals the mechanism of Hb F production through inhibition of HU-induced miRNA ⁽¹⁸⁾. Treatment with HU combined with HDAC2 knockdown increases gamma-globin expression. It was also reported that CD34 + cells treated with HU and MS-275 (HDAC inhibitors 1,2 and 3) had a relative induction of gamma-globin expression ⁽¹⁹⁾.

Curcumin is a decreasing expression of STAT3 mRNA gene and increases Hb F levels compared to 6-shogaol on K562 cells. While the combination of the two substances was not significant either in inhibiting STAT3 expression or HbF levels. The results of this study could be the basis for further research in vivo to reveal the signalling pathway in Hb F induction therapy ($\alpha_2\gamma_2$).

Conflict of Interest: Authors report no conflict of interest.

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Ethical Clearance: This study was approved by Medical and Health Research Ethics Committee (MHREC) Faculty of Medicine, Gadjah Mada University-DR.Sardjito General Hospital (Ref: KE/FK/1150/EC/2017).

References

- Bianchi N, Chiarabelli C, Borgatti M, Mischiati C, Fibach E, Gambari, R. Accumulation of γ -globin mRNA and Induction of Erythroid Differentiation After Treatment of Human Leukaemic K562 Cells with Tallimustine. *Br J Haematol.* 2001;113:951-961
- Fard AD, Hosseini SA, Shahjahani M, Salari F, Jaseb K. Evaluation of Novel Fetal Hemoglobin Inducer Drugs in Treatment of β -Hemoglobinopathy Disorders. *Int J Hematol Oncol Stem Cell Res.*2013;(3):47–54.
- Makala LH, Torres CM, Clay EL, Neumert C, Pace BS. Fetal Hemoglobin Induction β -Hemoglobinopathies : From Bench to Bedside. *J Hematol Transfus.* 2014;2(2):1018
- Dreuzy E, Bhukhai K, Leboulch P, Payen E. Current and Future Alternative Therapies for Beta-Thalassemia Major. *BMJ.*2016;39:24-38
- Foley HA, Ofori-Acquah SF, Yoshimurai A, Critz S, Baliga BS, Pace BS. Stat3 β Inhibit γ -Globin Gene Expression in Erythroid Cells. *J Biol Chem.*2002;277(18):16211-16219
- Chai E ZP, Shanmugam MK, Arfuso F, Dharmarajan A, Wang C, Kumar AP, et al. Targeting Transcription Factor STAT3 for Cancer Prevention and Therapy. *Pharmacology & Therapeutics.*2016;162:86-97
- Kim S-M, Kim C, Bae H, Lee JH, Baek SH, Nam D, et al., 6-shogaol Exerts Anti-Proliferative and Pro-Apoptotic Effects Through the Modulation of Stat3 and MAPKs Signaling Pathways. *Mol Carcinog.*2014;54(10):1132-1146
- Chaneiam N, Changtam C, Mungkongdee T, Suthatvoravut U, Winichagoon P, Vadolas J, et al. A Reduced Kurkuminoid Analog as A Novel Inducer of Fetal Hemoglobin. *Ann Hematol.*2013;92:379–386
- Ramakhrisnan V, Pace BS. Regulation of γ -globin Gene Expression Involves Signaling Through the p38 MAPK/CREB1 Pathway. *Blood Cells Mol Dis.* 2011;47:12–22
- Camacho-Barquero L, Villegas I, Sanche-Calvo JM, Talero E, Sanchez-Fidalgo S, Motilva V, et al. Kurcumin, a Curcuma Longa Constituent, Act on MAPK p38 pathway modulating COX-2 and iNOS expression in Chronic Experimental Colitis. *Int Immunopharmacol.* 2007;7(8):333–342
- Sankaran VG. Targeted Therapeutic Strategies for Fetal Hemoglobin Induction. *Hematology.*2011:459–465
- Bauer DE, Kamran SC, Orkin SH. Reawakening Fetal Hemoglobin: Prospects for New Therapies for The β -Globin Disorders. *Blood.* 2012;120(15):2945–2953
- Chai E ZP, Shanmugam MK, Arfuso F, Dharmarajan A, Wang C, Kumar AP, et al. Targeting Transcription Factor STAT3 for Cancer Prevention and Therapy. *Pharmacology & Therapeutics.*2016;162:86-97

14. Fu S, Kurzrock R. Development of Curcumin as an Epigenetic Agent. *Cancer*. 2010;116:4670–4676
15. Sunagawa Y, Katanasaka Y, Hasegawa K, Morimoto T. Clinical Application of Kurkumin. *PharmaNutrition*. 2015;67:1 5
16. Setyono J, Harini IM, Sarmoko S, Rujito L. Supplementation of curcuma domestica extract reduces cox-2 and inos expression on raw 264.7 cells. *Journal of Physics: Conf. 2019; Series, 1246 012059, IOP Publishing. doi:10.1088/1742-6596/1246/1/012059*
17. Ha SK, Moon E, Ju MS, Kim DH, Ryu JH, Oh MS, et al. 6-Shogaol, a ginger product, modulates neuroinflammation: A new approach to neuroprotection. *Neuropharmacology*. 2012;63:211-223
18. Pulle GD, Mowia S, Novitzky N, Wonkam A., Hydroxyurea Down-regulates BCL11A, KLF-1 and MYB Trough miRNA-mediated Action to Induce γ -Globin Expression : Implications for New Therapeutic Approaches of Sickle Cell Disease. *Clin Trans Med*. 2016;5:1–15
19. Esrick EB, McConkey M, Lin K, Frisbee A, Ebert BL. Inactivation of HDAC1 or HDAC2 induces gamma globin expression without altering cell cycle or proliferation. *Am J Hematol*. 2015;90(7):624-628

Introduction of Probiotic Type of Yogurt for the Treatment of Dysbiosis of Patients with Lymphogranulomatosis Under Polychemotherapy by BEACOPP-II Protocol

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Abstract

The efficacy of using probiotic preparations of the yogurt type was studied in 136 patients with lymphogranulomatosis, suffering from intestinal dysbiosis while taking antibiotic therapy and polychemotherapy (BEACOPP-II protocol). It was found that probiotics of this type are highly effective for the treatment of dysbiotic disorders of the intestines in cancer and hematological patients. Their use significantly reduces the risk of complications such as an unpleasant aftertaste in the mouth, belching, heartburn, diarrhea, constipation, flatulence, discomfort or periodic abdominal pain. It is recommended that prolonged therapy with a probiotic of the yogurt type be used in these groups of patients.

Keywords: Probiotic, dysbiosis, eubiosis, dyspepsia, lymphogranulomatosis, polychemotherapy.

Introduction

Every year, the problem of dysbiotic conditions of the gastrointestinal tract is increasing among the world's population in general and among Russian citizens in particular [1]. Along with other reasons, the use of antibacterial drugs is one of the main causes of intestinal dysbiosis. Currently, observed dysbiosis is mainly of natural microbial origin. This is due to a violation of homeostasis of the natural microflora of the gastrointestinal system, leading to the occurrence of intestinal dysbiosis (dysbiosis). The prevalence of this clinical condition among all age groups in the human population exceeds more than 90% and is constantly

increasing^[2]. This negatively affects the clinical course, diagnosis and treatment of various nosologies, leading to the aggravation of various diseases and their pathomorphism^[3,4].

Nowadays, lymphogranulomatosis has become one of the few highly liable diseases in the hematological practice. According to the German Hodgkin Study Group, achieving complete remission in patients with advanced stages is possible in 70-90% of cases, using effective polychemotherapy regimens in combination with or without radiation therapy^[5]. Thus, polychemotherapy regimes in lymphogranulomatosis is very important and such regime usually given with antibacterial therapy leads to dysbiosis. Traditionally, the correction of dysbiotic conditions is achieved by introducing microbial associations of a healthy person in the form of probiotics into the patient's digestive system^[6]. But most modern drugs all over the world are created on the basis of a limited number of bacterial strains, which are often poorly effective^[7,8]. Probiotics such as yogurt are especially recommended when conducting antibacterial

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therapy, taking cytostatics, as well as for correcting the microflora of the digestive system in people with lactase deficiency. Due to the simplicity of their administration and relatively high bioavailability. Probiotics of the yogurt type are widely used in the complex therapy of various pathological conditions, including diseases of the gastrointestinal tract, oncological diseases with long courses of chemotherapy, which are characterized by inhibition of normal microflora with the development of dysbiosis syndrome [9, 10, 11].

Purpose of the study: To analyse the effectiveness of probiotic therapy in patients with dysbiosis initiated by polychemotherapy and antibiotic therapy in conditions of cancer alertness. Also to determine the effectiveness of yogurt-type probiotic preparations in patients with the above conditions.

Materials and Method

The study was conducted according to the results of treatment of 136 patients with lymphogranulomatosis, suffering from intestinal dysbiosis with the background of chemotherapy (BEACOPP-II protocol) and concomitant antibacterial therapy. The study involved patients with excluded organic pathology of the digestive system such as scars, erosion, hernia of the esophagus, gastritis, peptic ulcer of the stomach and duodenum, ulcerative colitis, Crohn's disease, primary tumors of the gastrointestinal tract; diseases leading to excretory insufficiency of the liver and pancreas. Patients underwent a course of polychemotherapy in the Department of Hematology and Chemotherapy of the State Budgetary Healthcare Institution of the Republic of Crimea "Crimean Republican Oncological Clinical Dispensary named after V.M. Efetov" in Simferopol, from April 2015 to March 2017.

The preparation used in the study contained: a lyophilized microbial composition of live strains of lactobacilli (*Lactobacillus rhamnosus* and *Lactobacillus murinus*), which differ from other lactobacilli by more pronounced (40–45%) viability in the presence of antibiotics and have higher activity (35–40%) suppression of pathogenic and conditionally pathogenic microflora.

Statistical processing of the results was carried out using the Microsoft Office Excel 2013 program, with the calculation of the t-criterion by the Student method for relative values, the data were considered reliable at $t = 2$,

the reliability was $Pt = 95.5\%$, and the risk of error was $p < 0.05$.

In our study involving all human participants were in accordance with ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1964 and later amendments.

Research Results

136 patients with lymphogranulomatosis (Hodgkin's lymphoma) were examined, who received a course of polychemotherapy and suffered from intestinal dysbiosis that developed while taking antibacterial therapy.

An initial examination of patients revealed that in 47 (34.56%) patients, dysbiosis of the II degree was observed, and in 89 (65.44%) patients there was dysbiosis of the first degree. In 31 (22.79%) patients, dyspepsia/unstable stool type was observed and dyspepsia/constipation was observed in 18 (13.24%) of the examined patients. Flatulence was observed in 32 (23.53%) patients before probiotic therapy. 55 (40.44%) patients complained of discomfort and abdominal pain. Only the most pronounced subjectively and clinically significant syndrome complexes were taken into account.

The results of a retrospective analysis and dynamic examination of 136 patients before and after treatment of intestinal dysbiosis with and without antibiotic, radiation and polychemotherapy was observed (Table 1).

After 2 months of treatment with a probiotic type of yogurt in the study group, it was recorded that; II degree dysbiosis was not detected in the observed patients, but I degree dysbiosis was detected in 42 (30.88%) patients. Unstable stool, diarrhea after 2 months of treatment was determined in 3 (2.21%) patients. Constipation after treatment was observed in 2 (1.47%) patients. Flatulence was detected in 6 (4.41%) patients. Discomfort, abdominal pain were observed in 8 (5.9%) examined patients after the course of the treatment. In 23 (16.91%) patients it was observed that, after 2 months of treatment with a probiotic-type of yogurt, grade I dysbiosis was determined bacteriologically, despite the absence of any clinical symptoms and complaints of the digestive system from patients. In 94 (69.1%) patients, intestinal eubiosis was clinically and bacteriologically determined. The significance of differences for all of the above groups is $t = 2$, $Pt = 95.5\%$ and $p < 0.05$.

Table 1: The clinical condition of patients with intestinal dysbiosis before and after probiotic therapy.

Study Period	Prevailing of Clinical Syndromes (Number of Patients)			
	Unstable Stool, Diarrhea	Constipation	Flatulence	Discomfort, Abdominal Pain
Before Treatment	31	18	32	55
After Treatment	3	2	6	8

In the control group, after two months, no statistically significant changes were recorded. The observed patients still noted various disorders of the digestive system, such as belching, heartburn, diarrhea, constipation, flatulence, discomfort or periodic pain in the abdomen.

Conclusion

Probiotics such as yogurt demonstrate high efficiency in the correction of intestinal dysbiosis in oncological and hematological patients on the background of polychemotherapy and concomitant antibacterial therapy.

It has been proven that taking probiotics such as yogurt significantly reduces the incidence of dyspeptic disorders such as an unpleasant aftertaste in the mouth, belching, heartburn, diarrhea, constipation, flatulence, or periodical abdominal pain in patients suffering from dysbacteriosis, which has developed with the use of antibiotics.

Long-term therapy with a drug probiotic such as yogurt, which lasts more than 2 months, makes it possible to correct conditions such as grade I and grade II dysbiosis, contributing to intestinal eubiosis in a significant part of the observed patients.

Conflict of Interests: None declared.

Source of Funding: Self funding by authors

Ethical Clearance: In our study involving all human participants were in accordance with ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1964 and later amendments.

References

- Baohong Wang, Mingfei Yao, Longxian Lv., et al. The Human Microbiota in Health and Disease. Engineering (Zhejiang University, Hangzhou). 2017;3(1):71-82.
- Buttó L.F., Haller D. Dysbiosis in intestinal inflammation: Cause or consequence. International Journal of Medical Microbiology. 2017;306(5):302-309.
- Na-Ri Shin, Tae Woong Whon, Jin-Woo Bae. Proteobacteria: microbial signature of dysbiosis in gut microbiota. Trends in Biotechnology. 2015;33(9):496-503.
- Kau A.L., Ahern P.P., Griffin N.W., et al. Human nutrition, the gut microbiome and the immune system. Nature. 2011;474(7351):327-336.
- Kaliberdenko V.B., Shaduro D.V., Shanmugaraj K., et al. Analysis of polychemotherapeutic treatment with BEACOPP-14, BEACOPP-baseline and ABVD programs in patients with the advanced stages of hodgkin’s lymphoma. International Medical Journal. June 2020;27(3).
- Reid G. Probiotics: definition, scope and mechanisms of action. Best Practice & Research Clinical Gastroenterology. 2016;30(1):17-25.
- Gosálbez L., Ramón D. Probiotics in transition: novel strategies. Trends in Biotechnology. 2015; 33(4):195-196.
- Dasari S., Kathera C., Janardhan A., et al. Surfacing role of probiotics in cancer prophylaxis and therapy: A systematic review. Clinical Nutrition. 2016;8:348-352.
- Takahashi J., Rindfleisch J. A. Prescribing Probiotics. Integrative Medicine (Fourth Edition). 2018;105:986-995.
- Valdovinos M.A., Montijo E., Abreu A.T., et al. The Mexican consensus on probiotics in gastroenterology. Revista de Gastroenterología de México (English Edition). 2017;82(2):156-178.
- Giacchi V., Sciacca P., Betta P. Multistrain Probiotics: The Present Forward the Future. Probiotics, Prebiotics and Synbiotics. 2016; 19:279-302.

Influence of Mental Health and Social Relationships on Quality of Life among Myanmar Migrant Workers in the South of Thailand

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Abstract

Background: Previous studies indicated that mental health and social relationships have influence on quality of life. However, there are limited studies on the association between mental health and social relationshipson quality of life among Myanmar migrant workers in Thailand.

Method: This study aimed to determine the prevalence of quality of life and the influence of mental health and social relationships on quality of life among Myanmar migrant workers in the South of Thailand. This cross-sectional analytical study was conducted among 794 Myanmar migrants who were selected by using a multi-stage random sampling from 2 provinces in the South of Thailand to respond to a structured questionnaire interview. The generalized linear mixed model analysis was performed to determine the association between mental health and social relationships on quality of life when controlling other covariates.

Results: The prevalence of good quality of life among Myanmar migrant workers was 11.46% (95%CI:9.24-13.68). Mental health and social relationships were significantly associated with good quality of life were; no had depressive symptoms (adj. OR=3.83; 95%CI: 2.28-6.43, p-value < 0.001), had good relationship with employers (adj. OR=3.02; 95%CI: 1.71-5.31, p-value < 0.001) and had high level of involvement with peers (adj. OR=1.90; 95%CI: 1.09-3.32, p-value < 0.023). Significant covariates were average personal monthly incomes and received health information. About one-tenth of Myanmar migrant workers had a good quality of life. Mental health, social relationships and access to health information had influenced their quality of life.

Keywords: Myanmar migrant workers, Quality of life, Social relationships, Thailand.

Introduction

Quality of life (QOL) is a multidimensional level of an individual life's happiness where they live in societies to achieve their goal in life. QOL consists of 4 domains including physical, psychological, social relationships, and environmental domains⁽¹⁾. The concept of QOL is commonly used to describe the well-being among various susceptible populations, such as migrants, refugees, etc.⁽²⁻⁴⁾, since QOL describes the degree to which a person enjoys the important possibilities of his or her life⁽⁵⁾. There were a number of factors influencing QOL. Social relationships were one of the factors associated with QOL of which it increased the likelihood

of survival⁽⁶⁾. A study carried out in the Basque Country, Spain suggested that low social support was related to poor HRQOL, of which identifying the social support is a key in understanding health inequalities among immigrants⁽⁷⁾.

Migrating to a new country is an extremely complex and stressful process because it involves changes in all areas of life-socially, culturally and psychologically⁽⁸⁾. Psychosocial factors such as lack of social and emotional support from relatives and friends⁽⁹⁾ were common among migrant workers. Some studies indicated that migrant workers were refused by local citizens⁽¹⁰⁾ and lack of legal migration status in migration processes⁽¹¹⁾.

Depression, one of the most common mental health disorders, was identified as having a positive relationship with occupation injury⁽¹²⁾. Depression imposes an immense social burden which leads to functional impairment, decreased quality of life, low productivity and impaired interpersonal relationship⁽¹³⁾.

Thailand economic growth has attracted an increasing number of migrant workers from neighboring countries⁽¹⁴⁾. Migrant workers in Thailand are mostly involved in the “3 Ds” jobs (dangerous, dirty and degrading jobs). These 3Ds conditions push them at risk for health problems. One notable health hazard of migrant workers is the deterioration of mental health, which has been implicated to suicide that is more common among migrant workers than that of local citizens⁽¹⁵⁾. The Office of Foreign Worker Administration of Thailand reported that in July 2019 there were 2.83 million migrants residing in Thailand, and about 1.87 million were from Myanmar. About 358,530 Myanmar migrant workers were in the South region. Most of these migrants worked in the manufacturing sectors, agriculture and animal husbandry, fishery, and construction. Therefore, this study aimed to determine the prevalence of quality of life and the influences of mental health and social relationships factors on quality of life among Myanmar migrant workers in the South of Thailand.

Materials and Method

Study design and sampling: This cross-sectional analytical study was conducted in 2018. The populations were Myanmar migrant workers in the South of Thailand. The sample size was calculated by using the formula to estimate the sample size for logistic regression analysis of Hsieh⁽¹⁶⁾. The estimated sample size was 794. We recruited Myanmar migrant workers from 2 southern provinces by using multi-stage random sampling method.

Questionnaire: A structure questionnaire was developed based on the research questions and relevant literatures. The structured questionnaire consisted of 6 parts: A) Demographic and socioeconomic characteristics, B) Social relationships, C) Health behaviors and physical health status, D) the Perceived Stress Scale (PSS) of Cohen et al.⁽¹⁷⁾, E) The Center for Epidemiology Studies Depression Scale (CES-D)⁽¹⁸⁾, and F) WHOQOL-BREF was used to assess the quality of life. QOL scores were categorized into three groups: a) poor level (26-60 scores), b) moderate level (61-95

scores), c) good level (≥ 96 scores)⁽¹⁾. The questionnaire was undergone content validation by 5 experts and revised to improve its validity. The Cronbach's alpha coefficient of PSS, CES-D, and WHOQOL-BREF were 0.78, 0.70, and 0.85 respectively.

Statistic Analysis: All analyses were performed using Stata version 10.0 (StataCorp, College Station, TX). Demographic and socioeconomic characteristics of the participants were described by using frequency and percentage for categorical data as well as the mean and standard deviation for continuous data. A simple logistic regression was used for bivariate analysis to identify individual factor associated with QOL. In the bivariate and multivariable analysis, quality of life was classified into 2 groups using the cutoff score of ≥ 95 points which mean ‘had a good quality of life’. The independent factors that had p-value < 0.25 ⁽¹⁹⁾ were processed to the generalized linear mixed model (GLMM) analysis to identify the association between mental health and social relationships with QOL when controlling the effect of other covariates and reported the adjusted odds ratio (Adj. OR), 95% confidence interval (CI) and p-value < 0.05 as the magnitude of effect and statistical significant level.

Results

Majority of the Myanmar migrant workers were male (58.31%) with the average age of 32.79 (± 9.00) years old, 69.52% were married and 37.78% finished only primary education. Most of them lived in urban settings (81.74%), 75.19% lived with a family and 46.98% lived in a labor camp. The highest proportion worked in manufacturing (29.97%) followed by agriculture and animal husbandry, fishery and construction. Their average personal monthly incomes was 9,201.17 ($\pm 2,681.29$) Baht, of which 3,203.21 ($\pm 1,660.17$) Baht were average personal monthly expenditures. Almost all had health insurance (99.62%).

Most of the workers worked both indoor and outdoor (64.23%) and the rest (35.77%) worked only indoor. Most of them satisfied with their living and working conditions as well as the relationship with others, except that 58.56% had a limitation on traveling. About one-third were smokers (38.16%), 16.12% were drinkers. More than half of the migrant workers (54.91%) had a physical check-up and 11.08% had chronic diseases. Most of them (88.66%) had a moderate level of stress and more than half (52.77%) had depressive symptoms.

Concerning the quality of life, 85.77% (95% CI: 83.15-88.03) of the migrant workers had a moderate level, 11.46% (95% CI: 9.42-13.87) had a good level and 2.77% (95% CI: 1.82-4.17) had a poor level.

Factor associated with good quality of life: Bivariate analysis: The bivariate analysis results indicated that the independent variables that possibly

associated with good QOL (p-value<0.25) were; average personal monthly income, physical health check-up, involvement with peers, relationship with employers, relationship with co-workers, relationship with family, received health information and depressive symptoms. These factors have proceeded to the multi variable analysis (Table 1).

Table 1: Factors associated with good quality of life: Bivariate analysis

Factors	Number	% Good QOL	Crude OR	95% CI	P-value
Depressive symptoms					<0.001
Yes	419	6.21	1		
No	375	17.33	3.16	1.96-5.11	
Gender					0.261
Female	331	9.97	1		
Male	463	12.53	1.29	0.82-2.03	
Age (years)					0.270
< 30	427	10.30	1		
≥30	367	12.81	1.27	0.82-1.97	
Education					0.293
Primary school or lower	346	10.12	1		
Secondary school or higher	448	12.50	1.12	0.82-1.40	
Average personal monthly incomes (Baht)					0.032
<9,300	484	9.50	1		
≥9,300	310	14.52	1.61	1.04-2.50	
Average personal monthly expenditures (Baht)					
<3,000	327	11.31	1		0.913
≥3,000	467	11.56	1.02	0.65-1.59	
Physical health check-up					0.012
No	358	8.38	1		
Yes	436	13.66	1.77	1.12-2.82	
Involvement with peers					<0.001
Low to moderate	465	7.53	1		
High	329	17.02	1.90	1.60-3.94	
Relationship with co-workers					<0.001
Poor to average	445	7.87	1		
Good	349	16.05	2.23	1.43-3.50	
Relationship with family					0.001
Poor to average	229	6.11	1		
Good	565	13.63	2.42	1.34-4.37	
Relationship with employers					<0.001
Poor to average	474	6.12	1		
Good	320	19.38	3.68	2.31-5.88	
Chronic diseases					0.051
Yes	88	5.68	1		
No	706	12.18	2.30	0.90-5.83	
Received health information					0.009
No	433	8.78	1		
Yes	361	14.68	1.78	1.14-2.78	

Factors associated with good quality of life: multivariable analysis: The generalized linear mixed model analysis (GLMM) by Backward elimination indicated that mental health and some social relationships were associated with good quality of life which were; had no depressive symptoms (adj. OR=3.83;95% CI:2.28-6.43, p-value < 0.001), had good relationship with employers (adj. OR=3.02; 95% CI:1.71-5.31,

p-value < 0.001) and had high level of involvement with peers (adj. OR=1.90; 95% CI: 1.09-3.32, p-value < 0.023). Other significant covariates were had average personal monthly incomes $\geq 9,300$ Baht (adj. OR=1.62; 95% CI: 1.01-2.59, p-value = 0.043) and received health information (adj. OR=1.62;95% CI:1.00-2.61, p-value = 0.048) (Table 2).

Table 2: Factors associated with good quality of life: Multivariable analysis

Factors	Number	% Good QOL	Crude OR	Adjusted OR	95% CI	P-value
Depressive symptoms						<0.001
Yes	419	6.21	1	1		
No	375	17.33	3.16	3.83	2.28-6.43	
Relationship with employers						<0.001
Poor to average	474	6.12	1	1		
Good	320	19.38	3.68	3.02	1.71-5.31	
Involvement with peers						0.023
Low to moderate	465	7.53	1	1		
High	329	17.02	2.52	1.90	1.09-3.32	
Other covariates						
Average personal monthly incomes (Baht)						0.043
<9,300	484	9.50	1	1		
$\geq 9,300$	310	14.52	1.61	1.62	1.01-2.59	
Received health information						0.048
No	433	8.78	1	1		
Yes	361	14.68	1.78	1.62	1.00-2.61	

Discussion

The findings observed that most of the Myanmar migrant workers perceived of having a moderate level of QOL (85.77%), only 11.46% having good QOL. It might be that the situations where they lived and worked were as they expected. They were not much better. This study also observed that those who had no depressive symptoms had a significantly better quality of life in comparison with those who had depressive symptoms, of which similar with previous studies conducted in China^(20, 21). Besides, those who had a good relationship with employers had a significantly better quality of life in comparison with those who had a poor and average level which was similar with a study conducted in Thailand⁽²²⁾. It might be that the relationship with peer could result in job security and incomes. The migrant workers who had a high level of peer involvement had significantly better QOL than those who had low to moderate levels of peer

involvement which was similar to a study in Sweden⁽²³⁾. It might be that they could share various issues and able to release their tensions. Concerning personal monthly incomes, this study indicated that those who had average personal monthly incomes $\geq 9,300$ Baht were more likely to have good QOL in comparison with those who had lower incomes. A study conducted in China was also observed a similar finding⁽²⁰⁾. Concerning health, migrant workers who received health information were more likely to have a better quality of life in comparison with those who had not received health information. Migrants have usually accessed health information through social networks more than formal health service providers due to language and access barriers⁽²⁴⁾.

Conclusion

About one-tenth of Myanmar migrant workers in the South of Thailand had a good QOL. After adjusting

for other covariates which were personal monthly income and access to health information; mental health especially depressive symptoms and social relationships including had a good relationship with employers, and high level of peer involvement were found significantly associated with QOL.

Conflict of Interest: The authors declare that no conflict of interest.

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Ethical Clearance: Taken from the office of Khon Kaen University Ethical Committee in human research (HE 602370).

Reference

- 1 Division of Mental Health World Health Organization. WHOQOL-BREF introduction, administration, scoring and generic version of the assessment: Field trial version. Geneva: World Health Organization; 1996.
- 2 Browne S, Roe M, Lane A, Gervin M, Morris M, Kinsella A, et al. Quality of life in schizophrenia: Relationship to sociodemographic factors, symptomatology and tardive dyskinesia. *Acta Psychiatrica Scandinavica*. 1996;94:118–24.
- 3 Ghazinour M, Richter J, Eisemann M. Quality of life among Iranian refugees resettled in Sweden. *Journal of Immigrant and Minority Health*. 2004;6:71–81.
- 4 Group W. Development of the WHOQOL: Rationale and current status. *International Journal of Mental Health*. 1994;23:24–56.
- 5 Raphael, D., I. Brown, R. Renwick, M. Cava, N. Weir, and K. Heathcote. 1995. The quality of life of seniors living in the community: A conceptualization with implications for public health practice. *Canadian Journal of Public Health* 86(4): 228—233.
- 6 Holt-Lunstad J, Smith TB, Layton JB. Social relationships and mortality risk: a meta-analytic review. *PLoS Med*. 2010 Jul 27;7(7):e1000316.
- 7 Rodríguez Alvarez E, Lanborena Elordui N, Errami M, Rodríguez Rodríguez A, Pereda Riguera C, Vallejo de la Hoz G, et al. Relationship between migrant status and social support and quality of life in Moroccans in the Basque Country (Spain). *Gac Sanit*. 2009 Dec;23(Suppl 1):29–37.
- 8 Benish-Weisman M, Shye S. Life Quality of Russian Immigrants to Israel: Patterns of Success and of Unsuccess. *Social Indicators Research*. 2011;101(3):461-79.
- 9 Pannetier J, Lert F, Jauffret Roustide M, du Lou AD. Mental health of sub-saharan african migrants: The gendered role of migration paths and transnational ties. *SSM - population health*. 2017;3:549-57.
- 10 Benach J, Muntaner C, Chung H, Benavides FG. Immigration, employment relations, and health: Developing a research agenda. *American journal of industrial medicine*. 2010;53(4):338-43.
- 11 Meyer SR, Robinson WC, Chhim S, Bass JK. Labor migration and mental health in Cambodia: a qualitative study. *The Journal of nervous and mental disease*. 2014;202(3):200-8.
- 12 Ramos AK, Carlo G, Grant K, Trinidad N, Correa A. Stress, depression, and occupational injury among migrant farmworkers in Nebraska. *Safety*. 2016;2(4):23.
- 13 Pincus HA, Pettit AR. The societal costs of chronic major depression. *The Journal of clinical psychiatry*. 2001;62 Suppl 6:5-9.
- 14 Bank W. Labor migration in the greater Mekong sub-region: Synthesis report phase 1. Washington, DC: World Bank; 2006.
- 15 Nadim W, AlOtaibi A, Al-Mohaimed A, Ewid M, Sarhandi M, Saquib J, et al. Depression among migrant workers in Al-Qassim, Saudi Arabia. *Journal of affective disorders*. 2016;206:103-8.
- 16 Hsieh FY, Bloch DA, Larsen MD. A simple method of sample size calculation for linear and logistic regression. *Statistics in medicine*. 1998;17(14):1623-34.
- 17 Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. *Journal of health and social behavior*. 1983;24(4):385-96.
- 18 Radloff LS. The CES-D scale: A self-report depression scale for research in the general population. *Applied psychological measurement*. 1977;1(3):385-401.
- 19 Hosmer Jr DW, Lemeshow S, Sturdivant RX. *Applied logistic regression*: John Wiley & Sons; 2013.

- 20 Wong WKF, Chou K-L, Chow NWS. Correlates of Quality of Life in New Migrants to Hong Kong from Mainland China. *Social Indicators Research*. 2012;107(2):373-91.
- 21 Wang B, Li XM, Stanton B, Fang XY. The influence of social stigma and discriminatory experience on psychological distress and quality of life among rural-to-urban migrants in China. *Social science & medicine*. 2010;71(1):84-92.
- 22 Ti S, Somrongthong R. Health related quality of life of myanmar migrants in Takuapa and Kuraburi Districts, Phang-Nga Province, Thailand. *Journal of Health Research*. 2008;22(Suppl.): 79–83.
- 23 Puthooppambal SJ, Bjerneld M, Källestål C. Quality of life among immigrants in Swedish immigration detention centres: a cross-sectional questionnaire study. *Global Health Action*. 2015;8:10.3402/gha.v8.28321.
- 24 Pahud M, Kirk R, Gage J, Hornblow A. New issues in refugee research: the coping processes of adult refugees resettled in New Zealand. Switzerland: United Nations High Commissioner for Refugees. 2009.

Lumbosacral MRI Findings in Chronic Lower Back Pain

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Abstract

Background: Low back pain (LBP) is one of the most common musculoskeletal disorders demanding hospital visits. Intervertebral disc degeneration is a known cause of chronic low LBP back pain. The relation between changes in the lumbar spine and lower back pain is controversial.

Objectives: To assess LSS MRI findings in patients with CLBP, and to show the relation of disc degeneration with age and gender.

Material and Method: 218 adult patients with chronic lower back pain (pain more than 12 weeks) did Lumbosacral spine MRI, at Azadi Teaching Hospital/Kirkuk city, from March/2017 to April/2018, those with a positive history of spinal pathology other than osteoarthritis were excluded. The disc degenerative MRI changes at each lumbar disc were assessed and correlated according to age and gender.

Results: 146 of patients were male, and 72 of them were female, their age ranged from (16-73 years). Males and elderly patients were affected by disc degeneration more. 92.2% of patients had disc degeneration, followed by disc contour abnormality, facet joint arthrosis, high-intensity zone (HIZ), spinal canal stenosis, Modic changes (MC), Schmorl's nodes (SN), and spondylolesthesis. L4-L5 disc was the most commonly involved level by disc degeneration, followed by L5-S1 disc, the least level was L1-L2.

Conclusions: Most patients with CLBP have DDD. Older males are the most susceptible people to develop DDD which affect most commonly L4-L5 disc level, other findings may associate with DDD are MC, SN, HIZ, facet joint arthrosis, spinal stenosis, and spondylolesthesis.

Keywords: Chronic, lumbosacral, lower back pain, MRI.

Introduction

Low back pain (LBP) is one of the most common musculoskeletal problems demanding hospital visits, and the main contributing cause of disability in adults. LBP occurs in most of the people during any period of life. [1, 2, 3, 4, 5] Although several causes have been implicated

in low back pain, disc degeneration disease (DDD) is a known cause of this pain.^[6, 7] Chronic pain is defined as pain for more than 12 weeks.^[8]

DDD of the lumbosacral spine (LSS) in adults can start in the third decade of life.^[6] There are several risk factors related to disc degeneration in the LSS, including age, increased physical loading, obesity, and genetic influences.^[4, 9, 10]

Magnetic resonance imaging (MRI) is often requested and of choice in the management of patients with LBP as different abnormalities can be seen on spinal MRI.^[11, 12, 13] LSS MRI findings of DDD include decreased disc space, decreased signal intensity on T2W images which indicates disc dehydration.

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Disc degeneration on T2-weighted sagittal magnetic resonance images of the lumbar spine is appeared and graded as:

Grade (0): Normal No signal changes; Grade (1): the signal intensity of the nucleus pulposus is slightly decreased; Grade (2): seen as hypointense nucleus pulposus with preserved disc height; Grade (3): seen as hypointense nucleus pulposus with narrowing of disc space.^[14]

Disc degeneration may be associated with disc bulging/herniation, and high-intensity zone(HIZ).^[9, 15] Herniated disk is defined as a “focal displacement of nucleus, cartilage, a piece of annular tissue or fragmented apophyseal bone beyond the space of the intervertebral disc. Disc displacement most commonly is classified into five grades (normal, disc bulge, protrusion, extrusion, and sequestration).^[16, 17] (HIZ) represents tear in the annulus fibrosus of the disc, seen as very bright signal intensity on T2 weighted images at the posterior part of the disc.^[18] Other findings which associated with DDD include Modic changes (MC), Schmorl’s Nodes (SN), facet joint degeneration, spondylolesthesis, and spinal stenosis.^[19]

This study was done to assess LSS MRI findings in patients with CLBP, and to show the relation of DDD with age and gender.

Patients and Method

Subjects: Inclusion criteria: Two hundred eighteen (218) adult patients with chronic lower back pain (more than 12 weeks) were sent to MRI department at Azadi teaching hospital/Kirkuk city/Iraq, as a part of the management of lower back pain, over the period from March/2017 to April/2018. Their ages range from 16 to 73 years.

Exclusion criteria: Those who had a history of spinal surgery or back trauma, known spinal pathology,

malignant diseases, and athletes were excluded from the study. Clinical information was obtained from the documentation of physicians.

Imaging: All lumbosacral spine MRI examinations were done using the 1.5-T unit (Philips Acheiva, Netherl and 2010) with a dedicated lumbar coil, imaging protocol was as follows:

1. T1-weighted sagittal Turbo spin echo (TSE) with 8 msec echo time (TE) and 500 msec repetition time (TR).
2. T2- weighted sagittal TSE with 100 msec TE and 4000 TR.
3. T2-weighted axial TSE with 120 msec TE and 4000 TR, and
4. Myelography with 1000 msec TE and 8000 TR.

The images were interpreted by two board-certified radiologists with 7 years experience, any difference in opinion were settled by consensus. Each lumbar level of 218 patients was assessed for disc degeneration scoring, disc bulging and herniation, HIZ, presence of MC, SN, facet joint degeneration, spondylolesthesis, and spinal stenosis.

Statistical analysis: It was a cross-sectional analytic study. The study population demographic criteria including age in years, weight in kilograms (kg), and height in centimeters (cm) were expressed as means (SD). Percentage of Disc degeneration at different lumbar disc levels was assessed and related to gender and age, total degeneration score was estimated for each patient as average degeneration score of all lumbar disc levels and related to age, using Chi-square test. P-value level of less than 0.05 was required for significance. Percentage of disc bulge/herniation, HIZ, MC, SN, sponylolisthese, facet joint arthropathy, and spinal stenosis were also estimated. SPSS software, version 17, was used for the statistical analyses.

Results

The demographic criteria of the study sample were as seen in table 1.

Table 1: The demographic criteria of the study sample

Category	Male (a ^a N=146) Mean (SD)	Female (N=72) Mean (SD)	t- value	P value
Age (years)	43.5 (12.1)	42.5 (12.7)	0.5645	0.5730
Height (cm)	174.3 ± 6	161.3 ± 5.8	15.3747	0.0001
Weight (kg)	83.31 ± 14	74 ± 8	5.2332	0.0001

^aNumber.

There were 146 males and 72 females in the study sample; male to female ratio was 2:1, 141 males (96.6%) and 60 (83.4%) of females had disc degenerative changes in their LSS MRI.

Males were significantly more affected than females by disc degeneration ($P=0.0006$). Most of the patients had abnormal MRI findings 201 (92.2%), and only 17 (7.8%) had a normal MRI study. 32 patients were less than 35 years old, 140 patients were 36-55 years old, and 46 patients were more than 55 years old. 68.8% of < 35 years old group, 95% of 35-55 years old group, and All patients >55 years old group had disc degeneration change. The incidence of disc degeneration was

significantly increased with advancing age ($P<0.001$) as seen in table 2.

Table 2: Relation of disc degeneration with age.

Age	Disc Degeneration		Total
	Male	Female	
< 35	17	5	22
35-55	98	35	133
>55	26	20	46

The total number of the affected disc was 588 levels of a total of 218 patients. The most commonly affect level was L4-L5 in 32%, followed by L5-S1, L2-L3, L3-L4, and L1-L2 in 21.2%, 19.1%, 18%, and 9.2% respectively as seen in figure 1.

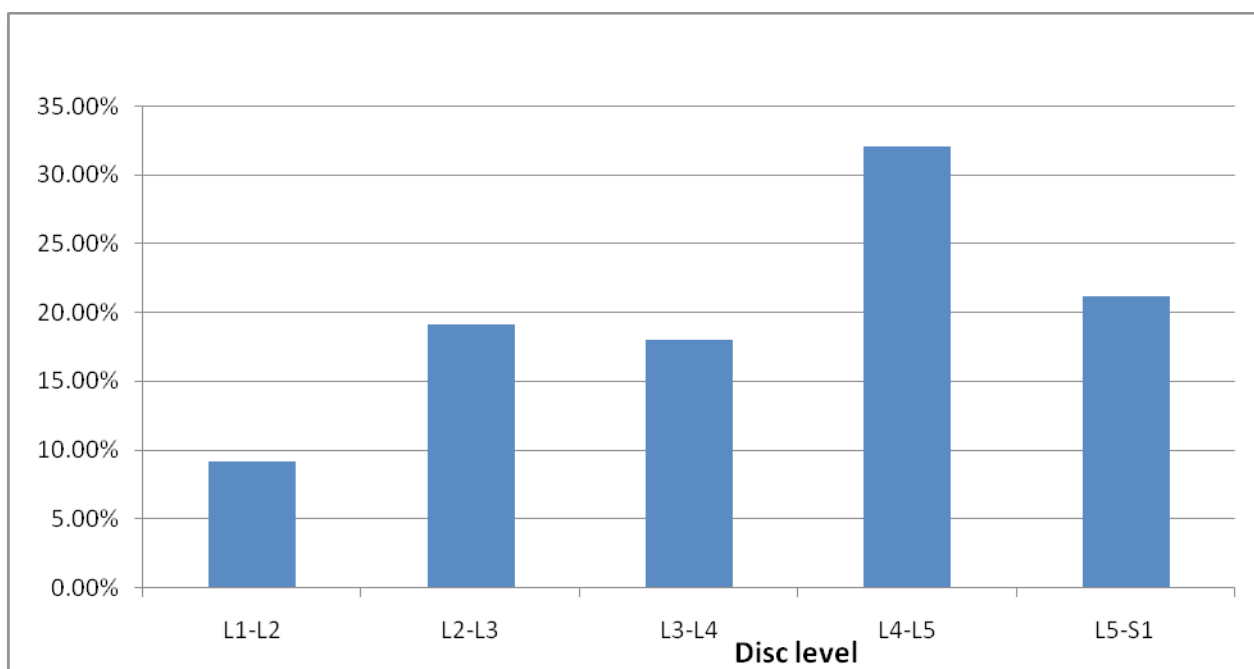


Figure 1- Distribution of disc degeneration according to disc level

Disc degeneration was present at one level in 25%, and multilevel in 75%. The average disc degeneration score of each patient was score 0 in 7.8% (17 patients),

score I in 30.1% (66 patients), score II in 37.2 (81 patients), and score III in 24.8% (54 patients) (Table 3).

Table 3: The relation between disc degeneration score and age

Age (Years)	Total Degeneration Score				Total
	0	I	II	III	
>35	10	18	4	0	32
36-55	7	40	61	32	140
55<	0	8	16	22	46
Total	17	66	81	54	218

Score 3 disc degeneration was not seen in <35 year's age group, and all patients who were <55 years old group had degeneration with different scores, the score of degeneration was significantly increased with increasing age ($P > 0.001$).

Other LSS MRI findings were as the following: disc contour abnormality (70.7%), HIZ (27.8%), SN in (12.9%), MC (19.3%), spinal stenosis (20.4%), facet joint degeneration (45.2%), and spondylolisthesis (6.4%).

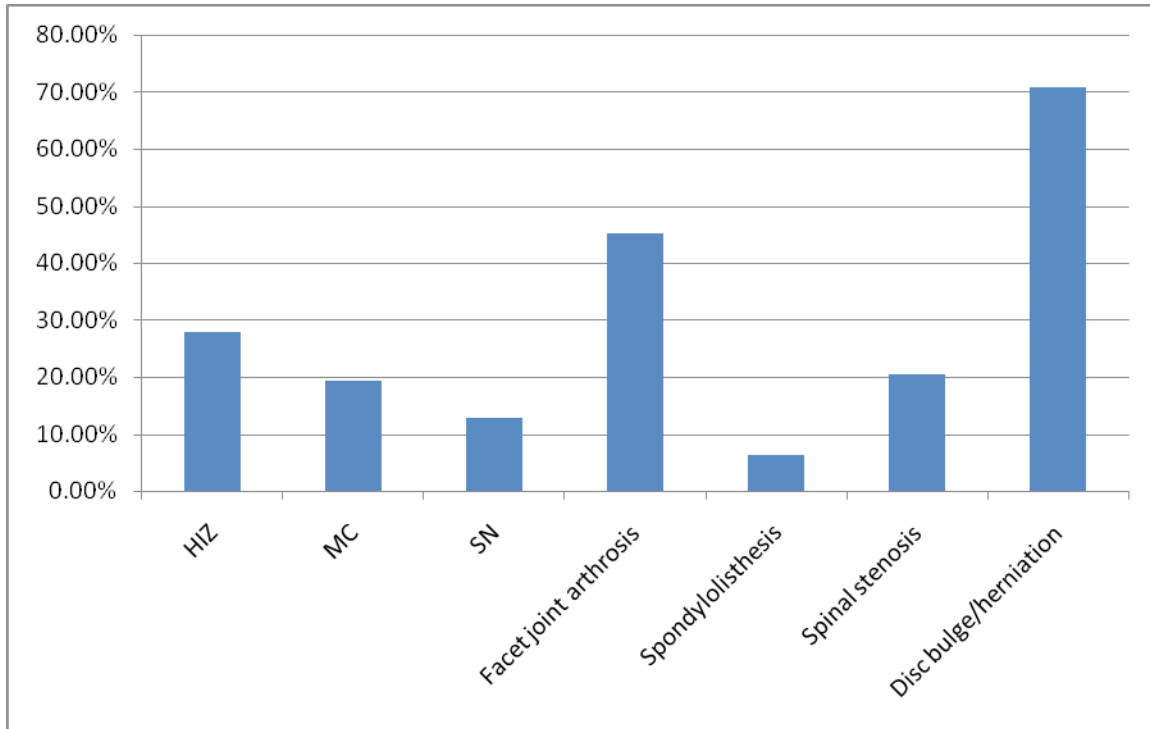


Figure 2: Percentage of MRI changes associated with disc degeneration

Discussion

Degenerative changes were seen in the majority (92.2%) of patients with chronic lower back pain; most of these changes were observed at L4/L5 and L5/S1 levels and lowest rate of involvement was noted at L1-L2 level. Similar outcomes had been perceived in most of the previous studies, due to the highest mechanical strain at these levels^[20, 21, 22, and 23].

Multiple disc level involvement was common as compared to the single-disc involvement; which was also in line with past studies.^[16, 24] In this study the incidence of disc degeneration significantly increased with age, due to aging process which involves decreased vascularization, and decreased delivery of nutrients and growth factors to the disc.^[25] This result was similar to several studies.^[20, 26] The fewer percentage of DDD that's seen in younger age group also noticed in other studies like us, its exact etiology is not clearly known,

but issues like genetic, autoimmune, and biochemical factors may play a role in the pathogenesis of disc degeneration.^[27]

Males were affected significantly more than females in our study which was comparable with other studies,^[28, 29] as men engage in jobs associated with heavy workload compared with women.^[30] Mechanical load that contributes to DDD might also have a role in the pathogenesis of disc contour abnormalities, HIZ, MC, and SN.^[31, 23, 33]

Conclusions

Most of patients with CLBP have DDD. Older males are the most susceptible people to develop DDD which affect most commonly L4-L5 disc level, other findings may associate with DDD including MC, SN, HIZ, facet joint arthrosis, spinal stenosis, and spondylolisthesis.

Conflict of Interest: None.

Source of Funding: None.

Ethical Approval: The permission was obtained from the Azadi Teaching Hospital Committee and informed consent was obtained from each individual before data collection was begun. Personal data was not explored.

References

- Leonid Kalichman, Paul Hodges, Ling Li, Ali Guermazi, and David J. Hunter. Changes in Paraspinal muscles and their association with low back pain and spinal degeneration: CT study. *Eur Spine J.* 2010; 19: 1136–1144.
- Dagenais S, Caro J, and Haldeman S. A systematic review of low back pain cost of illness Studies in the United States and internationally. *Spine J.* 2008; 8: 8–20.
- Roger Chou, Amir Qaseem, Vincenza Snow, et al. Diagnosis and Treatment of Low Back Pain: A Joint Clinical Practice Guideline from the American College of Physicians and the American Pain Society. *Ann Intern Med.* 2007; 147: 478–491.
- Livshits G, Popham M, Malkin I, et al. Lumbar disc degeneration and genetic factors are the Main risk factors for low back pain in women: the UK Twin Spine Study. *Annals of the Rheumatic Diseases.* 2011; 10:1740-5.
- Cheung KM, Karppinen J, Chan D, et al. Prevalence and pattern of lumbar magnetic resonance imaging changes in a population study of one thousand forty-three individuals. *Spine J.* 2009; 34: 934–40.
- Anderson D, and Tannoury C. Molecular pathogenic factors in symptomatic disc Degeneration. *Spine J.* 2005; 5: 260S-266.
- Masahiro Kanayama, Daisuke Togawa, Chihiro Takahashi, Tomoya Terai, and Tomoyuki Hashimoto. Cross-sectional magnetic resonance imaging study of lumbar disc degeneration in 200 healthy individuals. *Neurosurg Spine J.* 2009; 11(4): 501–507.
- Roger Chou, Rongwei Fu, John A Carrino, and Richard A Deyo. Imaging strategies for lowback pain: systematic review and meta-analysis. *The Lancet.* 2009; 373 (7): 463–72.10.
- Zhang YG, Sun ZM, Liu JT, Wang SJ, Ren FL, and Guo X. Features of intervertebral disc Degeneration in rat's aging process. *J Zhejiang UnivSci B.* 2009; 10: 522-527.
- Dino Samartzis, Jaro Karppinen, Danny Chan, Keith D. K. Luk, and Kenneth M. C. Cheung. The Association of Lumbar Intervertebral Disc Degeneration on Magnetic Resonance Imaging With Body Mass Index in Overweight and Obese Adults A Population-Based Study. *Arthritis & Rheumatism.* 2012; 64 (5): 1488–1496.
- F. M. K. Williams, N. J. Manek, P. N. Sambrook, T. D. Spector, and A. J. Macgregor. Schmorl's Nodes: Common, Highly Heritable, and Related to Lumbar Disc Disease. *Arthritis & Rheumatism.* 2007; 57 (5): 855–860.
- Lurie JD, Doman DM, Spratt KF, Tosteson ANA, Weinstein JN. Magnetic resonance Imaging interpretation in patients with symptomatic lumbar spine disc herniations. Comparison of clinician and radiologist readings. *Spine J.* 2009; 34(7):701–705.
- Tue Secher Jensen, Joan S Sorensen, Jaro Karppinen, and Charlotte Leboeuf-Yde. Vertebral Endplate signal changes (Modic change): A systematic literature review of prevalence and Association with. *Eur Spine J.* 2008; 17: 1407–1422.
- Samartzis, Jaro Karppinen, Danny Chan, Keith D. K. Luk, and Kenneth M. C. Cheung. The Association of Lumbar Intervertebral Disc Degeneration on Magnetic Resonance Imaging with Body Mass Index in Overweight and Obese Adults A Population-Based Study. *Arthritis & Rheumatism.* 2012; 64 (5): 1488–1496.
- Alison Endean, Keith T Palmer, and David Coggon. Potential of MRI Findings to Refine Case Definition for Mechanical Low Back Pain in Epidemiological Studies: A Systemic Review. *Spine J.* 2011; 36(2): 160–169.
- Van Rijn JC, Klemetsö N, Reitsma JB, et al. Observer variation in MRI evaluation of Patients suspected of lumbar disk herniation. *AJR...*2005;184: 299–303.
- Pokhraj Suthar, Rupal Patel, Chetan Mehta, and Narrotam Patel. MRI Evaluation of Lumbar Disc Degenerative Disease. *J Clin Diagn Res.* 2015; 9(4): TC04–TC09.
- Jeffrey G. Jarvik, and Richard A. Deyo. Diagnostic Evaluation of Low Back Pain with Emphasis on Imaging. *Ann Intern Med.* 2002; 137: 586-597.
- Yin-gang Zhang, Tuan-mao Guo, Xiong Guo, and Shi-xun Wu. Clinical diagnosis for discogenic low

- back pain. *Int J BiolSci.* 2009; 5(7):647-658.
20. Jim JJ, Noponen-Hietala N, Cheung KM, et al. The TRP2 allele of COL9A2 is an age dependent risk factor for the development and severity of intervertebral disc degeneration. *Spine J.* 2005; 30: 2735–42.
 21. Bakhsh A. Long-term outcome of lumbar disc surgery: an experience from Pakistan: Clinical Article. *Journal of Neurosurgery: Spine.* 2010; 12(6): 666-70.
 22. David G, Ciurea AV, Iencean SM, and Mohan A. Angiogenesis in the degeneration of the lumbar intervertebral disc. *Journal of medicine and life.* 2010; 3(2): 154.
 23. Skaf GS, Ayoub CM, Domloj NT, Turbay MJ, El-Zein C, Hourani MH. Effect of age and lordotic angle on the level of lumbar disc herniation. *Adv Orthop.* 2011;2011:950576.
 24. Takatalo J, Karppinen J, Niinimäki J, et al. Prevalence of degenerative imaging findings in lumbar magnetic resonance imaging among young adults. *Spine J.* 2009; 34(16): 1716-21.
 25. Rubin DI. Epidemiology and risk factors for spine pain. *Neurol Clin.* 2007;25(2):353-71.
 26. Cheung K, Fan J, Karppinen J, et al. Can age-related intervertebral disc degenerative changes be differentiated from degenerative disc disease? 4th Annual Meeting of International Society for the Study of the Lumbar Spine. June 10-14, 2007, Hong Kong, China.
 27. Urban JP, and Roberts S. Degeneration of the intervertebral disc. *Arthritis Research and Therapy.* 2003; 5(3): 120-38.
 28. De Schepper EI, Damen J, Van MeursJB, et al. The association between lumbar disc degeneration and low back pain: the influence of age, gender, and individual radiographic features. *Spine.* 2010; 35(5): 531-6.
 29. Wang YX, and Griffith JF. Effect of Menopause on Lumbar Disk Degeneration: Potential Etiology. *Radiology.* 2010; 257(2): 318-20.
 30. Punnett L, Prüss-Utün A, Nelson DI, Fingerhut MA, Leigh J, Tak S, et al. Estimating the global burden of low back pain attributable to combined occupational exposures. *Am J Ind Med* 2005;48:459-69.
 31. Albert HB, and Manniche C. Modic changes following lumbar disc herniation. *Eur Spine.* 2007; 16: 977- 982.
 32. Walwante R, Dhapate S, and Porwal S. Study of lumbar spine by MRI with special reference to disc degeneration and Modic changes in rural area . *Indian Journal of Clinical Anatomy and Physiology.* 2017; 4(4): 569-573.
 33. Mario Henríquez, and Bernardo Arriaza. Frequency and Distribution of Schmorl s Nodes in the Spine of Prehispanic Arica Populations: Evidence of Work Load on the Vertebral Column. *Chungara,* 2013; 45(2): 311-319.

Early Versus Conventional Postoperative Oral Feeding after Elective Colonic Anastomosis

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Abstract

Objective: The aim of this study was to assess the safety of early oral feeding after elective colonic anastomosis.

Method: The study was conducted upon 40 cases at Kasr Al- Ainy teaching hospital. The cases were divided into two groups: Group 1 (Early feeding): 20 patients began fluids on the first postoperative day and advanced to a regular diet within the next 24–48 h, as tolerated. Group 2 (Regular feeding): 20 patients were managed in the traditional way (nothing by mouth for five days).

Results: Anastomotic leakage was 0% in early feeding group versus 5% in conventional feeding group. Early oral feeding was tolerated in 90% of patients in early feeding group. The time to first passage of flatus was sooner in the early feeding group (1.05 ± 0.22) than the traditional group (1.95 ± 1.05), $p = 0.001$. The risk of wound infection was significantly reduced with the early feeding group (10.0%) when compared with the conventional feeding group (40.0%), $p = 0.028$. Length of hospital stay was significantly less in the early feeding group.

Conclusion: Early oral feeding after elective colonic anastomosis is safe and can be tolerated by the majority of patients. Early oral feeding is associated with early return of bowel habits and reduced length of hospital stay. It is also associated with reduced risk of wound infection.

Keywords: (Early feeding, Colonic anastomosis, Anastomotic leak).

Introduction

Conventional treatment after colonic anastomosis has typically entailed postoperative fasting with administration of intravenous fluids until passage of flatus, principally due to concerns over post-operative ileus.¹

This was based on the believe that oral feeding may not be tolerated in the presence of ileus and the

integrity of the newly constructed anastomosis may be compromised.²

However, small intestinal motility recovers 6–8 hours after surgical trauma and moderate absorptive capacity exists even in the absence of normal peristalsis.³

In addition several studies showed that early resumption of an oral diet accelerated gastro intestinal recovery, decreased the hospital length of stay and was associated with lower complication and mortality rate.⁴⁻⁶

So oral feeding can be started on the first postoperative day without waiting for the resolution of postoperative ileus. Thus, the patients can be protected from starvation and the related side effects.

Aim of Work: The aim of this study was to compare early and conventional postoperative oral feeding after

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elective colonic anastomosis as regards the risk of anastomotic leak, tolerance of early feeding, return of bowel habit, length of hospitalization, wound infection and serum electrolyte disturbance.

Material and Method

The study was conducted upon 40 cases at Kasr Al-Ainy teaching hospital during the period from March 2015 to September 2016.

The patients were then randomized into two groups. Randomization was achieved using sealed envelopes. After carefully explaining the purpose of the study, informed consent was taken from every patient.

Group 1 (Early feeding): 20 patients began fluids on the first postoperative day and advanced to a regular diet within the next 24–48 h, as tolerated.

Group 2 (Regular feeding): 20 patients were managed in the traditional way (nothing by mouth for five days).

In all the cases a detailed history was taken followed by clinical examination and relevant investigations including routine laboratory investigation (CBC, liver function tests, renal function tests), serum electrolytes and tumor markers.

It was assured that serum albumin level was at least 3 g/dl and hemoglobin level was at least 10 g/dl in all patients (for standardization).

Serum electrolytes (Na, K) were done preoperatively and then daily till the date of discharge to detect any electrolyte disturbance. According to the laboratory results correction was undertaken.

The patients were also assessed radiologically by barium enema, abdominal ultrasound, pelvic and abdominal CT, bone survey and chest X-ray in addition to colonoscopy and biopsy for diagnosis of colorectal cancer.

Chemical and mechanical bowel preparation was done for all patients. The anastomosis was done using

hand sewn technique, interrupted, 2 layers, using vicryl 3-0. Intra abdominal drain was inserted in all patients.

A nasogastric tube was inserted in all patients during surgery. The tube was removed immediately after surgery, and was reinserted after two episodes of vomiting of more than 100 mL over 24 hours in the absence of intestinal sounds.

The patients were monitored for vomiting, abdominal distension, length of ileus, tolerance of regular diet, length of hospitalization and complications including anastomotic leak, wound infection and electrolyte disturbances.

Findings: Group 1 (early feeding group) included 20 patients, 13 males (65%) and 7 females (35%) while group 2 (conventional feeding group) included 20 patients, 12 males (60%) and 8 females (40%). In group 1 (early feeding group) mean age was 39.4 ± 17.34 years (range 11–65 years) while group 2 (conventional feeding group) mean age was 45.05 ± 13.49 years (range 13–70 years).

Anastomotic leakage was 0% in early feeding group versus 5% in conventional feeding group. Anastomotic leakage occurred only in one patient in conventional feeding group after closure of colostomy and healed after conservative measures.

Early oral feeding was tolerated in 90% of patients in early feeding group. The time to first passage of flatus was sooner in the early feeding group (1.05 ± 0.22) than the traditional group (1.95 ± 1.05), $p = 0.001$.

The risk of wound infection was significantly reduced with the early feeding group (10.0%) when compared with the conventional feeding group (40.0%), $p = 0.028$.

Serum electrolyte disturbance was 5% in early feeding group versus 45% in conventional feeding group ($p = 0.003$).

Length of hospital stay which was significantly less in the early feeding group (5.95 ± 1.00) compared to conventional feeding group (7.70 ± 2.64), $p = 0.009$.

Table 1: Results of early feeding group

		No.	%
Sex	Female	7	35.0%
	Male	13	65.0%
Age	Mean \pm SD	39.40 \pm 17.34	
	Range	11–65	
Anastomotic leakage	Negative	20	100.0%
	Positive	0	0.0%
Tolerance of early feeding	Negative	2	10.0%
	Positive	18	90.0%
Time of passing flatus (days)	Mean \pm SD	1.05 \pm 0.22	
	Range	1–2	
Wound infection	Negative	18	90.0%
	Positive	2	10.0%
Electrolyte disturbance	Negative	19	95.0%
	Positive	1	5.0%
Hospital stay (days)	Mean \pm SD	5.95 \pm 0.99	
	Range	5–8	

Table 2: Results of conventional feeding group

		No.	%
Sex	Female	8	40.0%
	Male	12	60.0%
Age	Mean \pm SD	45.05 \pm 13.49	
	Range	13–70	
Anastomotic leakage	Negative	19	95.0%
	Positive	1	5.0%
Tolerance of early feeding	Negative	0	0.0%
	Positive	0	0.0%
Time of passing flatus (days)	Mean \pm SD	1.95 \pm 1.05	
	Range	1–4	
Wound infection	Negative	12	60.0%
	Positive	8	40.0%
Electrolyte disturbance	Negative	11	55.0%
	Positive	9	45.0%
Hospital stay (days)	Mean \pm SD	7.70 \pm 2.64	
	Range	5–15	

Discussion

Proper and adequate nutrition has so far been one of the major concerns in postoperative care. However, postoperative fasting until resolution of ileus, known as traditional feeding, is regarded as surgical dogma or doctrine.⁷

This belief was not supported by large number of studies which demonstrated that early feeding is safe, tolerated by most of the patients, reduced length of

hospital stay and was not associated with increased risk of complications.⁸⁻¹²

This prospective study was conducted in Kasr al Ainy hospital, and comprised 40 patients who underwent elective colonic anastomosis. Patients were divided into two groups; early feeding group (20 patients) and conventional feeding group (20 patients).

In this study, there was no significant difference in the risk of anastomotic dehiscence with the early feeding group when compared with the traditional feeding group. Anastomotic leakage was 0% in early feeding group versus 5% in conventional feeding group. It occurred only in one patient in conventional feeding group after closure of colostomy and healed after conservative measures.

The same result was reported by other studies. El Nakeeb et al. reported that anastomotic leakage was 1.66% in the early feeding group versus 3.33% in the traditional group. Also Le Zhuang et al. reported in their Meta-analysis of RCTs that early oral feeding did not reduce or increase the risk of anastomotic dehiscence compared with traditional oral feeding.^{2, 13}

These findings are opposite to the traditional belief that patients should not eat for several days after colorectal surgery in order to avoid anastomotic leakage.

In this study, 18 patients (90%) tolerated early oral feeding while 2 patients (10%) failed to tolerate early feeding and presented with recurrent vomiting and abdominal distension without intestinal sounds. Dag et al. reported similar results where the majority of the patients in the early feeding group (85.9%) tolerated the early feeding schedule.¹

The time to first passage of flatus was sooner in the early feeding group (1.05 \pm 0.22) than the traditional group (1.95 \pm 1.05), $p=0.001$. The same was reported by El Nakeeb et al where the time to first passage of flatus was seen on postoperative day 3.3 \pm 0.9 (2–8) in the early feeding group and on day 4.2 \pm 1.2 (2–9) in the traditional group ($P=0.04$).¹³

This was reflected on the length of hospital stay which was significantly less in the early feeding group (5.95 \pm 1.00) compared to conventional feeding group (7.70 \pm 2.64), $p=0.009$. Multiple studies reported the same results where early oral feeding was associated with reduced length of hospital stay.^{8, 14}

This reduction in the length of hospital stay may be due to that early feeding is associated with reduced length of postoperative ileus and early return of bowel movement, also early feeding is associated with reduced postoperative complications which may lead to decreased length of hospital stay.

In this study the risk of wound infection was significantly reduced with the early feeding group (10.0%) when compared with the conventional feeding group (40.0%), $p = 0.028$. While El Nakeeb et al, reported that wound complications occurred in 10% in early feeding group versus 11.67% in traditional feeding group. This variation in the incidence of wound infection may be due to variation in the definition of wound infection.¹³

The reduction in the incidence of wound infection among early feeding group may be due to that conventional feeding is associated with increased length of hospital stay so there may be increased risk of hospital acquired infection and wound infection.

In conclusion, early oral feeding after elective colonic anastomosis is safe and can be tolerated by the majority of patients. Early oral feeding is associated with early return of bowel habits and reduced length of hospital stay. It is also associated with reduced risk of wound infection. So, there is no obvious advantage in keeping patients nil by mouth after elective colonic anastomosis.

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References

1. Dag, Ahmet, et al. "A randomized controlled trial evaluating early versus traditional oral feeding after colorectal surgery." *Clinics* 66.12 (2011): 2001-2005.
2. Zhuang, Cheng-Le, et al. "Early versus traditional postoperative oral feeding in patients undergoing elective colorectal surgery: a meta-analysis of randomized clinical trials." *Digestive surgery* 30.3 (2013): 225-232.
3. Fujii, Takaaki, et al. "Benefit of oral feeding as early as one day after elective surgery for colorectal cancer: oral feeding on first versus second postoperative day." *International surgery* 99.3 (2014): 211-215.
4. Han-Geurts, I. J. M., et al. "Randomized clinical trial of the impact of early enteral feeding on postoperative ileus and recovery." *British Journal of Surgery: Incorporating European Journal of Surgery and Swiss Surgery* 94.5 (2007): 555-561.
5. Ng, Wai Quin, and Jane Neill. "Evidence for early oral feeding of patients after elective open colorectal surgery: a literature review." *Journal of clinical nursing* 15.6 (2006): 696-709.
6. Osland, Emma, et al. "Early versus traditional postoperative feeding in patients undergoing resectional gastrointestinal surgery: a meta-analysis." *Journal of parenteral and enteral nutrition* 35.4 (2011): 473-487.
7. Nematihonar, Behzad, et al. "Early versus delayed (traditional) postoperative oral feeding in patients undergoing colorectal anastomosis." *Advanced biomedical research* 7 (2018).
8. Smeets, Boudewijn JJ, et al. "Effect of early vs late start of oral intake on anastomotic leakage following elective lower intestinal surgery: a systematic review." *Nutrition in Clinical Practice* 33.6 (2018): 803-812.
9. Consoli, M. Lobato Dias, et al. "Early postoperative oral feeding impacts positively in patients undergoing colonic resection: results of a pilot study." *Nutricion hospitalaria* 25.5 (2010): 806-809.
10. Wallström, Åsa, and Gunilla Hollman Frisman. "Facilitating early recovery of bowel motility after colorectal surgery: a systematic review." *Journal of clinical nursing* 23.1-2 (2014): 24-44.
11. Boelens, Petra G., et al. "Reduction of postoperative ileus by early enteral nutrition in patients undergoing major rectal surgery: prospective, randomized, controlled trial." *Annals of surgery* 259.4 (2014): 649-655.
12. Lloyd, G. M., et al. "The RAPID protocol enhances patient recovery after both laparoscopic and open colorectal resections." *Surgical endoscopy* 24.6 (2010): 1434-1439.

13. El Nakeeb, Ayman, et al. "Early oral feeding in patients undergoing elective colonic anastomosis." *International Journal of Surgery* 7.3 (2009): 206-209.
14. Herbert, Georgia, et al. "Early enteral nutrition within 24 hours of lower gastrointestinal surgery versus later commencement for length of hospital stay and postoperative complications." *Cochrane Database of Systematic Reviews* 7 (2019).

Joint Effect Obesity and Oral Contraceptive Use towards Hypertension among Women in Thirteen Provinces in Indonesia

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Abstract

Introduction: Hypertension complications cause 9,4 million people died in the whole world every year. Hypertension in a woman is more dangerous than man, as they affect mortality and morbidity not only at herself but also the fetus in a pregnant woman. Hypertension is stimulated by many risk factors, some of them were obesity and using oral contraception. The purpose of this study is to evaluate obesity, oral contraceptives use and their joint effect on the risk of hypertension among women in Indonesia.

Method: A cross-sectional study from Indonesian Life Family Survey 5 data, including 10.270 women with age ≥ 18 years old lives in Indonesia. Weight, Height and Blood Pressure were measured. Hypertensive respondents if the blood pressure $\geq 140/90$ mmHg, while obese defined by body mass index $\geq 27,5$ kg/m². History of contraceptive used, smoking behavior and age were investigated. The effect between the independent and dependent variables in this study can be determined by Prevalence Ratio (PR) and estimated under Cox Regression Model.

Results: Our study showed that obesity, oral contraceptive used, and age significantly become risk factor of hypertension with PR (95% CI) respectively 2,12 (1,94–2,31); 1,21 (1,10–1,33); and 2,65 (2,42–2,91). Combination OC users and obesity significantly elevated the risk of hypertension by PR 2,149 (1,90–2,42) among women in Indonesia. Compared with OC, Obesity was more strongly associated with hypertension with PR 1,93 (1,74–2,13).

Conclusions: Obesity, OC users and their joint effects significantly increased the risk of hypertension among women in thirteen Provinces in Indonesia. The way better to prevent being obese than preventing using OC in the case of hypertension.

Keywords: *Hypertension; Obesity; Oral Contraceptive*

Introduction

Hypertension complications cause 9,4 million people died in the whole world every year.²⁶ Hypertension in a woman is more dangerous than man, as they affect mortality and morbidity not only at herself but also the fetus in a pregnant woman.⁷ Hypertension prevalence in people aged ≥ 18 years in Indonesia continues to increase from 2013 to 2018. Based on the basic health research 2013 and 2018, the prevalence of hypertension in Indonesia is 25.8% and 34.1% respectively.^{9,10} The proportion of hypertension in 2018 was 31.34% in men and 36.85% in women.¹⁰

Hypertension induced by obesity cause of adipocytes in obese people induced increase in renin-angiotensin system which increasing sodium absorption, fluid volume, and also activate sympathetic nervous system. Those adipocytes also induced inflammation and reduced insulin sensitivity which attends to become endothelial dysfunction and arterial stiffness or vasoconstriction which leads to hypertension.¹² Obesity has been defined by the World Health Organization (2000) and The National Heart, Lung and Blood Institute (1988) as a body mass index (BMI) ≥ 30 kg/m².² This classification not appropriate to describe the association of various diseases due to obesity in Asia, because the percentage of

subcutaneous fat in Asians is more than the Caucasian at the same age, sex and BMI.^{2,21,23} In 2004, WHO Expert Consultants suggested the classification of the latest BMI in terms of the risk of cardiovascular disease where the risk cut or point of obesity in the Asian population is ≥ 27.5 kg/m².²³ The prevalence of hypertension in the overweight and obese group is 40.8% while the prevalence of hypertension in the group with normal and thin BMI is 25.3%.¹⁴

Using oral contraceptives or pills containing estrogen and progesterone causes cardiac hypertrophy and increases the presenting response of angiotensin by involving the renin angiotensin system which causes high blood pressure.^{3,15,16} The prevalence of hypertensive patients increased in line with the long duration of oral contraceptive use. It is known that the prevalence of hypertension in women who do not use oral contraceptives, use less than 1 year, less than 2 years and more than 2 years in a row were 14.3%; 13.9%; 21.3%; 22.8%.¹⁶ Oral contraceptives is the second contraceptives most chosen by women 15-49 years old in Indonesia after giving birth to the last child is 8,5%, and the first one is injection every 3 months is 42,4%.¹⁰

A study using the 2013 basic health research data explained that women of childbearing age (WUS) who had a body mass index of more than 25 kg/m² had 2.7 fold risk of developing hypertension.¹¹ A cross-sectional study states that those who are obese (>25 kg/m²) have a risk of hypertension of 1,681 times compared to non-obese after being controlled by age variables, a history of family hypertension and physical activity.¹⁸ Hypertensive women and those without hypertension (adjusted) were 1.96 for oral contraceptive use >2 years and 1.22 for use at >1 year.¹⁶ Wang's research in 2011 showed the combined effect of obesity and the use of oral contraceptives at a risk of 8.02 times (OR 8.02, CI 5.05-12.74) greater than hypertension with an additive interaction of $P = 0.039$.²¹

Method

This study using cross-sectional design from Indonesian Life Family Survey 5 (IFLS-5) data. IFLS-

5 is the fifth survey was held in 13 of 27 province in Indonesia in 2014. This survey used household survey from IFLS data. The subjects of this study including 10.270 women 18-49 years old, live in Indonesia and have complete data for each variable would be analyzed in this study. Weight, Height and Blood Pressure were measured. Hypertensive respondents if the blood pressure $\geq 140/90$ mmHg, diagnosed by health workers, or consuming hypertension pills. While obese defined by body mass index $\geq 27,5$ kg/m² this cut off based on WHO Expert Consultant.²³ Oral contraceptive used, smoking behavior and age were investigated. Collecting, editing and analyzing data IFLS-5 using software STATA (v.12, StataCorp). The effect between the independent and dependent variables in this study can be determined by Prevalence Ratio (PR) with confidence intervals (CI) 95% and estimated using Cox Regression Model in constant time.

Results

Sociodemographic characteristic between hypertensive and non-hypertensive cases: Majority women with any kind of characteristic classified as not hypertension case. Our study showed that obesity, oral contraceptive used, and age significantly become risk factor of hypertension with PR (95% CI) respectively 2,12 (1,94–2,31); 1,21 (1,10–1,33); and 2,65 (2,42–2,91). This individual risk factors are shown in (Table 1).

Association obesity and the risk of hypertension: After adjustment for age, the obese women have 1,93 fold (PR 1,93, 95% CI 1,74-2,13) increased risk of hypertension compared with non-obese women. This effect less than PR before adjustment (PR 2,16, 95% CI 1,95–2,38) (Table 2).

Association oral contraceptive use and the risk of hypertension: After adjustment for age, the obese women have 1,22 fold (PR 1,22, 95% CI 1,07–1,38) increased risk of hypertension compared with non-obese women. This effect is the same with PR without adjustment (Table 2). There is association was observed between Obesity and OC users ($p < 0,001$) (data not shown).

Table 1: Analyses of Risk Factors for Hypertension in Women

Variable	Hypertension N(%)	Not Hypertension N(%)	RR	P-value	PAR (%)
Obesity					
Yes	899 (35,44)	1638 (64,56)	2,12 (1,94–2,31)	0,0001	35,97
No	1291 (16,69)	6442(83,31)	(Reff)		

Variable	Hypertension N(%)	Not Hypertension N(%)	RR	P-value	PAR (%)
Oral Contraception					
Yes	562 (24,75)	1709 (75,25)	1,21 (1,10–1,33)	0,0001	9,75
No	1628 (20,35)	6371 (79,65)	(Reff)		
Age					
34-49 years	1569 (31,34)	3438 (68,66)	2,65 (2,42–2,91)	0,0001	45,29
18-33 years	621 (11,80)	4642 (88,20)	(Reff)		
Smoking					
Yes	40 (25,48)	117 (74,52)	1,20 (0,87–1,64)	0,252	9,12
Ever	17 (26,98)	46 (73,02)	1,27 (0,78–2,04)	0,324	11,95
No	2133 (21,22)	7917 (78,78)	(Reff)		
Sleep Disturbance					
Yes	2007 (21,08)	7513 (78,92)	0,86 (0,74–1,00)	0,058	-
No	183 (24,40)	567 (75,60)	(Reff)		

Table 2: Obesity Combined with OC Use Associated with The Risk of Hypertension

Obesity	OC	Hypertension N(%)	Not Hypertension N(%)	Crude PR (95% CI)	P-value	*Adjusted PR (95% CI)	P-value
+	+	243 (38,27)	392 (61,73)	2,40 (2,08–2,76)	0,0001	2,11 (1,83–2,43)	0,0001
+	-	656 (34,49)	1246 (65,51)	2,16 (1,95–2,38)	0,0001	1,93 (1,74–2,13)	0,0001
-	+	319 (19,50)	1317 (80,50)	1,22 (1,07–1,38)	0,002	1,22 (1,07–1,38)	0,002
-	-	972 (15,94)	5125 (84,06)	(Reff)		(Reff)	

*Adjusted for age

Joint Effect obesity and OC users on the risk of hypertension: As shown in **Table 2**, before adjustment combination obesity and OC users significantly elevated the risk of hypertension by compared to among women in Indonesia with PR 2,4 (2,08–2,76). OC users slightly elevated the risk of hypertension among both obese and non-obese women. The joint effects of obesity and OC users significantly increase the risk of hypertension by 1,11 fold (PR 2,11, 95% CI 1,83–2,43). An antagonism biologic interaction between obesity and OC users was detected (p = 0,0174).

Discussion

From this cross-sectional study we evaluate that obesity, OC users and their joint effects on the risk of hypertension in women of 13 provinces in Indonesia. Our results indicated that Obesity and OC users were all risk factors for hypertension. We suggested a strong effect of obesity (BMI ≥ 27,5 kg/m²) on hypertension risk, which attribute 35,97% in population. Same study in Chinese population showed effect of increased BMI on hypertension attributed 32,51% of PAR (Population at Risk) with BMI ≥ 24 kg/m² vs BMI <24 kg/m².²¹

There are many studies emphasized whether biologic mechanism obesity induced hypertension,^{5,12} also their association around the world. This also proved in the present study, we verified that obesity was the risk factor for hypertension significantly. Therefore, in the future the body mass index (BMI) such as obesity should never be underestimated.

OC use as hypertension risk have attributable risk not as much as obesity was 9,75%. OC used is well known could change blood pressure by few millimeters and 2-3 fold increase incidence of hypertension.^{3,24} Both World Health Organization (WHO) and American College of Obstetricians and Gynecologists (AJOG) have formally offered that Hypertension was one of contradiction to use COC but AJOG would allow COC use in women with well-controlled hypertension in some circumstances.⁴ Low dose COC consist ethinyl estradiol dose less than 50 µg would increase risk of myocardial infraction and ischemic stroke approximately 2 fold in the general population of COC users.^{4,21,24} This cross-sectional study also confirmed OC as risk factor of hypertension significantly.

Interestingly we found there is joint effect between Obesity and OC use towards hypertension. Biologic Interaction identified by this study was antagonism although the risk of joint effect was bigger than independent risk of obesity or OC use. In the contrary, a case-control study in China also found joint effects general and central obesity, combined oral contraceptives (COC) use and hypertension, also shown a synergism interaction ($p = 0,039$).²¹ They found that the higher body mass index and the more longer respondent using COC therefore the risk of hypertension became a lot higher. The risk increased dramatically in combination of COC use with a BMI ≥ 28 kg/m² or Waist Circumference (WC) ≥ 90 cm with OR 8,02 (5,05–12,74) and OR 5,76 (3,65–9,12) respectively.²¹

This research found increasing risk to hypertension in joint effect obesity and OC use but have antagonism interaction. This might be caused by first, the operational definition of OC users had been used in this research was consist of women that using OC; women have used OC in her lifetime with proportion consecutively 11,20% and 10,92%. Women have used OC would have been stop for a long time ago or short time, a cohort study included 2112 hypertension people found that stopping OC in 6,6 \pm 7,5 months was an effective antihypertensive intervention in a clinical setting.¹³ The study showed there is association between stopping OC and improved prognosis as reduction of at least 10 mmHg in Diastolic Blood Pressure (DBP) or 20 mmHg in Systolic Blood Pressure (SBP) with OR 0,27 (CI 95% 0,06–0,90) adjusted by age, weight and drug prescription.¹³ Another study state that COC users would increase 5-6 mmHg of SBP and 1-2 mmHg in DBP.³ Besides, the period of time women who have a history used OC did not provide by RAND cooperation therefore we did not have information about that. Also as the limitation of our study, we did not identify the period of time using OC.

Second, there are two types of oral contraceptives used in Indonesia which were mini pil (progestin only pill/POP) and pil KB (Combination Oral Contraceptive/COCC), but this study was blinding that because there are no information about that. Although whether POP or COCC could increase blood pressure in experimental study in rats, which increasing blood pressures (systolic and diastolic) were higher in COCC user than POP.³ But, contrary in some study literature review and meta-analysis about POP and hypertension drawn conclusion no association POP and increasing blood pressure.^{6,8} This two condition affect the risk of OC and their

joint effect with obesity towards hypertension become antagonism. However, we found the risk of joint effect still bigger than the risk of obesity or OC users alone.

Conclusions

Our study indicated that obesity, OC users and their joint effects significantly increased the risk of hypertension among women in thirteen Provinces in Indonesia. The way better to prevent being obese than preventing using OC in the case of hypertension. For further research it would have been better if the variable not nominally categorized but depend on the usefulness and richness of the research. Also it would have been wonderful to include the long time using OC and using cohort design study. Besides, we recommend for future research for including waist circumference (WC), if the research conducted in Asian Population.

Ethical Considerations: This study was approved by The Research and Community Engagement Ethical Committee Faculty of Public Health Universitas Indonesia (Ket-605/UN2.F10/PPM.00.02/2019).

Competing Interests: The authors declared that no competing interests exist.

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References

1. American Academy of Family Physicians. JNC 8 Guidelines for the Management of Hypertension in Adults [Internet]. 2014 (cited 2019 April 20). Available from <https://www.aafp.org/afp/2014/1001/p503.pdf>.
2. Anuurad E, Shiwaku K, Nogi A, Kitajima K, Enkhmaa B, Shimono K, et al. The New BMI Criteria for Asians by The Regional Office for the Western Pacific Region of WHO are Suitable for Screening of Overweight to Prevent Metabolic Syndrome in Elder Japanese Workers. *Journal of Occupational Health*. 2003;45:335-343.

3. August P, Oparil S. Hypertension in women. *The Journal of Clinical Endocrinology and Metabolism*. 1999;84(6):1862–1866.
4. Beller JP, McCartney CP. Cardiovascular risk and combined oral contraceptives: clinical decisions in settings of uncertainty. *American Journal of Obstetrics and Gynecology*. 2013;39-41.
5. DeMarco VG, Aroor AR, Sowers JR. The pathophysiology of hypertension in patients with obesity. *Nat Rev Endocrinol*. 2014;10 (6): 364-376.
6. Glisic M, Shazad S, Tsoli S, Chadni M, Asllanaj E, Rojas LZ, et al. Association between progestin-only contraceptive use and cardiometabolic outcomes: A systemic review and meta-analysis. *European Journal of Preventive Cardiology*. 2018;25(10): 1042-1052.
7. Gudmundsdottir H, Høiegggen A, Stenehjem A, Waldum A, Os I. Hypertension in women: latest findings and clinical implications. *Therapeutic Advances in Chronic Disease*. 2012;3(3): 137-146.
8. Hussain SF. Progestogen-only pills and high blood pressure: is there an association? A literature review. *Contraception*. 2003;69(2004):89-97.
9. Kementerian Kesehatan. Hasil Riset Kesehatan Dasar 2013. Jakarta: Kemenkes; 2013.
10. Kementerian Kesehatan. Laporan Nasional RISKESDAS 2018. Jakarta: Kemenkes; 2019.
11. Kristina, Pangaribuan L, Bisara D. Hubungan Index Massa Tubuh Dengan Hipertensi Pada Wanita Usia Subur (Analisis Data Riskesdas 2013). *Media Litbangkes*. 2015:117-127.
12. Kotsis V, Stabouli S, Papakatsika S, Rizos Z, Parati G. Mechanism of Obesity-induced hypertension. *Hypertension Research*. 2010;33:386–393.
13. Lubianca JN, Moreira LB, Gus M, Fuchs FD. Stopping oral contraceptives: an effective blood pressure-lowering intervention in women with hypertension. *Journal of Human Hypertension*. 2005;19: 451–455.
14. Mardani S, Gustina T, Dewanto H, Priwahyuni Y. Hubungan antar indeks masa tubuh (IMT) dan kebiasaan mengkonsumsi lemak dengan tekanan darah. *Jurnal Kesehatan Komunitas*. 2011; 1(3): 129-135.
15. Pangaribuan L, Lolong DB. Hubungan penggunaan kontrasepsi dengan kejadian hipertensi pada wanita usia 15-49 tahun di Indonesia tahun 2013 (Analisis data RISKESDAS 2013). *Media Litbangkes*. 2015;25(2): 1-7.
16. Park H, Kim K. Associations between oral contraceptive use and risks of hypertension and prehypertension in a cross-sectional study of Korean women. *BMC Women’s Health*. 2013;13(39):1-7.
17. Ramadhani ET, Sulistyorini Y. Hubungan kasus obesitas dengan hipertensi di provinsi Jawa Timur tahun 2015-2016. *Jurnal Berkala Epidemiologi*. 2018;6(1):36-42.
18. Rohkuswara TD, Syarif S. Hubungan Obesitas dengan kejadian hipertensi derajat I pembinaan terpadu penyakit tidak menular (Posbindu PTM) Kesehatan Pelabuhan Bandung Tahun 2016. *Jurnal Epidemiologi Kesehatan Indonesia*. 2017; 1 (2): 13-18.
19. Rothman KJ, Greenland S, Lash TL. *Modern Epidemiology Third Edition*. Philadelphia: Lippincott Williams & Wilkins; 2008.
20. Strauss J, Witoelar F, Sikoki B. *The fifth wave of the Indonesia Family Life Survey: Overview and Field Report Volume 1*. California: RAND Corporation; 2016.
21. Wang C, Li Y, Bai J, Qian W, Zhou J, Sun Z, et al. General and central obesity, combined oral contraceptive use and hypertension in Chinese women. *American Journal of Hypertension*. 2011; 24 (12): 1324-1330.
22. Wei W, Li Y, Chen C, Sun T, Sun Z, Wu Y, et al. Dyslipidemia, combined oral contraceptives use and their interaction on the risk of hypertension in Chinese women. *Journal of Human Hypertension*. 2011; 25:364–371.
23. WHO Expert consultant. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *The Lancet*. 2004; 363: 157-163.
24. WHO Special Programme of Research, Development and Research Training in Human Reproduction. The WHO multicenter trial of vasopressor effects of combined oral contraceptives: 1. Comparison with IUD. *Contraception*. 1989; 40 (2): 129–145.
25. WHO Western Pacific Region. *The Asia-Pacific perspective: Redefining Obesity and its treatment*. Australia :Health Communications Australia; 2000.
26. World Health Organization. *A Global Brief on Hypertension Silent Killer, Global Public Health Crisis*. Geneva: WHO; 2013.

Comparison between the Antioxidant Activity of Volatile Oil and Hydrosol in *Eucalyptus Camaldulensis* (Young and Adult) Leaves

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Abstract

Essential oils have been reported as an important compounds in the pharmaceutical industries for their antibacterial and antioxidant activity. This study was conducted to investigate the antioxidant activity of *Eucalyptus camaldulensis* volatile oil and hydrosol obtained from young and adult leaves. Oil extraction was carried out by using steam distillation method. The antioxidant power was estimated by using the DPPH(2,2-diphenyl-1,1-picrylhydrazyl) and FRAP(ferric reducing antioxidant power) assays. Butylated hydroxy toluene (BHT) was used as positive control. The results show that young leaves of *E. camaldulensis* provide essential oil (2-4%), while in adult leaves the oil percentage was (1-2%). The IC₅₀ of volatile oil in young leaves for the DPPH and FRAP assays was (237.178 and 243.664 µg/ml) respectively while in adult leaves IC₅₀ was not observed. IC₅₀ of hydrosol in young leaves of DPPH and FRAP assays was higher as compared with control and adult leaves. The results also showed that the antioxidant activity of volatile oil and Hydrosol in adults leaves was more than in young leaves. The current study revealed the possibility of using this volatile oil and hydrosol as a natural antioxidants.

Keywords: Hydrosol, volatile oil, antioxidants, *Eucalyptus camaldulensis*.

Introduction

Aromatic plants are used in phytotherapy due to their essential oils and various biological activities such as antioxidant. Exogenous antioxidants can be a natural compounds like vitamins, flavonoids, anthocyanin but it can be also a synthetic like butylated hydroxy toluene⁽¹⁾. Natural antioxidants are an important compounds to prevent the free radicals during the interaction of oxygen with molecules⁽²⁾. These radicals are dangerous when they react with DNA and cell membrane⁽³⁾. Antioxidants delay or inhibit the oxidation processes by affecting the free radical or molecular oxygen⁽⁴⁾, so they prevent cellular damage and inhibit the pathway for cancer, aging and diseases^(5,6). They also used in foods and cosmetics industries to prevent undesirable oxidation processes. The synthetic antioxidants like butylated hydroxytoluene (BHT) and butylated hydroxyanisole (BHA) are possibly toxic. Finding natural antioxidants has been increased during the last years^(7,8). Some herbal extracts and oils formulations have been proved as an important antioxidant agents^(9,10). *Eucalyptus* belongs to Myrtaceae family, it has 500 species endemic to Australia and neighboring territories. Some species

have been introduced into Iraq, one of these species is *E. camaldulensis*⁽¹¹⁾. The leaves of this species is sensitive to dust pollution⁽¹²⁾ and change as the tree progress from juvenility to adulthood⁽¹³⁾, so it can be found as a young (growing tips), Mature (six mo.), aged (12-18 mo.).

The medicinal properties of *Eucalyptus* reside in its oil which is secreted and stored in the sub-dermal cavities⁽¹⁴⁾. The biological effects of this oil include: antiviral, antioxidants, antibacterial, antifungal and treat the respiratory infections as well as sinusitis⁽¹⁵⁾. The essential oil in association with hydrosol can be obtained through steam distillation process for the leaves of this aromatic plant. The hydrosol contains some of the water-soluble compounds of the essential oil which are the same of those present in volatile oil. Unlike essential oils that should be diluted prior to application attach the skin hydrosol can generally be used directly on the skin without further dilution⁽¹⁶⁾. Hydrosol has been used in different industries such as food and cosmetic as well as to the biological agriculture and soil fertilization⁽¹⁷⁾. This study was done to determine for the first time, comparison of the antioxidant activity for *Eucalyptus camaldulensis* leaves in Iraq. This work allowed

highlight in the influence of plant leaves maturity on the quantity, activity and chemical composition of essential oil and hydrosol.

Material and Method

Plant collection and extraction: Leaves (young and adult or aged) of *E. camaldulensis* Dehn were harvested in October 2018 from University of Baghdad. These leaves were washed and dried in shade for three days. Dried leaves of this plant were chopped and semi grinded into small pieces and submitted to steam distillation using the Clevenger apparatus for 4 h⁽¹⁸⁾. Yield percentage was calculated according to the oil ratio equation⁽¹⁹⁾.

$$\text{Extracted oil ratio} = \frac{\text{oil volume}}{\text{sample weight}} \times 100$$

The (DPPH) assay: 2,2-diphenyl-1,1-picrylhydrazyl: All the chemicals in this study were obtained from Sigma (Sigma-Aldrich GmbH, Germany). 2ml of samples at the concentrations (200, 400, 600, 800, 1000 µg/ml) were added to the volume (1ml) of the DPPH in methanol solution. The mixture was shaken and stand for half an hour in dark place. Spectrophotometer was used to measure the absorbance of the solution (yellow color) at 517 nm. Percentage (I%) of DPPH was collected as follow :

$$I\% = 100 \times \frac{A_{\text{control}} - A_{\text{sample}}}{A_{\text{control}}}$$

A control = Absorbance of control and A sample is the absorbance of test compound. Butylated hydroxytoluene (BHT) was used as a standard⁽²⁰⁾.

The FRAP (ferric reducing antioxidant power) method: Volatile oil and Hydrosol reducing powers were determined according to procedure of⁽²¹⁾. Different concentrations of the extracts were mixed

with phosphate buffer and 1% of water solution from potassium ferricyanide. This mixture was kept at 50 °C for 20 min. Trichloroacetic acid was added to the mixture and then centrifuged at 3000 rpm for 10 min. The supernatant was mixed with distilled water and FeCl₃ solution. The absorbance was read at 700 nm.

Statistical analysis: The data were reported by using mean ± standard deviation for three replicates. The IC₅₀ value µg/ml was calculated by using Excel programme depended on the logarithm (Log.) of each concentration.

Results and Discussion

Plant oil yield: The results show that young leaves of *E. camaldulensis* provide more essential oil (2-4%), while in adult leaves the oil percentage was (1-2%). These leaves provide quantitatively different yields. This result agree with⁽²²⁾ which referred that the aged leaves yield less oil than recently mature. On the other hand the different stages of growth affected the oil yield and its chemical compositions⁽²³⁾.

DPPH scavenging activity and Ferric Reducing Antioxidant power (FRAP) of volatile oil from Eucalyptus leaves: The results show that the antioxidant activity increased by increasing the concentrations. This activity of volatile oil in adult leaves was higher than young leaves in the two different assays (Figure 1 and 2). At the concentrations (200, 400 µg/ml), the highest value of DPPH activity was obtained from the volatile oil in adult leaves in addition to its highest FRAP activity for all concentrations as compared with control. On the other hand, the IC₅₀ (the half maximal inhibitory concentration) in both DPPH and FRAP assays was not observed in volatile oil of adult leaves while the IC₅₀ of volatile oil in young leaves for the two assays was (237.178 and 243.664 µg/ml) respectively, as compared with BHT (233.001 and 208.855 µg/ml).

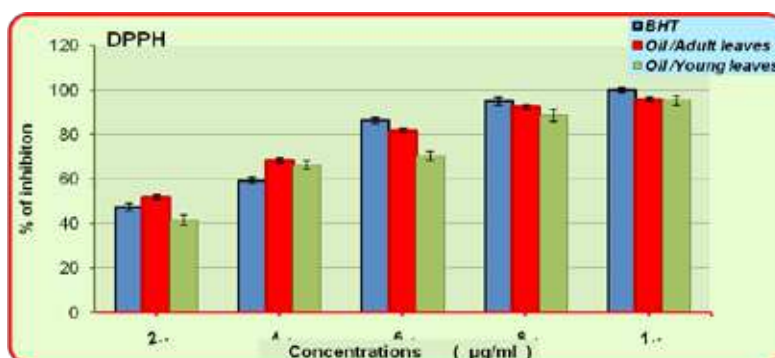


Figure 1: DPPH scavenging activity of *E. camaldulensis* volatile oil in adult and young leaves.

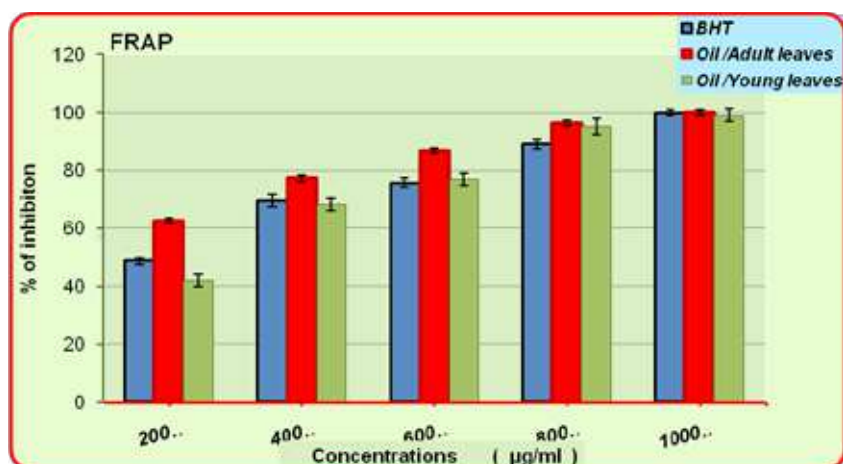


Figure 2: Ferric Reducing Antioxidant Potential of *E. camaldulensis* volatile oil in adult and young leaves.

DPPH scavenging activity and Ferric Reducing Antioxidant power (FRAP) of Hydrosol from *Eucalyptus* leaves: (Figure 3 and 4) show that the antioxidant activity of hydrosol in adult leaves was higher than young leaves in the two different assays. At FRAP assay the hydrosol of adult leaves at concentrations (400,600,800) revealed more activity as compared with control.

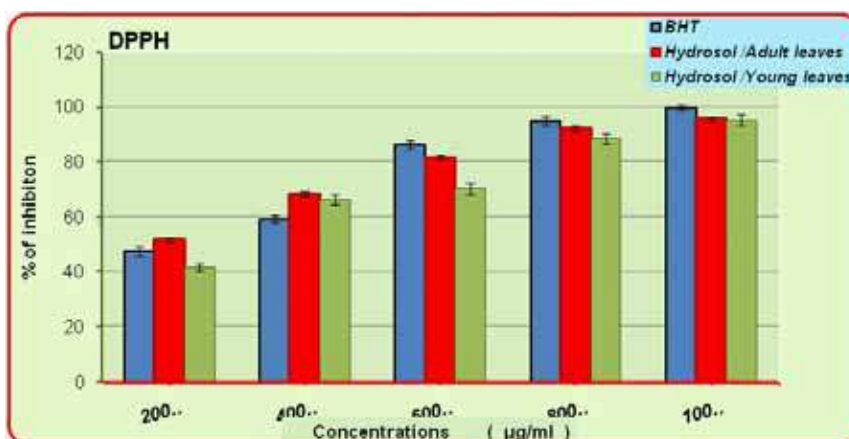


Figure 3: DPPH scavenging activity of *E. camaldulensis* Hydrosol in adult and young leaves.

On the other hand, IC50 of hydrosol in young leaves of DPPH and FRAP assays was higher as compared with control and adult leaves.

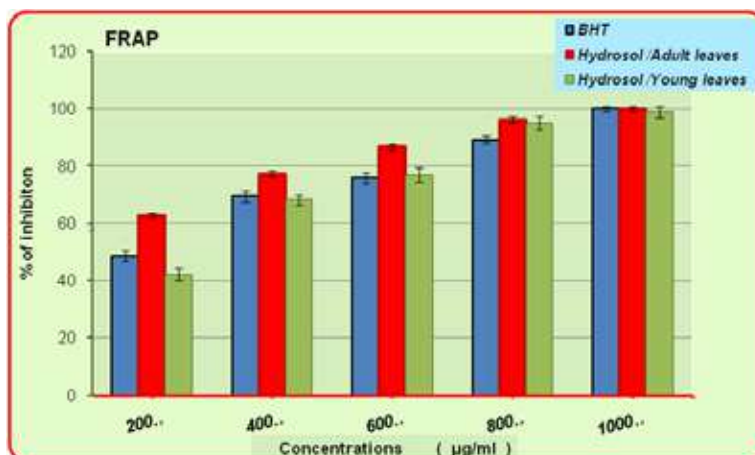


Figure 4: Ferric Reducing Antioxidant Potential of *E. camaldulensis* Hydrosol in adult and young leaves.

The differences in oils activity found in this experiment between different leaves may be related to the modifications of the oil composition during leaves maturation. The chemical analysis of *E. camaldulensis* essential oil revealed the presence of different compounds including: 1.8-cineole, limonene, α -pinene and p-cymene⁽²⁴⁾. The antioxidant activity of volatile oil belongs to these compounds and the differences in their concentrations. The stronger free radical inhibitors are active at low concentrations (lower IC50)⁽²⁵⁾. The disappeared of the IC50 in both DPPH and FRAP assays in volatile oil of adult leaves revealed that it could be appeared in lower concentration than 200 which represented the lower one in this study, so this study indicate that *E. camaldulensis* volatile oil in adult leaves was more active than the control itself.

Conclusion

The volatile oil and hydrosol of *Eucalyptus camaldulensis* can be used as a natural antioxidants. There is an economical importance by using hydrosol as a raw material in the cosmetic industry and food preservation.

Conflict of Interest: None

Funding: Self

Ethical Clearance: Not required.

References

- Litescu S, Eremia S, Diaconu M, Tache A, Radu G. Applications on Assessment of Reactive Oxygen Species and Antioxidants In: Somerse V(Ed.), Environmental Biosensors. In Tech. 2011.Pp:95-114.
- Bickers D, Athar M. Oxidative stress in the pathogenesis of skin disease. J. Invest. Dermatol. 2006. 126(12):2565-75.
- Lobo VA, Phatak A, Chandra N. Free radicals, antioxidants and functional foods: Impact on human health. Pharmacogn. Rev. 2010. 4(8):118-126.
- Pisoschi A, Negulescu G. Method for Total Antioxidant Activity Determination: A Review. Biochem. & Anal. Biochem. 2011. 1:106. doi: 10.4172/2161-1009.1000106.
- Finkel T, Holbrook NJ. Oxidant, oxidative stress and the biology of aging. Nature. 2002. 408(6809):239-247.
- Buyukokuroglu ME, Gulcin I, Oktay M, Kufrevioglu O. In vitro antioxidant properties of dantrolene sodium. Pharmacol. Res. 2001. 44:491-95.
- Krishnakumar V, Gordon I. Antioxidants- trends and development. Int. Food Ingeg. 1996. 5: 541-544.
- Lagouri V, Blekas G, Tsimidou M, Kokkini S, Boskou DZ. Composition and antioxidant activity of essential oils from Oregano plants grown wild in Greece. Z. Lebensm. Unters, Forch. 1993. 197: 20-23.
- Natarajan K, Narasimhan M, Shanmugasundaram K, Shanmugasundaram E. Antioxidant activity of a salt-spice-herbal mixture against free radical induction. J. Ethnopharmacol. 2006. 105:76-83.
- Olga A, Olena A, Natalia A, Valentina N. A new test method for the evaluation of total antioxidant activity of herbal products. J Agric. Food Chem. 2004. 52(1):21-25.
- Townsend CC, Guest E. Flora of Iraq. Vol.4. Part:1. Ministry of Agriculture. Republic of Iraq. 1959.
- AL-Taay MS, Al-Assie AA, Rasheed RO. Impact of bazian cement factory on air, water, soil, and some green plants in sulaimani city-Iraq. IJAS. 2018. 49(3):463-477.
- Pallardy S. Physiology of woody plants. 3rd ed. Academic Press. 2010. Pp:464.
- Silva J, Abebe W, Sousa S. Analgesic and anti-inflammatory effects of essential oils of Eucalyptus. J. Ethnopharmacol. 2003. 89:277-83.
- Sadlon A, Lamson D. Immune-Modifying and Antimicrobial Effects of Eucalyptus Oil and Simple Inhalation Devices. Altern Med Rev. 2010. 15(1): 33-47.
- Catty S. Hydrosols: The next Aromatherapy. Rochester, VT: Healing Arts press. 2001.
- Paolini J, Leandri C, Desjobert J, Barboni T, Costa J. Comparison of liquid-liquid extraction with headspace method for the characterization of volatile fractions of commercial hydrolats from typically Mediterranean species. J. Chromatogr. 2008. 1193(1-2):37-49.
- European Pharmacopeia. 4th ed.; Council of Europe: Strasbourg Cedex, France. 2002.
- Obeid SH, Jaber BM. Chemical composition and antioxidant activity of Pelargonium graveolens oil. IJAS. 2018. 49(5):811- 816.

20. Moreno S, Larrauri JS, Calixto F. A procedure to measure the antiradical efficiency of plant extracts. *J. Sci. Food Agric.* 1999. 76(2): 270-276.
21. Oyaizu M. Studies on products of browning reaction prepared from glucose amine. *Jpn. J. Nutr.* 1986. 44 (6): 307-315.
22. Coppen JJW. *Eucalyptus. The genus Eucalyptus.* Taylor and Francis. 2002.
23. Moghaddam M, Mehdizadeh L. Chemistry of Essential Oils and Factors Influencing Their Constituents. In: Grumezescu A and Holban A (Eds.), *Soft Chemistry and Food Fermentation.* 2017. p.379-419.
24. Ndiaye E, Gueye M, Ndiaye I, Diop SM, Fauconnier M. Chemical composition of essential oils and hydrosols of three *Eucalyptus* species from Senegal: *Eucalyptus alba* Renv, *Eucalyptus camaldulensis* Dehnh and *Eucalyptus tereticornis*. *Am. J. Essent. Oil. Nat. Prod.* 2017. 5(1): 01-07.
25. Ghasemzadeh A, Jaafar H, Ashkani S, Rahmat A, Juraimi A, Puteh A, Mohamed M. Variation in secondary metabolites production as well as antioxidant and antibacterial activities of *Zingiber zerumbet* (L.) at different stages of growth. *BMC Complement Altern. Med.* 2016. 16:104

E-Health Literacy of Medical Students at a University in Central Vietnam

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Abstract

Background: The study is to measure eHealth literacy of medical students at a university in central Vietnam and to examine factors influencing their skills.

Material and Method: This is a cross-sectional study. Data were collected through the self-administered structured questionnaire of 410 students who were randomly selected among general medical students and preventive medicine students in the fifth year at Hue University. The eHealth literacy scale was developed on the basis of eHEALS to measure skills for seeking and utilizing sources of eHealth information. Multiple linear regression model was used to identify factors influencing their eHealth literacy.

Results: The study found that the general mean score for eHealth literacy among participants is 27.03 (SD = 3.54). Factors influencing eHealth literacy are genders ($p=0.001$), training program ($p=0.013$), computer skills ($p=0.031$) and purpose of seeking and using medical information ($p<0.001$).

Conclusions: The findings showed that eHealth literacy of medical students in the study setting is still limited. In order to improve these skills of students, the educators should have relevant teaching strategies that promote the interest and skills of students to locate and evaluate eHealth resources.

Keywords: eHealth literacy, health resource, medical students, Vietnam.

Introduction

Along with the development of the digital technology, the internet provides more information than any tool ever to exist. People increasingly expect to interact with health information technology to promote their health.¹ According to Pew Research Center, among 80% of Internet users reported seeking health information online, 58% reported that the information found on their search impacted health decisions and 39% said that the information changed the way to cope with a chronic condition or manage pain.^{2,3} Those are referred

to as “eHealth” application. Facing information- rich environment, the concept of eHealth has been developed to response to challenges of accessing and effectively using health information technology.¹ Norman and Skinner (2006) defined eHealth literacy as the ability to seek, find, understand, and appraise health information from electronic sources and apply the knowledge gained to addressing or solving a health problem.⁴

eHealth literacy is an important issue for public, therefore health care providers need to have the appropriate skills to assess electronic health information. This will help them identifying issues and misinformation in the electronic resources and therefore improve health education to their target groups.⁵ Unfortunately, previous studies report that the level of eHealth literacy of health students was low and that they felt the need for improving their skills in eHealth literacy.⁵

Vietnam’s young population and low service costs give the country a higher internet penetration rate than

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most of its neighbors in Southeast Asia.⁶ According to a statistics, more than 50% of population accessed the internet at least once a month in 2016. Average daily time spent online among internet users in Vietnam was also high compared with neighbor countries.⁶ However, eHealth literacy is completely new concept in Vietnam. Scientific researches on this topic are still scarce. This study was conducted at University of Medicine and Pharmacy, Hue University with the aim of measuring eHealth literacy of medical students and examining factors influencing their skills. The findings of the study may provide basic information about eHealth literacy of future healthcare providers.

Material and Method

Site of Study: A descriptive cross sectional survey was conducted in Hue university of Medicine and Pharmacy, Hue University (HUMP). It is located in Hue city that is capital of Thua Thien Hue province, belonging to the central Vietnam. The University is responsible for training health professionals including both graduated and undergraduate levels who served people in all provinces in the central region and central highlands in the country.

Participants: Participants of the study were the fifth year medical students in the year 2017 because this cohort is provided nearly enough basis knowledge and skills of their professional. A sample size of 410 participants including 340 general medical students and 70 preventive medical students were randomly selected using proportional sampling method from a list of 1040 students who enrolled in those training programs. This list was provided from Department of undergraduate student management of the university. Data collection was implemented between July and December 2017.

Instrument: Data were collected using a self-report questionnaire. The questionnaire was structured into 3

parts: part 1 was demographic and socioeconomic profile of students, part 2 included questions about Internet access and electronic health information usage of the participants and part 3 was the eHealth Literacy Scale (eHEALS). eHEALS that was developed from eHEALS suggested by Norman and Skinner is a validated self-report tool to assess the comfort and skills for using electronic resources in health.⁷ The eHEALS is an 8-item scale with a 5-point Likert scale ranging from strongly agree to strongly disagree (scores between 1 and 5) was used. The minimum score is 8, maximum is 40, the higher scores correspond to the higher levels of eHealth literacy and vice versa. The reliability of the tool in Vietnamese language was evaluated using Cronbach's alpha by piloting among 50 students (overall Cronbach's alpha was 0.83).

Statistical Analysis: Data was analysed using SPSS software version 16.0. A multiple linear regression model was developed to identify the influence of individual characteristics, learning characteristics, internet accessibility and electronic health information usage on score of eHEALS. A p-value of less than 0.05 was considered statistically significant.

Findings:

Characteristics of Participants: Table 1 described that 80% of students aged 23 years old. More than half of them were male. Most of them lived in rented room. 12% of students whose households were classified as poor and near poor according to regulation of Government. The result of previous school year showed that 85.1% of students achieved good level. All students selected English as the foreign language. A few of them studied French as the second foreign language. The majority of students reported their English skills were not good (80.8%). There was 46.6% among them believed that their computer skill was good. Smartphone and laptops were popular facilities to access to internet.

Table 1. Characteristics of Students

Characteristics		N	%
Sex	Male	184	44.9
	Female	226	55.1
Age (years)	22	328	80.0
	23	73	17.8
	24	9	2.2

Characteristics		N	%
Place of residence	At home with family	34	8.3
	Student's hostel	15	3.7
	Rented room	352	85.8
	House of relatives	9	2.2
Economic condition of household	Near-poor, poor	48	11.7
	Normal	362	88.3
Learning result	Good	349	85.1
	Satisfaction	61	14.9
Foreign Language	English	410	100.0
	French	41	10.0
English level	Good	79	19.2
	Not good	331	80.8
Computer skill	Good	191	46.6
	Not good	219	53.4
Own a facility to access the internet	Yes	408	99.5
	No	2	0.5

eHealth Literacy: The purpose for students to use electronic health information is presented on the table 2. Electronic health information served mainly their learning tasks.

Table 2. Purpose of seeking electronic health information

Purpose	N	%
To look for a solution to health problem	298	72,7
To response to learning tasks	399	97,3
To improve knowledge about health and professional	336	82,0

The average total score on the eHEALS among participants was 27.03 (SD 3.54). Identifying the availability of health resources on the internet achieved the highest score of 3.72 (SD 0.78), followed by skill of finding helpful electronic health resources with mean score of 3.57 (SD 0.84). Skill to define quality of health information on the internet gained lowest score of 2.77 (SD 0.82). The skill of students to use confidently these resources in health decision making got also low score (3.22, SD 0.70) (Table 3)

Table 3. Self-reported eHEALS score of the medical students

eHEALS items	Mean	SD
I know what health resources are available on the Internet	3.72	0.78
I know where to find helpful health resources on the Internet	3.57	0.84
I know how to find helpful health resources on the Internet	3.43	0.84
I know how to use the Internet to answer my questions about health	3.53	0.73
I know how to use the health information I find on the Internet to help me	3.53	0.68
I have the skills I need to evaluate the health resources I find on the Internet	3.25	0.75
I can tell high quality health resources from low quality health resources on the Internet	2.77	0.82
I feel confident in using information from the Internet to make health decisions	3.22	0.70
Total	27.03	3.54

Factors related to eHealth literacy among medical students**Table 4. Factors related to eHEALS among medical students**

Predictors	B (SE)	p-Value	95% CI
Age	-0.01 (0.44)	0.988	-0.86 - 0.85
Sex (Female*)	1.3 (0.4)	0.001	0.55 - 2.10
Economic condition (No poor*)	-0.45 (0.58)	0.433	-1.58 - 0.68
Training program (Preventive medicine *)	1.3 (0.50)	0.013	0.27 - 2.25
Learning classification (Not good *)	0.96 (0.58)	0.096	-0.17 - 2.09
The number of foreign languages studied (one foreign language *)	0.59 (0.46)	0.204	-0.32 - 1.50
English level (Not good *)	0.72 (0.50)	0.148	-0.26 - 1.71
Computer skill (Not good *)	0.89 (0.41)	0.031	0.08 - 1.69
Own a facility to access the internet (Yes *)	- 3.19 (2.65)	0.230	- 8.39 - 2.02
Purpose of seeking electronic health information To look for a solution to health problem (No*)	- 0.04 (0.41)	0.93	-0.85 - 0.78
To response to learning requests (No*)	0.88 (1.13)	0.44	- 1.34 - 3.10
To improve knowledge about health and professional (No*)	1.87 (0.48)	< 0.001	0.93 - 2.80
Constant	24.85 (10.09)	0.014	5.82 - 44.68

* level 0 of dummy variables

Table 4 revealed results of the multiple linear regression analysis. Sex of students, their training program, computer skill and purpose to access health resources on the internet influenced their eHEALS. Mean score of eHEALS in male students is higher 1.3 points than that of females ($p = 0.001$). Similarly, general medical students showed better level of eHealth literacy than preventive medical students ($p = 0.013$). The students who were confident of their computer skill gained mean score of 11% higher than others ($p = 0.031$). The students who accessed electronic health information with the aim at improving their knowledge about health and professional achieved 1.87 points higher than their counterparts ($p < 0.001$). The study did not find a significant association between eHEALS score with other characteristics of the participants.

Discussion

Mean score for eHEALS of medical students in HUMP was 27.03 (SD= 3.54) which are lower than those in previous studies on health students.^{8,9} In Iran, a study revealed that the mean score for eHEALS of the medicine and health science university students was 28.21 (SD=6.95).⁵ Park and Lee reported that mean eHEALS score of nursing students in Korea in 2014 was 27.06 (SD= 4.2).⁸ The mean eHEALS score of

541 nursing students in Jordan was 28.96 (SD= 4.64).⁹ Accessibility to internet and availability of online health information sources are considered as contributing factors to eHealth literacy.^{5,10} According to statistics in 2017, the internet penetration rate among population in Vietnam was 53% while this rate was 70% and 73% in Iran and Jordan, respectively.^{11,12} In addition, a report of Ministry of Health (2010) revealed that dissemination of health information via the webs were still limited and sharing these sources among electronic libraries of health science universities in Vietnam had restricted because of lack of interconnection system.¹³

Among eHEALS items, skills of participants to differentiate between good and poor quality of health resources was evaluated at the lowest level. This finding was supported by many previous studies.^{5,8,9} Authors indicated that health science students could access health related website but they could not identify a trustable information sources.⁵ Medical students will be future health care providers who are considered as a reliable health information source. This skill will help them identifying misinformation in the social media, therefore provide better advise to their target groups.⁵ Besides, this will meet demand of clients in utilizing eHealth to promote and sustain their health in context of the digital era. Authors suggested that eHealth literacy skills should

be incorporate into the curriculum of health science students in general and medical students in special.^{8,9}

Multiple linear regression analysis showed that eHEALS of male students was better than those of females. Our result is similar to that of Dasti et al (2017).⁵ In some communities, the young male are more convenient to access internet compared to the female. They had opportunity to spend more time on the internet. Level of access to the internet was suggested to be one of factors improving eHealth literacy.¹⁰ However the relationship between gender and eHealth literacy was found inconsistently among former studies.^{14,15,16} The difference in culture of study settings, participants of studies might result in these various findings.

Training program was other factor that influenced eHealth literacy in the study. General medical students had higher eHEALS score than preventive medical students. Compare to training program of preventive medicine, the one of general medicine program is larger. It requires more professional knowledge and skills. More utilization of eHealth resources to respond learning task and improve professional knowledge could result in higher level of eHealth literacy among general medical students.

Levels of proficiency in web usage have direct impact on eHealth literacy because they include capacity to effectively search, navigate using links and scroll in web page. These are essential to develop computer literacy that is one of six components of eHealth literacy.^{4,10} Understandingly, good computer skills of participants had positively impact on eHealth literacy.

The current study revealed potential limitations. First, a self-report tool measuring eHealth literacy was adapted for medical students in Vietnamese language. Although pilot research showed that the scale was good internal consistency with Cronbach alpha = 0.83. It is necessary to validate translated tool in the future study in Vietnam. Second, the study included students in the fifth year of two training programs, they are not representative for all medical students in HUMP. However this is the first study measuring eHealth literacy among medical students in the Vietnam, the findings can provide preliminary evidences to enhance eHealth literacy to meet the needs of health care in the new digital era.

Conclusions

This study indicated that eHealth literacy of medical

students in HUMP is still limited. It is suggested that eHealth literacy concepts should be introduced to medical students as a topic of subject “health education and communication”. Educators should encourage relevant teaching strategies that promote the interest and skills of medical students to locate and evaluate health resources available on the internet.

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Ethics Statement: Approval for the study proposal was obtained from HUMP. In addition, approval for implementing the study at the classes was obtained from Department of Student Management of the University. The self-report questionnaire was given to students with their permission after they were introduced adequate information about the study in a consent form. Ethical principles of research on human subjects such as autonomy, beneficence, and justice were introduced in this form. The vulnerable populations did not present in our study.

References

- Collins SA, Currie LM, Bakken S, Vawdrey DK, Stone PW. Health Literacy Screening Instruments for eHealth Applications: A Systematic Review. *J Biomed Inform.* 2012; 45(3): 598–607.
- Kathrynz Z. Generations 2010. Pew Research Center: Internet & Technology. <https://www.pewinternet.org/2010/12/16/generations-2010/>; 16 Dec 2010 [accessed 2018 Dec 4].
- Susannah F. Health Information is a Popular Pursuit Online. Pew Research Center: Internet & Technology. <https://www.pewinternet.org/2011/02/01/health-information-is-a-popular-pursuit-online/>; 2011 [accessed 2018 Jan 29].
- Norman CD, Skinner HA. eHealth Literacy: Essential Skills for Consumer Health in a Networked World. *J Med Internet Res.* 2006; 8(2): e9. doi: 10.2196/jmir.8.2.e9
- Dashti S, Peyman N, Tajfard M, Esmaeeli H. E-Health literacy of medical and health sciences university students in Mashhad, Iran in 2016: a pilot study. *Electron Physician.* 2017; 9(3): 3966–3973.
- Rahul C. Vietnam Online: Digital Usage and

- Behavior, 2015-2020. eMarketer. In Vietnamese. <https://www.slideshare.net/VNguynThyDung/emarketer-vietnam-online-digital-usage-and-behavior-20152020>; 2016 [accessed 2018 Sept 5].
7. Norman CD, Skinner HA. eHEALS: The eHealth Literacy Scale. *J Med Internet Res.* 2006; 8(4): e27. doi: 10.2196/jmir.8.4.e27
 8. Park H, Lee E. Self-reported eHealth literacy among undergraduate nursing students in South Korea: a pilot study. *Nurse Educ Today.* 2015; 35(2): 408-413. doi: 10.1016/j.nedt.2014.10.022
 9. Tubaishat A, Habiballah L. eHealth literacy among undergraduate nursing students. *Nurse Educ Today.* 2016; 42: 47-52. doi: 10.1016/j.nedt.2016.04.003
 10. Werts N, Rogers LH. Barriers To Achieving E-Health Literacy. *Am J Health Sci.* 2013; 4(3): 115–119.
 11. Electronic Health Administration, Ministry of Health of Vietnam. Preliminary research on issues of “digital citizen”. In Vietnamese. <http://ictmoh.gov.vn/Index.aspx?action=News&newsId=44151>; 2017 [accessed 4 Dec 2018].
 12. Simon K. Digital Yearbook: Digital Data for Every Country in the World. We are social. <https://wearesocial.com/special-reports/digital-in-2017-global-overview>; 24 Jan 2017 [accessed 2018 Dec 4].
 13. Joint Annual Health Review (JAHR). E-health Report. In Vietnamese <http://jahr.org.vn/downloads/Nghien%20cuu/Thong%20tin%20y%20te/Ehealth.doc?phpMyAdmin=5>; 2010 [accessed 2018 Dec 12]
 14. Civilcharran S, Hughes M, Maharaj M. Uncovering Web search tactics in South African higher education. *SA J Inf Manag.* 2015; 17.
 15. Fung IC-H, Hao Y, Cai J, Ying Y, Schaible BJ, Yu CM, Tse ZTH, Fu KW. Chinese Social Media Reaction to Information about 42 Notifiable Infectious Diseases. *PLoS ONE.* 2015; 10(5): e0126092. doi:10.1371/journal.pone.0126092
 16. Tomas CC, Queiros PJP, Ferreira TJR. Analysis of the psychometric properties of the portuguese version of an eHealth literacy assessment tool. *Rev. Enf. Ref.* 2014; IV(2): 19-28. doi:10.12707/RIV14004

Phenomenological Study: Nurses Experiences in Collaboration with Physician and Witch-doctors in Initial Management of Emergency Trauma Patient in Puskesmas of East Sumba Regency, East Nusa Tenggara, Indonesia

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Abstract

Introduction: Communities in the area of East Sumba in meeting its health is influenced by cultural traditions and handling of traditional treatment. The provision of health services at the community health center (*Puskesmas*) is often referred to health centers requires collaboration among health professionals. Medical collaboration process influenced by the culture and traditions of the people so do also the collaboration process traditionally by witch-doctors in the initial treatment of trauma patients in the *Puskesmas*. The aim of research to explore the nurses experience collaborate with doctors and witch-doctors in the initial handling emergency trauma patients at the *Puskesmas* East Sumba, East Nusa Tenggara.

Method: The research method of qualitative research design using interpretive phenomenological approach. Participants totaled 7 nurse health center, taken by purposive sampling. Collecting data through semi-structured interviews with in-depth interviews and open-ended question. Data were analyzed using phenomenology interpretative analysis (IPA).

Result: The results of this study obtained four themes, namely theme 1: Responsible for performing their duties in collaboration, theme 2: Pros Cons collaborative process with witch-doctors, theme 3: Receiving treatment witch-doctor but under close supervision, and theme 4: Feeling strange but true to the success of the witch-doctor. The process of collaboration between health professionals by nurses and doctors as well as traditional collaboration with witch-doctors in the early treatment of trauma is done in the *Puskesmas*. Traditional treatment options by witch-doctor is a tradition that is believed to be public, proven and successful cure the patient. Nurses as health workers in *Puskesmas* receive the tradition but remains under close supervision by nurse.

Conclusion: Initial management of trauma patients is done in the *Puskesmas* in the process of collaboration between nurses, doctors and witch-doctors to save the patient. Witch-doctor collaboration process in the initial treatment of trauma can not be avoided but successful and remain in the supervision of health workers in *Puskesmas*. Important local cultural considerations in nursing care based on the culture of early trauma treatment in the *Puskesmas*.

Keywords: Nurses experiences, Collaboration with physician, Collaboration with witch-doctors, Initial management, emergency trauma.

Introduction

According to the World Health Organization (WHO), trauma has a very high prevalence of more than 9 people die every minute due to trauma and violence. Trauma caused more than 1 million deaths each year

and about 20 million to 50 million people suffered severe injuries that trauma is the leading cause of death worldwide⁽¹⁾. In developing countries, significantly more than 90% of accidents occur as a result of a motor vehicle, and projected mortality due to these accidents

increased by 80% in countries of low and middle income⁽¹⁾. Trauma treatment in East Sumba, East Nusa Tenggara, Indonesia, treated myself as much as 78.3%, traditionally treated as much as 19.8% and treated by medical personnel as much as 19.3%⁽²⁾.

In Indonesia, there is community health centers called *Puskesmas* as a primary care role to give early treatment in case of such as trauma cases⁽³⁾. Nurses in community health centers (*Puskesmas*) in dealing with trauma patients requires collaboration among professionals in the handling of such collaboration with physicians and other health workers in health centers⁽³⁾. Initial management of trauma patients in the *Puskesmas* East Sumba influenced by the habits of the local community in deciding the treatment of trauma that would be done medically, traditional and treated themselves. Nursing staff are also required to provide professional nursing care based on cultural characteristics that already exists in the local community⁽⁴⁾.

Basic theory of nursing that can be used according to the customs and culture of the local community based Transcultural nursing theory by Madeleine M. Leininger. Nurses provide nursing care to individuals, groups, communities within the context of diverse health decisions and actions have to be traditional treatments, the practice of professionals nursing care or medical-care. It could affect the preservation, negotiation and restructuring of cultural care to improve the health and well-being of the client⁽⁵⁾.

Interviews with nurses in *Puskesmas* conducted during preliminary studies in several *Puskesmas* East Sumba, obtained the data that nurses conduct collaborative medical treatment and also traditionally like the handling of closed or open fractures, sprains and dislocations. Massage witch-doctor allow health workers perform simple massage, but do not allow to touch the wound was cleaned.

This is supported by statements of other participants who have ever come across cases of trauma patients, underwent the process of initial treatment in the *Puskesmas* and will be referred immediately but relatives of patients choose traditional treatments. In addition, the patient's family chose to call witch-doctor to treat patients. Furthermore, the families asked the patient is discharged to receive more traditional treatment at home.

Phenomenological study approach to explore more deeply related to the real experience of facing the nursing

profession in the health center in the first treatment of trauma patients. Through this approach, the nursing perspective, uniqueness and justification of nursing disciplines ever experienced nurses will not be lost but can be explored more in depth⁽⁶⁾. Therefore, researchers are interested in more depth about the experience of the nurse collaboration with doctors and witch-doctors in the initial treatment of trauma patients in the *Puskesmas*.

Method

This study was a qualitative research approach interpretive phenomenology⁽⁷⁾. The number of respondents were taken by purposive sampling is seven nurses *Puskesmas* in East Sumba, East Nusa Tenggara. Method of data collection using semi-structured interviews with in-depth interview to the participants and used open-ended question. Analysis of the data is interpretative phenomenology analysis (IPA) to the stages of reading and re-reading, initial noting, developing emergent themes, searching for connections across emergent themes, moving the next cases, looking for patterns across cases.

Findings and Discussion

The result of this research is a theme that is generated from the data analysis process research results that there are 4 themes as a result of this research and has been adapted to the purpose of research on the process of collaboration in the initial treatment of trauma patients. The findings of this study four themes along with the discussion are as follows:

Theme 1: Responsible for performing their duties in collaboration: This theme is a process of collaboration between health professionals and an important component in improving the quality of health services in *Puskesmas* as primary basic level that can be reached by the public. This theme is there based on the statements of participants who were interviewed are:

R3: "...the process of teamwork in the ER, we conduct management ... the emergency accident that should be referred...handling pas came we clean the wound, treat wounds, post infusion, the observation first, lest he vomit...check out the state...patients with suspected severe head injury, we observed the first few minutes...usually we will refer the patient to hospital..."

R7: "...an accident..that hit these two girls...we've been working in a team to give early treatment..."

R5: "...from the beginning we have collaboration with doctors...see the general situation..."

R5: "...patients with accident...I help the doctor...sew all her veins...continue straight closed...while it also directly refer..."

R2: "...the decision of the doctor, if the doctor does not exist, remains to be consul to doctor while we handle...doctor who instructed the therapy until the decision to do the referral process..."

The process of collaboration between nurses and physicians in the initial management of trauma in the form of teamwork in the ER. This is done in accordance with the responsibilities of each task and sometimes a nurse helps the doctor or a physician assistant in the treatment of trauma patients such as suturing. Collaboration is woven well and done in the form of teamwork health outposts can meet the needs of the initial treatment of trauma.

Collaboration among health professionals is also necessary to meet the needs of a range of public health services in underdeveloped areas.⁽⁸⁾ It collaboration among healthcare professionals in health center practice environment at the primary level as the health center must be run in accordance with the role of each profession so complementary in running nursing practice, medical and traditional. This can be done in accordance with the wishes of the patient and family, or the decision to accept the process of handling.⁽⁹⁾ Previous studies also suggested that the collaborative model implemented at all levels of government to empower the community in accordance with the performance indicators of each stakeholders to improve public health in terms of early detection, prevention and control of non-communicable diseases.⁽¹⁰⁾

Theme 2: Pro Cons collaborative process with the witch-doctor: This theme is based on the statement of the participants in the interviews conducted as follows:

R1: "...we give the understanding...this can be conducted...but we are afraid of there is infection if only massaged..."

R2: "...if the kinds of cons we're afraid if they take home medicine, that we prohibited, we always said should not take the medicine at the same village and medical drugs...we have no control..."

R3: "...not all of our nurses and doctors who allowed

so...to deal with witch-doctor...not all cases..."

R2: "...it was hard to talk, knowing already the Sumba right cannot be separated from the village medicine...depending on customs and their beliefs..."

R5: "...we want to oppose but difficult ...if myself received and not received has it...the family wants to sort...responsibility... especially if in the village with the conditions here, it is tradition..."

R5: "...people believe about it...there are herbs that can be affixed and the evidence they recovered ...a trauma patient such as fracture...of the family...ask a masseur or bring a masseur here...it is tradition..."

Collaboration with the witch-doctor performed in the *Puskesmas* to assist in the initial handling trauma patients even though there are pros and cons to it. Nurses have a sense of worry about the complications that may occur as a result of handling witch-doctor on infection and treatment. There is a ban for not taking the drugs simultaneously medical and traditional, but nurses cannot go against the tradition because it was believed by the local communities related to the handling of the witch-doctor. The patient's family or society already believe and trust in the proven tradition of handling quack cure. Tradition witch-doctor handling cannot be challenged by the nurse health center, otherwise the nurse resigned to the tradition of handling witch-doctors believed and proved to cure the patient.

Partnership collaboration culture-based health workers can affect the improvement of health outcomes and involvement of community participation in health services⁽¹¹⁾, Collaboration traditional witch-doctor tradition of collaboration with real success in handling, restoring and maintaining the health of patients adjusted well to the confidence and trust of the public and health professionals about the culture⁽⁵⁾.

Theme 3: Receive witch-doctor handling practices but under close supervision: This theme is in accordance with the statement of the participants are:

R4: "...the only way there should be a collaboration... could not only his own actions...must ask the help of other people...who have other skills...without going through formal education...bring a masseur that helped... to save people...a decision we have to take..."

R4: "...so masseur already we call and it was believable..."

R7: "...there was...family who asked...sometimes closed fracture if any accident they say should be massage...it's tradition...we respect that decision..."

R2: "...sometimes we work together...if only normal trauma, the patient's family asked the witch-doctor to come at the health center to massage...to be in front of the nurse...should not without supervision...calling the witch-doctor or sprayed so...we also conduct collaboration... medicine medical still be served, but the massage with drugs remaining..."

R7: "...there is supervision and we do not let that... his fracture was irregular...it is not allowed..."

The nurse stated that there is a process of collaboration with herbalists traditional massage in cases of trauma such as a fracture or dislocation in the *Puskesmas*. Nurses receive treatment collaboration witch-doctor, knowing that cannot be alone in taking action early treatment. Nurses also need the help of others even though the person is not through a formal health education but is believed to help provide early treatment. Decisions collaboration with the witch-doctor is the only way that can be taken to help nurses initial handling for the sake of patient safety. Nurses accept and respect the decision of the family choose quack but the handling of supervision of nurses in *Puskesmas*. This decision is influenced by family who is used to use traditional treatment.

Collaboration with the witch-doctor has become a habit the local community and is considered a tradition that affect the behavior of people who believe the witch-doctor in cases of trauma such as fractures and dislocations. Behavior in finding where the handling of public health issues is also influenced by the concept of healthy and sick trusted by the local community such as culture and tradition to follow a traditional treatment that affects the concept of beliefs, attitudes and behaviors of people who agreed to elect to undergo the process of handling by herbalists⁽¹²⁾.

Theme 4: Feel strange but true to the success of the witch-doctor: This theme is in accordance with the statement of the participants are:

R4: "...we are at odds...with our medical science has...a collaboration that we did...even if one track...but what can we do...yes it is...like a strange thing is not real but it is real...eight trauma patients was massaged and it worked...from the initially hesitant...but all are safe, and

also collaboration is also established with good..."

Nurses feel strange for the success of the witch-doctor in dealing with trauma patients. The nurse stated that witch-doctors have another without going through formal education related to the handling of cases of trauma, but strangely or witch-doctor miraculously managed to handle trauma patients. Handling traditionally by witch-doctors massage has become a local tradition in dealing with cases of trauma such as a fracture or dislocation. The success led to nurse feels strange witch-doctor as believers do not believe it but the real observed that witch-doctors successfully handle trauma patients.

Successful handling of witch-doctor profitable and has become a local culture can be preserved, accommodation and re-negotiated or modified in accordance with the Transcultural nursing theory by Madelenie M. Leininger, known as culture-based nursing care⁽⁵⁾. Improvement of health and health behaviors can be done with the involvement of people who are already receiving and trusting culture related to the tradition of handling traditional so it can be developed as an innovative approach to patient care in underdeveloped areas where people still believe in the tradition that is handling or traditional treatment is proven to provide relief for patients⁽¹¹⁾.

Conclusions

Initial management of trauma patients is done in the *Puskesmas* requires a collaborative process, whether it is a medical collaboration between nurses and doctors or traditional collaboration involving witch-doctor massage. This was done with the aim of saving the lives of patients. The process of initial treatment of trauma involving collaboration with herbalists massage becomes a matter that cannot be avoided, but still in control of health workers in *Puskesmas*. This is due to the strong culture of the people who still believe in the traditional treatment by a witch-doctor, so that their culture be important for consideration by nurses in *Puskesmas* to provide nursing care based on the local culture in the initial treatment of trauma.

Conflict of Interest: There is no conflict of interest in this study.

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Ethical Clearance: This study was approved by ethics committee ethical clearance from the Medical Faculty of Nusa Cendana Kupang, East Nusa Tenggara Indonesia with numbers: 04/UN15.16/KEPK/2019.

References

1. ATLS. Advanced trauma life support course student manual. Chicago: American College of Surgeons; 2018. Available from: <https://www.passeidireto.com/arquivo/53236360/advanced-trauma-life-support-atls-student-course-manual-2018/2>,
2. Riskesdas. Basic health research Temggara province of East Nusa. In: RI KK, editor. The first edition ed. Jakarta: Institute for Publishing and Development Agency; 2013. p. 292.
3. Ministry of Health. Infodatin data center and information, Health of Ministry of the RI Jakarta Selatan 2017.
4. Woo BFY, Lee JXY, Tam WWS. The impact of the advanced practice nursing role on quality of care, health central outcomes, patient satisfaction, and cost in the emergency and critical care settings: A systematic review. *Human Resources for Health*. 2017; 15 (63): 1-22.
5. Alligood MR. *Nursing theorists and their work* 8ed. Singapore: Elsevier; 2017.
6. Alase A. The interpretative phenomenological analysis (IPA): A guide to a good qualitative research approach. *International Journal of Education and Literacy Studies*. 2017; 5 (2): 9-19.
7. Moleong LJ. *Qualitative research method*. Revised ed. Bandung: PT Remaja Rosdakarya; 2014.
8. Engel J, Prentice D. The ethics of interprofesional collaboration. *Nursing Ethics*. 2013; 20 (4): 426-35.
9. Schadewaldt V, McInnes E, Hiller JE, Gardner A. Experiences of nurse practitioners and medical practitioners working in collaborative practice in primary healthcare models in Australia - a multiple case study using mixed method. *BMC Family Practice*. 2016; 17 (99): 1-16.
10. Yandrizal., Machmud R, Noer M, Hardisman., Afrizal., Lipoeto NI, et al. Stakeholder collaboration to empower integrated model of health education centers for non-communicable diseases: A study in Bengkulu. *Indian Journal of Public Health Research & Development*. 2018; 9 (1): 133-8.
11. Cyril S, Smith BJ, Inesedy AP, Renzaho AMN. Exploring the role of community engagement in improving the health of disadvantaged Populations: A systematic review. *Global Health Action*. 2015; 8: 1-12.
12. Graaf PD, Pavlic DR, Zelko E, Vintges M, Willems S, HANSSENS L. Primary care for Roma in Europe: Position paper of the European forum for primary care. *National Institute of Public Health*. 2016; 55 (3): 218-24.

Determinant Factors of Alcohol Consumption by Adolescents

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Abstract

Objectives: The harmful use of alcohol was a causal factor in more than 200 diseases and injury conditions. The percentage of alcohol consumption at age 15-19 years in Indonesian were male (3.4%) and female (1.5%). Alcohol consumption is associated with a risk of developing health problems, such as mental and behavior disorder which includes alcohol dependence and major non-communicable disease.

Method: This was an analytic observational research with Cross Sectional design. The population were all students of Senior High School or the equal, in Yogyakarta City. Sample size in the research are 380 students. Technic sampling is used Multi-stage random sampling. The Research used questionnaire as the instrument. To analyze the data is used univariate analysis and bivariate analysis (chi-square).

Results: The results show that 40.1% of adolescent in Yogyakarta City consume or once consumed alcohol, while 26.6% were alcohol dependence/harmful alcohol dependence. Bivariate analysis results in the following. Knowledge ($p=0.000$; $RP=0.541$); attitude ($p=0.000$; $RP=2.510$); self-confidence ($p=0.001$; $RP=1.566$); family role ($p=0.016$; $RP=1.396$); teacher role ($p=0.000$; $RP=1.960$); peer role ($p=0.000$; $RP=2.953$); information resources ($p=0.436$; $RP=1.103$).

Conclusions: There was relationship among knowledge, attitude, self-confidence, family role, teacher role, and peer role, and alcohol consumption by adolescent. There is no correlation between information sources and alcohol consumption by adolescent.

Keywords: Knowledge, attitude, self confidence, family, teacher's role, peers, information sources, alcohol consumption, adolescent.

Introduction

Excessive use of alcohol is the causal factor of more than 200 diseases and injuries. 5.1% of them are caused by alcohol consumption. In addition, it causes disability and fatality. Among the age group of 20-39 years old, 25% of total fatality is caused by alcoholism. In 2012, 3.3 million of death is caused by alcoholism, or 5.9% of the total mortality number.¹ Alcohol consumption in South East Asia of the age group above 15 years old,

per capita, is 3.4 liters of pure alcohol. It is projected to increase in 5-10 years along with the increasing number of adolescents. Thus, it increases the potential consumers. In 2010, the proportion of alcohol consumption in Southeast Asia, of the age group of 15-19, showed 5.9% of ex-drinker and 8.2% drinkers.²

In 2010, the alcohol consumption per capita in Indonesia showed that male consumed 1.1 liter of alcohol, while female took 0.1 liter.³ The percentage of alcohol consumption in the country for the age group of 15-19 years old are 3.4% and 1.5% for male and female, respectively. The number is small but it is a clear evidence that Indonesian youngsters consume alcohol.⁴

Alcohol consumption may influence individuals' behavior. Alcohol has encouraged the youth to commit crime, reaching 2%.⁵ Juvenile delinquency in Indonesia, particularly in Yogyakarta Special Region Province,

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is categorized as severe by the evidence of several incidence, such as school brawling, getting drunk, unwed pregnancy, and so on. Being rebellious is not an only cause of misbehavior. Instead, child rearing or environment may be another factor.⁶ This research aims to know the relation among predisposing, reinforcing, and enabling factor and alcohol consumption by adolescents in Yogyakarta.

Materials and Method

This study belongs to observational analytic research with cross sectional design. The research is conducted in all senior high schools, and the equal, in Yogyakarta City, of which all the students become the population, as many as 36.360 students. The samples were taken using Multi-stage random sampling. Sample size among this research is 380 adolescents. The instruments include questionnaires to measure the variables of knowledge, attitude, confidence, family roles, teachers' role, peer roles, and information sources. The research used the instrument adopted from The Alcohol Use Disorders

Identification Test published by WHO. The analysis data employed Chi square.

Results

They have low level of knowledge and consume alcohol (27.8%). 129 adolescent (51.4%) who consume alcohol have high level of knowledge. There was relation between knowledge and consume alcohol among adolescent ($p=0.000$; $RP=0.541$; $CI95\%=0.43-0.69$). There was relationship between attitude and alcohol consumption ($p=0.000$; $RP=2.510$; $CI 95\%= 1.972-3.196$). There was relationship between self-confidence and alcohol consumption ($p=0.001$; $RP=1.566$; $CI95\%=1.25-1.96$). There was relation between family roles and alcohol consumption ($p=0.016$; $RP=1.396$; $CI95\%=1.098-1.775$). There was relation between teachers' roles and alcohol consumption ($p=0.000$; $RP=1.960$; $CI95\%= 1.604-2.397$). There was relationship between peers' roles and alcohol consumption ($p=0.000$; $RP=2.953$; $CI95\%=2.362-3.692$). There was no relation between information resources and alcohol consumption ($p=0.436$; $RP=1.103$; $CI95\%= 0.885-1.374$).

Table 1: Determinant Factors of Alcohol Consumption by Adolescents in Yogyakarta City, Indonesia

Variable	Alcohol Consumption				Number		RP	CI 95%	p
	Yes		No						
	n	%	n	%	n	%			
Knowledge									
Low	64	27,8	166	72,2	230	100	0,541	0,43-0,69	0,000
High	129	51,4	122	48,6	251	100			
Attitude									
Negative	63	23,9	201	76,1	264	100	2,510	1,97-3,19	0,000
Positive	130	59,9	87	40,1	217	100			
Self Confidence									
Low self-confidence	47	57,3	35	42,7	82	100	1,566	1,25-1,97	0,001
Confident	146	36,6	253	63,4	399	100			
Family Role									
Less participating	44	52,4	40	47,6	84	100	1,396	1,09-1,78	0,016
Participating	149	37,5	248	62,5	397	100			
Teachers' Role									
Less Participating	72	64,3	40	35,7	112	100	1,960	1,60-2,39	0,000
Participating	121	32,8	248	67,2	369	100			
Peers									
Participating	120	69,8	52	30,2	172	100	2,953	2,36-3,69	0,000
Less participating	73	23,6	236	76,4	309	100			
Information Sources									
Low	107	42	148	58	255	100	1,103	0,89-1,37	0,436
High	46	38,1	140	61,9	226	100			

Discussion

The Correlation between Knowledge and Alcohol

Consumption: Adolescents who have low knowledge as a protective factor not to consume alcohol. This situation is because teenagers who do not consume alcohol have no knowledge of the type of alcohol and the aroma of alcohol. While someone who consumes alcohol at least more often see, have physical contact with, know, and obtain the information about alcohol compared to those who do not. They get the information through their senses, particularly sight and hearing.⁷ Individual who have learned the effects of drinking will think twice to consume it. Indeed, it is more likely that they will avoid it. Those who take good care of their life will not harm themselves.⁸ Previous research showed there is a relation between poor knowledge about the effects of alcohol and the drinking behavior of adolescent where the higher is the score of poor knowledge, the higher is the number of alcohol drinking by adolescence.⁹

The Correlation between Attitude and Alcohol

Consumption: Attitude influences alcohol consumption by adolescents in Yogyakarta. Attitude is the second level of behavior before an individual takes an action. Attitude is a readiness to act, but it is not an implementation of a motive. It is a response that involves opinion and emotion.⁷ Previous research shows there is a relation between attitude and alcohol consumption by adolescent. The occurrence of those with negative attitude is 14.88 times compared to adolescents who have positive attitude.¹⁰ Another research show there no relation between attitude and the prevention of alcohol consumption.¹¹

Attitude is part of the process of changing behavior. It means that attitude is not yet operate in an action or behavior. It is not always manifested in a real action. An action can be illustrated by attitude of like-dislike, or agree-disagree. However, the attitude can influence particular behavior, such as preventing alcohol consumption. An individual has the opinion and tendency to avoid alcohol consumption, but pressure, lack of confidence, or other factors may cause the attitude cannot manifest in the real action.

The Correlation between Self-confidence and alcohol consumption:

Confidence influences an individual's attitude and behavior. An individual's belief in his capability or confidence will lead him to do what he wants. Meanwhile, those who lack of confidence tend to doubt his action. Indeed, they tend to avoid the action.

Self-confidence is the key factor in making an individual feel more optimistic and try to adapt the environment. Nevertheless, self-confidence for conducting negative may harm others. It is supported by the idea that self-confidence is a positive assessment on a self, which raises the individual's motivation to respect himself.¹²

Frequently, adolescents drink alcohol to gain self-confidence and eliminate shyness, stress, and depression. Alcohol belongs to anti-depressant of central nerve system that presses the control shyness and avoidance, as well as influencing the conscience.¹³ Thus, drinking individuals cannot control their behavior and conscience, allowing them to gain more confidence. If this continues, the individuals will be addicted and they will experience a kind of mental disorder, leading to other health problems.

Other research that is in line with the result concludes that self-confidence contributes to juvenile delinquency, but it has negative correlation value. It means that the higher the self-confidence, the less the occurrence of juvenile delinquency. Alcohol consumption belongs to one of the mentioned delinquency.¹⁴

The relation between family and alcohol

consumption: In families less participating, the number of alcohol consumption is higher compared to those whose family have greater roles. The family's participation in preventing youth from drinking alcohol is not enough to encourage the youth to leave it. Family role is not the only factor in this case. Theoretically, parents' role will root within an individual to interact with himself or with others.⁸ Good interaction will help to shape adolescence's behavior.

The research is supported by another research conducted to underage inmates, ranged from 15 to 18 years old. It shows that children's attachment to their father, particularly when it decreases, lead to improve the numbers of juvenile delinquency.¹⁵ The most influential factor of adolescent alcohol consumption is their parents.¹⁶ The quality of parents-children relationship reflects the level of warmth, security, confidence, positive affective, and response.¹⁷

The Correlation between Teacher's role and alcohol consumption:

In this study, it is known that teacher has not been fully capable of encouraging adolescents not to drink alcohol, apart from other influencing factors, such as environment and peers. The previous research shows that 80.6% of students perform

unhealthy behavior because their teachers do not concern much about them. The relation is significant.¹⁸ Children and adolescents tend to imitate the adults. In this case, teachers are the adults they see at school. It is expected that the policies, regulation, and sanctions arranged by the teachers help the adolescents to behave better.

Teachers can strengthen students in performing good deeds. This strengthening factor is concomitant factor following the behavior, such as giving sanction, incentive, or punishment upon the behavior. Teachers also participate in maintaining or eliminating the behavior.¹⁹ Teachers have the power to influence the values and characters of the students in three ways: be an effective caregiver by loving and respecting the students; be a good model inside and outside the classroom; and be an ethical counselor by providing moral teaching.²⁰

The Correlation between Peers and alcohol consumption: The role of friends becomes a reinforcing influence for adolescents to consume alcohol. Previous research show that one of the reasons causing an individual to drink is the environment.²¹ Youth who spend their time with peers who drink alcohol are likely to develop drinking habit. Other research supports the results, showing that there is positive and significant relation between peers' attachment and juvenile delinquency. The finding indicates that attachment to peers is the risk factor that causes juvenile delinquency, one of them is alcohol consumption.¹⁵

Adolescents have more time to spend with their peers rather than to their family. Indeed, it is common that peers come first before the parents, for individuals tend to easily actualize themselves and live their own choices without their parents.⁸ Mostly, drinking alcohol becomes the main social activities of male adolescents. It also becomes their social symbol.²²

Peers are influential social agent for individuals. These individuals are willing to do anything to join their peers in a group, such as smoking, drinking, or any other activities.²³ Previous research shows significant relation between peers giving negative influence and alcohol consumption by adolescents. It reached OR=9.64, meaning that the occurrence of alcohol consumption is 9.64 times bigger in adolescents receiving negative influence than those receiving positive influence.¹⁰

The relationship between Information Sources and Alcohol Consumption: Information sources do not relationship with alcohol consumption by adolescents

in Yogyakarta City. A study shows that the respondents exposed by alcohol advertisement indicate an increase in their willingness to drink compared to those who are exposed to non-alcoholic advertisement. Warning advertisement of the effects of alcohol indirectly contributes to decrease alcohol consumption.²⁴ Mass media becomes strong influence in shaping public opinion and behavior. Other study found that mass media causes assertive behavior and the tendency of juvenile delinquency.²⁵ Youth behavior that leads to alcohol consumption can be influenced by advertisement. It results in significant relation between cigarette advertisement and smoking behavior by students of junior high schools.²⁶

However, the present study shows that information sources or mass media does not give negative effect. The problem is not on the type or the number of mass media, but from the characteristics (positive or negative) and the attitude of the receiver of information. Conversely, information sources can give positive impact.²⁷ If the information provided by the mass media is positive, it brings good knowledge which leads to good attitude reflected in the real life. The higher the access to positive information sources, the more knowledge obtained and the more positive the behavior.

Conclusion

There was relationship between knowledge, attitudes, self-confidence, family role, teacher's role, and peer role with alcohol consumption in adolescents. There was no relationship between information sources and alcohol consumption in adolescents in the city of Yogyakarta. Provide understanding to adolescents about healthy living behaviors such as avoiding alcohol consumption and involving parents, teachers and friends in supporting teenagers to avoid alcohol consumption.

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References

1. World Health Organization. Fact Sheet Alcohol [Internet]. World Health Organization. 2015 [cited 2017 Jan 20]. Available from: <http://www.who.int/mediacentre/factsheets/fs349/en/>
2. World Health Organization. Global Status Report on Alcohol and Health 2014 [Internet]. World Health Organization. Geneva: World Health Organization; 2014 [cited 2017 Jan 23]. p. 1–376. Available from: http://www.who.int/iris/bitstream/10665/112736/1/9789240692763_eng.pdf
3. World Health Organization. Cancer Country Profile Indonesia [Internet]. World Health Organization. 2014 [cited 2017 Feb 8]. p. 1–2. Available from: http://www.who.int/cancer/country-profiles/idn_en.pdf?ua=1.
4. Global Information System on Alcohol and Health. Youth and alcohol [Internet]. Global Information System on Alcohol and Health. 2014 [cited 2017 Feb 9]. Available from: <http://apps.who.int/gho/data/node.main.A1206?lang=en>
5. Badan Pusat Statistik. Profil Kriminalitas Remaja Tahun 2010 [Internet]. Badan Pusat Statistik. 2010 [cited 2017 Jan 28]. Available from: <https://www.bps.go.id/index.php/publikasi/3514>
6. Sit. Kenakalan Remaja di Indonesia khususnya DIY Sudah Sangat Parah [Internet]. Pemerintah Daerah Kabupaten Bantul. 2012 [cited 2017 Feb 11]. Available from: <https://bantulkab.go.id/berita/1507.html>
7. Notoatmodjo S. Ilmu Perilaku Kesehatan. Jakarta: Rineka Cipta; 2010.
8. Elfiky I. Terapi Berpikir Positif. Jakarta: Zaman; 2014.
9. Arshad MRM, Omar M, Shahdan NA. Alcoholism Among Youth: A Case Study in Kuala Lumpur, Malaysia. *Int J Cult Hist*. 2015;1(1):21–8.
10. Wijaya IPA. Faktor-Faktor Yang Mempengaruhi Tingginya Konsumsi Alkohol pada Remaja Putra di Desa Keramas Kecamatan Blahbatuh Kabupaten Gianyar. *J Dunia Kesehat*. 2016;5(2):15–23.
11. Mananggal YA, Maramis FR., Engkeng S. Hubungan Antara Pengetahuan dan Sikap dengan Tindakan Pencegahan Mengonsumsi Alkohol pada Pelajar di SMA N 1 Siau Barat Kab. Kepulauan Sitaro. *Pharmacoon*. 2016;5(1):211–8.
12. Thursan H. Mengatasi Rasa Tidak Percaya Diri. Jakarta: Puspa Swara; 2002.
13. Hasan ABPH. Pengantar Psikologi Kesehatan Islami. Jakarta: Rajawali Pers; 2008.
14. Fatchurahman M, Pratikno H. Kepercayaan Diri, Kematangan Emosi, Pola Asuh Orang Tua Demokratis dan Kenakalan Remaja. *Pers J Psikol Indones*. 2012;1(2):77–87.
15. Fitriani W, Hastuti D. Pengaruh Kelekatan Remaja dengan Ibu, Ayah dan Teman Sebaya terhadap Kenakalan Remaja di Lembaga Pembinaan Khusus Anak (LPKA) Kelas II Bandung. *J Ilmu Kel dan Konsum*. 2016;9(3):206–17.
16. Amalia A. Peran Orang Tua Terhadap Konsumsi Alkohol Pada Remaja Putra Di Desa Sidorejo Kecamatan Sugio Kabupaten Lamongan Tahun 2015. *J Kebidanan dan Keperawatan Aisyiyah*. 2019;11(2):126–34.
17. Lestari S. Psikologi Keluarga Penanaman Nilai dan Penanganan Konflik dalam Keluarga. Jakarta: Kencana; 2012.
18. Diana FM, Susanti F, Irfan A. Pelaksanaan Program Perilaku Hidup Bersih dan Sehat (PHBS) di SD Negeri 001 Tanjung Balai Karimun. *J Kesehat Masy*. 2014;8(1):46–51.
19. Green LW, Kreuter MW. Health Promotion Planning: an Educational and Environmental Approach Second Edition. California: Mayfield Publishing Company; 2000.
20. Lickona. Pendidikan Karakter Panduan Lengkap Mendidik Siswa Menjadi Pintar dan Baik Diterjemahkan oleh: Lita (2014). Bandung: Nusa Media; 2008.
21. Tes AA, Puspitawati T, Marlinawati VU. Fenomena Perilaku Mengonsumsi Minuman Keras Mahasiswa Program Studi S-1 Kesehatan Masyarakat Universitas Respati Yogyakarta. *J Formil KesMas Respati*. 2017;2(1):25–31.
22. Saputro FAD, Hastuti YD, Arisdiani T. Pengaruh Peran Teman Sebaya Terhadap Perilaku Konsumsi Alkohol pada Remaja Putra. *J Ilm Permas*. 2014;4(2):70–81.
23. Ratna W. Sosiologi dan Antropologi Kesehatan (dalam Perspektif Ilmu Keperawatan). Yogyakarta: Pustaka Rihama; 2010.
24. Stautz K, Frings D, Albery IP, Moss AC, Marteau TM. Impact of alcohol-promoting and

- alcohol-warning advertisements on alcohol consumption, affect, and implicit cognition in heavy-drinking young adults: A laboratory-based randomized controlled trial. *Br J Health Psychol.* 2017;22(1):128–50.
25. Sriyanto, Abdulkarim A, Zainul A, Maryani E. Perilaku Asertif dan Kecenderungan Kenakalan Remaja Berdasarkan Pola Asuh dan Peran Media Massa. *Psikologi.* 2014;41(1):74–88.
26. Kustanti AA. Hubungan antara Pengaruh Keluarga, Pengaruh Teman dan Pengaruh Iklan terhadap Perilaku Merokok Pada Remaja di SMP 1 Slogohimo, Wonogiri. Universitas Muhammadiyah Surakarta; 2014.
27. Sarwono SW. *Psikologi Remaja.* Jakarta: Rajawali Pers; 2016.

The Effects of Infant Massage on the Physical Development of Baby in Indonesian Rural Areas

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Abstract

Introduction: Infant massage has been a long time and common practice. Mother plays an important role in ensuring the effectiveness of infant massage. This research attempts to find out the effects of infant massage training and education on the infant's physical development for mother in rural areas in Indonesia.

Material and Method: This study was designed to compare two groups, namely, the first group of 17 mothers with infant massage education and training intervention since the third trimester, and the second group of 17 mothers without intervention. Body weight, body length, circumference of the upper arms, suckling frequency and suckling duration of the babies in the two groups were compared one month after delivery.

Results: One month after the group of mothers giving massage to their babies, there were significant differences ($p < 0.05$) in body weight, body length, suckling frequency of the babies in the two groups, while none for circumference of upper arms and suckling duration. Comparing the effects of massage on babies before and after giving infant massage, there were significant differences in suckling durations and body weight of the babies.

Conclusion: Our study suggests that, after receiving an education on infant massage, mothers with babies are recommended to give massage to their babies. Infant massage brings various benefits to the babies, and it can be performed in natural contexts, including in rural setting.

Keywords: *Infant massage, baby development, mother-child interaction, rural setting, Indonesia.*

Introduction

The benefits of massage for babies have been long recognized. Massage stimulates babies to have better physical growth and become a powerful stimulus to the early life of a baby¹. It also creates a closer mother-infant bonding². Newborn babies receiving massage are known to make a quickly health recovery when they are sick³.

Since mothers in many cultures are responsible for the well-being and care of their babies, then they could play strategic roles in stunting prevention. The data issued by the World Bank reveal that, in 2013, as many as 37% of Indonesian children under five years of age or equal to 9 million children suffered from stunting⁴. The number decreased to 30% in 2018⁵. The data from the Indonesian Ministry of Health show that most cases of child stunting occur in rural areas.

Mothers should be empowered, among others, through infant massage training. Most existing researchers so far have discussed infant massage in the contexts of hospitals or other health facilities. As far as the researcher is concerned, a very few studies have been carried out with regard to discussions on the effects of infant massage to infant growth, and how mothers get involved in the activity in the natural contexts of their daily life. This research is then an attempt to examine the effects of mother's involvement in infant massage in the context of rural areas in Indonesia.

Material and Method

This research, involving 34 mothers having pregnancy in their third trimester, was conducted in the Village of Perlis, an area under the supervision of Tangkahan Durian Health Center, and Pangkalan

Brandan, Langkat Regencies, North Sumatra Province in Indonesia. This is a quasi-experimental research⁶ by having two groups. The first group, the intervention group, is the mothers who were given infant massage training, a note book and leaflet on infant massage. The second group, the non-intervention group, is the mothers who only had note book with them.

The intervention group received trainings in infant massage for 4 consecutive days. The trainings were led by instructors and the object of massage was infant phantom. Trainings were carried out simultaneously in the village maternity clinic. Leaflet provided extra information about infant massage.

After giving birth, the mothers got the same trainings for 4 consecutive days. The mothers were asked to massage their babies twice a day- when the babies were taking a bath in the morning and in the afternoon- for the duration of 30 days. The researcher supervised the process of infant massage. Before massage was given, the weight, length, and circumference of the upper arms of the babies were measured. The researcher also interviewed the mothers about the suckling frequency and suckling duration of their babies. The data were recorded in the note book distributed to each mother before.

Meanwhile, the non-intervention group received note book and leaflet. The mothers in this group accepted explanation of how important massage is for their babies. However, they did not receive any training in infant massage. The measurements of baby weight, length, circumference of the upper arms, and suckling frequency and duration were made every week until the fourth week.

Infant massage took place for 25 minutes. Massage started in the face area, then chest, stomach, arms, legs, and back of the head. Each area was slowly and gently massaged. When giving the massage, the mother maintained eye contact and “communicated” with her baby. A series of massage was done 6 times for 8 seconds each. Baby oil was used for the infant massage.

The body weight of baby (in grams) was measured with a special weight scale, GEA. The measurement results were converted into NCHS category, namely, standard deviation (SD) <-3 to <-2 and SD -2 to SD 2. The body length of baby (in centimetres) was measured with a paper measuring gauge. The measurement results were also converted also into NCHS

category like the body weight. The circumference of the upper arms of baby was measured with an arm gauge for baby, and categorized into >0,5 cm/month or < 0,5 cm/month. Suckling frequency of baby was categorized into >10 time suckling frequency/day or <10 time suckling frequency/day. Suckling duration of baby was categorized into >15 minutes or <15 minutes.

Each group and between the intervention and non-intervention groups were compared and were tests with 95% CI.

Results

This study involved 34 mothers who were in the third trimester of pregnancy. All mothers had safe delivery with the total of 19 male babies and 15 female babies. Most female babies (65%) were from the non-intervention group. Seen from pregnancy interval and mother parity, the profiles of the two groups were similar. The majority of mothers’ latest pregnancy interval was 2 years. Most were multiparous women (70.6% of multiparity in each group). In the intervention group, 64.7% of mothers were in their 20-≤30 years of age while in the non-intervention group were little bit older (see Table 1).

Table 2 provides the differences of the two groups. In the intervention group, all mean variable values increase significantly after 4-week intervention. There are increases in body weight as much as 26.8%, body length as much as 5.2%, circumference of upper arms as much as 11.8%, suckling frequency as much as 44.7%, and suckling duration as much as 61.6% after intervention. All changing conditions are statistically different (p-value <0.05).

The babies in the non-intervention group undergo the following conditions. There are increases in body weight as much as 22%, body length as much as 1%, and circumference of upper arms as much as 11.9%. There are slightly difference in suckling frequency (13.2%) and suckling duration (52.4%). All changing conditions, but body length, in this group have statistical values (p)<0.05.

The differences between the intervention group and non-intervention group come up with different statistical test results. For body weight, body length, and suckling frequency variables, the differences are statistically significant (p<0.05), while circumference of upper arms and suckling duration variables do not indicate any difference.

The differences between the groups are clearly seen in Picture 1. It indicates weekly changes in each variable. Body weights of all babies increase steadily until the third week yet several babies gain significant body weights in the fourth week. The maximum gain weight for several babies in the intervention group is 1000 grams while in the non-intervention group, 700 grams. The same pattern also applies to the body length of the baby. In the first two weeks, the body length reach of the babies in the two groups is relatively the same. However, from the

third to the fourth weeks, the babies in the intervention group grow more significantly in body length compared to those in the non-intervention group. Picture 1 part c presents the changes in the circumference of upper arms. Striking changes are seen in third and then fourth weeks. Suckling frequency and suckling duration of the babies in the intervention groups are much better than those in the non-intervention group when intervention enters the third week.

Table 1. Comparison of mother's demographics and infant characteristics in intervention and non-intervention groups

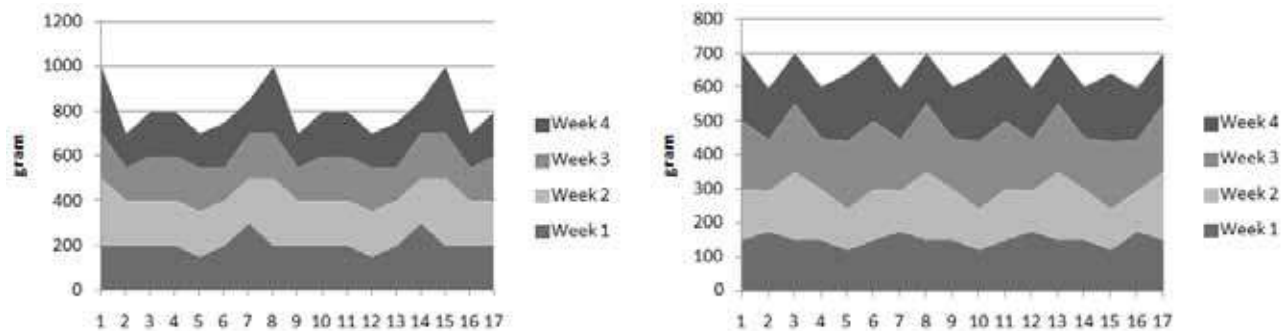
Characteristics	Intervention group		Non-intervention group	
	n	(%)	N	(%)
Mother's Age				
>30 years of age	6	35.3	9	52.9
20-≤30 years of age	11	64.7	8	47.1
Pregnancy interval				
2 years	12	70.6	12	70.6
> 2 years	5	29.4	5	29.4
Mother parity				
Multiparity	12	70.6	12	70.6
Grande multiparity	5	29.4	5	29.4
Gender of baby				
Female	9	53	6	65
Male	8	47	11	35
Birth Weights (in grams)				
2,500-3,000	8	47	13	76
3,000-3,250	9	53	4	24
Birth Length (in cm)				
47 cm	4	24	6	35
48 cm	5	29	4	24
49 cm	8	47	7	41
Circumference of upper arms after birth (in cm)				
8	2	12	4	24
8.5	4	24	5	29
9	10	58	7	41
9.5	1	6	1	6

Table 2. The difference of mean and SD in the intervention and non-intervention groups: before, after, and between groups

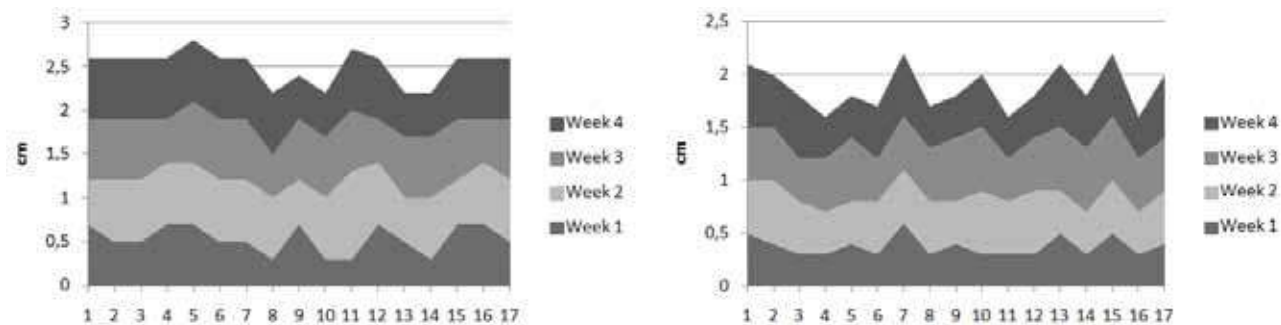
Variable	Intervention group		Non-intervention group	
	Mean ± SD	P value	Mean ± SD	P value
Body weight				
Before	3000.12 ± 567.28	0.001 ^{a)}	2941.18 ± 276.83	0.001 ^{a)}
After	3806.00 ± 552.79		3588.24 ± 270.65	
Δ change	805.88 ± 105.89		647.06 ± 48.25	0.001 ^{b)}

Variable	Intervention group		Non-intervention group	
	Mean ± SD	P value	Mean ± SD	P value
Body length				
Before	48.24±0.83	0.001 ^{a)}	48.06±0.89	0.445 ^{a)}
After	50.75 ± 1.01		48.54±0.88	
Δ change	2.51±0.19		0.47±0.05	0.001 ^{b)}
Circumference of upper arms				
Before	8.79±0.39	0.001 ^{a)}	8.17±2.03	0.007 ^{a)}
After	9.83 ± 8.42		9.16±2.05	
Δ change	1.04±0.13		0.98±0.13	0.295 ^{b)}
Suckling Frequency				
Before	7.47±0.51	0.001 ^{a)}	7.82±0.39	0.001 ^{a)}
After	10.94 ± 1.39		8.60±0.69	
Δ change	3.34 ± 1.48		1.04 ± 1.28	0.001 ^{b)}
Suckling Duration				
Before	9.65±1.27	0.001 ^{a)}	8.71±0.99	0.007 ^{a)}
After	15.51 ± 1.93		13.09±2.26	
Δ change	5.95±2.27		4.57±2.32	0.094 ^{b)}

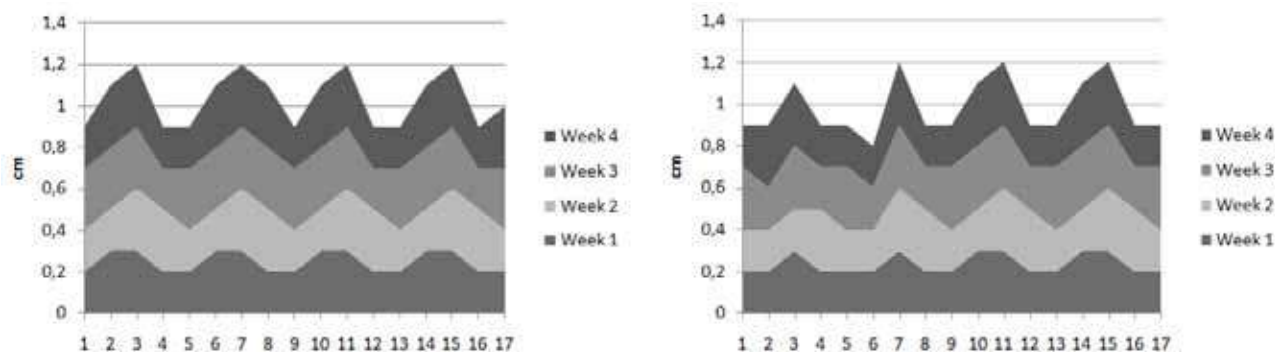
a) P value Paired (Wilcoxon test), b) P value Independent Sample test/Mann-Whitney U test



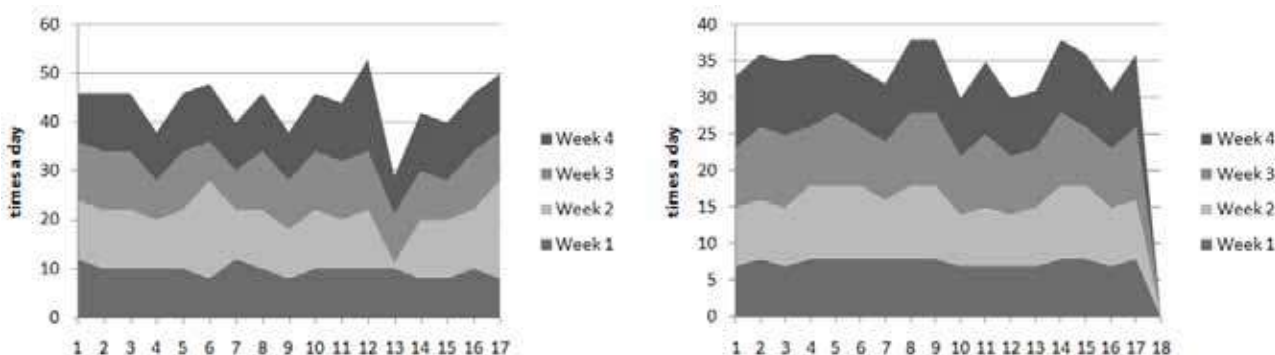
(a) body weight



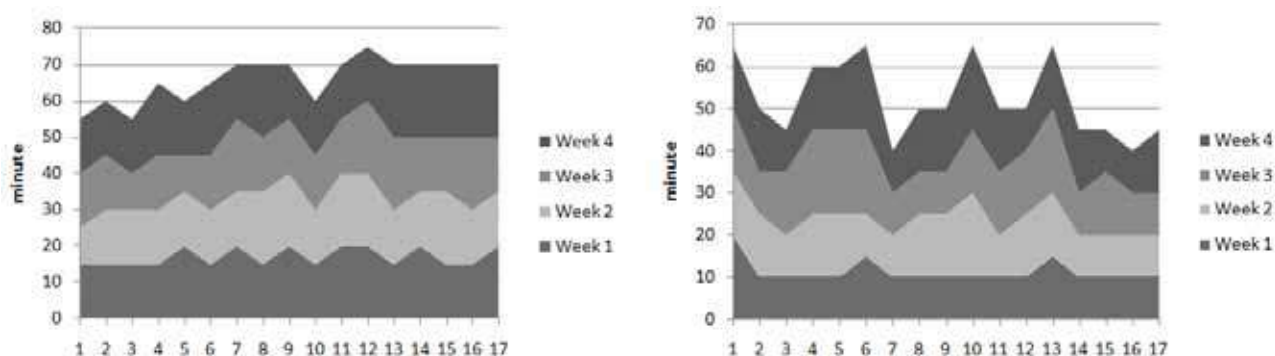
(b) body length



(c) circumference of upper arms



(d) suckling frequency



(e) suckling duration

Picture 1. Weekly development of babies in the intervention and non-intervention groups

Discussion

Educating mothers about infant massage certainly has beneficial effects on their babies. The best time for mothers to receive infant massage education is during the period of entering the third trimester of pregnancy to one month after delivery. Babies having massage undergo physical development in terms of body weight, body length, and circumference of upper arms. They look comfortable during breastfeeding. This condition indirectly create an intimate connection between mother and her baby.

Previous study reveals that after having one-year massage right after their birth, babies record higher scores for motor and mental development. The babies pain responses are low and have shorter LoS (length of stay) in hospital³.

This study also suggests that appropriate infant massage techniques performed by the mother stimulate her baby to gain body weight significantly^{7,8}. Infant massage and physical exercises could cause rapid weight gain for pre term infants as well⁹. With massage and physical exercises, babies show significant growth

in their bone length as shown in their increasing body length¹⁰.

Babies who are given massage have a better sleep quality than those who are not¹¹. Babies need to get enough sleep for healthy growth as shown in their increasing body weight and length. This is possible because infant massage improves blood circulation of the baby¹². Another hypothesis regarding infant massage is that stroking the muscles of a baby activates a receptor in the baby's body. This receptor is responsible for stimulating effective baby metabolism which in turn promoting rapid physical growth of the baby¹³.

In addition, infant massage seems to be closely related to quality of baby suckling. This study reveals that the suckling frequency and suckling durations of the babies of the mothers in the intervention group are better than those in the non-intervention group (see pictures 1d and 1e). Weight and length gain of babies do correlate strongly with breastfeeding at least during the early six months of infancy¹⁴.

However, it is important to recognize the psychological effects created by skin-to-skin contact between mother and her baby. This study finds out that mothers who massage their babies in fact establish positive relationships with their babies. These positive relationships maintain the emotional stability of the mothers which in turn stimulates mothers to improve their breast milk production¹⁵. Positively psychological condition allows mothers to produce adequate quantity of milk their babies.

The importance of infant massage has been recognized for a long time^{12,16}. New studies also confirm that infant massage helps mother to develop affection for her baby¹⁵. It does not only meet the physical needs of the baby but also facilitates both mother and her baby to build positive relationships¹⁷. Compared to the mothers who do not participate in infant massage training, those who join the infant massage trainings for 8 weeks report of better self-confidence in fulfilling their role. The trainings help them to build more intimate and positive relationships with their babies¹⁸. For the mothers, massage could become an activity to channel affection for their babies¹⁹. A relaxed emotional state enables mothers to have much better sleep quality¹¹.

Like in other cultures, it is the common and traditional role of Indonesian mothers, especially those living in rural areas, to bath their baby. Therefore, mothers do not

need to spare specific time to massage their baby since it could be done during bath time because giving infant massage during bath is a natural process a mother could perform²⁰. Since many mothers lack adequate knowledge about infant massage techniques,²¹ it is then necessary to train and educate them on infant message from the final phase of their pregnancy to one month after giving birth.

Conclusion

This study proves that infant massage is an effective way to improve baby's physical profiles and suckling quality. It supports the argument that infant massage trainings and education for pregnant women are important to ensure the well-being of both mothers and their babies. This study indicates that mother plays a very important role in ensuring the life quality of her baby in the future.

Conflict of Interest: The author has none to declare

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References

1. Heath A, Bainbridge N. *Baby Massage*. London: Dorling Kindersley Limited; 2004.
2. Bagshaw J, Fox I. *Baby Massage for Dummies*. Indianapolis, Indiana: Wiley Publishing, Inc; 2005.
3. Abdallah B, Kurdahi L, Hawwari M. Infant Behavior and Development The efficacy of massage on short and long term outcomes in preterm infants. *Infant Behav Dev* [Internet]. 2013;36(4):662–9. Available from: <http://dx.doi.org/10.1016/j.infbeh.2013.06.009>
4. The World Bank. *Indonesia Accelerates Fight Against Childhood Stunting* [Internet]. Who We Are/News. 2018. Available from: <https://www.worldbank.org/en/news/feature/2018/06/26/indonesia-fights-stunting-commitment-convergence-and-communities>
5. MoH. *Basic Health Research 2018*. Jakarta; 2019.
6. Zaluchu F. *Metodologi Penelitian Kesehatan*. Bandung: Cipta Pustaka Media; 2006.

7. Ferber SG, Kuint J, Weller A, Feldman R, Dollberg S, Arbel E, et al. Massage therapy by mothers and trained professionals enhances weight gain in preterm infants. *Early Hum Dev.* 2002;67:37–45.
8. Lee H. The Effects of Infant Massage on Weight, Height, and Mother-Infant Interaction. *J Korean Acad Nurs.* 2006;36(8):1331–9.
9. Diego MA, Field T, Hernandez-reif M. Early Human Development Preterm infant weight gain is increased by massage therapy and exercise via different underlying mechanisms. *Early Hum Dev* [Internet]. 2014;90:137–40. Available from: <http://dx.doi.org/10.1016/j.earlhumdev.2014.01.009>
10. Field T, Diego M, Hernandez-reif M. Preterm infant massage therapy research: A review. *Infant Behav Dev* [Internet]. 2010;33(2):115–24. Available from: <http://dx.doi.org/10.1016/j.infbeh.2009.12.004>
11. Field T, Gonzalez G, Diego M, Mindell J. Infant Behavior and Development Mothers massaging their newborns with lotion versus no lotion enhances mothers' and newborns' sleep. *Infant Behav Dev* [Internet]. 2016;45:31–7. Available from: <http://dx.doi.org/10.1016/j.infbeh.2016.08.004>
12. Field T, Diego M, Hernandez-reif M. Massage therapy research. *Dev Rev.* 2007;27:75–89.
13. Field T, Hernandez-reif M, Diego M, Feijo L, Vera Y, Gil K. Massage therapy by parents improves early growth and development. *Infant Behav Dev.* 2004;27:435–42.
14. Küpers LK, Abée CL, Bocca G, Stolk RP, Pieter J. Determinants of Weight Gain during the First Two Years of Life — The GECKO Drenthe Birth Cohort. *PLoS One.* 2015;1–15.
15. Gurol A, Polat S. The Effects of Baby Massage on Attachment between Mother and their Infants. *Asian Nurs Res (Korean Soc Nurs Sci).* 2012;6:35-41.
16. Reissland N, Burghart R. The Role of Massage in South Asia: Child Health and Development. *Soc Sci Me.* 1987;25(3):231–9.
17. Clarke CL, Gibb C, Hart J, Davidson A, Clarke CL. Infant massage: developing an evidence base for health visiting practice. *Clin Eff Nurs.* 2002;6:121-8.
18. Vicente S, Verissimo M, Diniz E. Infant Behavior and Development Infant massage improves attitudes toward childbearing, maternal satisfaction and pleasure in parenting. *Infant Behav Dev* [Internet]. 2017;49(December 2016):114–9. Available from: <http://dx.doi.org/10.1016/j.infbeh.2017.08.006>
19. Porter LS, Porter BO, Mccoy V, Bango-sanchez V, Kissel B, Williams M, et al. Blended Infant Massage-Parenting Enhancement Program on Recovering Substance-Abusing Mothers' Parenting Stress, Self-Esteem, Depression, Maternal Attachment, and Mother-Infant Interaction. *Asian Nurs Res (Korean Soc Nurs Sci)* [Internet]. 2015;9(4):318–27. Available from: <http://dx.doi.org/10.1016/j.anr.2015.09.002>
20. Cooke A. Infant massage: The practice and evidence-base to support it. *Br J Midwifery.* 2015;23(3):166–70.
21. Wati AM, Renityas NN. The Effect of Health Education to Baby Massage Skill. *J Ners dan Kebidanan.* 2014;1(1):62–7.

Relationship between Polishing Techniques and Bacterial Count on Different Denture Base Materials

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Abstract

Introduction: Wearing of dentures cause alteration in the oral microflora and increasing in number of bacteria and candida. The polished and fitting surfaces of the denture are both affected. Different polishing techniques influence the total count of bacterial accumulation on the denture surface.

Aim: To count the bacterial colonies after polishing three denture base materials before and after six months of denture wearing by different polishing techniques.

Materials and Method: Eighteen patients were randomly selected for construction of maxillary partial denture. They were divided into 3 groups: Group 1: Patients received conventional heat-cured PMMA (Acrostone) denture. Group 2: Patients received thermoformed polyamide (NEWULTRA) denture. Group 3: Patients received thermoformed acetal (Bio Dentaplast) denture. In each group, three patients had their dentures polished by pre polishing with brown rubber disc and fine pumice with wet rag wheel, and the other three patients with the same technique but followed by tripoli compound with dry rag wheel. Evaluation of bacterial counting was conducted before denture wearing and after six months of denture wearing. Swabs were taken from the palate of the patients and bacteria were counted.

Findings: No significant difference was found between technique no. I and no. II in decreasing the bacterial count between the tested materials. Thermoformed polyamide showed the highest bacterial count after six months of wearing denture polished by technique no. II followed by thermoformed acetal and heat-cured PMMA.

Conclusion: The second polishing technique produced less surface roughness and bacterial colonization on the tested materials than the first one.

Keywords: Polishing techniques, bacterial count, denture base materials.

Introduction

Wearing removable dental prosthesis (either complete or partial dentures) causes an alteration in the oral microflora^[1].

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The surfaces of soft and hard tissues of the oral cavity covered with a 0.5-1.5 μ m thick layer which consists of: salivary glycoprotein, immunoglobulin and microorganisms that normally formed within about thirty minutes after tooth brushing and is called "pellicle"^[2].

Microorganisms found in this pellicle such as: oral streptococci, staphylococci, enterococci^[3] and oral yeast which is known as candida albicans.

With many oral environmental factors, salivary pellicle is the strongest factor for microbial colonization

of oral hard surfaces such as teeth, restorations and prosthetic appliances^[4].

Bacteria and Candida commonly causes dental caries and less frequently cause more severe disease, such as pneumonia or endocarditis^[5]. The medically important diseases maybe caused by the bacterial pathogens; that occasionally colonize the oral cavity^[6].

The alteration in the oral microflora considers as a common cause for the development of a particular condition: dental prosthetic stomatitis or denture associated stomatitis. Denture stomatitis is characterized by mucosal inflammation and redness underneath a denture^[7]. It is caused by the microbial biofilm on the fitting surface of the denture rather than on the mucosal surface, especially in the maxilla^[8].

Available literature makes it known that bacterial and fungal adhesion to the prosthetic materials is a complicated phenomenon and depends on such factors as, coarseness of those materials and their ability to attract water and the proteins in saliva, which facilitate adhesion of micro-organisms^[9].

Smooth and highly polished denture surface are of utmost importance for patient comfort and denture longevity, and it is desired for reducing microorganism's retention^[10]. It can improve good aesthetical results, oral hygiene and low plaque retention, preventing oral diseases^[11].

The aim of the polishing procedure of the denture is to make the denture glassy without changing its contour. For obtaining this aim, all scratches and rough areas must be removed. A series of progressive finer abrasive is used to produce a shiny surface on the denture^[12].

Polishing procedure is either mechanical or chemical^[12&13]. The mechanical polishing procedure uses abrasives which produces wear of the surface in a selective controlled manner and this reduces the surface roughness of the material^[13]. Mechanical polishing is preceded by finishing using stone bur and sand paper in order to make the acrylic denture reach to the final form before polishing^[14].

As Manufacturer's recommendations for polyamide suggest the material can be used as partial denture framework including clasps, due to its flexural properties^[15].

Mustafa MJ^[16] stated that effect of finishing and polishing technique on the surface polyamides have been reported as being difficult to finish and polish due to their low melting temperature, Fraying at the margins of the polyamide specimens was noticed occasionally during polishing of the samples in study, which may have occurred due to overheating of the surface and exposure of fibers.

A study^[17] was conducted on the effect of denture cleansers on the formation of candida biofilms on a polyamide resin and a PMMA resin. The study showed that candida biofilms had significantly higher growth on polyamide compared with PMMA indicating that polyamide could present a convenient surface for microbial colonization.

A recent study by Mekkawy MA et al^[18]; revealed that acetal resin showed the highest mean value of surface roughness after polishing among materials tested, but within the accepted threshold level. Due to the high crystalline feature of acetal resins, which provides excellent properties as it increases the hardness, it might be the cause of the increased surface roughness value^[19].

So the aim of this study was to count the bacteria on three denture base materials before and after denture wearing for six months.

Materials and Method

18 patients were selected from Removable Prosthodontics Department. Faculty of Dentistry. Minia University.

Inclusion Criteria: Patients were free from any systemic diseases especially autoimmune disease or patients under corticosteroids therapy. Age ranged between 45 to 55 years (males or females). Partially edentulous maxillary arch with recent extractions and completely edentulous mandibular arch. Patients with good oral hygiene, measured by modified gingival index (MGI).

Exclusion Criteria: Sensitive patients (allergic) to heat-cured PMMA or thermoformed materials were excluded. Allergy test was applied for each patient using the patch test^[20]. No previous history of denture wearing.

Ethical Consideration: Thesis protocol was approved by the research ethical committee. Faculty of Dentistry. Minia University.

Patient Categorization:

Patients were categorized into three groups:

Group 1: Patients received conventional heat-cured PMMA (Acrostone) removable partial denture.

Group 2: Patients received thermoformed polyamide (NEWULTRA) removable partial denture.

Group 3: Patients received thermoformed acetal (Bio Dentaplast) removable partial denture.

The in-vitro investigations of an earlier study by EldinMS^[21] concluded that polishing technique that used pre polishing rubberizing with brown rubber disc 1500 rpm for one minute, followed by fine pumice with wet rag wheel, 1500 rpm for two minutes (technique no. I)^[16] and the same technique but followed by tripoli compound with dry rag wheel, 1500 rpm for two minutes (technique no. II)^[16]; showed the least surface roughness values for heat-cured PMMA and thermoformed specimens. Accordingly, for each group, three patients had their dentures polished with technique no. I, and the others three patients with technique no. II.

Patient Evaluation: Patients were evaluated by collection of swabs from the palatal mucosa by the aid of sterile cotton swabs (sterile swab stick)^[22]. Swabs were taken within area of (2 × 2 cm line) by using a transparent pattern. This transparent pattern was made for each patient. Sterile cotton swab was moistened with phosphate buffered saline (PBS) and then applied using horizontal strokes for one minute to the swabbed areas then recapped again and transferred immediately to the microbiology laboratory for processing. Swabs were taken in the morning between 11 and 12 o'clock.

Evaluation Time:

a. Before denture wearing.

b. After six months of denture wearing.

Bacterial Counting: Bacterial concentration was conducted on blood agar enriched with 5% sheep blood^[22]. Samples were prepared under aseptic condition and were incubated for 24 hours at 37°C^[23]. Bacteria were counted manually and counting was repeated 3 times. Colonies growth recorded as total colony forming units per milliliter for liquids (CFU/ml)^[24].

$$CFU = (\text{Bacterial Colony Count} / \text{Volume used} \times \text{Reciprocal of dilution})$$

Statistical Analysis: Data were presented as mean (μ) and standard deviation (SD). Data were explored for normality using Kolmogorov-Smirnov and Shapiro-Wilk tests. Data showed a parametric distribution. In this study; independent t-test and dependent t-test were used.

Findings: Patients were: ten patients Kennedy's class I, five patients Kennedy's class II, two patients Kennedy's class III with long edentulous area, one patient Kennedy's class IV. They were twelve males and six females.

Table 1 showed that group 1 had no significant difference in bacterial counting after polishing with technique no. I and II before denture wearing (P value=0.172), but showed a significant higher difference of technique no. I than technique no. II after denture wearing (P value=0.022) with (Mean: 3.88 and 2.49) respectively. Group 2 showed no significant difference in bacterial counting after polishing with technique no. I and II before denture wearing (P value=0.548) and after denture wearing (P value=0.434). Group 3 showed no significant difference in bacterial counting after polishing with technique no. I and II before and after denture wearing (P value=0.073) & (P value=0.208) respectively.

		Techniques				p-value
		Technique I		Technique II		
		Mean	SD	Mean	SD	
GP 1	Before Polishing	4.86	.03	4.47	.52	0.172 NS
	After Polishing	3.88	.89	2.49	.17	0.022*
GP 2	Before Polishing	4.69	.88	4.32	.56	0.548 NS
	After Polishing	3.51	.88	3.01	.59	0.434 NS
GP 3	Before Polishing	5.21	.49	4.41	.55	0.073 NS
	After Polishing	3.45	.21	2.84	.53	0.208 NS

In table 2, it was clarified that dentures that were polished by technique no. I; before and after denture wearing showed no significant difference in bacterial counting for group 1&3; (P value=0.109 and 0.124) respectively. But group 2 had a significant higher difference before wearing denture than after denture wearing (Mean: 4.69 and 3.51) respectively. Group 1 that was polished by technique no. II; showed a

significant higher difference before and after denture wearing (Mean: 4.47 and 2.49) respectively. Group 2 that was polished by technique no. II; showed a significant higher difference before denture wearing than after denture wearing (Mean: 4.32 and 3.01) respectively. Group 3 that was polished by technique no. II; showed a significant higher difference before and after denture wearing (Mean: 4.41 and 2.84) respectively.

			Polishing				p-value
			Before Polishing		After Polishing		
			Mean	SD	Mean	SD	
Polishing technique	Technique I	GP 1	4.86	.03	3.88	.89	0.109 NS
		GP 2	4.69	.88	3.51	.88	0.04*
		GP 3	5.21	.49	3.45	.21	0.124 NS
	Technique II	GP 1	4.47	.52	2.49	.17	0.002*
		GP 2	4.32	.56	3.01	.59	0.004*
		GP 3	4.41	.55	2.84	.53	0.008*

Discussion

Patients selected were free from any systemic diseases as autoimmune disease or under corticosteroids therapy which would cause osteoporosis. Their age range were between 45 and 55 years to assure that the mandibular arch were completely dentulous and the maxillary arch was with recent extraction of the teeth to prevent extreme bone resorption after long time extraction or overeruption of the mandibular teeth.

None of the selected patients were previously wearing dentures to assure that there was no effect of any previous treatment in the results^[25].

This present study used a transparent pattern (2×2 cm) for taking a swab from each patient for idealization of the area of swab. Swab that was taken in this study were from the palate only and not from the fitting surface of the prosthesis as within the limitations of Al-AkhaliMA^[26] study, it can be concluded that the mucosa under the acetal denture base retains more microorganisms than the mucosa under the metallic denture base. However, the fitting surface of the metallic denture base retains more micro-organisms than the fitting surface of the acetal resin denture base. This difference was found to be non-statistically significant; the adhesion of micro-organisms on mucosa and denture base of either the metal or acetal denture increased by time^[26].

The present study revealed that few of the patients had reduced (CFU/ml). However, such a finding was not necessarily indicative of a total absence of microbial presence on the prosthesis and in this study it could be due to the limitations of over swabbing efficiency or due to the small sample size.

This study concluded that no significant difference between technique no. I and no. II in decreasing the bacterial count between the tested materials. However, thermoformed polyamide showed the highest bacterial count after six months of wearing denture polished by technique no. II followed by thermoformed acetal and heat-cured PMMA.

From the research of Glantz et al^[27], it arises that acrylic has smaller surface potential, but it absorbs water which causes a significant increase of adhesion strength and adsorption of a relatively large amount of prosthesis plaque.

It was demonstrated that polyamides had rougher surface than other resin materials, and it caused more bacterial and fungal colonization^[28].

Ata So^[29] reported that, whiteacetal resin was more porous and showed less color stability than pinkacetal resin.

This study was followed for only six months which is a reasonable period to give an idea about the bacterial adhesion on different denture base materials after using polishing techniques.

Conclusion

The use of tripoli compound in polishing different denture base materials caused decreasing in the total count of bacterial adhesion on denture surfaces as it caused less surface roughness of these materials, however this decrease was non-significant.

Conflict of Interest: None.

Source of Funding: Self-funding.

Ethical Clearance: Procedures were in accordance with institutional and national ethical standards and with the Helsinki declaration.

References

- Girard B Jr, Landry RG, Giasson L. Denture stomatitis: etiology and clinical considerations. *J Can Dent Assoc.* 1996;62:808-12.
- Shay K. Denture hygiene: a review and update. *JCDP.* 2000;1:28-41.
- Van der Mei HC, Free RH, Elving GJ, Weissenbruch RV, Albers FWJ, Busscher HJ. Effect of probiotic bacteria on prevalence of yeasts in oropharyngeal biofilms on silicone rubber voice prostheses in vitro. *J Med Microbiol.* 2000;49:713-718.
- Papaoiannou W, Gizani S, Nassika M, Kontou E, Nakou M. Adhesion of *Streptococcus mutans* to different types of brackets. *Angle Orthod.* 2007; 77:1090-1095.
- Coulthwaite L, Verran J. Potential pathogenic aspects of denture plaque. *Br J Biomed Sci.* 2007;64:180-9.
- Reddy MS. Reaching a better understanding of nonoral disease and the implication of periodontal infections. *Periodontol* 2000. 2007;44:9-14.
- Spratt D. 4.1. Dental plaque and bacterial colonization. In: Medical biofilms. Jass J, Surman S, Walker J, editors, John Wiley and Sons Ltd. 2003;175-98.
- Olsen I. Denture stomatitis. Occurrence and distribution of fungi. *Acta Odontol Scandinav.* 1974;32:329-33.
- Okita N, Orstavik J, Ostby K. In vivo and vitro studies on soft denture materials: microbial adhesion and tests for antibacterial activity. *Dent Mater.* 1991;7:155-160.
- Verran J, Maryan CJ. Retention of *Candida Albicans* on acrylic resin and silicon of different surface topography. *JPD.* 1997;77:535-539.
- Taylor R, Maryan CJ, Veran J. Retention of oral microorganisms on cobalt-chromium alloy and dental acrylic resin with different surface finishes. *JPD.* 1998;80:592-597.
- Kuhar M, Furduk NN. The effect of polishing technique on the surface roughness of acrylic denture base resin. *JPD.* 2005;93:76-85.
- Jefferies SR. Abrasive finishing and polishing in restorative dentistry: a state-of-the-art review. *Dent Clin North Am.* 2007;51:379-397.
- Barbosa CMR, Gabriotti MN, Silva-Concilio LR, Joia FA, Ribeiro MC. Surface roughness of acrylic resins processed by microwave energy and polished by mechanical and chemical process. *Braz J Oral Sci.* 2006;5:977-981.
- Abuzar MA et al. Evaluating surface roughness of a polyamide denture base material in comparison with poly (methyl methacrylate). *J Oral Sci.* 2010;52:577-581.
- Mustafa MJ, Amir HM. Evaluation of *Candida albicans* attachment to flexible denture base material (valplast) and heat cure acrylic resin using different finishing and polishing techniques. *J Bagh Coll Dent.* 2011;23:36-41.
- de Freitas FFS, Pereira-Cenci T, da Silva WJ, Filho AP, Straioto FG, Del Bel Cury AA. Efficacy of denture cleansers on *Candida* spp. biofilm formed on polyamide and polymethyl methacrylate resins. *JPD.* 2011;105:51-58.
- Mekkawy MA, Hussein LA, Alsharawy MA. Comparative study of surface roughness between polyamide, Thermoformed polymethyl methacrylate and acetal resins flexible denture base materials before and after polishing. *Life Sci J.* 2015;12:90-95.
- Fitton JS, Davies EH, Howlett JA, Pearson GJ. The physical properties of a polyacetal denture resin. *Clin Mater.* 1994;17:125-129.
- Garner LA. Contact dermatitis to metals. *Dermatol Ther.* 2004;17:321-327.
- El-Din MS, Badr AI, Agamy EM, Mohamed

- GF. Comparison between Heat Cured Polymethylmethacrylate, Thermoplastic Polyamide and Thermoplastic Acetal in Regarding to their Surface Roughness: In Vitro Study". *EC Dental Science*. 2017;12:156-167.
22. Murray PR , Baron EJ, Jorgensen JH, Pfaller MA, Tenover FC, Tenover FC. *Manual of clinical microbiology*. 8th ed. American Society for Microbiology. Washington, D.C. 2003. p120. ISBN: 1555812554 9781555812553. p 120.
23. Soomro MA, Maqsood S, Ansari SA, Riffat A. Adhesion of Oral Candida and bacteria on prosthodontics and orthodontic appliances. *JPDA*. 2012;21:223-227.
24. Williams DW, Chamary N, Lewis MAO, Milward PJ, McAndrew R. Microbial contamination of removable prosthodontics appliances from laboratories and impact of clinical storage. *Br Dent J*. 2011;211:163-166.
25. Srividya S, Nair CK, Shetty J. Effect of Different Polishing Agents on Surface Finish and Hardness of Denture Base Acrylic Resins: A Comparative Study. *IJOPRD*. 2011;1:7-11.
26. Al-Akhali MA, El-Kerdawy MW, Ibraheim ZA, Abbas NA. Comparative study on the microbial adhesion to acetal resin and metallic removable partial denture. *IJDentistry*. 2012;3:1-4.
27. Glantz P, Baier R, Goupil D. Intraoral adhesion to a well-defined surfaces. *Acta Odontol Scand*. 1981;39:169-177.
28. Vojdani M, Giti R. Polyamide as a Denture Base Material: A Literature Review. *JOD SUMS*. 2015;16:1-9.
29. Ata SO, Yavuzylmaz H. In vitro comparison of the cytotoxicity of acetal resin, heat-polymerized resin, and auto-polymerized resin as denture base materials. *J Biomed Mater Res B: Appl Biomater*. 2009;91B:905-909.

Determination of Dyspnea in Mechanically Ventilated Patients

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Abstract

Introduction: Although dyspnea is the most common suffering and devastating symptom in the mechanically ventilated patients (MVPs), it is not routinely measured.

Aim of the Study: To assess dyspnea and factors contributing to it in MVPs.

Design: A descriptive research design

Settings: Intensive Care Units of Alexandria Main University Hospital.

Subjects: Forty critically ill conscious adult MVPs

Tool of Data Collection: Dyspnea assessment tool used to collect the data.

Results: 55% of the study sample had dyspnea and 86.4% of dyspneic MVPs had moderate to intense level of dyspnea.

Conclusion: Dyspnea is present in more than half of the MVPs. Moderate to intense dyspnea is more frequent in MVPs.

Keywords: *Dyspnea, Mechanical ventilation, Modified Borg Scale.*

Introduction

Dyspnea is a subjective experience of breathing discomfort described as air hunger, heavy breathing or choking.^(1,2) It is a common and often debilitating symptom that affects up to half of patients admitted to acute tertiary care hospitals and 25% of patients admitted to acute tertiary care hospitals seeking care in ambulatory settings.^(3,4) Presence of dyspnea is a strong predictor of patient's clinical course and mortality and neglecting it cause suffering, complicate and extend length of stay, and counterbalance physiological benefits in terms of clinical outcomes.^(4,5,6) Therefore, mechanical ventilation which is a commonly used technological treatment in ICUs,⁽⁷⁾ aims to maintain adequate oxygenation, alleviate the patient's respiratory symptoms, reduce the work of breathing (WOB), and improve patient comfort.^(1,6)

However and at the same time, patients on MV

may experience distressing symptoms such as anxiety, dyspnea, pain or discomfort, confusion, agitation, and sleep disturbances.⁽⁸⁾ In other words, dyspnea can persist, reappear, or re-increase after the initiation of MV. This can reveal many complications (such as pneumothorax, pneumonia, cardiac failure, anemia, etc.), air leaks, increased airway resistance, decreased lung compliance, inappropriate ventilator settings, anxiety and pain.^(6, 9) Therefore, dyspnea could be used as a useful clinical management tool for the MVPs.⁽⁶⁾

The critical care nurses had an essential role in providing patient-centered care to maintain oxygenation and ventilation adequacy, breathing comfort, and patient-ventilator synchrony.⁽¹⁰⁾ Responsibilities of the critical care nurse related to ventilator management may vary among acute care settings, but no doubt the nurse is the "first-line manager" challenged with MVPs related problems.⁽⁹⁾ Therefore, it is very important that they

should do their best effort to develop their knowledge and skills needed for effective management of MVPs. ⁽⁹⁾

As dyspnea is the most suffering and devastating symptom.⁽¹¹⁾ A patient-centered approach of nursing care should include routine assessment for dyspnea using an appropriate instrument.^(5,9,12) Unfortunately, dyspnea is still not routinely assessed in critically ill patients, except during patient weaning from MV.⁽⁶⁾ During the last decades, manufacturers and researchers increase their attention on the patient-ventilator interactions.⁽¹³⁾ However, dyspnea has not been studied to any great extent in MVPs.⁽⁶⁾ In general critical care nurses have a sense of security that, because the patients are supported by the MV, they are receiving adequate ventilation and they are not suffering from dyspnea however, in fact, dyspnea is common and more frequent problem in MVPs. In addition, there is a knowledge gap in the understanding of dyspnea in those patients. Therefore, this study aimed to assess dyspnea in mechanically ventilated patients.

Materials and Method

Design: A descriptive research design was used to assess dyspnea in MVPs.

Sample: A convenience sample of 40 critically ill conscious patients above 18 years old intubated and attached to MV for more than 24 hours

Settings: Casualty and general ICU of Alexandria Main University Hospital.

Instrument: Dyspnea assessment tool used to collect the data and was developed after reviewing the related literature.^(5,6,9,14) It consisted of **two parts**. **The first part** consisted of the patients' characteristics, MV parameters and the respiratory distress manifestations associated with dyspnea. Arterial blood gases (ABG), peripheral oxygen saturation (SPO₂), vital signs, anxiety, pain level, blood hemoglobin level (Hb) were also assessed. **The second part** of the tool consisted of the dyspnea scale. The Modified Borg Scale (MBS)^(5, 15) was used to assess dyspnea in MVPs. It is a 12-point scale (0, 0.5, 1–10) with numbers corresponding to descriptions regarding the amount of dyspnea, with no dyspnea rated as 0 and worst maximal dyspnea rated as 10.

Data collection: The patient's characteristics and health relevant data were recorded. The manifestations of respiratory distress associated with dyspnea, were continuously observed.

If any abnormality in breathing dynamics was present, dyspnea assessment was done by asking patients first "do you have trouble breathing". If the answer was yes, then they were asked to rate the intensity by telling the patients the items of Modified Borg Scale (MBS) and ask them to select the dyspnea level. Finally mechanical ventilation settings, vital signs, Hb level, ABG and SpO₂ were assessed and documented. Pain and anxiety were also assessed by visual analog scales (10-cm VASs to evaluate anxiety ("no anxiety" to intolerable anxiety") and pain (no pain" to "intolerable pain").

Data Analysis: Patient were categorized according to the dyspnea as "present" or "absent" and therefore defining two groups of patients. The patients groups were compared using Wilcoxon rank sum tests for quantitative variables and the Fisher's exact test for qualitative variables. A multiple logistic regression with a backward stepwise model selection was used to identify factors independently associated with dyspnea. All tests were two sided, and p values < .05 were considered statistically significance. The statistical analyses were performed using SPSS version 17.

Results

Result of this study shows that more than half of the study sample had dyspnea (55%) and the mean age of dyspneic patients was 53.39 ± 17.0 . The majority of the study sample (77.5%) was males (90.9% of them were dyspneic). One half of the study sample suffered from pulmonary disorders and 59.1% of them had dyspnea. The mean score of dyspnea modified Borg scale was 6.0 ± 1.8 and this reflect the moderate to intense level of dyspnea. This table also shows that there was significant difference between dyspneic and non dyspneic patients in term of hemoglobin level.

Findings of current study revealed that 31.8% of the dyspneic patients had fever, 27.3% of them had pain and 63.6% of them had anxiety. Dyspneic patients exhibited abnormalities in breathing dynamics (using of accessory muscle) while, non dyspneic ones did not exhibit any abnormality in breathing dynamics. Also dyspneic patients were more attempting to sit up in bed, had higher respiratory rate (RR), higher HR, higher systolic blood pressure (SBP) and diastolic blood pressure (DBP), lower Hb level, lower SpO₂, lower FiO₂%, lower Vt, lower flow rate, lower PEEP, higher PS, and higher PAP than non dyspneic patients. There were statistically significant differences between dyspneic and non dyspneic patients

regarding RR, HR, SBP, DBP, Hb level and SpO₂. It was observed that dyspneic patients were on assist control ventilation (ACV) mode and PSV mode while, non dyspneic patients were on biphasic positive airway pressure (BIPAP), synchronized intermittent mandatory ventilation (SIMV), and continuous positive airway pressure (CPAP) modes and there were statistically significant differences regarding ventilator modes, PAP in dyspneic and non dyspneic patients.

Also it was found that 86.4% of the patients had moderate to intense level of dyspnea. Of those 50% had moderate dyspnea and 36.4% had intense dyspnea. There were statistically significant differences between dyspnea intensity level (mild, moderate and severe dyspnea) regarding abnormalities in breathing dynamics, RR, HR, SBP, and PAP.

Discussion

Poor patient-ventilator interaction causes discomfort and dyspnea.⁽¹⁶⁾ Optimizing patient comfort is a main concern in the ICU and relieving immediate suffering is indeed a natural mission of all caregivers.⁽¹⁷⁾ Therefore, the aim of this study is to assess dyspnea in MVPs.

Regarding the **presence and intensity level of dyspnea in MVPs**, the findings of this study highlight that dyspnea is more frequent in MVPs and our result revealed that more than half of the study sample had dyspnea and the majority of them experienced moderate to intense level of dyspnea. This may be related to assessment of dyspnea in MVPs is neglected due to safety feeling of critical care nurses that MV provide support to patients attached to it. In addition, lack of knowledge and skills related to dyspnea in MVPs. These findings are consistent with Bissett et al⁽¹⁸⁾ and Twibell et al⁽¹⁹⁾ findings who reported that patients had moderate and high levels of dyspnea during MV. On the contrary, Decavèle et al⁽²⁰⁾ and Merchán-Tahvanainen et al⁽²¹⁾ results which revealed that MVPs had low to moderate levels of dyspnea.

In relation to **the characteristics of the study sample**, one half of the sample diagnosed with pulmonary disorders. This may be due to that the majority of subjects were adult male and more than one third of them were elderly. This may be due to smoking history and aging which affecting on the lung volume. As people are older, their lung functions start to decline (Veljković, 2019).⁽²²⁾

In our study, Dyspneic and non dyspneic patients did not differ significantly in term of patients' diagnosis. This may be due to presence of many factors which contribute to dyspnea in MVPs. This result is in agreement with Schmidt et al. (2011)⁽⁶⁾ who found that intensity, characteristics and prevalence of dyspnea did not depend on the cause of respiratory failure and this result suggests that dyspnea may be caused by pathophysiology of disease. Indeed, patients with pulmonary disorders reported dyspnea that is may be related to the hyperinflation-induced volume restriction as in COPD patients.^(17, 23)

Mechanical ventilation and critical illness induce great anxiety and distress in hospitalized patients. **Anxiety and pain** may increase dyspnea by stimulating ventilatory drive.⁽²⁴⁾ We found that there were no statistically significant differences between dyspneic and non dyspneic patients regarding anxiety and pain in MVPs. This may be due to MVPs may be unable to communicate their distress, anxiety and pain. It was reported by Schmidt et al⁽⁶⁾ that pain and anxiety were more frequent in dyspneic than in non-dyspneic MVPs and dyspnea was significantly associated with anxiety.

As **hemoglobin** is a common generator of dyspnea, and at the same time there was an association between anemia and failure of weaning from MV.⁽²⁵⁾ So, it is of most importance to assess hemoglobin level and correlate it with dyspnea in MVPs. Dyspneic patients had lower hemoglobin level than non dyspneic patients and there was statistically significant difference between dyspneic and non dyspneic patients in term of hemoglobin level. Multivariate analysis showed that there was no significant association between dyspnea and hemoglobin. This is similar to Schmidt et al. (2011)⁽⁶⁾ who found that there was no association between dyspnea and hemoglobin.

Ventilatory settings might be involved in the genesis of dyspnea, in addition to **ventilatory mode**. In the present study, dyspneic patients were usually on ACV and PSV modes and there were statistically significant differences regarding ventilator modes, PAP in dyspneic and non dyspneic patients. This may be due to higher respiratory rate in ACV which increase inspiratory efforts and hence increase work of breathing. Schmidt et al (6) reported that ACV was the principle cause of dyspnea and found that the ACV mode was independently associated with dyspnea⁽¹⁷⁾

Regarding **Pressure support ventilation**, there were no statistically significant differences between dyspneic and non dyspneic patients. This may be due to that the mean pressure support in dyspneic patients is to some extentsimilar tonon dyspneic patients. On the contrary, Vaporidiet al (2019)⁽²⁶⁾ who found low pressure support levels have also been associated with a sense of excessive inspiratory effort and there was a trend toward more dyspnea in those who received a pressure support ventilatory mode with a pressure support level < 15 cm H₂O.⁽⁶⁾

Other factor may contribute to dyspnea in MVPs is a low **tidal volume**. We found that there was no statistically significant difference between dyspneic and non dyspneic patients in relation to tidal volume. This may be also related to small variations in the value of the tidal volume in the dyspneic and non dyspneic patients. This is against Rauxet al (2019)⁽²⁷⁾ found that low tidal volumes were associated with air hunger.

Moreover, the **inspiratory flow** is among the ventilator settings that may be lead to dyspnea. Our findings indicate that dyspneic patients had a lower inspiratory flow than non dyspneic patients. This may be due to that ventilator flow rate is not adjusted to match the high respiratory demands of critically ill patients. Also there was no statistically significant difference between dyspneic and non dyspneic patients in the term of inspiratory flow. These findings are consistent with Schmidt et al.⁽⁶⁾and Binks et al (2017)⁽²⁸⁾ findings that an inspiratory flow below 1 l/sec equates to a risk of generating dyspnea.

Conclusion

It can be concluded that dyspnea is present in more than half of the MVPs. Moderate to intense dyspnea is more frequent in MVPs. Assessment of dyspnea in the MVPs is feasible and applicable.

Ethical Clearance: The Research and Ethical Committee of the Faculty of Nursing, Alexandria University approved the study, and an ethical clearance was issued. Permissions were requested from hospitals' management and unit's managers. Participation in the study was voluntary and an informed written consent was obtained from patients after explaining aim of the study. The right to refuse to participate or to withdraw from the study was emphasized to patients. Confidentiality of participants was maintained.

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References

1. Branson R, Blakeman T Robinson B. Asynchrony and Dyspnea. *Respiratory Care* 2013; 58 (63): 973-989.
2. Lansing R, Gracely R, Banzett R. The Multiple Dimensions of Dyspnea: Review and Hypotheses. *Respir Physiol Neurobiol* 2009; 167 (1): 53-60.
3. Parshall M, Schwartzstein R, Adams L, Banzett R. An Official American Thoracic Society Statement: Update on the Mechanisms, Assessment, and Management of Dyspnea. *Am J Respir Crit Care Med*.2012; 185(4): 435-452.
4. Laviolette L, Laveneziana P. Dyspnoea: a Multidimensional and multidisciplinary approach. *Eur Respir J* 2014; 43: 1750–1762.
5. Spector N, Klein D, Connolly M, Carlson K. Dyspnea: Applying Research to Bedside Practice. *AACN Advanced Critical Care* 2007; 18 (1): 45-60
6. Schmidt M, Demoule A, Polilo A. Dyspnea in mechanically ventilated critically ill patients. *Critical Care Med*. 2011; 39 (9): 2059-2065.
7. Chlan L, Savik K. Patterns of Anxiety in Critically Ill Patients Receiving Mechanical Ventilatory Support. *Nurs Res*. 2011; 60 (3 Suppl): 50-57.
8. Tracy M, Chlan L. Nonpharmacological Interventions to Manage Common Symptoms in Patients Receiving Mechanical Ventilation *Critical Care Nurse* 2011; 31 (3): 19-28 www.ccnonline.org
9. Grossbach I, Chlan L, Tracy M. Overview of Mechanical Ventilatory Support and Management of Patient- and Ventilator-Related Responses. *Critical Care Nurse* 2011; 31(3): 30-44.
10. Chlan L, Tracy M, Grossbach I. Achieving Quality Patient-Ventilator Management: Advancing Evidence-Based Nursing Care. *Critical Care Nurse*. 2011; 31(6) :46-50.
11. Parveen S, Thaniwattananon P, Matchim Y. Dyspnea Experience and Dyspnea Management in Patients with Chronic Obstructive Pulmonary Disease in Bangladesh. *Nurse Media Journal of Nursing* 2014; 4 (1): 703-714.
12. Hansen-Flaschen J. Dyspnea in the ventilated patient: a call for patient-centered ventilation. *Respir Care* 2000; 45(12):1460-1467.

13. Pierson D. Patient-Ventilator Interaction. *Respiratory Care* 2011; 56 (2): 214-228.
14. Campbell M, Templin T, Walch J. A Respiratory Distress Observation Scale for Patients Unable to Self-Report Dyspnea. 2010; 13(3): 285-289.
15. Grgic J, Sabol F, Venier S, Mikulic I, Bratkovic N, Schoenfeld BJ, Pickering C, Bishop DJ, Pedisic Z, Mikulic P. What dose of caffeine to use: acute effects of 3 doses of caffeine on muscle endurance and strength. *International Journal of Sports Physiology and Performance*. 2019 Sep 9;1(aop):1-8.
16. Blanch L, Villagra, Sales B, Montanya J. Asynchronies during mechanical ventilation are associated with mortality. *Intensive Care Med*. Published online: 2015.
17. Schmidt M, Banzett R, Raux M. Unrecognized Suffering in the ICU: Addressing Dyspnea in Mechanically Ventilated Patients. *Intensive Care Med*. 2014; 40(1): 1-10.
18. Bissett BM, Leditschke IA, Neeman T, Boots R, Paratz J. Inspiratory muscle training to enhance recovery from mechanical ventilation: a randomised trial. *Thorax*. 2016; 1;71(9):812-9.
19. Twibell R, Siela D, Mahmoodi M. Subjective perceptions and physiological variables during weaning from mechanical ventilation. *American Journal of Critical Care*. 2003;1;12(2):101-12.
20. Decavèle M, Similowski T, Demoule A. Detection and management of dyspnea in mechanically ventilated patients. *Current opinion in critical care*. 2019 1;25(1):86-94.
21. Merchán-Tahvanainen ME, Romero-Belmonte C, Cundín-Laguna M, Basterra-Brun P, San Miguel-Aguirre A, Regaira-Martinez E. Patients' experience during weaning of invasive mechanical ventilation: A review of the literature. *Enfermería Intensiva (English ed.)*. 2017 1;28(2):64-79.
22. Veljković D, Deljanin Z. Incidence trend of chronic obstructive pulmonary disease. *Acta Medica Medianae*. 2019;58(2):16-21.
23. Rock LK, Schwartzstein RM: Mechanisms of dyspnea in chronic lung disease. *GUTT Opin Support Palliat Care* 2007; 1: 102-108.
24. Jafari H, Courtois I, Van den Bergh O, Vlaeyen JW, Van Diest I. Pain and respiration: a systematic review. *Pain*. 2017 Jun 1;158(6):995-1006.
25. Docherty A, Walsh T. Anemia and blood transfusion in the critically ill patient with cardiovascular disease. *Critical Care* 2017; 21:61.
26. Vaporidi K, Akoumianaki E, Telias I, Goligher EC, Brochard L, Georgopoulos D. Respiratory drive in critically ill patients: pathophysiology and clinical implications. *American journal of respiratory and critical care medicine*. 2019 22(ja).
27. Raux M, Navarro-Sune X, Wattiez N, Kindler F, Le Corre M, Decavele M, Demiri S, Demoule A, Chavez M, Similowski T. Adjusting ventilator settings to relieve dyspnoea modifies brain activity in critically ill patients: an electroencephalogram pilot study. *Scientific reports*. 2019 ;12;9(1):1-0.
28. Binks AP, Desjardin S, Riker R. ICU clinicians underestimate breathing discomfort in ventilated subjects. *Respiratory care*. 2017 1;62(2):150-5.

The Effect of Self-Regulated Learning Strategy in Motor Hyperactivity and Learning the Performance of Skill of Jump Shot in Basketball for Freshmen High School Students

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Abstract

The study aims to identify the effect of the strategy of self-regulated learning in the motor hyperactivity and learning the performance of the jump shot skill of the basketball for freshmen high school students. The researchers used the experimental design with the experimental and control groups in pre and post. This study was conducted at Al-Fursan High School, the General Directorate for Education of Al-Rusafa II for the academic year 2017-2018. Male students aged 15-16-years were surveyed using hyperactivity scale to detect the phenomenon that correspond to the study problem. Students who scored (28) on this scale were purposively selected to represent (36.842%) of the original community. They were divided into two equal groups; study and control. Each group included (14) students. The researchers prepared six educational units that are applied in the physical education lesson for the study group. The study results revealed that the self-regulated learning strategy has proved its effectiveness in reducing hyperactivity and its good investment in the physical education lesson. The self-regulated learning strategy proved its effectiveness in learning the performance of jump-shot in basketball for freshmen high school. The researchers recommend that it is necessary to pay attention to the periodic psychometry in the physical education lesson in the high school to detect unwanted behaviors and change them into active and productive behaviors, and training teachers and develop their own abilities in the application of educational strategies in the physical education lesson and caring for the modern of such strategies.

Keywords: *Self-Regulated Learning; Motor Hyperactivity; Jump-Shot*

Introduction

The teaching process should be viewed as a unit that includes (objective, content, and method), and that the lesson; as a whole or parts, is closely linked to these three factors,” said Ahmed. “Some of the specialists in the field of physical education teaching that the content of the physical education lesson includes some components, including a compound set of concepts, standards, and facts, and a range of sports performance method⁽⁶⁾.

“It is necessary to assess the level of motor development that a student reaches to determine what skills he has learned and what he has not yet learned,” said Mona and Jamal. ⁽⁷⁾

Pintrich and Zeidner define the self-regulated learning (SRL) strategy as “a meaningful and active

process. Learners set their educational goals and then attempt to monitor, organize, and control their cognitive, motivational, and behavioral characteristics, and their orientations in the learning environment”.⁽¹⁰⁾

“The aim of self-regulation is to regulate the personal, behavioral, and environmental factors that influence the learner’s performance in learning situations,” said Youssef Mohamed. ⁽⁹⁾

The learner leaders in the learning groups after roles assignment among them acquire personal and professional skills at a high level, which deepens the concept of learning as the practice facilitates the learning process of the less-experienced students in an organized and supported manner ⁽¹¹⁾.

Hyperactivity is defined as “excessive, inappropriate behavior of the position, no direct goal, inappropriate

development of the child's age, negatively affecting and accumulating behavior and increasing in males more than females."⁽⁵⁾

The academic researcher specialized in motor learning and teaching method should differentiate between the types of these behaviors for the purpose of controlling them by adopting the scientific method. Thus, they can control the system in the lesson and enable the teacher to achieve his objectives, shaping the future student personality, in addition to maintaining the spirit of teamwork and cohesion among students. This calls for continuing the scientific efforts to supply the educational process; particularly the physical education lesson, with specialized research including the psychological studies that deal with the study of behavior at different stages of life. The importance of this study lies in the importance of diagnosing and analyzing hyperactivity among middle school students.

Self-regulated learning involves metacognitive (planning, self-monitoring, evaluation, reflection) and motivational (effort, self-efficacy) processes engaged by learners to reach self-set goals ⁽⁶⁾.

One of the duties of the school is to create and organize a safe learning environment for students who are inherently descended from different social environments and families. This difference is associated with many factors. Usually, such a difference leads them to seek self-affirmation among their peers. This clearly appears in his behavior of dealing with peers which takes different forms. The researchers; throughout their visits to the schools, noticed different, unwanted behaviors including hyperactivity against others that arises among cohort in the physical education lesson, which allows them to move freely and play unrestrictedly compared to other restricted classroom environments. This enables those meant by exploring to observe these behaviors, which require careful measurement with objective tools within the parameters of the psychometric measurement of the methodology of scientific research to suit the students' characteristics, their age, level, and then the educational institutions service to prepare the programs for it later. The problem of the study lies in the researchers' attempt to achieve this diagnosis to find the scientific answer to the following question: Does the SRL strategy help in investing the organization of the excessive students' movement in favor of learning the skillful performance of jump-shot in basketball?

The study aims to (1) identify the influence of the SRL strategy on the hyperactivity of freshmen high school students, and (2) recognize the influence of the SRL strategy on learning the performance of jump-shot skill in basketball for these students.

The researchers hypothesized the following:

1. There are statistically significant differences in the hyperactivity and learning the performance of jump-shot skill in basketball between the pretest and posttest between groups.
2. There are statistically significant differences in the hyperactivity and learning the performance of jump-shot skill in basketball between for the posttest time between groups.

Method

An experimental, pretest-posttest design with two groups; study and control, was used to guide this study.

The boundaries of the research community in this study were represented by the high school freshmen. The study included 76 male students, age 15-16-years, who were recruited from Al-Fursan High School in Al-Rusafa side in Baghdad City. for the academic year (2017/2018). The study participants were selected by surveying using a scale for hyperactivity. Students who score 8 or above on this scale would be involved ($n = 28$) who were purposively selected. They represent (36.842%) of this society. Twenty students were assigned in the pilot study to test the modified version of the scale. Participants in the main study sample were assigned using the simple random sample method; 14 students in each group.

Measuring tools and study procedures: In order to diagnose hyperactivity, the hyperactivity scale developed by Abdul- Ameer⁽²⁾ was adopted. It consists of 15 items with a total score of (15). Minor modifications and adapting it to 20 students to find the scientific bases. The researchers designed a performance evaluation form that includes three sections of performance the jump-shot in the basketball of (10) degrees. This performance is revealed after the students' videotaping and presented to three specialists in basketball tests.

After preparing the measuring tools for the study experiment, the educational units were prepared using the SRL strategy to employ excess energy from excessive activity in the sense of the concept of hyperactivity by

directing the students well according to the determinants of motor performance of the skill. At the same time, the educational units aim to regulate the cognitive information pertinent to that skill and the harnessing of the learner's energy for proper performance since it is not limited to the accuracy of the scoring, but the movement and harmony of the body parts of the requirements of the optimal performance that helps to such an accuracy later. The teacher's duty is to create the educational environment appropriate for applying such a strategy to be a lesson that is free from restrictions, be concerned with the learners' directions and feedback of self-

regulation. Such strategies are considered as meaningful and active learning strategies sought by modern learning schools in various sciences. The educational units have been applied among students with hyperactivity for 45-days in an average of one educational unit per week for the academic year 2017-2018 after finishing the formal school time. Data were analyzed using the statistical package for social sciences (SPSS) version 24. The statistical measures of percentage, arithmetic mean, standard deviation, independent-sample T-test, and paired-sample T-test were used.

Results

Table 1. The equivalence of the study groups in the pretest

Tests	Study Group (n = 14)		Control Group (n = 14)		t	Sig.	Sig. Level
	Mean	SD	Mean	SD			
Hyperactivity	10.5	1.653	10.14	1.875	0.535	0.597	NS
Performance of jump-shot skill	2	0.961	2.43	1.089	1.104	0.28	NS

Significant at $p \leq 0.05$ at 0.05, degree of freedom $n-2 = 26$

Table 2. Pretest and posttest tests for the study and control groups

Tests and measurement Unit	Group	Pretest		Posttest		Mean Difference	Std. Error Mean	t	Sig.	Ass.
		Mean	SD	Mean	SD					
Hyperactivity	Study	10.5	1.653	4.5	0.65	6	1.922	11.683	0.000	S
	Control	10.14	1.875	6.57	0.646	3.571	2.065	6.472	0.000	S
Performance of jump-shot skill	Study	2	0.961	7.71	0.469	5.714	1.069	20	0.000	S
	Control	2.43	1.089	5.29	0.469	2.857	1.167	9.158	0.000	S

$n = 14$ for each group; Significant at $p \leq 0.05$, degree of freedom = 13 at 0.05; S = Significant

Table 3. The equivalence of the study groups in the posttest

Tests	Study Group (n = 14)		Control Group (n = 14)		t	Sig.	Sig. Level
	Mean	SD	Mean	SD			
Hyperactivity	4.5	0.65	6.57	0.646	8.453	0.000	S
Performance of jump-shot skill	7.71	0.469	5.29	0.469	13.706	0.000	S

Significant at $p \leq 0.05$ at 0.05, degree of freedom $n-2 = 26$; S = Significant

Reviewing the results of Table (2) reveals improvements in the values of the variables of the study and control groups. Reviewing Table (3) displays that the students in the study group members outweighed their counterparts in the control group pertinent to the dependent variables. This finding could be attributed to the role of SRL strategy that enabled the students to reorganize their experiences and information, improve

excessive and random movement in the class, and guide it towards proper skill performance that requires aesthetic and quality determinants in the three skill sections. Thus, two objectives were met by one action that is positively reflected on the psychological status in its improvement whatever the reasons for such opportunities. At the same time, the skilled performance that requires regulating the experience and information as indicated to regulate the

movement. As well as, it helped to increase the number of units to six for one skill in improving the values of skill improvement for the performance of this skill in basketball. For the students in the control group, the researchers attribute the improvements to the role of the sports education lesson, and it achieves of educational and learning goals.

Al-Busidistated that SRL differs from self-learning developed by Skinner or using computers. In his theory, Deutsch could determine the relationship form between different organizations of mutual social interdependence⁽¹⁾.

Qatami stated that “The aim of Uzbel is to study the cognitive structure of the learner and the higher mental processes in order to achieve a meaningful learning and increase the efficiency of the processes of cognitive processing of the information using multiple cognitive processes and at reasonable times that facilitate the task of storing these knowledge, their transfer, and integration into the learner’s cognitive structures”⁽⁸⁾.

Thorndike stated that “The teacher and the learner must determine the characteristics of the good performance so that the practitioner can be organized to be able to diagnose errors and not repeated them and the difficulty to modify,”⁽⁴⁾

Conclusions and Implications:

1. The SRL strategy has proved its effectiveness in reducing hyperactivity and good investment in the physical education lesson among freshmen.
2. The SRL strategy has proved its effectiveness in learning the performance of jump-shot in basketball for freshmen.

The researchers recommend the following:

1. It is necessary to pay attention to the process of periodic psychometry in the physical education lesson in the high school to detect unwanted behaviors and turn them into active and productive behaviors.
2. It is necessary to train teachers and develop their own abilities in the application of educational strategies in the physical education lesson and paying attention to the modern of such strategies.

Conflict of Interest: The researchers report no conflict of interest.

Funding: This study did not receive any funding from any agency.

Ethical Clearance: A permission to conduct this study was obtained from the ethical committee in the College of Basic Education, University of Mustansiriyah

References

1. Ahmed IM. Curricula and teaching method in physical education. Cairo: Dar Al-Fikr Al-Arabi for Printing; Publishing, and Distribution; 1998.
2. Al-Busidi UB. Preferred learning styles among a sample of secondary school students in Mascot City and their relationship with each of gender, academic achievement, and specialty. [unpublished master thesis],[Mascot, Oman], College of Education, Sultan Qaboos University; 1999.
3. Abdul-Ameer HO. Effect of playing therapy for children with hyperactivity who age 8-10-years. Journal of Sciences of Physical Education, 2013, 1(6), 80.
4. Abu Jado SM. Educational psychology. 3rd ed. Amman: Dar Al-Maseerah for Printing and Distribution; 2003.
5. Al-Hadeedi M & Al-Khateeb J. Learning strategies for students with special needs. Amman: Dar Al-Maseerah for Printing and Distribution; 2005.
6. Zimmerman BJ. Development and adaptation of expertise: Therole of self-regulatory processes and beliefs. (2006). In K. A. Ericsson, N.Charness, P. J. Feltovich, & R. R. Hoffman (Eds.), The Cambridge handbook of expertise and expert performance (pp. 705–722). New York, NY:Cambridge University Press.
7. Al-Husaini S. An introduction to research in education. Amman: Dar Al-Maseerah for Publishing and Distribution; 2013.
8. Qatami, Y. M. Cognitive theory in learning. Amman: Dar Al-Maseerah for Publishing and Distribution; 2010.
9. Qatami, Y. M. Theories of learning and education. Cairo: Dar Al-Fikr Al-Arabi for Printing Publishing, and Distribution; 2005.
10. Pintrich, P.R. & Zeidner, M. (2000). The role of goal orientation in self-regulated learning. Cited in Boekaerts, M.(Eds.). Handbook of self-regulation. San Diego: CA: Academic; 2000.

11. Morton, J. P. (2008). Learning to be a sport and exercise “scientist”: evaluations and reflections on laboratory-based learning and assessment. *Journal of Hospitality, Leisure, Sport & Tourism Education (Oxford Brookes University)*, 7(2), 93–100. Retrieved from <https://search-ebshost-com.ezproxy.okcu.edu/login.aspx?direct=true & db=s3h & AN=35367925 & site=ehost-live>

The Influence of Tactical Approach Exercises on the Tactical Behavior of Some the Attack and Defense Skills by Foil (Fencing)

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Abstract

The study aimed at identifying the effect of tactical approach exercises on the planning behavior of some offensive and defensive skills of the foil in the research sample. Use the experimental method by designing the experimental and control groups with pre- and post-test on a sample of second stage students. The experimental group that learns the skills under study using the planetary approach exercises. After the implementation of the curriculum and post-test, Then statistical treatments concluded that the tactical approach exercises carried out by the experimental group in learning the skill performance have positively influenced the analysis of the results of the planning behavior of some offensive and defensive skills in the foil better than the control group that did not develop in the analysis of planning behavior. In light of the conclusion, it is recommended to adopt the tactical approach exercises in developing the planning behavior of some offensive and defensive skills in the foil..

Keywords: Exercises, Planetary Approaches, Planned Behavior, foil.

Introduction

When teaching or training to the fence, the learner must reach a degree of progress so that you clearly understand the end of the kinetic sentence you perform and why? They must know the purpose of their efforts, they should also be encouraged to control skills, learn about their performance situations and learn how to apply them⁽¹⁾Therefore, we find several basic elements within the process of learning and training fencing sport and these elements (rapid decision-making, response speed, behavioral planning correct behavior) in order to carry out a kinetic sentence ending with atouch of the competitor, with high flexibility in thinking, where these factors are very important for the player Fencing, and the lack of availability leads to the failure to ensure the fulfillment of technical and tactical duties (technical and planning skills) and the rapid adaptation of the reactions of competitors of different planning behavior⁽⁴⁾

When you look at the exercises approach planners as one of the method used to learn and develop the basic skills, the characteristics of these exercises became clear by creating an atmosphere similar to the atmosphere of competition and close to it, as the learner performs during

the performance of these exercises skills and planning, and thus linking learning skills and plans, as it is one The method that gain the learners how to perform the skill in the competition according to gradual steps, and the purpose of using this method is to develop performance in play and interaction to unify the planning and the implementation of the skill in the conduct of the correct plans ends with a legal touch.

Through the above, the researchers considered conducting a study in which they try to pay attention to the planning side along with their interest in the skill side through the use of exercises that make the learners learn in an atmosphere similar to the atmosphere of competition, namely exercises approach approaches to know their role in performing the correct planning behavior of the performance of offensive and defensive skill in the arm For students to improve the educational process for the better.

Search Problem: Through the follow-up and informed the researchers being a teacher of physical education and sports science noticed that there is a discrepancy between learners in learning the planning aspects of some fencing skills, and also found it difficult

to perform learners when linking more than one skill with each other, especially the skills of the foil, and most learners are able to perform some fencing skills, but they find it difficult to perform the same skills when placed in the atmosphere of competition with associates, and maybe the reasons for this is to pay attention to the physical side and skills and a greater degree than the interest in the planning side and therefore find it difficult learners in choosing the most appropriate plan and Best behavior among several actions.

Therefore, the researchers considered the development of solutions to this problem through the use of exercises approach planners, which urges the learner to perform skills with the implementation of the plans and thus know the role of these exercises in the planning of the performance of offensive and defensive skill in the arm of the foils educated students.

Research Objective: Identify the impact of the tactical approach exercises in the planning behavior of some offensive and defensive skills of the foil at the research sample.

Research hypothesis: Planned approach exercises have a positive effect on the planning behavior of some offensive and defensive skills of the foil at the research sample.

Defining terms:

Planetary Approaches Exercises: It is an encouraging approach to solve the planning tasks and a coherent link between learning and mastering the planning skills and moving within gradual steps that give the learner how to learn the performance of skill in the competition and the purpose of using this method is to develop performance in the game and interaction to unify the planning and implementation of the skill⁽⁹⁾

Planned behavior: It is the achievement of the goal mentally before the performance or is a prediction of the movement coupled with performance, implemented through a movement or a group of movements used to solve a certain duty based on the prediction of the movement of the tool or opponent or colleague and others⁽³⁾

Research Methodology and Field Procedure:

Research Methodology: Use the experimental approach with controlled design to design the

experimental and control groups with pre- and post-test to suit the nature of the problem to be studied.

Research community and sample: The research community identified the second stage students in the College of Physical Education and Sports Sciences for girls/University of Baghdad for the academic year

(2018-2019) and the number of 106 students distributed over 4 divisions, and through the draw was selected Division (A) number of 26 students representing the experimental group, which learn skills under The study using the planners approach exercises, and Division (C) and the number of 28 students representing the control group, which learnt he skills of fencing according to the usual teaching method followed (skill exercises and physical), and thus the total number of the main experiment sample (54) students and a percentage of (51%) of the total community, Tjan was confirmed O The two samples are valued through pretest.

Analysis of the planning behavior of some offensive and defensive skills of the foil: For analyzing the offensive and defensive planning behavior in the foil for the educated in practice, individual competitions were conducted, each student competing for scientific research, and then the analysis of tribal rivalries by three tribunals after filming, by taking the arithmetic mean of the degrees of the courts according to the competition analysis from approved in previous studies⁽⁶⁾The objective of the analysis of the competition was to identify the level of planning behavior of members of the research sample.

Main trial procedures:

Pre-test: After, the survey was conducted on 25-2-2019 the pre-test of the experimental and control groups was conducted to analyze the planning behavior of some offensive and defensive skills of the Blind weapon through video shooting, on 3-3-2019, according to competitions for scientific research in the fencing hall. The pre-test was used for homogeneity and equivalence of the two research samples as in Table (1) show in pag6.

Prepare an educational curriculum using the Planetary Approach exercises: An educational curriculum has been prepared using the tactical approach exercises for the skills of the fencing weapon in the fencing according to the vocabulary of the sectoral sector.

Therefore, to learn the offensive and defensive skills according to exercises close to the competition conditions. And against any competitor. What are the opponent’s weaknesses and strengths? In order to perform this kind of attack or defense movement. The curriculum was implemented from the date of 4-3-2019 to 6-5-2019 on the experimental group; the control group remains the usual way (physical and skill exercises) to learn the offensive and defensive skills of the Blind.

Post-test: The experimental and control groups were analyzed after the experimental and control groups to analyze the planning behavior of some offensive and defensive skills of the Blind on 7-5-2019, in the fencing hall. Taking into account all the temporal and spatial conditions conducted in the pretest.

Statistical means: The statistical package (SPSS) was used to process the results according to the following laws:

- Arithmetic mean.
- Standard deviation.
- The law of interconnected samples.
- Law for independent samples discussion of results:

Presentation of the results of pre-posttests in the experimental research group: Table (2) page 6 showed that there were significant differences between the values of the arithmetic media and the values of the standard deviations of the pre and post-tests in the experimental group. This means that there are significant differences in the interest of the post-test in the experimental sample the development of the experimental group is attributed to the use of tactical approach exercises when learning the skills of the Blind weapon. Through the tactical approach exercises, learners generate programs about their behavior that store these programs in memory, which helps to realize the required attitudes and

behavioral plans after the stimulus has occurred and in the form of mental processes⁽⁸⁾

In addition, the competing teammates always try to hide as much of their actions as possible. The more it assimilates all the information and analyzes it properly, the more it will be able to react quickly. Therefore, “understanding and analyzing competition is the knowledge of the overall competition relationships, the position of competitors and their strategic objectives⁽⁵⁾

Planned approach exercises place the learners during skill learning in situations that make them think about the action and planning required, in order to develop their mental and cognitive ability by giving them information to organize the competition and to take appropriate action. This theoretical information was applied in the form of exercises that serve the tactical behavior of some offensive and defensive skills in the foil.⁽⁷⁾

Presentation of the pre- and post-test results of the control group and their discussion: Table (3) page 6 showed that there were no significant differences between the values of the arithmetic media and the values of the standard deviations of the pre- and post-tests of the control group. This means that there were no significant differences in the control sample. As the information is given to the control group and the skill performance performed emphasizes the skilled technique and is of no value even if performed skillfully during the stages of learning and training, unless the learners can apply what they learn from skills during the actual competition, and they can analyze each new situation, and realize any Of the movements and plans that can or cannot be used in it, for example, if we note “the movement of the arrow in the fencing depends on the element of surprise and speed in performance, and lead when the opponent leads one of the attacks and return to standby, so that the distance between the opponents is large and the attacker initiates Iha.⁽²⁾

Table 1: Shows the statistical parameters between the two research groups in the pretest tests for homogeneity and equivalence

Significance of differences	.Sig	T-Test	.Sig	The value of Levin	± p	s		Analysis of the planning behavior of some offensive and defensive skills
Immaterial	0.268	1.12	0.758	0.096	1.29	4.65	Expert mental	
					1.35	4.25	Officer	

Significant at significance level ≤0.05

Table (2) shows the statistical parameters to find the differences between the pre-post tests in the experimental group

Significance of difference S	.Sig	T-Test	P	Q.	± p	S		Analysis of the planning behavior of some offensive and defensiveskills
Moral	0.000	35.4	1.82	12.69	1.29	4.65	before me	
					1.19	17.34	after me	

Significant at 0.05 level

Table 3: Shows the statistical parameters to find the differences between the pretest-posttests in the control group

Significance of difference S	.Sig	T-Test	P	Q.	± p	s		Analysis of the planning behavior of some offensive and defensive skills
Immaterial	0.113	1.87	1.74	0.62	1.35	4.2	before me	
					1.99	4.8	after me	

Significant at 0.05 level

Conclusions and recommendations: After the statistical treatments, it was concluded that the tactical approach exercises carried out by the experimental group in learning the skill performance have positively influenced the analysis of the results of the planning behavior In light of the conclusion, it is recommended to adopt tactical approach exercises in the development of the planning behavior of some offensive and defensive skills in the arm of the Blind, the fact that these exercises give the learner a positive analysis.

Conflict of interest & Source of Funding: University of Baghdad

Ethical Clearance just before the references and resubmit: By Turntin program

Ethical Clearance: Taken from as attached last page issued from University of Baghdad/higher education department.

Source of Funding: Self

References

- Esraa Qahtan Jameel:** Exercises of concentration of attention and mental perception in the accuracy and speed of response to some of the attacks of fencing (Ph.D. thesis, College of Physical Education for Girls, University of Baghdad,2007) p42.
- Raheem Helou:** The impact of special exercises in the development oft he level of behavior and intelligence of offensive planning for advanced fencing players with a weapon. (Ph.D. thesis, College of Physical Education and Sport Sciences, University of Basra, 2010)p47.
- Adel Fadel Ali:** The impact of some uses of knowledge base systems in learning programs without a symbolic model to learn the skills of offensive fencing. (Ph.D. thesis, College of Physical Education and Sports Science, University of Baghdad, 2000)p15.
- Aida Ali Hussein and Fatima Abdel-Maleh:** The Effect of a Training Program Using Kinetic Response Speed Exercises to Develop Counter-Attack Attacks and Their Relation to the Results of the Shutdowns of the Blind (Second International Scientific Conference, Faculty of Physical Education for Girls, Zagazig University,2007)p45.
- Abdul Khaliq Ibrahim; the impact of a proposed curriculum using the method of comparative competitiveness in learning the performance of the skills of the movement of legs and stabbing Blind. (Master Thesis, College of Physical Education and Sport Sciences, Anbar University, 2010)p39.
- Fatima Abdul Maleh: The Effect of a Proposed Training Curriculum for Developing Schematic

- Knowledge and the Level of Planned Behavior for Some Offensive Skills in the Blind (Ph.D. Dissertation, Faculty of Physical Education and Sport Sciences, Basra University, 2002).
7. Fatima Abdul Maleh and others; I 1: (Jordan, Arab Society Press,2010)p132,p177.
 8. Fatima Abdul Maleh and others; Sports preparation in fencing; i 1: (Al-Faisal Press, Baghdad, 2017).
 9. Fatima Abdul Maleh and ZerNamous Al-Taie; basics of fencing training. I 1: (Jordan, Arab Society Press,2015)p224.

Influence Organizational Citizenship Behavior (OCB) on Performance Nurses Public Health Centre in the District Tuban

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Abstract

Organization will successfully when employees not only do their tasks anyway but also want to do duty extra as wants to work, help one another, give advice, participate effectively, giving best services, and want to use time it works effectively but not all an employee with like willingly want to do¹. A nurse having organizational behavior citizenship behavior (OCB) the atmosphere than last year in order to have a comfortable so as to cause a working relationship which harmonious in order to increase performance workers to reach organizational goals².

The study was observational analytic, population nurses public health centre in the district tuban were 24 people, a random sampling of sampling simple .Independent variable organizational citizenship behavior and dependent variable performance nurses and research instruments using sheets kuisisioner with data analysis spearman use the rank.

Is the organizational citizenship behavior (OCB) of performance nurse.

Keywords: *Organization, citizenship, behavior, performance nurse, public health centre.*

Introduction

Human resources have a very crucial role in addition to the other. owned organization. An organization can run well and get completely as performance produced by every other component running smoothly and mutually supported³.

One attitude or behavior to improve the performance of nurses in the structure of course behavior that leads to positive things that are known as organizational behavior (ocb) citizenship that is the individual that exceeds demand and the role of. But not all employees voluntarily want to does more their formal task on their job description contains⁴

One of the ways to enhance the performance of nurses is by the presence of organizational behavior (ocb) citizenship in organization so that it will give rise to the atmosphere a harmonious work⁵. Hence, very important a nurse having organizational behavior citizenship behavior (OCB) the atmosphere than last year in order to have a comfortable so as to cause a working relationship which harmonious in order to increase performance workers to reach organizational goals⁶.

Material and Method

This research design of observational analytic, the population is nurses public health centre in the district tuban a total of 24 people, simple sampling technique random sampling .The independent variable citizenship organizational behavior and the dependent variable for the performance of nurses and an instrument the research uses a sheet of the questionnaire was test with data analysis using the spearman rank⁷.

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Findings:

1. The distribution of respondents ocb nurse

No.	OCB	f	Prosentase
1	Height	16	69,6%
2	Medium	4	17,4%
3	Low	3	13,0%
	Total	23	100%

Based on the table above can be seen from 23 (100%) respondents said that the majority of 16 (69,6%) respondents own high of ocb

2. The distribution of respondent based on the nurses

No.	Performance nurse	f	Prosentase
1	Good	12	52,2%
2	Medium	10	43,5%
3	Low	1	4,3%
	Total	23	100%

Based on the table above can be seen from 23 (100%) respondents said that the majority of 12 (52,2%) respondents have a good performance.

3. The influence of organizational behavior citizenship (ocb) on the performance of nurses

OCB	Performance Nurse			Total
	Good	Medium	Low	
Height	11 (68,8%)	5 (31,3%)	0 (0,0%)	16 (100%)
Medium	1 (25,0%)	3 (75,0%)	0 (0,0%)	4 (100%)
Low	0 (0,0%)	2 (66,7%)	1 (33,3%)	3 (100%)
Total	12 (52,2%)	10 (43,5%)	1 (4,3%)	23 (100%)
Value	$\alpha = 0,05$	$p = 0,005$		$r = 0,563$

From the table above it can be seen from 23 (100%) of respondents that almost most of which have ocb high with a good track record in 11 (68.8%) of respondents, having ocb being with the performance of being 3 (75,0%) and that has ocb low with the medium of performance 2 (66.7%)

Based on an analysis by using spss for windows with the spearman rank $\alpha = 0,05$ obtained the $p = 0,005$ value $p < \alpha$ so variable ocb have significant influence on performance a nurse with the correlation was ($r = 0,564$) and direction positive correlation means the higher ocb better performance nurse at work.

Discussion

1. **Behavior identification organizational citizenship (OCB) in nurses:** Most of nurses in public health centre in the district tuban having organizational citizenship behavior (OCB) the height.

Organizational citizenship behavior (OCB) in generally believed that to achieve excellence must have their individual performance of as high as, because basically individual performance influences the performance as a whole ocb organization is the act of someone out kewajibanya not consider

the interests of the himself[8]. This behavior have changed in line how passionate organization on welfare levels individual and appreciation organization against their contribution⁹. The majority of respondents having ocb high, because some aspects of: alturism, civic virtue, conscientiousness, courtesy, sportmanship.OCB also is the unique individual activities in working and is the customs or manners performed voluntarily, no formal is part of the job, and indirectly identified by a system of rewards¹⁰. So it can be concluded that ocb also called the behavior extra role of concurrent given individual exceeds main function⁴.

This research result indicates that there are 16 respondents own ocb high and 3 respondents own ocb. lowIt is in because the willingness of nurses to take the role of (role) that exceeds a lead role in an organization, so called as behavior any extra roles (extra role).It is to achieve the success of an organization when its members not only working on his main job just, but also want to do extra duty, like the will to cooperate, help each other, provide input into, actively involved, provide service extra, as well as wanting to use the hours are effectively.

2. **Identification performance nurse:** Performance is the result of a work or process of an end of a activities. The performance is a motion or action that have been carried out in a conscious geared to achieving a goal or a specific target. The performance was a result of working to the awards by a person or a group of people in accordance with their respective authorities and responsibilities of each party, as forms of businesses in achieving legally organizational goals, not unlawful and in accordance with moral and ethical¹¹.

The performance is an illustration of the level of achievement of implementing a program or policy activities in realizing the target, the purpose of, the vision and mission of the organization that was poured through strategic planning an organization .For that reason the performance of individual basically can be influenced by a number of factors such as the quality of, the quantity, the effectiveness of, timeliness and independence¹².

From the research the majority of respondents having a good track record .It was because the performance of supported by a factor of an external and an internal, the internal factor, that is, that deals with the properties of a person .While the external factor that is the factors that influences the performance someone who originated in the neighborhood¹³.

As behavior, attitude, and the colleague, subordinate or leadership of, work facilities and climate organization .Where factors that might have an impact on working system given by organization or the hospital .Individual ocb influences the performance, and therefore this behavior is leading to the social interaction of members of an organization are more reliable, reducing the conflict, and improve the efficiency¹⁴.

3. **The influence of organizational citizenship behavior (OCB) on the performance of nurses:** The result of this research is the organizational citizenship behavior (OCB) on the performance of nurses. OCB influential positive and significantly to the performance of individual⁸. It is anyone had showed that the of individuals having an attitude of my doubts but towards their job of his colleagues or help with the work of his colleagues the more one is high performance general of the agriculture ministry, of individuals having an inclination to favor the relevant organisation s with the role of and

decrease the participation in a central organization, of individuals having the level of consciousness of doing things which includes in this data collection referred to the dispatch priorities the presence of the use of the time of work¹⁵. The individual had tinggat awareness in working eat, employee performance will be good too individuals having a polite and manners, organization individuals having sportifits in working involving a willingness to tolerate discomfort true and risk jobs without the complaining employees own attitude sportsmanship in working for the good performance these individuals¹⁶.

Research conducted by researchers from the data can be proved the organizational citizenship behavior (OCB) by means of distributing the sheets for two times a week.This is evidenced by the results of research of 23 (100) percent of respondents said that almost entirely having ocb high performed well 11 (68,8%), respondents having ocb was with performance and 3 (75,0%) and who has low ocb with performance and 2 (66,7%).This karenakan willingness nurse to take the roles of (role) beyond, primary role in an organization so called as the behavior of the role of extra (extra-role).

It is to achieve the success of an organization when its members not only do, main function of only but also want to do the extra, as a willingness to cooperate,, help each other inform, active, provide service extra, and will want to make use of their working time effectively¹⁷.

Conclusion

The influence of organizational behavior citizenship (ocb) on performance tuban public health centre in the district nurse

Ethical Clearance: Ethical clearance of this study was taken from Ethical Committee of PublicHealth Faculty Airlangga University, Indonesia.

Source of Funding: This study was self funding by authors.

Conflict of Interest: There is no conflict of interest in this study.

References

- 1 “Pengaruh Kepuasan Kerja, Motivasi Kerja Dan Komitmen Organisasi Terhadap Kinerja Melalui Organizational Citizenship Behavior (OCB)

- Sebagai Variabel Intervening,” *Econ. Educ. Anal. J.*, 2017.
- 2 Muttaqillah dkk, “Pengaruh Stres Kerja dan Motivasi Kerja terhadap Kinerja Perawat serta Implikasinya pada Kinerja Badan Layanan Umum Daerah Rumah Sakit Jiwa (BLUD) Aceh,” *J. Manaj. Pascasarj. Unsyiah*, 2015.
 - 3 S. W. M. Hafidz, M. S. Hoesni, and O. Fatimah, “The relationship between organizational citizenship behavior and counterproductive work behavior,” *Asian Soc. Sci.*, 2012.
 - 4 E. M. Eatough, C. H. Chang, S. A. Miloslavic, and R. E. Johnson, “Relationships of role stressors with organizational citizenship behavior: A meta-analysis,” *J. Appl. Psychol.*, 2011.
 - 5 M. C. Bolino, H. H. Hsiung, J. Harvey, and J. A. LePine, “‘Well, i’m tired of tryin’!’ organizational citizenship behavior and citizenship fatigue,” *J. Appl. Psychol.*, 2015.
 - 6 Y. Putrana, A. Fathoni, and M. M. Warso, “Pengaruh Kepuasan Kerja dan Komitmen Organisasi Terhadap Organizational Citizenship Behavior Dalam Meningkatkan Kinerja Karyawan PT. Gelora Persada Mediatama Semarang,” *J. Manage.*, 2016.
 - 7 Nursalam, “Konsep Dan Teori Metodologi Penelitian Ilmu Keperawatan,” *Salemba Med.*, 2008.
 - 8 D. W. Organ, “Organizational Citizenship Behavior,” in *International Encyclopedia of the Social & Behavioral Sciences: Second Edition*, 2015.
 - 9 E. R. Lestari, N. Kholifatul, and F. Ghaby, “Pengaruh Organizational Citizenship Behavior (OCB) terhadap Kepuasan Kerja dan Kinerja Karyawan The Influence of Organizational Citizenship Behavior (OCB) on Employee’s Job Satisfaction and Performance,” *J. Teknol. dan Manaj. Agroindustri*, 2018.
 - 10 W. Harwiki, “The Impact of Servant Leadership on Organization Culture, Organizational Commitment, Organizational Citizenship Behaviour (OCB) and Employee Performance in Women Cooperatives,” *Procedia - Soc. Behav. Sci.*, 2016.
 - 11 M. A. Hafid, “Hubungan kinerja perawat terhadap tingkat kepuasan pasien pengguna yankestis dalam pelayanan keperawatan di rsud syech yusuf kab. gowa,” *J. Kesehat.*, 2014.
 - 12 R. Winasih, Nursalam, and N. Dian, “Budaya organisasi dan Quality of Nursing Work Life Terhadap Kinerja dan Kepuasan Kerja Perawat Di RSUD Dr. Soetomo Surabaya,” *Ners*, 2015.
 - 13 R. Royani, J. Sahar, and M. Mustikasari, “Sistem Penghargaan Terhadap Kinerja Perawat Melaksanakan Asuhan Keperawatan,” *J. Keperawatan Indones.*, 2012.
 - 14 I. N. Budiawan, K. Suarjana, and I. P. G. Wijaya, “Hubungan Kompetensi, Motivasi dan Beban Kerja dengan Kinerja Perawat Pelaksana di Rumah Sakit Jiwa Provinsi Bali,” *Public Heal. Prev. Med. Arch.*, 2015.
 - 15 S. Berkow, K. Virkstis, J. Stewart, and L. Conway, “Assessing new graduate nurse performance,” *Nurse Educ.*, 2009.
 - 16 M. D. Naylor and E. T. Kurtzman, “The role of nurse practitioners in reinventing primary care,” *Health Affairs*. 2010.
 - 17 S. Fox, P. E. Spector, A. Goh, K. Bruursema, and S. R. Kessler, “The deviant citizen: Measuring potential positive relations between counterproductive work behaviour and organizational citizenship behaviour,” *J. Occup. Organ. Psychol.*, 2012.

Skeletal Stability Using Adjustable Versus Mini Plates Following Bilateral Sagittal Split Ramus Osteotomy (BSSRO): A Randomized Clinical Trial

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Abstract

Background and Objective: This study aimed at assessing the skeletal stability of adjustable miniplates in comparison to conventional miniplates following bilateral sagittal split ramus osteotomy (BSSRO)

Materials and Method: Fourteen patients were divided into 2 equal groups. Patients in both groups underwent BSSRO and mandibular setback. In the study group, the bone segments at the osteotomy site were stabilized using the adjustable plates and four 2.0 mm monocortical screws. In the control group, bone segments at the osteotomy site were stabilized using conventional miniplates and four 2.0 mm monocortical screws. Each patient was assessed in terms SNB, mandibular plane angle (MPA) recorded in degrees (°) and horizontal and vertical changes of the B-Point recorded in millimeters (mm).

Results: Skeletal stability was contemporaneous in both groups with an insignificant difference regarding the assessment criteria. However, adjustable plates showed the advantage of decreasing operative time when occlusion is not perfect at the release stage and adjustments were required.

Conclusion: The choice of the fixation method should combine between sufficient stability for early jaw mobilization and elasticity to allow for intraoperative and early postoperative corrections. Such requirements were met by the adjustable plates.

Keywords: BSSRO, adjustable plates, fixation.

Introduction

Dentofacial deformity signifies significant unconventionalities from ordinary scopes of the maxillomandibular complex. In 1907, *Angle* described Class III malocclusion as when “the lower first molar is in a mesial positioned in relation to the upper first molar”. This type of deformity includes a relatively trivial segment of the regular orthodontic run through. However, these cases are among the most challenging to be treated effectually and productively.⁽¹⁾

Skeletal class III malocclusions were alleged to be solely accredited to an oversized and/or prominent mandible, this was till the 1970s. But in reality, it can be the product of mandibular prognathism with a customarily situated maxilla, maxillary retrognathism with a normal mandible or mixture of maxillary retrognathism and mandibular prognathism.⁽²⁾

The prime goals of successful orthognathic surgery are the restoration of normal jaw function, optimal facial esthetics, and long-term stability. The most common orthognathic practice is a bilateral sagittal split ramus osteotomy (BSSRO) to setback or advance the mandible. From a surgeon’s point of view, long-term stability following BSSRO may be the most imperative thing to accomplish.⁽³⁾

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Several method of fixation are used to achieve

acceptable postoperative stability, including bicortical screws or miniplates. These means are used to position the proximal and distal segment after BSSRO. Several studies have been conducted comparing the postoperative skeletal stability between different types of osteosynthesis.⁽⁴⁾

The presented study is to investigate the postoperative skeletal stability following BSSRO in mandibular setback surgeries using adjustable versus monocortical miniplates by identifying the horizontal and the vertical changes of mandibular position through lateral cephalometry.

Materials and Method

Study group: The plates used in our study were the 2.0 Dr. SABOYE adjustable plates on site manufactured by GlobalD, France. The plate was 1 mm thickness and consisted of 2 vertical plates—a long and a shorter one - connected by two adjustable arms. The long plate is was 15mm and the short one was 12mm. The distance between the two plates was 17mm having an adjustable joint in each arm that could be modified using plate-specific pliers accompanying the kit, the joints were either expanded or compressed to achieve the desired result. This was to allow anterior, posterior, clockwise and counter-clockwise directional change.

Comparator Group: Conventional 4-hole with space monocortical miniplates and screws were used.

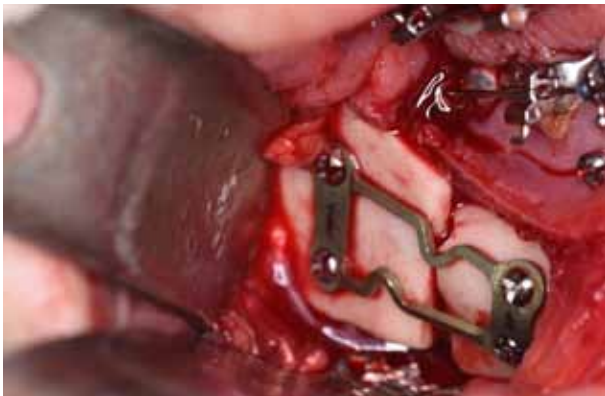


Fig. 1: Adjustable plate placement after osteotomy

Study Population: 14 patients were selected suffering from class III skeletal relationship. The history and detailed medical examination data for each patient was collected in a chart prepared specially for this study. Standard preoperative patients' photographs were taken. Fabrication of intermediate and final dental splint was carried out on the surgical model conventionally.

Clinical data: Mandibular range of motion, occlusion, wound healing, temporomandibular joint dysfunction syndromes and inferior alveolar nerve paresthesia in addition to other complications as infection or facial nerve injury was evaluated for each patient.

Radiographic data: Radiographic follow-up was achieved through lateral cephalometric radiographs. Panoramic radiographs were ordered immediately postoperatively to check the condylar position and the location of plates and screws. Lateral cephalometric radiographs were ordered immediate postoperative (F1), 3 months (F2), 6 months (F3), and 1 year postoperatively (F4) to develop cephalometric analysis which compared that performed preoperatively (F0) to evaluate the surgical changes and the amount of relapse. All radiographs were traced using Dolphin software using Wits and Stener analysis.

The Data collected included angular measurements, SNB (the angle formed between the anterior cranial base (S-N) and a line drawn through N and B point), MPA (The angle formed between the mandibular plane (Go-Me) and the anterior cranial base (S-N)) recorded in degrees (°) and horizontal and vertical changes of the B-Point (the innermost point on the contour of the mandible) recorded in mm.

Horizontal changes at B-point were measured and calculated by a perpendicular line to Frankfort horizontal plane (FH)(The plane demonstrated by a line through the orbitale and porion) passing through Nasion (N) point. Vertical changes at B-point were measured and calculated from perpendicular to FH line. Changes to these landmarks were recorded at 2 different time intervals, F0-F1 (representing the surgical change) and F1-F4 (representing the amount of relapse). Posterior movement of the mandible was represented by negative values while anterior movement was represented by positive values. On the other hand, superior movement of the mandible was represented by positive values while inferior movement was represented by negative values.

Results

Male to female ratio was 0.75 (6 males and 8 females) with average age group of 24.1 (22–27 y). All patient had class III skeletal relationship, eight required bimaxillary surgery and only six patients required only mandibular setback.

Surgical Results: For all patients, the surgical procedures were performed without any major complications. All inferior alveolar nerves were either embedded in the distal segment or visible but embedded in the distal segments. However, in two cases a bad split occurred on the left side of the mandible in one case and on the right side in the other during splitting and the decorticated fragment was fixed again in place using miniplates.

Clinical Results: The early postoperative period for all patients went uneventful with no significant complications. All patients showed postoperative edema with variable degrees. Patients who underwent single jaw surgery had mild edema which had resolved within 1-2 weeks, while patients who underwent bimaxillary

surgery showed severe edema which resolved in 2–4 weeks. Early mandibular function was started for both groups. All patients were satisfied with the esthetic results.

Radiographic Results

SNB and MPA: Concerning SNB, for the mean percentages of relapse showed no statistically significance differences between the two groups at F0 to F4. However, there was a statistically significant difference between the two groups regarding the mean percentages of relapse. Concerning MPA, there was no statistical differences between the two groups regarding the mean percentages of relapse.(Table 1)

Table 1: Comparison of the means and standard deviation values of SNB and MPA in the different time periods

		F0		F1		F2		F3		F4		Relapse %	
		Mean ± SD	P-value	Mean ± SD	P-value	Mean ± SD	P-value	Mean ± SD	P-value	Mean ± SD	P-value	Mean ± SD	P-value
SNB	Group I	84.82±4.20	0.749	79.17±2.74	1.000	79.82±2.85	0.485	80.35±3.16	0.302	80.82±3.35	0.239	2.02±0.72	0.000*
	Group II	86.1±4.93		79.81±4.57		81.34±4.72		82.62±4.58		83.42±4.42		4.55±0.84	
MPA	Group I	34.77±3.06	0.994	31.6±3.0	0.757	32.27±3.1	0.485	32.75±3.0	0.305	33.25±3.01	0.239	4.99±1.0	0.226
	Group II	34.75±3.61		31.65±3.64		32.42±3.72		33.08±3.66		33.75±3.72		6.25±1.76	

Point horizontal and vertical: For B horizontal, the mean percentages of relapse showed no statistically significant differences between the two groups at F0-F1 and F1-F4. In addition, there was no statistical differences between the two groups regarding the

mean percentages of relapse. For B vertical, the mean percentages of relapse showed no significant differences between the two groups at F0-F1 and F1-F4. There was a statistical difference between the two groups regarding the mean percentages of relapse (Table 2).

Table 2: Comparison of the means and standard deviation values of B point in a horizontal and vertical direction in the different time periods.

		F0-F1		F1-F4		Relapse %	
		Mean±SD	P-value	Mean±SD	P-value	Mean±SD	P-value
B Horizontal	Group I	-4.87±1.46	0.075	1.47±0.30	0.850	32.76±12.76	0.357
	Group II	-5.02±1.31		1.87±0.45		38.23±8.5	
B Vertical	Group I	1.67±0.60	0.321	-0.66±0.16	0.478	44.43±18.93	0.461
	Group II	2.07±0.80		-0.73±0.20		38.22±10.33	

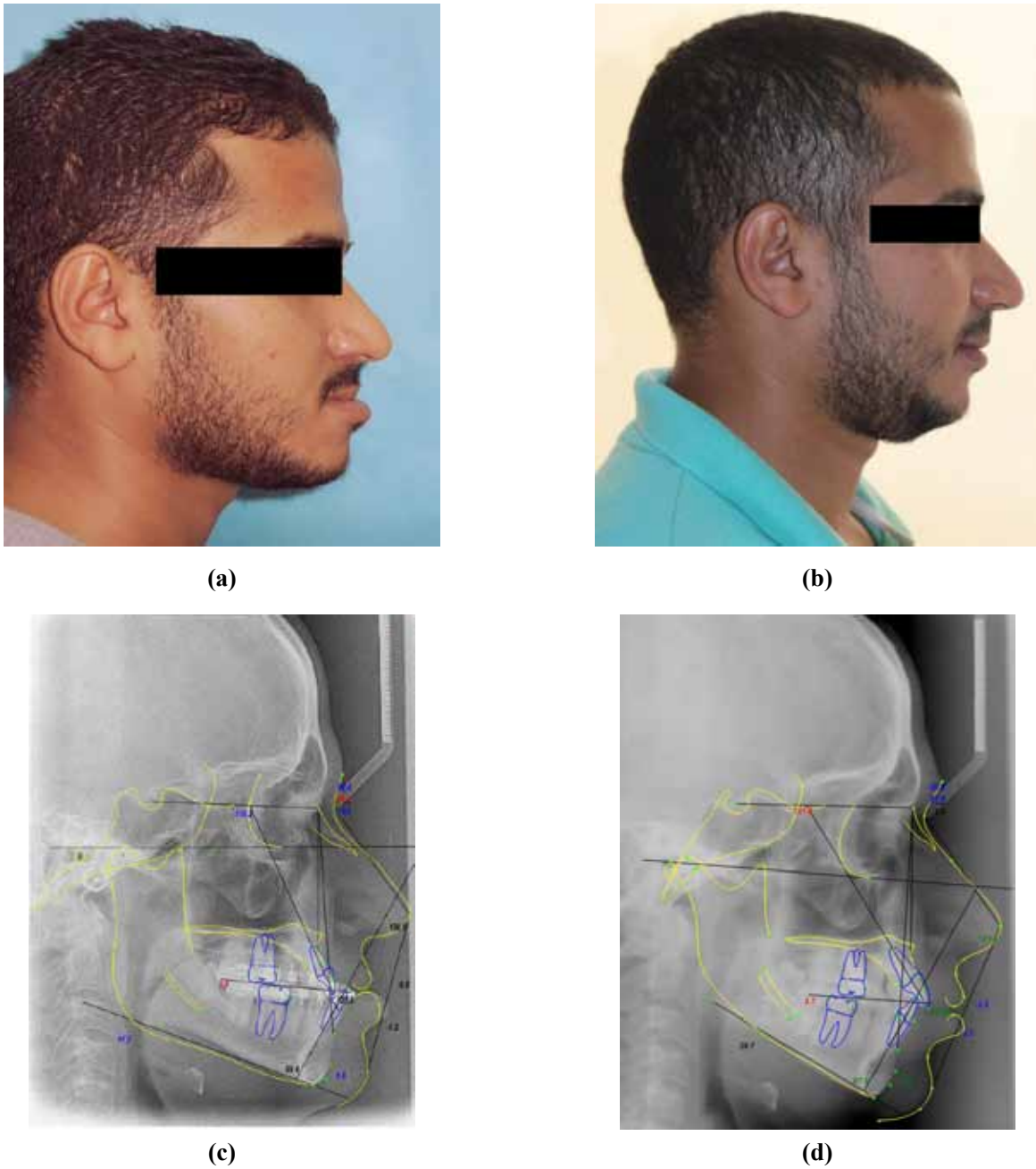


Fig. 2: (a) Preoperative clinical photo, (b) postoperative clinical photo, (c) Preoperative lateral cephalometry, (d) 12 months post-operative lateral cephalometry

Discussion

BSSRO is the gold standard surgical technique used for mandibular advancement and setback. Postoperative relapse is the most common drawback. With the advent of rigid internal fixation across the osteotomy site, uncontrolled skeletal relapse is unlikely to occur. Skeletal remodeling at the site of osteotomy and the mandibular condylar heads may postoperatively continue up to one year. At the time of the sagittal splitting of the mandible,

it is imperative to precisely position the proximal mandibular segment prior to fixation application.⁽⁵⁾

Many factors can influence the postoperative stability of the mandible, including the amount of setback, postoperative re-orientation of the pterygomasseteric sling, the bowing effect of the proximal segments, occlusal disharmony, and positional changes of the mandibular condyle and proximal segment.⁽⁶⁾

Adjustable plates have the advantage of decreasing operative time when occlusion is not perfect at the release stage and adjustments are required. Using the plate-specific pliers accompanying the kit, the joints can be either expanded or compressed to achieve the desired result. This allows anterior, posterior, clockwise and counter-clockwise directional change.

In the current study the age ranged between 22 and 27 years in order to avoid the effect of age on postoperative stability. **Joss and Vasalli** in their systematic review did not report post-surgical growth of the mandible after BSSO setback because the age was between 20 and 32 years.⁽⁷⁾

Data was aggregated in the form of mean and standard deviation (SD). 95% CI together with 0.05 P-value will be additionally reported. Data was analyzed using IBM SPSS advanced statistics (Statistical Package for Social Sciences), version 21 (SPSS Inc., Chicago, IL). The stability of mandibular position was described as mean and standard deviation. The Mann-Whitney U test was performed to test the significance between the 2 groups at each time period. Friedman's test followed by multiple comparisons test was performed to test the significance between the 4 time periods within each group. In addition, correction of p-value was done using Bonferroni adjustment to avoid hyperinflation of type 1 error that arises from multiple comparisons. A p-value ≤ 0.05 was considered statistically significant. All tests were two tailed.

For both groups F0-F1 was characterized by posterosuperior mandibular movement. This was accompanied by a decrease in SNB and MPA. Autorotation of the mandibular distal segment resulted during surgery and lead to superior movement of B point. For both groups, F1- F4 was characterized by anteroinferior mandibular movement.

Righi et.al and **Fujioka et.al** concluded a similar anteroinferior mandibular movement which took place during the follow-up period. They proposed that the "shearing force is the most noteworthy load affecting the maxillomandibular system stability after osteotomy". In case of BSSRO, these "shearing stresses" act on the osteotomy site and causes clockwise rotation of the distal segment and counterclockwise rotation of the proximal segment.^(8,9)

Lee et al reported that postsurgical skeletal changes after surgery-first approach BSSRO setback were also

in the anterosuperior direction.⁽¹⁰⁾ In contrast, **Kim et al** reported that changes were in the anteroinferior direction and they postulated that the possible reasons for this difference were mandibular counterclockwise rotation after surgical splint removal and differences of facial types among patients.⁽¹¹⁾

Previous studies fixated on postoperative skeletal stability and the extent of relapse after BSSRO mandibular setback depending on fixation method. **Abeltins et al.** stated that the mean (SD) horizontal relapse at B point was 1.4 mm.⁽¹²⁾ **Ballon et al.** reported the point B point horizontal relapse was 1.05 mm.⁽¹³⁾ **Landes and Ballon** reported that horizontal relapse at point B was 2.0 mm.⁽¹⁴⁾ These authors all used four-hole sliding plates to fix the mandibular bony segments.

Rao et.al evaluated the skeletal stability after BSSO in advancement and setback cases using miniplates. In the setback group, mandibular plane had a statistically significant change position of 1.4 mm (paired t-test, $p = 0.03$). The SNB angle, remained constant during the follow-up period. In advancement cases, the relapse was seen from the third month postoperative period but in setback cases, the relapse was noted from the sixth month onward and the skeletal relapse in these cases were noticed cephalometrically.⁽¹⁵⁾

Hsu et.al evaluated mandibular prognathism stability corrected by BSSO comparing bi-cortical osteosynthesis and monocortical miniplates, the percentage of relapse in the miniplates group was 25%.⁽¹⁶⁾ A reasonable explanation for the difference in mean mandibular relapse results is the length of the follow up period (6 months only).

Veysiére's study on the preliminary effect of an adjustable S-shaped plate on 15 consecutive cases showed good results, with respect to the mechanical reliability of this plate for three months postoperatively corresponding to the bone-healing period. Radiographic observations did not show any significant displacement at the osteosynthesis site. Class III patients showed good clinical results without any occlusal relapse. From the radiographic study of this group, no patient has presented significant postoperative bone movements.⁽¹⁷⁾

In addition to time saving, the integrity of the bone at the site of fixation was preserved, instead of screws removal and re-drilling which could compromise the integrity of the bone. This is an additional comfort we have chosen to adopt in our study. Finally, the simplicity

of the adjustment of these plates after centric relation check avoids any compromise in occlusion at the end of the surgery.

Other than our results, the choice of the fixation method should combine between sufficient stability for early jaw mobilization and elasticity to allow for intraoperative and early postoperative corrections. We think that the adjustable plates meet these criteria.

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Competing Interests: No conflict of interest.

Ethical Approval: The Ethics and research committee, Faculty of Dentistry, Cairo University approved the study and patients' consent was obtained.

References

1. Angle, E. L. Treatment of malocclusion of the teeth. Classification and Diagnosis of malocclusion(7thed.)1907. <http://doi.org/10.1017/CBO9781107415324.004>
2. Ackerman, J. L., Proffit, W. R., & Sarver, D. M. The emerging soft tissue paradigm in orthodontic diagnosis and treatment planning. *Clinical Orthodontics and Research* 1999;2(2), 49–52. <http://doi.org/10.1111/ocr.1999.2.2.49>
3. Bell WH, Scheideman GB. Correction of vertical maxillary deficiency: stability and soft tissue changes. *J Oral Surg* 1981;39:666.
4. Roh Y-C, Shin S-H, Kim S-S, Sandor GK, Kim Y-D. Skeletal stability and condylar position related to fixation method following mandibular setback with bilateral sagittal split ramus osteotomy. *J Cranio-Maxillofacial Surg* [Internet]. Elsevier Ltd; 2014;42(8):1958–63.
5. Khechoyan DY. Orthognathic surgery: General considerations. *Semin Plast Surg*. 2013;27(3):133–6.
6. Van Sickels, J. E., Larsen, A. J. & Thrash, W. J.: Relapse after rigid fixation of mandibular advancement. *J. Oral Maxillofac. Surg.* 1986: 44: 698-702.
7. Joss CU, Vassalli IM. Stability After Bilateral Sagittal Split Osteotomy Setback Surgery With Rigid Internal Fixation: A Systematic Review. *J Oral Maxillofac Surg*. 2008;66(8):1634–43.
8. Righi, E., Carta, M., Bruzzone, A. A., Lonardo, P. M., Marinaro, E., & Pastorino, A. Experimental analysis of internal rigid fixation osteosynthesis performed with titanium bone screw and plate systems. *J Craniomaxillofac Surg*. 1996: 24(1), 53–57. doi:10.1016/s1010-5182(96)80078-3.
9. Fujioka, M., Fujii, T., & Hirano, A. Comparative Study of Mandibular Stability After Sagittal Split Osteotomies: Biocortical Versus Monocortical Osteosynthesis. *The Cleft Palate-Craniofacial J*: 2000 37(6), 551–555. doi:10.1597/1545-1569(2000)037<0551.
10. Lee NK, Kim YK, Yun PY, Kim JW; *J Craniomaxillofac Surg*: 2013 41:47.
11. Kim CS, Lee SC, Kyung HM, et al: Stability of mandibular setback surgery with and without presurgical orthodontics. *J Oral Maxillofac Surg*: 2014 72:779.
12. Abeltins A, Jakobsone G, Urtane I, et al. The stability of bilateral sagittal ramus osteotomy and vertical ramus osteotomy after bimaxillary correction of class III malocclusion. *J Craniomaxillofac Surg* 2011;39:583–7.
13. Ballon A, Laudemann K, Sader R, et al. Segmental stability of resorbable P(L/DL)LA-TMC osteosynthesis versus titanium miniplates in orthognathic surgery. *J Craniomaxillofac Surg* 2012;40:e408–14.
14. Landes CA, Ballon A. Skeletal stability in bimaxillary orthognathic surgery: P(L/DL)LA-resorbable versus titanium osteofixation. *Plast Reconstr Surg* 2006;118:703–22.
15. Rao SH, Lankupalli AS, Selvaraj L. Skeletal Stability after Bilateral Sagittal Split Advancement and Setback Osteotomy of the Mandible with Miniplate Fixation. 2014;600077:9–15.
16. Hsu SSP, Huang CS, Chen PKT, Ko EWC, Chen YR. The stability of mandibular prognathism corrected by bilateral sagittal split osteotomies: A comparison of bi-cortical osteosynthesis and mono-cortical osteosynthesis. *Int J Oral Maxillofac Surg*. 2012;41(2):142–9.
17. Veyssiere A, Leprovost N, Ambroise B, Prévost R, Chatellier A, Bénateau H. Study of the mechanical reliability of an S-shaped adjustable osteosynthesis plate for bilateral sagittal split osteotomies. Study on 15 consecutive cases. *J Stomatol Oral Maxillofac Surg*. 2018 Feb;119(1):19-24. doi: 10.1016/j.jormas.2017.11.003.

Factors Influencing Rate of Chest Compression in Cardio Pulmonary Resuscitation (CPR) by Nurses as a First Responder

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Abstract

Introduction: Cardiac arrest is a condition of the cessation of blood circulation in the body. First aid cardiac arrest is cardiopulmonary resuscitation consisting of chest compression and ventilation. Chest compression is a factor that affects the return of spontaneous circulation (ROSC) patients. In addition to the depth of chest compressions, the chest compression rate is a major factor that can increase the chances of the patient's life shortly after suffering a cardiac arrest.

Aim: The purpose of this study is to determine the factors that affect the rate of the chest compressions performed by nurses as a first responder.

Method: The method used in this study is analytic cross sectional correlative to 107 respondents. Chest compression rate measurement using a chest compression CPR Help Zoll's Real product was analyzed using an application Rescue Net Code Review.

Finding: Preliminary study results showed that the factors that affect the rate of the chest compression is gender, age, BMI, education, the last time attend to BLS training and the last time giving chest compressions. Based on the results of the linear regression analysis, gender is a factor that most affects to the rate of the chest compression ($\beta = -7.8$). It explains that the male responder provide a faster compression 8x/min compared with female responder.

Conclusion: In conclusion, gender, the last time attends to BLS training and the last time provides chest compression significantly affect to the rate of the chest compression.

Keywords: *Cardiac arrest, Rate, Chest Compression.*

Introduction

Cardiac arrest is a condition in which the cessation of blood circulation caused by heart failure in effectively contract⁽¹⁾, Cardiac arrest that persists for ten minutes can result in the death of vital organs in the body. Such conditions require immediate action. If there is a delay in the delivery of the action, the likelihood of success is reduced 7-10% every minute⁽²⁾, The incidence of sudden cardiac arrest in the United States an estimated 200,000 patients annually⁽³⁾, In Indonesia, the incidence of sudden cardiac arrest patients is still not clear data obtained, but it is estimated around 10,000 people in one year or 30 people every day⁽⁴⁾.

Preliminary studies showed that patients who had a cardiac arrest and need a Basic Life Support (BLS) procedure in private hospital on 1 January 2018 and May 2018 in 38 patients. As for the number of patients who visit the diagnosis of coronary artery disease and are at risk of sudden cardiac arrest as many as 910 patients.

Sudden cardiac arrest can occur in hospital and out of hospital. In hospital cardiac arrest is a major cause of death of patients hospitalized⁽⁵⁾. Cardiopulmonary resuscitation (CPR) is an action that should be given to patients with sudden cardiac arrest⁽⁶⁾.

Cardiopulmonary resuscitation (CPR) consists of chest compression and ventilation. Chest compression

aims to deliver blood to the vital organs such as the heart and brain and stimulate the return of spontaneous circulation (ROSC) in patients⁽⁷⁾. Medical personnel should provide chest compressions as soon as possible when met patients with cardiac arrest. A nurse who on duty for 24 hours is a potential first responder for the patients⁽⁸⁾.

Quality chest compressions includes five components, namely the average rate giving chest compressions as much as ≥ 100 -120 x/min, chest compression depth around 5-6 cm, the return of the chest, hand position and no interruption more than 10 seconds⁽⁹⁾. Components of rate chest compression is one of the main factor that can increase the chances of the patient’s life shortly after cardiac arrest⁽¹⁰⁾ But the quality of chest compressions given today by nurses is below standard⁽¹¹⁾.

A study reports that there is a decline in the quality of chest compressions in the first minute are only able to provide 98%-quality chest compressions, and in the fifth minute only able to provide 18% of the expected target of chest compressions ⁽¹²⁾.

Based on a study involving subjects with age 31 years $\pm 5:34$, mentions that there is no correlation between age responder with the quality of chest compressions given⁽¹³⁾.

Other studies mention that the responder with a BMI > 24 is able to provide better chest compressions than responder with a BMI <24⁽¹⁴⁾, but other research said that the subject of women with a BMI <26 were able to give chest compressions faster than female subjects with a BMI > 26⁽¹⁵⁾.

Based on the literature, researchers wanted to determine the factors that influence the rate of the chest compression in cardiopulmonary resuscitation (CPR) provided by nurses as a first responder.

Method

The research design used in this study are correlative analytic with cross sectional study. In this study were recruited on voluntary basis, conducted between January and April 2019.

The population in this study was nurses who work in private hospital. The sampling technique used purposive sampling was 107 nurses with the following inclusion criteria: male or female age 21-43 years, minimum

education level diploma and maximum bachelor of nursing (BN), respondents had attended training Basic Life Support (BLS) procedure according to American Heart Association (AHA) 2015 guidelines. The exclusion criteria were pregnant and chronic diseases that make the responden weak and disable do physical exercise.

Before the data collection process, the respondents should fill the agreement form. Then, researchers will measure the height and weight of respondents, as well as provide relevant demographic data questionnaire respondents. The next process, researchers will give a presentation case of cardiac arrest in the hospital, and assess the response to the case.

Respondents are expected to provide chest compression for a minute on props. The data has been recorded, stored in CPR Help Zoll’s Real product, and then analyzed using an application Rescue Net Code Review.

This study already gets ethical clearance by the Health Research Ethics Commission in Faculty of Medicine, *Universitas of Brawijaya* with number series 54/EC/KEPK–S2/02/2019.

Finding:

Table 1: Distribution Characteristics of Respondents by Age, Body Mass Index (BMI), When Was the Last BLS Training and When Was the Last Giving Chest Compression

Variables	Min-Max	Mean \pm SD
Age (Years)	21-43	28.16 \pm 4.5
BMI (Kg/M ²)	16-32	22.13 \pm 3.4
The last BLS training (Month)	1-60	14.26 \pm 1.1
Last giving Chest compression (Month)	0-36	8.71 \pm 1.2

According to the table 1, it can be explained that the average age of respondents was 28 years, with a minimum age of 21 years and maximum 43 years. Furthermore, the average BMI was 22, with a minimum value of 16 and a maximum value of 32.

The average last training BLS of respondents is 14 months ago, with a minimum last training is 1 month ago and maximum last training is 60 months ago. the averaged last giving chest compressions is 8 months ago, with minimum last giving chest compression is less than 1 month and maximum is 36 months ago.

Table 2: Distribution Characteristics of Respondents by Gender and Education Background Respondents

Variables	N	%
Gender		
Man	36	33.6
Woman	71	66.4
Education		
Diploma	78	72.9
BN	29	27.1

According to the table 2, it can be explained that the gender most are women that are 71 respondents (66.4%), education background of respondents the most is a Diploma as many as 78 respondents (72.9%), but only 29 respondents (27,1%) are diploma.

Table 3: Chest Compression Rate in One Minute

Variables	Min-Max	Mean ± SD
Chest Compression rate	84 -190	139 ± 1.7

Based on table 3, it can be seen that the average rate of the chest compressions is 139x/min. The minimum rate is 84x/min and maximum rate is 190x/min.

Table 4: Linear Regression Analysis of Factors influencing Chest Compression Rate

Variables	R	P	R Square
Gender	-7.88	0,025	.151
Last BLS training	-0.32	0,018	
Last giving Chest compression (Month)	-0.30	0,023	

Based on the linear regression analysis, age, education background and BMI did not significantly influence the compression rate.

According to the table 4, the factors that influence the rate of the chest compression are gender, when the last BLS training and when the last giving chest compression with all p value <0,05. The three factors to explain the variable compression rate of 15.1%.

Any increase in the last 1 month long training conducted by a nurse will reduce chest compression rate of 0,32 after controlling for other variables. If the chest compressions performed by a male nurse will faster 7x/min when compared to women. The last experience giving chest compressions significantly affect the rate of the chest compression. Any increase in the last 1 month

long experience of giving chest compressions will reduce the rate of chest compressions as much as 0,30.

Discussion

A study explains that the greater number of chest compression rate will increase the possibility of return of spontaneous circulation or (ROSC)⁽¹⁶⁾.

Based on this study, male nurses provide faster compression when compared to female nurses, it is likely due to greater muscle mass is owned by male nurses, as well as a larger body size than female nurses⁽¹⁷⁾. However, other studies explained that gender significantly influence the chest compression rate with p value = 0.00, but the study also explains that the female respondents giving chest compressions faster when compared to the male respondents⁽¹⁵⁾.

Other studies mention that the male respondents (20%) were able to give chest compressions is more than 200 times in two minutes when compared to female respondents (0.03%)⁽¹⁸⁾. The ability of male respondents in providing chest compressions faster when compared to female respondents likely due to the size of the female body that is lighter and shorter than the size of the male body.

BLS training is one of the factors that play a role in improving skills and knowledge of the respondent to provide basic life support in patients with cardiac arrest. One important component in the training of BLS is cardiopulmonary resuscitation (CPR). Cardiopulmonary resuscitation (CPR) is the first aid to be provided by a nurse as the first responden before the code blue team came.

In addition to gender, according to this study, when the last attend to BLS training significant effect on the rate of the chest compression. The longer the respondents did not attend training BHD, it will decrease the rate of chest compressions. This was due to the declining ability and knowledge of respondents about the up to date basic life support.

Another study explains that the skill level of the respondents is 18.7% before training, after training increased to 93.5%. However, after 10 weeks of training this value decreased to 82.5% and after two years of training, the value declined significantly to 36.8%⁽¹⁹⁾. BLS is the instructional media training that includes knowledge and skills in providing basic life support.

BLS periodic training is expected to enhance the skills and knowledge of nurses, so nurses more confident and competent when faced with a patient with cardiac arrest.

In addition to gender and last BLS training, other factors that affect the rate of the chest compression is when the last experience giving chest compressions. Nurses often give chest compressions on a patient reported to be rapidly exhausted in giving chest compressions⁽¹⁸⁾. Other study states that the medical officer who works in the emergency room with chest compression condition often do not get tired when giving chest compressions when compared with medical personnel who work in the other room⁽²⁰⁾.

BLS training must often give to nurses as medical personnel that play a role into the first responden of cardiac arrest in the hospital.

Another study said that rate.

Conclusion

Based on the results of multiple linear regression analysis, there are three factors that influence the rate of the chest compression is gender, when the last BLS training and when the last giving chest compression. All three of these factors have a significant influence with each value -7.88, -0.327 and -0.303. This study can be used as a reference to hospitals and health care workers in an effort to improve the quality of chest compressions, especially on chest compression rate.

Conflict of Interest: In this Study, there is no conflict of interest.

Source of Funding: In this study, a whole funding is accounted on the researcher independently. There are no other funding sources.

Reference

1. Brunner, Suddart. Medical Surgical Nursing. karyasa WAYAJKIm, editor. Jakarta: EGC; 2002.
2. Aelen PD. chest paid for automated CPR. resuscitation journal. 2012;84(11):1625-32.
3. Brooks S, Hassan N, Bigham B, Morrison L. Mechanical versus manual chest compressions for cardiac arrest. the Cochrane library. 2014.
4. Suharsono T, Ningsih D. Penatalaksanaan Henti Jantung Di Luar Rumah Sakit. Malang: UMM Press; 2009.
5. Sandroni C, Nolan J, Cavallaro F, Antonelli M. In-hospital cardiac arrest: incidence, prognosis and possible measures to improve survival. Intensive care med. 2007;33(2):237-45.
6. Sutton R, Nadkarni V, Abella B. "Putting It All Together" to Improve Resuscitation Quality. emerg Med Clin North Am. 2012;30(1):105-22.
7. Berg RA, Hemphill R, Abella BS, Aufderheide TP, Cave DM, Hazinski MF, et al. Part 5: Adult Basic Life Support, American Heart Association Guidelines for Cardiopulmonary Resuscitation and emergency cardiovascular care. circulation. 2010;122(18):685-705.
8. Mchugh M, Rochman M, Sloane D, Berg R, Mancini M, Nadkarni V, et al. Better Nurse Staffing and Nurse Work Environments Associated With Increased Survival of In-Hospital Cardiac Arrest Patients. Medical Care. 2016;54(1).
9. Hazinaki M, Shuster M, Donnino M, Travera A, Samson R, Sohexnayder., et al. highlights of the 2015 American Heart Association Guidelines update for CPR and ECC. America: AHA; 2015.
10. Depth and rate of chest compressions during CPR impact survival in cardiac arrest [Internet]. ScienceDaily. 2015 [cited November 28, 2018]. Available from: www.sciencedaily.com/releases/2015/02/150205155638.htm.
11. Sutono., Ratnawati R, Suharsono T. the differences between chest compression and ventilation in Basic Life Support (BLS) training to Bachelor of Nursing Student with instructor feedback, Audiovisual Feedback and both of them in Yogyakarta. 2016. 2016-05-27;3(2):15. Epub 2016-05-27.
12. Pozner C, Almozlino A, Elmer J, Poole S, McNamara D, Barash D. Cardiopulmonary resuscitation feedback improves the quality of chest compression provided by hospital health care professionals. the American Journal of Emergency Medicine. 2011;29(6):618-25.
13. Zhang F, Li Y, Huang S, Jun. Correlations between quality indexes of chest compression. World J Emerg Med., 2013;4(1).
14. Sayee N, McClusky D. Factor influencing performance of cardiopulmonary (CPR) by foundation year 1 hospital doctors. Ulster Med. 2012;81(1):14-8.

15. Jaafar A, Abdulwahab M, Al-Hashemi E. influence of rescuer's gender and body mass index on cardiopulmonary resuscitation according to the American Heart Association 2010 resuscitation guidelines. Hindawi Publishing Corporation international scholarly research notice. 2015;2015.
16. Sanders., Kern., Berg., Hilwig., Heidenrich., Ewy. Survival and neurologic outcome after cardiopulmonary resuscitation with four different chest compression-ventilation ratio. *annals of Emergency Medicine*. 2002;40(6):553-62.
17. Kamińska H, Wiczorek W, Matysiuk P, Czyzewski L, Ladny J, Smereka J, et al. Factors influencing high quality chest compressions during cardiopulmonary resuscitation scenario according to 2015 American Heart Association Guidelines 2018.
18. Rad M, Rad M. a study of factors related to cardiopulmonary resuscitation physical fatigue and the quality of resuscitation. *Acta facultatis medicae naissensis*. 2017;34(1):43-53.
19. Nori JM, Saghafinia M, Motamedi MH, Hosseini SM. CPR Training for Nurses: How often Is It Necessary? *Iranian Red Crescent Medical Journal*. 2012;14(2):104-7.
20. Foo NP, Chang JH, Lin HJ, Guo HR. Rescuer fatigue and cardiopulmonary resuscitation positions: a randomized controlled crossover trial. *resuscitation journal*. 2010;81(5):579-84.

A Comparative Study between the Use of Atropine Alone and in Combination with Glycopyrrolate in Acute Organophosphorus Poisoning in Minia Poison Control Center

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Abstract

Objectives: To evaluate and compare the effectiveness of atropine alone and the combined therapy of atropine and glycopyrrolate in treatment of patients with acute organophosphate poisoning (OP).

Patients and Method: Forty patients with history of OP poisoning were included in the study with in the period from 1st of March 2017 to 28th of February 2018. The study is a prospective randomized controlled trial that was carried out on patients admitted to Poison Control Center of Minia University Hospital. These patients were divided in to two groups of 20 patients each. Group I was treated with atropine alone while group II was treated with atropine in combination with glycopyrrolate.

Results: The majority of the patients were females (55%). The outcomes of these two groups were analyzed and compared including percentage of mortality, percentage of recovery, duration of hospital stay, need for mechanical ventilation, incidence of intermediate syndrome and percentage of adverse reactions. The percentage of recovery and percentage of mortality were the same between the 2 groups with p=1. However, there was reduction in hospitalization days and incidence of adverse drug reactions of the used drugs in group II when compared to group I.

Conclusion: The study suggests that treatment with combined therapy of atropine and glycopyrrolate was more effective than therapy with atropine alone regarding the reduction in the duration of hospital stay and incidence of adverse reactions of the used drugs.

Keywords: Organophosphorus poisoning, atropine, glycopyrrolate.

Introduction

Organophosphorus (OP) compounds are largely used as pesticides worldwide. Their easy availability and lack of knowledge about their seriousness resulting increase in accidental and suicidal poisoning. According

to a World Health Organization (WHO) report, every year three million cases of poisonings with insecticides occur worldwide resulting in approximately 200,000 deaths.¹

OP insecticides are irreversible acetyl cholinesterase (AChE) enzyme inhibitors. The clinical manifestations are caused by excess acetylcholine (ACh) at the muscarinic receptors, nicotinic receptors and in CNS. Manifestations of OP poisoning occur in three phases: Acute cholinergic crisis (first 48 hours), intermediate syndrome (IMS) (24-96 hours after poisoning) and OP induced delayed polyneuropathy.²

Anticholinergics are competitive antagonist to ACh and reverse all muscarinic effects both in CNS and

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peripheral nervous system. Glycopyrrolate is a synthetic quaternary amine with peripheral effects similar to those of atropine. It is longer acting drug and doesn't cross the blood brain barrier and therefore, it has lesser effect on CNS.³

Aim of the work: The aim of this study is to evaluate and compare the effectiveness of atropine alone and the combined therapy of atropine and glycopyrrolate in treatment of patients with acute organophosphate poisoning (OP).

Patients and method: The study is a prospective randomized controlled trial that was carried out on patients admitted to Poison Control Center of Minia University Hospital. Forty patients were collected within the period from 1st of March 2017 to 28th of February 2018. Written informed consent was obtained from relatives of all patients.

Patients: Forty patients with acute OP toxicity of both sexes aging from 20 to 60 years were included in the study. Diagnosis was made by history of exposure to OP compound, clinical manifestations and by measuring pseudocholinesterase enzyme level. These patients were divided in to two groups of 20 patients each. Group I was treated with atropine alone while group II was treated with atropine in combination with glycopyrrolate.

The cases included in the study were chosen as they have no history of previous diseases including hepatic, renal, cardiovascular, respiratory or CNS illness. Patients were excluded from the study if they had concomitant ingestion of other drugs in a suicidal attempt. Patients with trauma, patients with drug or alcohol abuse and patients presented to emergency department 24 hours after OP exposure were also excluded.

Atropine was given either as a continuous infusion or intermittent dosing (the end-point of atropinisation was drying of secretions, flushing, tachycardia and mydriasis). Continuous infusion was started as 0.02-0.08 mg/kg per hour and intermittent dosing was performed using atropine in the doses of 2 mg IV and then 2 mg after every 5-10 minutes till the signs of atropinisation appeared. After achieving atropinisation, the interval between the doses was increased so as to maintain adequate atropinisation. Atropine was then slowly withdrawn over a period of 3-5 days.

Glycopyrrolate was given at a dose of 7.5 mg infused in 200 ml saline till the desired effects of dry mucous membranes. It has also been given at a dose of 0.2 mg IM and repeated every 6 hours if required.

Outcome: All the patients were observed for short-term outcomes either complete recovery or death and total duration of hospital stay.

Complications: All patients observed for the complications developed during hospital stay e.g intermediate syndrome, respiratory tract infection, need for mechanical ventilation, CNS toxicity and other adverse effects.

Statistical analysis: Statistical analysis was performed using the SPSS software for Windows v. 20 (SPSS Inc., Chicago, IL). For comparing quantitative data, Kruskal Wallis test and Mann Whitney tests were performed. For comparing qualitative data, Fisher exact test was performed. A probability value ($p=0.05$) was considered statistically significant.

Results

During one year study forty patients with acute OP poisoning were evaluated. The majority of the patients were females (55%). Group I consisted of 20 patients with the mean age of 25.3 ± 6.2 mostly from rural areas (80%). Group II also consisted of 20 patients having mean age of 34.3 ± 13.6 and most of them belonged to rural areas (70%). There was no significant difference in demographic data and time of arrival between the 2 groups. As regard percentage of recovery and percentage of mortality there was no significant difference in patients treated with atropine alone and patients treated with a combined therapy of atropine and glycopyrrolate ($P=1$) However, there was reduction in hospitalization days in group II when compared to group I (Table I).

There was no significant difference in need for mechanical ventilation and incidence of intermediate syndrome between the 2 groups with $P=1$ (Table II). It was found that the combined treatment of atropine with glycopyrrolate reduces dose of atropine with $P=0.278$ (Table III) with subsequent decrease in atropine adverse effects. Incidence of confusion, hallucinations and tachyarrhythmias were significantly more in group I when compared with group II with $P>0.001$ (Table IV).

Table I: Outcome data between the study groups

		Group I	Group II	P value
		N=20	N=20	
Hospital stay	Median	5	4	0.066
	IQR	(4-6)	(3-5)	
Outcome	Recovery	18(90%)	18(90%)	1
	Died	2(10%)	2(10%)	

IQR: Interquartile range, Significant level at P value < 0.05

Table II: Complications between the study groups:

		Group I	Group II	P value
		N=20	N=20	
Ventilation Required	No	16(80%)	16(80%)	1
	Yes	4(20%)	4(20%)	
Intermediate Syndrome	No	18(90%)	18(90%)	1
	Yes	2(10%)	2(10%)	
Respiratory Tract infection	No	14(70%)	16(80%)	0.465
	Yes	6(30%)	4(20%)	

*: Significant level at P value < 0.05

Table III: Doses of atropine used in treatment between the study groups

		Group I	Group II	P value
		N=20	N=20	
Atropine	Median	55.5	49.5	0.278
	IQR	(42-90)	(31-70)	

IQR: Interquartile range, Significant level at P value < 0.05

Table IV: Adverse effects of the drugs between the study groups

		Group I	Group II	P value
		N=20	N=20	
Confusion	No	2(10%)	14(70%)	<0.001*
	Yes	18(90%)	6(30%)	
Hallucinations	No	2(10%)	14(70%)	<0.001*
	Yes	18(90%)	6(30%)	
Tachyarrhythmias	No	0(0%)	10(50%)	<0.001*
	Yes	20(100%)	10(50%)	
Fever	No	6(30%)	12(60%)	0.057
	Yes	14(70%)	8(40%)	

*: Significant level at P value < 0.05

Discussion

Organophosphates are one of the most common causes of poisoning especially in developing countries

with mortality rates reaching up to 10-20%. So early diagnosis and appropriate treatment is often life saving.⁴

The antidotes of OP poisoning are anticholinergic drugs such as atropine and glycopyrrolate, atropine being the older of the two medications. Muscarinic effects of OP poisoning are reversed by these drugs. Conventional treatment with atropine may lead to CNS toxicity, although control of secretions may still be inadequate.⁵

Glycopyrrolate (glycopyrronium bromide) is a quaternary ammonium with anti-muscarinic activity and peripheral actions like to that of atropine, however glycopyrrolate is twice as potent as atropine for peripheral effects. It can be safely used during pregnancy as it doesn't cross the placental barrier. Glycopyrrolate can't pass through the BBB so it does not have any detectable central anti-cholinergic effects.⁶

Atropine is universally accepted antidote most frequently used for the patients of OP poisoning. Some of the previous studies revealed that atropine treatment is effective, however it often causes agitation, hallucinations and confusion. Other effects of atropine treatment are hyperthermia, bowel ileus, urine retention and tachycardia, however the use of combined therapy of atropine and glycopyrrolate improves tachycardia with no changes in body temperature and CNS stimulation hence glycopyrrolate can't pass through the BBB.⁷ Out of all the forty patients included in the study confusion and hallucinations were seen in 24 (60%) cases and 18 cases of them were from Group I. Incidence of confusion and hallucinations is significantly more Group I when compared to group II with P<0.001.

So it was found that the combined treatment of atropine with glycopyrrolate reduces dose of atropine with P=0.278 and also reduces the central adverse effects associated with it improving the quality of treatment.

Other clinical manifestations seen were intermediate syndrome in 2 (10%) case in group I and 2 (10%) cases in group II. Respiratory infection was seen in 10 patients, 6 (30%) cases of them from group I explaining that combined therapy of atropine and glycopyrrolate provides better control on chest secretions. Out of 40 cases 36 patients recovered and 4 patients died. Incidence of mortality is not statistically significant between both groups.

Our study found that there was no significant difference in mortality between patients treated with

atropine alone and patients received combined therapy of atropine and glycopyrrolate, how ever there was reduction in the duration of hospital stay and incidence of adverse reactions especially CNS toxicity associated with atropine treatment. This agreed with results of a study done by Khalid et al. (2017) and Anju et al.(2011) whom study revealed that both the groups had the same efficacy but atropine showed a very distinct CNS toxicity,^{3,7} but it was in contrast with Arendse et al.(2009) who had found that the infusion of a combination of atropine and glycopyrrolate had a lower mortality rate but the occurrence of atropine toxicity was unchanged between the 2 groups.⁸

Conclusion

The study suggests that treatment with combined therapy of atropine and glycopyrrolate was more effective than therapy with atropine alone regarding the reduction in the duration of hospital stay and incidence of adverse reactions of the used drugs.

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References

1. Eddleston M, Eyer P, Worek F, Mohamed F, Senarathna L, von Meyer L, Juszczak E, et al. Differences between organophosphorus insecticides in human self-poisoning: a prospective cohort study. *The Lancet*. 2005; 366(9495), pp.1452-9.
2. Abdollahi M, Karami-Mohajeri S. A comprehensive review on experimental and clinical findings in intermediate syndrome caused by organophosphate poisoning. *Toxicology and applied pharmacology*. 2012; 258(3), pp.309-14.
3. Anju N, RH SR, Nalini P. Comparison of Efficacy and Safety of Atropine Sulphate and Glycopyrrolate in the Treatment of Organophosphorus Poisoning at St. Martha's Hospital, Bangalore. *Indian Journal of Pharmacy Practice*. 2011; 3(1).
4. Chowdhary S, Bhattacharyya R, Banerjee D. Acute organophosphorus poisoning. *Clinica chimica acta*. 2014; 431, pp.66-76.
5. Kumaran Senthil S, Chandrasekaran VP. Combined atropine and glycopyrrolate in organophosphorous poisoning. *JIST* 2007; 3(1).
6. Thunga G, Sam KG, Xavier VR, Verma M, Vidyasagar S, Pandey S. Effectiveness of Combination of Atropine and Glycopyrrolate in the Treatment of Mixed organophosphorus Poisoning. *The Internet Journal of Anesthesiology*. 2009; 20(2), pp.1-9.
7. Khalid A, Kazi MA, Bibi I, Memon HN, Khan M, et al. Effect of Atropine and Glycopyrrolate in patients with Organophosphate poisoning. *Indo American Journal Of Pharmaceutical Science*. 2017; 4(11), pp.4370-4374.
8. Arendse R, Irusen E. An atropine and glycopyrrolate combination reduces mortality in organophosphate poisoning. *Human & experimental toxicology*. 2009; 28(11), pp.715-20.

Implant Materials Used for Orbital Floor Reconstruction

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Abstract

Purpose: To review different available implant materials used for orbital floor reconstruction regarding their indications, advantages and disadvantages.

Summary: Review of literature revealed the presence of a wide variety of implant options for repair of orbital floor defects. They can be broadly classified into biological materials, metals and polymers which are further divided into resorbables and non resorbables. The choice could be based on an algorithm for the defect size, the anatomical location, or the remaining structural support. Small defects may heal solely by the formation of scar tissue, whereas larger defects, especially those associated with enophthalmos, need material of a sufficient strength to support the orbital contents.

Keywords: Blow-out fractures, Titanium, resorbable polymers.

Introduction

Fractures of the orbit are seen in many patients who have blunt trauma to the face and skull. The prominent position of the orbit in the craniofacial skeleton predisposes this region to injury.¹

Blow-out fracture is a special type of fracture of the orbital floor. Rene Le Fort concluded that blow-out fractures occurred through force transmission from the more rigid infraorbital rim to the relatively weak orbital floor, known as the buckling theory.² This theory was challenged by Pfeiffer in 1948, who observed a case series of globe-directed trauma resulting in blowout fractures, leading him to propose the hydraulic theory, which states that hydraulic pressure from the globe is transmitted to the bony orbit resulting in fracture of the thin orbital floor.³

In the repair of orbital fractures, the value of an implant is to regain function and aesthetic appearance by repairing the traumatic defect and bringing the globe into its correct position. In addition to the timing and method of reconstruction, a third essential factor in orbital fracture surgery is the choice of reconstruction material.⁴

Advances in biotechnology continue to introduce new implant materials for reconstruction of orbital floor fractures. Which material is best fit for orbital floor reconstruction has been a controversial issue.⁵

Characteristics of an ideal orbital reconstruction material⁶:

- 1. Stability and fixation:** The implant should be strong enough to support the orbital content and related forces, do not deform (sagging of material into maxillary sinus) under load and can be fixed to surrounding structures
- 2. Contouring and handling:** Restores adequate volume to treat enophthalmos and diplopia, easy to shape to fit the orbital defect and regional anatomy and has smooth surface.
- 3. Biological behavior:** Ideal implant is biocompatible with no infection, migration, foreign body reaction,

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non-allergenic and non-carcinogenic. It should be osteosynthetic and shows high tissue incorporation but easily dissectable in implant removal during secondary reconstruction

4. **Drainage:** Spaces within the implant should be present to allow drainage of orbital fluids
5. **Donor site morbidity:** The implant should not increase surgical complication rate or donor site morbidity (pain, swelling, etc.)
6. **Radiopacity:** The implant should be radiopaque to enable radiographic evaluation without artifacts.
7. **Availability and cost-effectiveness:** Ideal implant should be readily available in sufficient quantities and acceptable costs

Types of materials used for orbital reconstruction:⁶

1. Biological materials:

- *Autografts/autogenous materials:*
 - i. Autologous bone: calvarium, iliac crest, rib, mandibular symphysis, maxillary sinus wall
 - ii Autologous cartilage: nasal septum or concha, auricle, rib
 - iii Autologous fascia: Tensor fascia lata, temporal fascia
 - iv Autologous periosteum
- *Allografts:* Lyophilized dura mater; demineralized human bone, lyophilized cartilage, irradiated fascia lata.
- *Xenografts and animal-derived materials:* porcine sclera, porcine skin gelatin/Gelfilm, bovine bone or sclera
- *Biological ceramics (inorganic, non-metallic):* Porous hydroxyapatite (HA) and other calcium phosphates.

2. Metals: Titanium, Cobalt alloys

3. Polymers (plastics):

- *Non-porous non-resorbable (permanent) implants:* Silicone, nylon (SupraFOIL; Supramid), polytetrafluoroethylene (PTFE; Teflon, Gore-Tex), hydrogels, PEEK (poly ether ether ketone).

- *Non-porous resorbable implants:* Hyaluronate/ carboxymethylcellulose (HA/CMC; Seprafilm).
- *Porous non-resorbable implants:* Porous polyethylene (PE; Medpor)
- *Porous resorbable (absorbable) implants:* Poly(lactic acid) (PLA), poly(glycolic acid) (PGA), PLA/PGA implants Polydioxanone (PDS), polyglactin 910/PDS implants (Ethisorb)

4. Composites:

HA-reinforced high density composite

Titanium/PE composite implant (Medpor Titan)

HA/PLA/polycaprolactone (PCL) sheet

Bone morphogenetic protein-loaded gelatin hydrogel

Advantages and disadvantages of currently available reconstruction materials:

- **Biological materials:** Biological materials are defined as grafts harvested from the same or another human or animal and include autografts, allo-grafts, and xenografts.⁶

Since the 18th century, autologous bone has been the 'gold standard' biomaterial for the reconstruction of bony defects in the craniofacial area.⁷ Autologous bone grafts are used in orbital surgery because of their strength, rigidity, vascularization potential, and incorporation into the orbital tissues with minimal acute and chronic immune reactivity (i.e. infection, extrusion, collagenous capsule formation, and ocular tethering).⁸ Donor site morbidity remains a general drawback for autologous bone harvesting.⁶

Allografts (homografts) are transplanted tissues (e.g. lyophilized dura mater or banked (demineralized) bone) from another human being. Their advantages include a decreased surgical time, preoperative customizability, absence of donor site morbidity, and abundant availability of banked bone.⁴ Lyophilized dura (Lyodura) was a standard in the past for the reconstruction of smaller orbital defects because of its strength and absence of tissue reactions.⁹ However, it became controversial following a case of Creutzfeldt–Jakob prion disease in a patient who received dura originating from a cadaver.¹⁰ Consequent to this report, lyophilized dura sterilization was no longer performed with gamma irradiation but with sodium hydroxide.¹¹ The

disadvantages of allografts include a resorption rate substantially higher than that of autologous tissue,⁸ the need for immunosuppressive pharmacotherapy, and the risk of viral transmission, such as hepatitis C virus and HIV.¹²

- **Metals**

Titanium has been used extensively in craniofacial surgery and dentistry in the form of implants, plates, and screws.¹³ With its high biocompatibility and physico-mechanical properties, it could be an ideal implant for covering large anatomical defects (categories III–V) and globe malposition if implant-stabilizing surrounding bone or a distal landmark (a ‘bony ledge’) is absent.¹⁴

Titanium mesh is strong, rigidly fixable, widely available, and is subject to osseointegration with minimal foreign body reaction.¹⁵ However, titanium is costly and may have irregular edges if not cut properly, which may impinge soft tissue. Furthermore, fibrous tissue will incorporate the mesh-holes, which can make implant replacement technically complex.¹⁵ Late unwanted effects such as infection, corrosion, and toxic metal ion release have been reported with the use of titanium implants.¹³ One Randomized Control Trial (RCT) has evaluated the effects of titanium implants as compared to perforated (PDS) foil for small orbital floor fracture reconstruction, and found no significant differences in the clinical outcomes.¹⁶ A pilot study without controls used a low-profile 0.25-mm titanium plate in large defects (categories II and III) and found successful clinical outcomes without complications in 93% of the cases; at the 6-month follow-up, no functional or aesthetic concerns were observed.¹⁴

- **Polymers:** Polymers (or plastics) are large molecules comprising multiple repeated subunits and can be categorized into absorbable and non-absorbable (permanent) types.⁶

Non-absorbable permanent polymer implants: Porous ultra-high density polyethylene (**PE; Medpor™**) sheets of various sizes and thicknesses (0.4–1.5 mm) have been used widely to cover smaller floor defects since the 1990s. This widespread use is a product of the ability to easily cut the sheets into various shapes and the ability of orbital tissue to move freely over the smooth surface. Connective tissue and vascular components grow into the pores with minimal foreign body reaction.¹⁷ In a prospective cohort study of floor reconstructions, PE sheets showed satisfactory surgical outcomes and infection rates similar to autografts.¹⁸

Polytetrafluoroethylene (PTFE; Teflon) is biologically and chemically inert, non-antigenic with minimal foreign body reaction, sterilizable, and easily mouldable. However, this polymer has not yet been subject to comparative clinical studies.⁶

Relatively new in orbital floor repair is the use of nylon foil, a non-porous poly-amide. Nylon foil has provided favourable results in preliminary non-comparative studies.¹⁹

Resorbable Osteosynthesis implants: Although the performance and biocompatibility of metallic and titanium fixation in osteosynthesis has been reported as satisfactory, a number of disadvantages have been associated with its use, including stress shielding of bone or osteopenia²⁰, impairment in imaging evaluation²¹ and its restricted use in certain specific circumstances such as pediatric craniofacial surgery.²²

Resorbable materials have been used widely for over 30 years in many fields of surgical practice,²³ and are of interest because of their more predictable absorption rates than biological grafts, as well as their high level of customizability and control.²⁴

Chemistry and mechanism of action: Bioresorbable polymers are mainly high-molecular-weight aliphatic polyesters with repeating units of α -hydroxy acid (HOCHR-COOH) derivatives manufactured by ring-opening polymerization. The absorption of these polymers begins with depolymerization through the hydrolysis of their ester bonds and subsequent metabolism, probably by macrophages, in the citric acid cycle into water and carbon dioxide.²⁵

The first clinically used bioresorbable polymer was polyglycolic acid (PGA), a highly crystalline and high-molecular weight molecule with limited clinical use for osteosynthesis because of its susceptibility to rapid degradation. Approximately 4–7 weeks after implantation, a duration which is insufficient to allow complete bone healing, PGA loses its mechanical strength in vivo. In addition, the side effects of PGA have been detected during its clinical use; these are due to the difficulty in clearing the accumulated acid degradation products. These negative effects have resulted in the minimal use of pure PGA in osteosynthesis.²⁶

Poly-lactic acid (PLA) is another high-molecular-weight bioresorbable polymer; its optically active carbon in lactic acid generates 2 stereoisomeric forms,

namely poly- L -lactide (PLLA) and poly- D -lactide (PDLA). Since the early 1990s, PLLA has been used as an osteosynthesis material.²⁷ Due to its crystallinity and hydrophobicity, PLLA is fairly resistant to hydrolysis, and thus bioresorption with complete loss of its strength in vitro does not occur within the first 2 years of implantation. PDLA, on the other hand, has a lower crystallinity and is less resistant to hydrolysis. Because of its slower degradation rate, PDLA has been reported to be highly biocompatible, although crystalline particles resistant to degradation may elicit some inflammatory response.²⁷

By copolymerization of different derivatives of α -hydroxy acids, a variety of different mechanical qualities and degradation rates can be achieved. Copolymers of L -, D -lactides, for example, SR-P(L/DL)LA 70/30, a copolymer composed of 70% PLLA and 30% PDLA, loses all its strength in vitro after 48 weeks of implantation.²⁸ Copolymers of L -lactide and glycolide (PLGA) have been extensively used owing to the wide range of physiochemical properties of the components.²⁹

Advantages and disadvantages of resorbable implants: The main advantages are easy handling and contourability, smooth surface and smooth edge, do not necessarily require rigid fixation, ideal for pediatric fractures, thin and can be applied in multiple layers in larger orbital volume displacement and without late implant related complications as infection, migration and extrusion.⁶

On the other hand, these materials can be radiolucent on postoperative imaging.⁶ Some authors believed it may not provide enough support to orbital contents in large fractures and demonstrated an increase in orbital volume as a late complication.³⁰

In a RCT, the administration of an absorbable copolymer of PLA and PGA had functional and aesthetic outcomes and complications similar to auricular cartilage implants in orbital blowout fractures with or without medial wall involvement.³¹ In addition, PLA 70/30 plates were studied in a controlled trial and showed similar surgical outcomes and complications as compared to autografts in category II and III floor defects, without MRI evidence of foreign body reaction.³²

Discussion

Depending characteristics of the different materials

of orbital implants, it was feasible to postulate clinical recommendations for materials in specific cases.

Treatment algorithm for orbital wall fractures⁶:

1. Small-sized, low-complexity defects (class I): Most materials are suitable; biological behaviour is most important and resorbables may be used in these cases.
2. Medium-sized, medium-complexity defects (class II): Apart from the bio-logical behaviour of an implant, the experience of the surgeon with specific types of orbital implants will benefit the outcome. Various materials can be used, from autologous materials to alloplasts.
3. Large-sized, high-complexity defects (classes III–VI): Stability and contour become more significant and pre-bent or patient-specific titanium mesh is the preferred reconstruction material.

Conclusion

The debate on the clinical recommendations for orbital reconstruction material will likely continue because of the absence of RCTs and best practice clinical studies. Controversy exists regarding the best material features, which can be defined broadly by whether the implant is: (1) autogenous or allogenic, (2) non-resorbable or resorbable material and (3) malleable or preformed anatomical plates.

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References

1. Kuhn F and D P. ocular trauma : principles and practice. New york: Thieme, 2002, p. 385-8.
2. Tessier P. The classic reprint. Experimental study of fractures of the upper jaw. I and II. Rene Le Fort, M.D. *Plast Reconstr Surg.* 1972; 50: 497-506.
3. Pfeiffer RL. Traumatic Enophthalmos. *Trans Am Ophthalmol Soc.* 1943; 41: 293-306.
4. Bairo F. Biomaterials and implants for orbital floor repair. *Acta Biomater.* 2011; 7: 3248-66.

5. Avashia YJ, Sastry A, Fan KL, Mir HS and Thaller SR. Materials used for reconstruction after orbital floor fracture. *J Craniofac Surg.* 2012; 23: 1991-7.
6. Dubois L, Steenen SA, Gooris PJ, Bos RR and Becking AG. Controversies in orbital reconstruction-III. Biomaterials for orbital reconstruction: a review with clinical recommendations. *Int J Oral Maxillofac Surg.* 2016; 45: 41-50.
7. Tessier P, Woillez M, Lekieffre M and Asseman R. [Posttraumatic diplopia and osseous grafts. Observations]. *Bull Mem Soc Fr Ophtalmol.* 1960; 73: 271-91.
8. Chowdhury K and Krause GE. Selection of materials for orbital floor reconstruction. *Arch Otolaryngol Head Neck Surg.* 1998; 124: 1398-401.
9. Lühr HG and Maerker R. Transplantation of homologous dura in reconstruction of the orbital floor. *Trans Int Conf Oral Surg.* 1973; 4: 340-4.
10. Prichard JV, Thadani R and E. K. Rapidly progressive dementia in a patient who received a cadaveric dura mater graft. *MMWR Morb Mortal Wkly Rep.* 1987; 36: 49-50.
11. Guerra MF, Perez JS, Rodriguez-Campo FJ and Gias LN. Reconstruction of orbital fractures with dehydrated human dura mater. *J Oral Maxillofac Surg.* 2000; 58: 1361-6.
12. Aho AJ, Hirn M, Aro HT, Heikkilä JT and Meurman O. Bone bank service in Finland. Experience of bacteriologic, serologic and clinical results of the Turku Bone Bank 1972-1995. *Acta Orthop Scand.* 1998; 69: 559-65.
13. Mackenzie DJ, Arora B and Hansen J. Orbital floor repair with titanium mesh screen. *J Craniomaxillofac Trauma.* 1999; 5: 9-16.
14. Dubois L, Steenen SA, Gooris PJ, Mourits MP and Becking AG. Controversies in orbital reconstruction--I. Defect-driven orbital reconstruction: a systematic review. *Int J Oral Maxillofac Surg.* 2015; 44: 308-15.
15. Schubert W, Gear AJ, Lee C, et al. Incorporation of titanium mesh in orbital and midface reconstruction. *Plast Reconstr Surg.* 2002; 110: 1022-30.
16. Dietz A, Ziegler CM, Dacho A, et al. Effectiveness of a new perforated 0.15 mm poly-p-dioxanon-foil versus titanium-dynamic mesh in reconstruction of the orbital floor. *J Craniomaxillofac Surg.* 2001; 29: 82-8.
17. Dougherty WR and Wellisz T. The natural history of alloplastic implants in orbital floor reconstruction: an animal model. *J Craniofac Surg.* 1994; 5: 26-32.
18. Wajih WA, Shaharuddin B and Razak NH. Hospital Universiti Sains Malaysia experience in orbital floor reconstruction: autogenous graft versus Medpor. *J Oral Maxillofac Surg.* 2011; 69: 1740-4.
19. Park DJ, Garibaldi DC, Iliff NT, Grant MP and Merbs SL. Smooth nylon foil (SupraFOIL) orbital implants in orbital fractures: a case series of 181 patients. *Ophthalmic Plast Reconstr Surg.* 2008; 24: 266-70.
20. Paavolainen P, Karaharju E, Slati P, Ahonen J and Holmstrom T. Effect of rigid plate fixation on structure and mineral content of cortical bone. *Clin Orthop Relat Res.* 1978; 136: 287-93.
21. Fiala TG, Novelline RA and Yaremchuk MJ. Comparison of CT imaging artifacts from craniomaxillofacial internal fixation devices. *Plast Reconstr Surg.* 1993; 92: 1227-32.
22. Orringer JS, Barcelona V and Buchman SR. Reasons for removal of rigid internal fixation devices in craniofacial surgery. *J Craniofac Surg.* 1998; 9: 40-4.
23. Francel TJ, Birely BC, Ringelman PR and Manson PN. The fate of plates and screws after facial fracture reconstruction. *Plast Reconstr Surg.* 1992; 90: 568-73.
24. Lyu S and Untereker D. Degradability of polymers for implantable biomedical devices. *Int J Mol Sci.* 2009; 10: 4033-65.
25. Pietrzak WS. Principles of development and use of absorbable internal fixation. *Tissue Eng.* 2000; 6: 425-33.
26. Vasenius J, Vainionpää S, Vihtonen K, et al. Comparison of in vitro hydrolysis, subcutaneous and intramedullary implantation to evaluate the strength retention of absorbable osteosynthesis implants. *Biomaterials.* 1990; 11: 501-4.
27. Pihlajamäki H, Bostman O, Hirvensalo E, Tormala P and Rokkanen P. Absorbable pins of self-reinforced poly-L-lactic acid for fixation of fractures and osteotomies. *J Bone Joint Surg Br.* 1992; 74: 853-7.
28. Tormala P, Pohjonen T and Rokkanen P. Bioabsorbable polymers: materials technology and surgical applications. *Proc Inst Mech Eng H.* 1998; 212: 101-11.

29. Pietrzak WS and Kumar M. An enhanced strength retention poly(glycolic acid)-poly(L-lactic acid) copolymer for internal fixation: in vitro characterization of hydrolysis. *J Craniofac Surg.* 2009; 20: 1533-7.
30. Cordewener FW, Bos RR, Rozema FR and Houtman WA. Poly(L-lactide) implants for repair of human orbital floor defects: clinical and magnetic resonance imaging evaluation of long-term results. *J Oral Maxillofac Surg.* 1996; 54: 9-13.
31. Kruschewsky Lde S, Novais T, Daltro C, et al. Fractured orbital wall reconstruction with an auricular cartilage graft or absorbable polyacid copolymer. *J Craniofac Surg.* 2011; 22: 1256-9.
32. Al-Sukhun J and Lindqvist C. A comparative study of 2 implants used to repair inferior orbital wall bony defects: autogenous bone graft versus bioresorbable poly-L/DL-Lactide [P(L/DL)LA 70/30] plate. *J Oral Maxillofac Surg.* 2006; 64: 1038-48.

Recent Trends in Management of Rhegmatogenous Retinal Detachment

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Abstract

Purpose: To review different method for management of rhegmatogenous retinal detachment (RRD), different indications, advantages and recent modifications for each technique.

Summary: Rhegmatogenous retinal detachment (RRD) is caused by retinal break which held open by vitreoretinal traction and causes accumulation of liquefied vitreous under the neurosensory retina separating it from the retinal pigment epithelium (RPE). There are three lines for surgical management of RRD; pneumatic retinopexy, scleral buckling and pars plana vitrectomy (PPV) with different new modifications aiming for easier surgeries and better results.

Keywords: Rhegmatogenous retinal detachment, pneumatic retinopexy, scleral buckle, vitrectomy.

Introduction

Rhegmatogenous retinal detachment (RRD) affects about 1 in 10.000 of the population each year and may affect both eyes in about 10% of cases. It is characterized by the presence of a retinal break which held open by vitreoretinal traction and causes accumulation of liquefied vitreous under the neurosensory retina separating it from the retinal pigment epithelium (RPE).⁽¹⁾

One of the most common risk factors of RRD is posterior vitreous detachment (PVD). with age, collagen fibers are fragmented and proteoglycans are aggregated around these fragments and these changes may be responsible for liquefaction of vitreous which can pass into the subhyaloid space and separate the posterior vitreous surface from the internal limiting membrane(ILM) of the retina producing a true PVD.⁽²⁾

Other factors that accelerate vitreous liquefaction include enzymatic vitreolysis with ocriplasmin, cataract surgery, high myopia, ocular inflammation, and trauma.⁽³⁾

Proliferative vitreoretinopathy (PVR) represents one of the most common complications of RRD causing failure of surgical repair. It develops when RPE cells are dispersed into the vitreous cavity through a retinal break and form membranes on the inner retinal surface which lead to the reopening of retinal breaks or the creation of new ones causing retinal re-detachment.⁽⁴⁾

There are different risk factors for development of PVR as presence of large retinal breaks or giant tears, vitreous hemorrhage, multiple previous eye surgeries, previous ocular trauma, preexisting PVR, prolonged ocular inflammation, viral infections of the posterior segment and prolonged chorioretinitis.⁽⁵⁻⁷⁾

There are three lines for surgical management of RRD; pneumatic retinopexy, scleral buckling and pars plana vitrectomy(PPV) with primary success rates of up to 90%.⁽⁸⁾

The purpose of that review is to identify the current management and recent modifications in techniques for treatment of RRD.

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Pneumatic Retinopexy: Pneumatic retinopexy is a minimally invasive procedure for correction of RRD. It consists of injecting an expandable gas and applying retinal cryotherapy or laser photocoagulation to close retinal breaks yielding good results in carefully selected patients.⁽⁹⁾

This technique was first described by Rosengren in 1938, then it was widely practiced after the publication of Hilton and Gizzard's seminal paper in 1986, in which they described what was known as modern pneumatic retinopexy.⁽¹⁰⁾

Pneumatic retinopexy is indicated for uncomplicated RRD without PVR. The ideal cases are those with one break or a group of breaks within 1 clock hour and retinal breaks involving the superior 8 clock hours of the retina.⁽⁹⁾

In appropriately selected patients, outcomes are comparable to alternative techniques, and it has the benefits of reduced morbidity, reduced costs and faster postoperative recovery.⁽¹¹⁾

A review of 81 studies including 4,138 eyes undergoing pneumatic retinopexy revealed a single operation success rate of 74.4% and a final success rate of 96.1% after further scleral buckling or vitrectomy procedures.⁽¹²⁾

Careful preoperative examination is essential for that technique, including scleral indentation to examine the far peripheral retina, transconjunctival cryopexy is applied over the peripheral retinal break, or laser retinopexy may be used if the tear was posterior and must be performed 24–48 hours after gas injection, paracentesis, then the gas either C3F8 or SF6 at 100% expansible concentration is injected. Insertion of needle is perpendicular to the sclera directed to the center of the vitreous cavity, then the needle is withdrawn to leave 2–3 mm of it within the globe, then brisk injection of the gas to avoid fish-egg gas bubbles.⁽⁹⁾

Scleral buckling (SB): SB surgery was introduced in 1951 by Charles Schepens, which had a high rate of success and became the treatment of choice for RRD.⁽¹³⁾ It is indicated for RRD in young age, phakic eyes, and in limited retinal detachment, particularly with an inferior detachment.⁽¹⁴⁾

The aim of SB is to reduce the vitreous traction and close the retinal break as the sclera is pressed inward so that the vitreous traction is lessened to close the retinal

break.⁽¹⁵⁾ It has several advantages over PPV, including early visual rehabilitation and prevention of cataract formation⁽¹⁵⁾ but there are some difficulties to learn it due to the steep learning curve, declining mastery over indirect ophthalmoscopy and poor ergonomics associated with the surgery, and so there are some modifications to some of the steps of SB to make them safer, more precise and make the process of learning the art of SB easier.⁽¹⁶⁾

As regards localization of break and retinopexy, chandelier-assisted SB using a chandelier and a wide-angle fundus viewing system has the advantages of better visualization, familiarity to the predominantly vitrectomy trained surgeons and improved ergonomics⁽¹⁷⁾, also an illuminated scleral depressor is a new technique to improve localization.⁽¹⁶⁾

Sutureless buckling is simple, fast, and safe technique which can be performed in most eyes with RRD specially with localized areas up to 1½ clock hours or ½ a quadrant, also more than one explant can also be placed in multiple quadrants in eyes with multiple breaks.⁽¹⁸⁾

In eyes with a single retinal break, an intrascleral buckle can be placed by creating scleral pocket to house the silicone segment, then silicone segment is placed in the scleral pocket, and a single suture is used to close the pocket. This is an extremely localized buckle and does not cause much refractive change.⁽¹⁶⁾

Minimal segmental buckling is also a fast, simple, effective technique for repair of RD and it is suitable for cases with single break or breaks restricted to few clock hours (ideally <3 clock hours). In this technique, a silicon segment is placed either circumferentially for multiple breaks and retinal dialysis or radially for horseshoe tear, then suture bites are oriented parallel to the limbus for circumferential segments and radially for radial segments as the buckling effect is achieved with suture. It is preferable to use this technique in cases with the absence of other lesions which can predispose to RD in rest of the quadrants. Minimal segmental buckling needs minimal manipulation and may have less postoperative pain.⁽¹⁹⁾

To avoid complications of subretinal fluid drainage, trans-scleral needle drainage technique may be alternative using 26 gauge ½ inch needle to perforate the sclera and drain the SRF with advantage of small entry site decreasing the risk of hemorrhage and incarceration.²⁰

Also, infusion-assisted drainage can be used to prevent the hypotony during drainage by placing a 25G infusion as in vitrectomy and turned on during SRF drainage to ensure maintenance of intraocular pressure during drainage and also assists in draining. The infusion cannula is placed in the same quadrant of drainage site and is placed just before drainage of SRF to avoid inadvertent kinking of the cannula and lens trauma when rotating the eye for visualizing the drainage site.⁽¹⁶⁾

A new technique has recently been described for suprachoroidal buckling, in which an illuminated catheter is inserted into the suprachoroidal space and directed to any desired location where peripheral breaks are present, and then long-lasting hyaluronic acid filler can be injected to create internal choroidal indentation. This can be performed without or in combination with vitrectomy and has been used successfully for the treatment of RRD.⁽²¹⁾

Pars Plana Vitrectomy (PPV): PPV is currently the most commonly used procedure for the repair of RRD⁽²²⁾. Over last decades, this procedure has been progressively improved due to advanced technology, such as the development of small-gauge instrumentation and the use of intraocular perfluorocarbon liquid, silicone oil, and gases. All of these have played a part in making PPV a highly effective technique for repair of simple and complex RRDs, and new modifications are still being made.⁽²³⁾

There are multiple risk factors for surgical failure after PPV include longer duration of symptoms, older age, larger extent of RD, macular detachment, inferior detachment, absence of detectable retinal breaks, high myopia, hypotony, and PVR-related risk factors such as pseudophakia, aphakia, uveitis, vitreous hemorrhage, and preoperative PVR.⁽²⁴⁾

The internal limiting membrane (ILM) was first named by Pacini in 1845 and represents the barrier between the retina and the vitreous body.⁽¹⁾

The inverted ILM flap technique was compared with ILM peeling only in a retrospective study which revealed higher rates of macular hole closure and retinal reattachment, significant improvement in the final visual acuity with this technique and it has been suggested that the inverted ILM flap may stimulate the proliferation of glial cells that aid in closing the hole.⁽²⁵⁾

Another comparative study has also investigated

the effectiveness of combining a macular buckle with PPV and ILM peeling in highly myopic eyes and RD with macular hole and revealed a higher rate of retinal reattachment and macular hole closure in combined surgery group.⁽²⁶⁾

For treatment of macular folds, which may complicate RRD surgery and have significant implication on the visual prognosis, induced detachment of the macula can be performed by the subretinal injection of balanced salt solution, as well as the addition of filtered air, under these conditions, the action of gravity of the perfluorocarbon liquid in the vitreous cavity combined with an active globe manipulation may achieve successful flattening of the macula.⁽²⁷⁾

Recent studies have evaluated the potential of high-frequency electric welding (HFEW) for creation of immediate chorioretinal adhesion to obviate the need for long-term tamponade and used it in a rabbit model of retinal tear and one study reported that it was able to create an immediate retinopexy equal in strength to mature laser retinopexy.⁽²⁸⁾

Development of ERM is one of complications of PPV for repair of RRDs has been reported to range from 4.4% to 12.8%⁽²⁹⁾ specially in cases with multiple or large retinal breaks⁽³⁰⁾, equatorial breaks and a longer duration of macular detachment.⁽²⁹⁾

Various studies compared PPV with ILM peeling versus PPV without ILM peeling in patients with RRD and revealed a lower incidence of postoperative ERM in patients with ILM peeling.⁽³¹⁾

For management of severe PVR, soft-shell technique may improve retinal flattening and prevent passage of perfluorocarbon liquid into the subretinal space by injecting ophthalmic viscoelastic devices (OVDs) over areas of retinal folds with possible retinal breaks, this protective layer allowed the perfluorocarbon liquid placed over it to achieve retinal flattening and prevented it from entering the subretinal space.⁽³²⁾

In recent years, partially fluorinated alkanes (FALKs) were introduced as long-term heavy tamponades, which are heavier than water and may be beneficial especially in the treatment of lower RRD or PVR. A recent study investigated the use of F6H8 in combination with silicone oil, in cases with inferior RRD with PVR, where F6H8 was used to flatten the retina and was later partially mixed with silicone oil

for long-term tamponade. This combination resulted in a clear tamponade allowing postoperative visualization of the retina, with no emulsification, inflammation, or other complications. The best results were reported with F6H8/SO ratios between 50/50 and 30/70.⁽³³⁾

Two-step surgery is another option for severe PVR as an initial surgery is done first to repair the retinal detachment in which perfluorocarbon liquid tamponade is left for 2 to 3 weeks, followed by a second procedure in which it is removed. A recent study reported good results with this technique in 44 eyes with retinal detachment complicated by grade C PVR.⁽³⁴⁾

Conclusion

There are different techniques for surgical management of RRD and every day there are new modifications in these techniques which aim at easier surgeries and more satisfactory results for the patients.

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References

1. Wollensak G, Spoerl E, Grosse G, Wirbelauer C. Biomechanical significance of the human internal limiting lamina. *Retina*. 2006;26(8):965-8.
2. Neal RE, Bettelheim FA, Lin C, Winn KC, Garland DL, Zigler JS, Jr. Alterations in human vitreous humour following cataract extraction. *Exp Eye Res*. 2005;80(3):337-47.
3. Stalmans P, Benz MS, Gandorfer A, Kampik A, Girach A, Pakola S, et al. Enzymatic vitreolysis with ocriplasmin for vitreomacular traction and macular holes. *N Engl J Med*. 2012;367(7):606-15.
4. Pennock S, Haddock LJ, Mukai S, Kazlauskas A. Vascular endothelial growth factor acts primarily via platelet-derived growth factor receptor alpha to promote proliferative vitreoretinopathy. *Am J Pathol*. 2014;184(11):3052-68.
5. Girard P, Mimoun G, Karpouzas I, Montefiore G. Clinical risk factors for proliferative vitreoretinopathy after retinal detachment surgery. *Retina*. 1994;14(5):417-24.
6. Duquesne N, Bonnet M, Adeleine P. Preoperative vitreous hemorrhage associated with rhegmatogenous retinal detachment: a risk factor for postoperative proliferative vitreoretinopathy? *Graefes Arch Clin Exp Ophthalmol*. 1996;234(11):677-82.
7. Yanyali A, Bonnet M. [Risk factors of postoperative proliferative vitreoretinopathy in giant tears]. *J Fr Ophtalmol*. 1996;19(3):175-80.
8. Hafez E, Sena DF, Fallano KA, Crews J, Do DV. Pneumatic retinopexy versus scleral buckle for repairing simple rhegmatogenous retinal detachments. *Cochrane Database Syst Rev*. 2015;7(5).
9. Stewart S, Chan W. Pneumatic retinopexy: patient selection and specific factors. *Clin Ophthalmol*. 2018;12:493-502.
10. Hilton GF, Grizzard WS. Pneumatic retinopexy. A two-step outpatient operation without conjunctival incision. *Ophthalmology*. 1986;93(5):626-41.
11. Goldman DR, Shah CP, Heier JS. Expanded criteria for pneumatic retinopexy and potential cost savings. *Ophthalmology*. 2014;121(1):318-26.
12. Chan CK, Lin SG, Nuthi AS, Salib DM. Pneumatic retinopexy for the repair of retinal detachments: a comprehensive review (1986-2007). *Surv Ophthalmol*. 2008;53(5):443-78.
13. Schepens CL, Okamura ID, Brockhurst RJ. The scleral buckling procedures. I. Surgical techniques and management. *AMA Arch Ophthalmol*. 1957;58(6):797-811.
14. Haring G, Wiechens B. Long-term results after scleral buckling surgery in uncomplicated juvenile retinal detachment without proliferative vitreoretinopathy. *Retina*. 1998;18(6):501-5.
15. Park SW, Lee JJ, Lee JE. Scleral buckling in the management of rhegmatogenous retinal detachment: patient selection and perspectives. *Clin Ophthalmol*. 2018;12:1605-15.
16. Shanmugam PM, Ramanjulu R, Mishra KCD, Sagar P. Novel techniques in scleral buckling. *Indian J Ophthalmol*. 2018;66(7):909-15.
17. Gogia V, Venkatesh P, Gupta S, Kakkar A, Garg S. Endoilluminator-assisted scleral buckling: our results. *Indian J Ophthalmol*. 2014;62(8):893-4.
18. Shanmugam PM, Singh TP, Ramanjulu R,

- Rodrigues G, Reddy S. Sutureless scleral buckle in the management of rhegmatogenous retinal detachment. *Indian J Ophthalmol.* 2015;63(8):645-8.
19. Kreissig I. View 1: minimal segmental buckling without drainage. *Br J Ophthalmol.* 2003;87(6):782-4.
 20. Agarwal MK. Modified needle drainage. A safe and efficient technique of subretinal fluid drainage in scleral buckling procedure: *Indian J Ophthalmol.* 2004 Dec;52(4):342-3; author reply 343.
 21. El Rayes EN, Mikhail M, El Chewieky H, Elsayah K, Maia A. Suprachoroidal Buckling for the Management of Rhegmatogenous Retinal Detachments Secondary to Peripheral Retinal Breaks. *Retina.* 2017;37(4):622-9.
 22. Schwartz SG, Flynn HW, Jr., Mieler WF. Update on retinal detachment surgery. *Curr Opin Ophthalmol.* 2013;24(3):255-61.
 23. Nemet A, Moshiri A, Yiu G, Loewenstein A, Moisseiev E. A Review of Innovations in Rhegmatogenous Retinal Detachment Surgical Techniques. *J Ophthalmol.* 2017;4310643(10):7.
 24. Adelman RA, Parnes AJ, Michalewska Z, Ducournau D. Clinical variables associated with failure of retinal detachment repair: the European vitreo-retinal society retinal detachment study report number 4. *Ophthalmology.* 2014;121(9):1715-9.
 25. Matsumura T, Takamura Y, Tomomatsu T, Arimura S, Gozawa M, Kobori A, et al. Comparison of the Inverted Internal Limiting Membrane Flap Technique and the Internal Limiting Membrane Peeling for Macular Hole with Retinal Detachment. *PLoS One.* 2016;11(10).
 26. Ma J, Li H, Ding X, Tanumiharjo S, Lu L. Effectiveness of combined macular buckle under direct vision and vitrectomy with ILM peeling in refractory macular hole retinal detachment with extreme high axial myopia: a 24-month comparative study. *Br J Ophthalmol.* 2017;101(10):1386-94.
 27. Barale PO, Mora P, Errera MH, Ores R, Paques M, Sahel JA. Treatment of Macular Folds Complicating Retinal Detachment Surgery Using Air for Retinal Unfolding. *Retin Cases Brief Rep.* 2018;12(3):228-30.
 28. Umanets N, Pasychnikova NV, Naumenko VA, Henrich PB. High-frequency electric welding: a novel method for improved immediate chorioretinal adhesion in vitreoretinal surgery. *Graefes Arch Clin Exp Ophthalmol.* 2014;52(11):1697-703.
 29. Martinez-Castillo V, Boixadera A, Distefano L, Zapata M, Garcia-Arumi J. Epiretinal membrane after pars plana vitrectomy for primary pseudophakic or aphakic rhegmatogenous retinal detachment: incidence and outcomes. *Retina.* 2012;32(7):1350-5.
 30. Katira RC, Zamani M, Berinstein DM, Garfinkel RA. Incidence and characteristics of macular pucker formation after primary retinal detachment repair by pars plana vitrectomy alone. *Retina.* 2008;28(5):744-8.
 31. Fallico M, Russo A, Longo A, Pulvirenti A, Avitabile T, Bonfiglio V, et al. Internal limiting membrane peeling versus no peeling during primary vitrectomy for rhegmatogenous retinal detachment: A systematic review and meta-analysis. *PLoS One.* 2018;13(7).
 32. Yamakiri K, Uchino E, Sakamoto T. Soft shell technique during vitrectomy for proliferative vitreoretinopathy. *Graefes Arch Clin Exp Ophthalmol.* 2016;254(6):1069-73.
 33. Tosi GM, Marigliani D, Bacci T, Romeo N, Balestrazzi A, Martone G, et al. F6H8 as an Intraoperative Tool and F6H8/Silicone Oil as a Postoperative Tamponade in Inferior Retinal Detachment with Inferior PVR. *J Ophthalmol.* 2014;956831(10):2.
 34. Sigler EJ, Randolph JC, Calzada JI, Charles S. Pars plana vitrectomy with medium-term postoperative perfluoro-N-octane for recurrent inferior retinal detachment complicated by advanced proliferative vitreoretinopathy. *Retina.* 2013;33(4):791-7.

Study the Composition of Fatty Acids in Blood Serum Parts During the Fasting Month (Ramadan)

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Abstract

This study dealt with the measurement of several variables in the blood serum for a group of people in the case of fasting (Ramadan) for (14-16) hours, where the blood serum was withdrawn from people during daylight hours after fasting (5-8) hours and then follow the same people After (15) days of fasting and then after (25) days as well as blood serum samples were collected for the same people one month after the end of the month of Ramadan and the age of people ranged between (19-80)years and both sexes (males and females) are healthy people and do not suffer from any apparent disease. The study focused on measuring the percentage of fatty acids in the three segments separated from serum (cholesterol ester, triglyceride and phospholipids) which were separated by thin layer chromatography and then the esterification of the separated fatty acids was carried out using (BF₃/methanol) method. Percentage of fatty acids (SFA, MUFA and PUFA) using a capillary gas chromatography device The results of this study indicated a significant increase in the percentage of saturated fatty acids, a non-significant decrease in the percentage of monounsaturated fatty acids, and a non-significant decrease in the percentage of polyunsaturated fatty acids in The serum cholesterol ester portion of the fasting group compared with the control group The results of this study indicated a significant increase in the percentage (SFA), a non-significant decrease in the percentage (MUFA), and a non-significant increase in the percentage (PUFA) in the Tricyclic serum for serum group The results of this study showed a significant increase in the percentage (SFA), a significant decrease in the percentage (MUFA), and a significant non-significant decrease in the percentage (PUFA) in the serum phosphate fat portion of the fasting group compared with Control group.

Keywords: *Fatty acids, cholesterol ester, fasting, saturated fatty acid.*

Introduction

This study was designed to identify the effect of fasting on the level of chemotactic variables and the percentage of fatty acids in serum. Fasting is an integral part of many religions in terms of the pattern, duration and limits of fasting that differ between different religions [1], and fasting in biochemical conditions is to refrain from eating calories for (12-14) hours (2). Ramadan is the ninth month of the Islamic calendar during this month and it is expected that all healthy adult Muslims, males and females abstain from foods, liquids, oral medications and smoking from dawn to sunset and this type of fasting is addressed in our study, which lasts (29 to 30 days) [3] Fasting affects many metabolic processes in the human body and physiological indicators return to normal after the end of the month of fasting, indicating the safety of fasting for healthy people. [1]. The human diet is a complex mixture of reactive components that

cumulatively affect health^[2]. and fast e An excellent model of how dietary modifications affect lipid profile^[3]. studies have shown beneficial changes in serum on chemotactic variables in terms of high variables (HDL) and low variables (TG, TC, LDL) that are considered to be the main risk factors For coronary heart disease and cerebro vascular disease^[4] diet modification (fasting) is a treatment for hyperlipidemia and is also taken in conjunction with drug therapy in people with coronary heart disease risk . Fasting also affects the percentages of fatty acids in the three parts of the blood serum, as this effect is positive and the percentage of fatty acids with different varieties is balanced in the three parts of the blood serum.^[1]

Materials and Method

Blood samples were collected for healthy people who were fasting after a period days and then follow

up the people themselves after (20) days of fasting and control group where the samples were collected for the period (17/5-16/6 (2018), where (5) milliliters of blood was withdrawn for each person and then the samples are left for Serum is separated. After that, the serum divided into two parts.

Section 1: Measurement GLU, TC, HDL, LDL, TG, PL by Kits and VLDL was theoretically calculate.

The second section kept in freezing at (-18)°C until the start of the analysis of fatty acids.

The percentage of fatty acids of the three parts of the serum (CE, PL and TG) was measured after the separation of each of the three parts using (TLC) technique. These parts are distributed on the used silica gel plate resulting from the separation of serum components blood using a solvent system consisting of (hexane/ether/formic acid) in percentages (2:20:80) (V/V/V). [5]

The fatty acids are then re-esterified for each of the three previously separated parts using BF₃/Methanol (16%)^[6] and then diagnosis and analysis of the percentage of fatty acids for each part using standard models.

Percentage of fatty acids: The serum fatty acid content of the above three components was estimated by means of injecting (1) micro-liters of the model prepared for measurement in the (CGC)^[7] Figure (1) shows the graph resulting from the analysis and measurement of the ratio of (23) fatty acid standard using the device (CGC).

Table (1): Standard fatty acids

Fatty Acids	Retention Time	Percentage
C 4:0	2.28	0.09
C 6:0	3.62	0.14
C 11:0	6.47	0.15
C 12:0	10.81	0.172
C 14:0	13.23	0.084
C 15:0	15.71	0.18
C 16:0	18.12	0.086
C 18:0	20.51	0.17
C 18:1trans	21:25	0.095
C 18:1cis	22:79	0.036
C 18:2	23:46	0.048
C 18:3	27:47	0.068
C 20:0	25:22	0.363
C 21:0	29.73	0.338

Fatty Acids	Retention Time	Percentage
C 22:0	30.33	0.01
C 22:1	31.48	0.039
C 20:4	33.67	0.178
C 23:0	34.34	0.03
C 22:2	35.70	0.024
C 24:0	37.32	0.323
C 20:5	38.74	0.031
C 24:1	39.23	0.015
C 22:6	40.73	0.099

Statistical analysis: The results were analyzed for the levels of chemotherapeutic variables (Glu, TC, LDL, HDL, VLDL, TG and PL) as well as percentage analysis of fatty acids in the three segments separated from serum lipids. Blood using t-test for groups of equal number and different totals to compare the results of people fasting with the control group in general, where the acceptable probability level is (P> 0.05) [8].

Results and Discussion

The results of this study showed a significant decrease in (Glu) concentration in the fasting group compared with the control group. This may be attributed to lower calorie intake during Ramadan compared to other months as well as the nature of muscular effort and sleep during fasting month. [9] The results indicated a significant decrease in (TC) concentration in the fasting group compared to the control group. This is consistent with several studies that indicated this decrease during fasting. Insulin sensitivity. The results also indicated a significant increase in (HDL-C) level in the fasting group compared to the control group. This corresponds to several studies in the case of fasting. The role of hepatic lipase, which controls the level of (HDL-C) and during fasting, is an increase in the effectiveness of hepatic lipase which leads to an increase in the level of this type of cholesterol during the fasting period and low level of (TC) [10]. This study indicated a significant decrease in (LDL-C) level in the fasting group compared with the control group. This corresponds to a number of studies that indicated the possibility of (LDL-C) level during the fasting period [11]. There was a significant decrease in the (TG) in serum in the fasting group compared with the control group. This can be due to the nature of food intake during the fasting period as the concentration of this type of fat depends on the level of neutral triglycerides, which are directly related to the food [12]. (LDL/HDL) is an important clinical indicators to diagnose the risk of

disease Cardiovascular [13]. The increase or decrease in this ratio is an indication of the progression of metabolic processes within the normal level and the normal ratio should be less than 3.3 [14]. The ratio (TC/HDL) refers to this ratio. The risk of developing cardiovascular disease and its probability of occurrence is more specific than the total cholesterol level of serum [15]. The results of this study indicated a significant decrease in this percentage of the total fasting compared with the control group, and the ratio (TG/HDL). This is one of the important indicators on the occurrence of atherosclerosis and the higher this percentage increased the probability of developing atherosclerosis [16]. The results of this study showed a significant decrease in this ratio to the fasting group compared to the control group. This indicates the usefulness of fasting affecting the insulin level. The results of this study indicated a significant decrease in (PL) in the fasting group compared to the control group. The hepatic lipase enzyme is effective during fasting, leading to increased lipolysis in general and phospholipids in particular [17]. All results shown in Table (2).

Table (2): Biochemical parameters in control group and fasting group

Biochemical Parameters	Control	Fasting	P value
N mmol/l	50	50	
Glucose	5.04±0.94 *	4.13±0.78*	0.001 <
TC	4.91±0.81	4.60±0.97	0.093
HDL-C	1.27±0.42	1.43±0.43	0.059
LDL-C	3.68±0.70	3.13±0.85	0.001
VLDL-C	0.58±0.30	0.44±0.14	0.009
TG	1.40±0.71	1.044±0.53	0.004
TC/HDL-C	3.86±1.66	3.55±1.12	0.262
LDL-C/HDL-C	2.89±1.02	2.51±1.00	0.334
TG/HDL-C	1.05±0.62	0.79± 0.46	0.051
PL mg/100ml	126±34.3	80.3±2.97	0.017

* Mean±SD

Fatty acids in the cholesterol ester: The results of this study showed a significant increase in the percentage of (SFA) for the fasting group compared with the control group. A significant decrease in the percentage of (MUFA) for the fasting group compared with the control group. There was a significant decrease in the ratio of (PUFA) to the fasting group compared to the control group as shown in Fig. 2 and Table 3. Lipid triglycerides in adipose tissue (ATGL) that oxidize and metabolize fats, especially cholesterol ester and triglycerides in adipose tissue [18][19]. Located in food with their

serum levels and give an indication of the usefulness of fasting in affecting the proportion of fatty acids of all kinds in this part of the blood serum [20][21].

Table (3): Fatty acids in the cholesterol ester

Fatty Acid	Control	Fasting
SFA	n=25	n=25
6:0	5.22±0.16*	4.40±1.49
11:0	1.95±0.16	4.25±1.70
12:0	2.35± 0.18	4.84±1.36
14:0	2.55±0.18	3.71±0.33
15:0	2.27± 0.14	4.44±1.84
16:0	2.35±0.19	8.78±3.89
18:0	2.16±0.11	2.42±0.33
20:0	2.74±0.10	2.13±0.52
21:0	5.85±0.12	4.08±1.18
22:0	1.86±0.01	2.49±0.47
23:0	2.51±0.02	2.31±0.88
24:0	2.66±0.23	1.99±0.49
Total	34.47± 1.6	45.83± 15.48
MUFA		
18:1trans	5.00± 0.12	3.76±0.19
18:1cis	2.55±0.21	1.58±0.46
22:1	2.12±0.28	0.61± 0.01
24:1	2.32±0.17	2.81±0.67
Total	11.99±0.78	8.76±1.33
PUFA		
18:2 n6	2.51±0.17	2.51±0.45
18:3 n6	2.50±0.28	2.15±0.45
20:4 n6	2.91±0.21	1.92±0.34
22:2 n6	2.06±0.28	3.03± 1.42
20:5 n3	2.59±0.19	2.24±0.33
Total	12.57±1.13	11.85±2.99

* Mean±SD

Fatty acids in the triglyceride: The results of this study indicated a significant increase in (SFA) for the fasting group compared with the control group as . This may be due to insulin sensitivity during the fasting period. There is an inverse relationship between insulin sensitivity and fatty acid level [22]. This is due to the effect of fasting on a number of specific enzymes. By removing saturation and elongation which plays an important role in increasing . This may be due largely to food intake in addition to the effect of fasting on enzymes that regulate lipolysis [23] which leads to the formation of a greater percentage of polyunsaturated fatty acids through increased fat oxidation and de-saturation of some short-chain acids and converted to long chain (PUFA) and this

corresponds to a number of recent studies in the field of fasting^[24]. The percentage of fatty acids indicates and its installed in triple part of the serum in general to the amount of fatty acids within the existing food intake, as the proportion of fatty acids in this part of the blood serum are highly correlated associated with the nature and the amount of fatty acids present in the intake of food during the fasting period^[25].

Fatty acids in the phospholipids: The results of this study indicated a significant increase in the (SFA) of the fasting group compared with the control group . This may be due to the role of the liver during the fasting process as the liver plays an essential role in the formation or demolition of this type of phospholipids by controlling the amount of (SFA) entering or exiting the blood serum to the liver, which affects the percentage of this type of acid as the process of demolition of fat increases during the fasting period and the liver plays a major role in this process ^[26] and to The presence of a significant decrease in the level of fatty acids This may be attributed to the fact that fasting affects the body mass rate in the first stage by activating the activity of the enzyme lipop utinlayase and thus affecting the rate of formation of triglycerides. The results of this study indicated that there was increase in the percentage of fatty acid (22: 2n6) of serum dimple, fasting group compared with the total This can be attributed to insulin sensitivity, which in turn affects the action of de-saturating enzymes, since the action of these enzymes is closely related to The results of this study indicated that there is a variation in the percentage of fatty acids in this part of the blood serum compared ester cholesterol and triglycerides, which is consistent with many studies in this area. As the proportion of fatty acids in this part of the blood serum.^[27] It is an indication of the importance of fasting by increasing compatibility and hepatogenesis of both (SFA), especially fatty acid (16: 0) and (PUFA) n: 3, as phospholipids are a good vector for recycling fatty acid of fatty proteins it promotes the health of the body through the redistribution and transmission of fatty acids between different parts of the serum ^[28].

Conclusions

1. The study indicated a significant decrease in serum(TC) level in the fasting group compared to the control group, which indicates the usefulness of fasting in reducing the risk of high serum cholesterol. High serum cholesterol leads to an increased risk of heart disease and atherosclerosis.

2. The study indicated a significant rise in(HDL) level and a significant decrease in LDL level. This proves the role of fasting in controlling metabolism in general and fat metabolism in particular. The body fats fat during fasting as a major source of energy during the fasting period and then the body returns to normal after breakfast.
3. The study indicated the effect of fasting on the level of fatty acids (PUFA/MUFA/SFA) in the three parts of the serum where the effects were different from high percentage of fatty acids and low percentage of (MUFA). The multicomponent compared with control groups demonstrating the role of fasting in influencing the metabolism of all types of fatty acids in different parts of the serum.

Ethical Clearance: All samples were taken from colleges at dept. of chemistry-Mosul university, according to their agreement.

Source of Funding: Self-funding.

Conflict of Interest: Nil.

References

1. Chtourou H. Effects of Ramadan Fasting on Health and Athletic Performance. 2013. 3–6 p.
2. M. RJS. Changes in blood glucose and lipid profile during Ramadan Fasting. JAMC. 2000;12(3):13–5.
3. H. S. The effect of ramadan fasting on the body fat. Ann Biol Res. 2012;3(8):3958–61.
4. H. E. Effect of Ramadan Fasting on Blood Levels of glucose, triglyceride and cholesterol. J Public Health (Bangkok). 2006;1(3):203–6.
5. Junior A. Metabolism during fasting and starvation understanding the basics to glimpse new boundaries. J Nutr Diet. 2017;1(1):102.
6. M. F. Effect of intermittent fasting on lipid profile and hematological parameters in healthy volunteers in Jordan. Univers J Med Dent. 2012;1(1):5–9.
7. Barkia A. fatty acid in Fasting. J Heal Popul. 2011;29(5):486–93.
8. S.S. Effect of ramadan fasting on waist circumference, blood pressure lipid profile. Mal Nutr. 2005;11(2):143–50.
9. Folsom M. plasma fatty acid composition as an indicator of habitual dietary fat intake in middle-age adults. AmJ Clin Nutr. 1995;62(3):564–671.

10. Desgupta A. Clinical chemistry, immunology and laboratory quality control. 2014. 88–89 p.
11. Leonard J. The Ways and Means of Statistics. 1979. 490–495 p.
12. B. L. The effect of ramadan fasting on fasting serum glucose in healthy adults. *MedJMalaysia*. 2003;58(5).
13. J. G. Effect of Ramadan fasting on glucose homeostasis and adiponectin levels in healthy adult males. *J Diabetes Metab Disord*. 2015;14(55).
14. S. Kamal. Effect of Islamic fasting on lipid profile ... *Natl J Med Res*. 2012;2(4):407–10.
15. Khan N. Effect of Ramadan fasting on glucose level ... *East MedHealth J*. 2017;23(4):274–9.
16. Fernandez M. The LDL to HDL cholesterol ratio as a valuable tool to evaluate coronary heart disease risk. *J AmGol*. 2008;27(1):1–5.
17. Pinto X. Lipidos sericosy prediccion delriesgo cardiovascular.... *Clin Invest Arter*. 2000;12:267–84.
18. J. Genest. High density lipoproteins in health and in disease. *J Invest Med*. 2003;47:31–42.
19. Miller M. Investigators, Impact of triglyceride levels beyond LDL-C... *JAmCollCardiol*. 2008;51(7):724–30.
20. R. Murray. Harper s Biochemistry. 2000.
21. Sauvat A. Trans-Fats Inhibit Autophagy induced by Saturated Fatty Acids. *E BioMedicine*. 2018;
22. M. Sabin. Fasting Nonesterified Fatty Acid profiles in childhood.... *J Am Acad Pediatr*. 2014;10(15):189.
23. Marks K. Fasting enriches liver TG with n-3 PUFA... *GenesNutrDoi*. 2015;10(1007).
24. P. Salo. Fatty acids composition of serum CEs as a reflector of low.... *ActaPaediat*. 2000;89:399–405.
25. A. Nigam. Relationship between n-3 and n-6 plasma fatty acid levels *Nuti Meta.and Card Dis*. 2009;19:264–70.
26. B. Vessby. The risk to develop NIDDM is related to the fatty acid composition of CEs. *AmPiaAss*. 1994;43:1353–7.
27. J. Cardona. Profile of free fatty acids and fraction of PL, CE, and TG... *Nutrients*. 2016;8(54):3390.
28. Innis S. Dietary TG Structure and its role in infant Nutrition. *AmSoc.for Nutr*. 2011;2:275–83.

Expression of Amylin and Preptinin Iraqi Patients with Type 2 Diabetes Mellitus

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Abstract

Diabetes mellitus is one of the most worldwide spread chronic diseases, and its complications are very serious if it is untreated. Type-2 diabetes mellitus (T2DM) is reported to be caused by obesity and sedentary life style. DM plays a role in accelerating the hardening and narrowing of the arteries. Preptin and amylin are pancreatic hormones which participate in glucose homeostasis. In T2DM patients amylin peptides can be toxic to β -cells of pancreas due to Amyloid deposits within these cells, supporting the idea that islet amyloid might have an important role in the pathogenesis of T2DM. Preptin is a peptide hormone that is secreted with insulin and amylin from the pancreatic β -cells. The study planned to investigate the relationship between serum amylin and preptin levels in patients with T2DM compared to healthy controls and to study their associations together (preptin and amylin) with serum levels of insulin and HOMA-IR. Sixty-four (64) patients were recruited from the Endocrine Outpatient clinic in Al-Imamain Al-Kadhmain city hospital from March of 2018 to May of 2018. Fasting serum samples were obtained on enrolment. (mean age, 61.73 ± 8.05 years; mean duration of diabetes, 8.77 ± 2.66 years; mean HbA1c, 8.1 ± 1.7) with T2DM and body mass index (BMI) $> 25.1 \text{ kg/m}^2$ underwent examination. Age, sex and (BMI) matched with thirty eight (38) healthy controls were also included. Serum preptin and amylin levels were measured by ELISA technique. There was statistically significant difference between patients and controls serum amylin ($p=0.023$) and preptin ($p=0.01$). Patients with T2DM had significantly higher blood glucose ($p=0.0001$), HbA1c ($p=0.0001$), insulin ($p=0.0001$), and homeostatic model assessment of insulin resistance (HOMA-IR) ($p=0.001$) compared to healthy control, while total cholesterol was positively related ($p=0.111$) triglyceride, low-density lipoprotein cholesterol values were ($p<0.001$ for each), and significantly lower high-density lipoprotein cholesterol levels compared with the control group ($p<0.0001$). The preptin level demonstrated a significant positive association with insulin and HOMA-IR compared with healthy control. (for healthy control group: $r=0.381, p=0.146$, $r=0.133, p=0.438$) respectively; for T2DM group: ($r=0.411, p=0.02$, $r=0.332, p=0.003$), The amylin level also showed a significant positive correlation with insulin and HOMA-IR compared with healthy control. (for healthy control group: $r=0.188, p=0.309$, $r=-0.039, p=0.911$) respectively; for T2DM group: ($r=0.279, p=0.002$, $r=0.291, p=0.003$), Conclusions: There were significant differences between healthy control and patients with T2DM concerning amylin and preptin levels. Serum Amylin and preptin increase in association with insulin in diabetic conditions. The present study suggests a potential role of amylin and preptin in the pathogenesis of T2DM.

Keywords: Amylin, preptin, type 2 Diabetes Mellitus.

Introduction

Diabetes mellitus (DM) is a metabolic disorder characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both⁽¹⁾. Typical presentation of Diabetes mellitus includes symptoms like thirst, polyuria, blurring of vision, and weight loss⁽¹⁾.

T2DM results from defect in insulin action in hepatic and peripheral tissues, especially muscle tissues and adipocytes⁽²⁾. The specific etiologic factors are not known but genetic input is much stronger in T2DM than type 1 diabetes mellitus (T1DM)⁽²⁾. Human islet amyloid polypeptide (hIAPP) which named as amylin, 37 amino acid, that is co-secreted with insulin from pancreatic islet β cells. This peptide when accumulates and aggregates

forms fibrils, Amyloid deposits is associated with β cells degeneration which considered as a hallmark of non-insulin dependent diabetes mellitus (NIDDM)⁽³⁾. The prevalence of diabetes for all age-groups worldwide was estimated to be 2.8% in 2000 and expected to be 4.4% in 2030⁽⁴⁾. The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030. According to International Diabetes Federation data, there were some 425 million patients with diabetes worldwide in 2017, and this number is estimated to reach 629 million by 2045^(5,6,7). Amylin is produced via gene expression on chromosome 12. It is transcribed as an 89-amino acid prepolypeptide, which is cleaved to form the mature peptide in the β cells of the pancreas, where it is stored along with insulin and C-peptide in the same granules⁽⁸⁾.

Amylin, which is co-secreted with insulin, regulates post-prandial glucose levels in part by inhibiting gastric emptying and suppressing glucagon release while not affecting glucose uptake⁽⁹⁾. Amylin has been shown to mirror insulin secretion in healthy subjects⁽¹⁰⁾, obese subjects, prediabetes (subjects with impaired glucose tolerance)^(11,12), and patients with T2DM⁽¹⁰⁾. These findings suggest an active role for plasma amylin levels in modulating glucose metabolism⁽¹³⁾.

As an endocrine peptide, preptin is thought to activate the insulinlike growth factor receptor 2 (IGF2R), and as a result, induces calcium-dependent insulin secretion in association with protein C and phospholipase C when the glucose concentration is high⁽¹⁴⁾. In addition, preptin has insulin-like effects on bone metabolism, such as boosting cellular differentiation and affecting the functions of osteoblasts and osteoclasts⁽¹⁵⁾. Preptin is a 34-amino acid peptide hormone co-secreted from the cells of pancreas along with insulin, amylin, and pancreastatin^(16,17). Females have higher preptin level than males⁽¹⁸⁾. Preptin is believed to be a physiological enhancer of insulin secretion induced by glucose. There is a strong correlation between obesity, hyper-insulinemia and insulin resistance, and these associations get stronger with increasing body weight⁽¹⁹⁾. Therefore, the relationship between BMI and preptin level would be a worth investigation. Hence, this study was carried out to evaluate amylin and preptin in patients with T2DM.

Subjects, Material and Method

Subjects: This study comprised sixty four

consecutive patients of T2DM (26 male and 38 female) and 38 healthy control (18 male and 20 female) were recruited from the Endocrine outpatient clinic in Al-Imamain Al-Kadhmain city hospital from March 2018 to May 2018.

All of the patients were asked to provide socio-demographic data, medical history, and family history. Other questions included were: the duration of disease, age of onset of the disease, any treatment taken.

Inclusion criteria: Patients who are suffering and diagnosed as T2DM patients.

Exclusion Criteria: T1DM patients, Pregnant women, Presence of other autoimmune disease like Hashimoto's thyroiditis, SLE, patients with liver disease, renal disease, recent history of cardiovascular disorder, hypertension, neurological disease, or, obese subjects with history of acute or chronic infections, any other chronic diseases, under cortisol treatment or suffering from any autoimmune disease, were excluded from the study.

Blood Sampling: Blood samples (7 ml) were collected from T2DM patients diagnosed according to the WHO protocol, and control subjects in serum separator vacutainers (BD Vacutainer Systems, Plymouth, UK). Sera were separated and immediately stored at -20° C until analysis.

Serum Amylin and preptin: The quantitative determination of Amylin levels and preptin were conducted by ELISA technique, using a commercial available kit, (human Amylin ELISA kit Catalog No. MBS72142 Mybiosource.com) and (human Preptin ELISA kit Catalog No. MBS764034 Mybiosource.com), respectively.

Statistical analysis: All data were coded and entered using the program statistical package for social sciences (SPSS) version 25 under windows XP. Descriptive data was summarized using mean, standard deviation (SD), $P < 0.05$ were considered statistically significant.

Results

Serum levels of Amylin and preptin were estimated in 64 patients with T2DM, compared with 38 healthy control, age and sex matched. As expected, the patients with T2DM had significantly higher level of Amylin levels than the healthy controls ($P=0.023$), as shown in table (1) and Figure(1).

The concentrations of preptinlevel, are presented in Table (1) are significantly higher in T2DM patients as compared with normal subjects(p=0.01).As shown in figure(2), The mean levels of amylin and preptin in normal healthy subjects and T2DM pateints was depicted in Table 1.

Table:(1): The Anthropometric and biochemical variables between the studied groups.

Parameters	Healthy Control Mean± SD	Type 2 DM Mean ± SD	P-value
NO.	38	64
Age (Years)	58.3 ± 9.1	61.73± 8.05	0.0001
BMI	26.5 ± 3.2	29.2 ± 4.2	0.411
FPG (mg/dL)	78.8± 8.1	188.3± 38.1	0.0001
HBA1c (%)	4.1 ± 1.3	8.1 ± 1.7	0.0001
Insulin (µU/L)	6.67 ± 4.76	4.33 ± 2.53	0.0001
HOMA-IR	1.21 ± 0.16	1.77± 0.38	0.001
TotalCholesterol (mg/dL)	165.7 ± 22.3	191.7 ± 26.3	0.111
Triglyceride (mg/dl)	96.8± 29.3	187.6 ± 63.6	0.0001
HDL-C (mg/dL)	44.3 ± 4.1	34.5 ± 2.8	0.0001
LDL-C (mg/dL)	105.4± 26.3	181.4 ± 41.8	0.293
Amylin (pg/ml)	133.46±68.47	244±73.74	0.023
Preptin (pg/ml)	383.11±18.47	546.68±19.62	0.01

Values are Mean ± SD.,BMI: body mass index HOMA-IR: homeostatic model assessment-insulin resistance, FPG: fasting plasma sugar, HBA1c: hemoglobin A1C, HDL-C: high-density lipoprotein-cholesterol, LDL-C: low-density lipoprotein-cholesterol, P < 0.05 is considered statistically significant

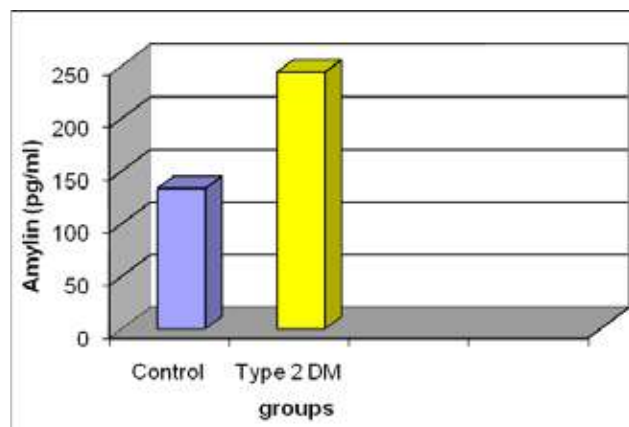


Figure (1): Mean levels of Amylin in patients with Type 2 DM compared to healthy controls.

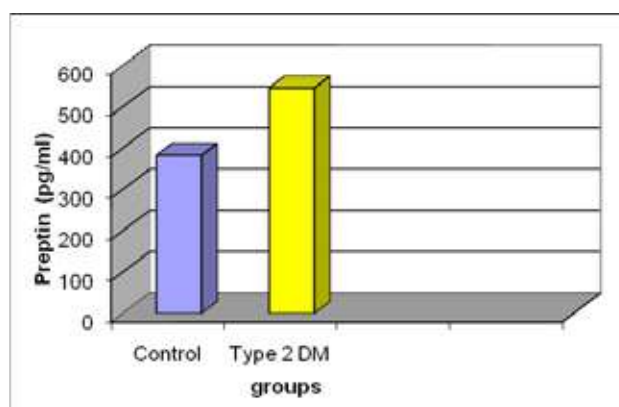


Figure (2): Mean levels of Preptinin T2DM patients compared to healthy controls

The amylin level demonstrated a significant positive correlation with insulin and HOMA-IRcompared with healthycontrol(r=0.279,P=0.002),(r=0.291,P=0.003). Also preptin level showed a significant positive correlation with insulin and HOMA-IRcompared with healthy control.(r=0.411,P= 0.02),(r=0.332,P= 0.003)

Discussion

In T2DM, the levels of amylin are raised in parallel with the increased demand for insulin, and this is thought to induce concentration-dependent amylin aggregation⁽²⁰⁾. Islet amyloid formation is associated with reduced β-cell mass⁽²¹⁾ and human amylin ‘oligomers’ (small, soluble aggregates) are toxic to cultured islet cells⁽²²⁾ suggesting that they could contribute to progressive islet β-cell failure. Amylin oligomers can disrupt membranes⁽²³⁾ and inflict oxidative damage to cells⁽²⁴⁾. In the present study amylin was measured and compared in type 2 DM and control, there was significant statistical difference between type 2 DM and control group where the p-value was 0.023. Researchers mentioned that islet amyloid deposits are found in >90% of T2DM patientsat autopsy⁽²⁵⁾, and action⁽²⁶⁾. Amylin has been. However,the mechanisms and the precise role of amylin in the pathophysiology of T2DM remain unclear.

In the present study The concentrations of preptin level significantly higher in T2DM patients as compared with normal subjects (p=0.01), as illustrated in Table (1). These results agree with other results done by Yang et al.⁽²⁷⁾ who found higher levels of preptin in T2DM patients compared with control group. Higher preptin levels have also been reported in studies of patients with gestational DM and polycystic ovary syndrome⁽²⁸⁻³⁰⁾.

Preptin is a physiological enhancer of insulin secretion induced by glucose. Recent studies have revealed that there is a potential association between preptin and insulin resistance in humans⁽³¹⁾. About diabetes mellitus, this association was also significant and this is confirmed by literature where it was shown that the concentration of preptin levels were higher in DM patients⁽³²⁾.

Statistical analysis revealed that Amylin significantly related to the variations seen in HOMA-IR in the present study, indicating a connection between amylin and insulin resistance in patients with T2DM. In the present study preptin level showed a significant positive relation with insulin and HOMA-IR compared with healthy control. These results consistent with other results that showed strong association between preptin levels and HOMA-IR in obese subjects as previously mentioned⁽³³⁾. Similar to our research, the preptin level showed a positive correlation with insulin, HOMAIR, glucose, and HbA1c levels in a study conducted by Yang et al.⁽²⁷⁾. Therefore, it is expected that a possible relation between amylin and preptin levels might exist. In the present study these two peptides (amylin and preptin) increase independently in T2DM patients; however, both indices demonstrated a positive correlation with insulin levels and HOMA-IR values.

Conclusion

Amylin and preptin may have an important role in the pathogenesis of T2DM, and ultimately in the degeneration and death of pancreatic islet cells. These findings provided a new rationale and opening up additional avenues of research into the etiology, pathogenesis and the treatment of T2DM. The findings of this investigation may provide significant data for in future research.

Conflict of Interest: None

Funding: Self

Ethical Clearance: Not required.

References

1. Definition, Diagnosis and classification of diabetes mellitus and its complications: World health organization, Geneva, 1999P: 2,17, 19,22.
2. Babalola O,Ojo LO, Akinleye AO. Status of lead and selected trace elements in type 2 diabetes mellitus patients in Abeokuta, Nigeria. African

- Journal of biochemistry research, 2007. Vol. 1 No.7, P:127-131.
3. Hiddings H, Eberhardt N. Intracellular amyloidogenesis by human islet amyloid polypeptide induces apoptosis in COS-1 cells. American journal of pathology, 1999. Vol.154, No.4, P:1077-1088.
4. Wild S, Bchir MB, Roglic G, Green A,Sicree R, King H. Global prevalence of diabetes. Diabetic care, 2004. Vol. 27, P:1047-1053.
5. American Diabetes Association. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-Diabetes Care 2018;41:S13–27.
6. International Diabetes Federation. IDF Diabetes Atlas. 8th edition. Brussels: International Diabetes Federation, 2017.
7. Akin S, Erdem ME, Kazan S, Aliustaoğlu M. The relationship between helicobacter pylori infection and glycemic regulation in type 2 diabetic patients. Nobel Med; 2014. 10:32–5.
8. Cooper G, Willis A, Clarkt A, Turnert R, Sim R, Reid K. Purification and characterization of a peptide from amyloid-rich pancreases of type 2 diabetic patients (amino acid sequence/calcitonin gene-related peptide/insulin A chain/Alzheimer disease/pancreatic islet). Proc. Natl. Acad. Sci., 1987. Vol. 84, P: 8628-8632.
9. Weyer C, Maggs DG, Young AA, Kolterman OG. Amylin replacement with pramlintide as an adjunct to insulin therapy in type 1 and type 2 diabetes mellitus: a physiological approach toward improved metabolic control. Current pharmaceutical design.2001. 7:1353-1373.
10. Pullman J, Darsow T, Frias JP. Pramlintide in the management of insulin-using patients with type 2 and type 1 diabetes. Vasc Health Risk Manag. 2006. 2:203-212.
11. Reinehr T, de Sousa G, Niklowitz P, Roth CL. Amylin and its relation to insulin and lipids in obese children before and after weight loss. Obesity (Silver Spring). 2007. 15:2006-2011.
12. Cai K, Qi D, Hou X, Wang O, Chen J. MCP-1 upregulates amylin expression in murine pancreatic Î² cells through ERK/JNK-AP1 and NF-κB related signaling pathways independent of CCR2. PLoS One. 2011. 6: e19559.
13. Sanke T, Hanabusa T, Nakano Y, Oki C, Okai K. Plasma islet amyloid polypeptide (Amylin) levels and their responses to oral glucose in type 2 (non-

- insulin-dependent) diabetic patients. *Diabetologia*. 1991. 34:129-32.
14. Cheng KC, Li YX, Asakawa A, Ushikai M, Kato I, Sato Y. Characterization of preptin-induced insulin secretion in pancreatic β -cells. *J Endocrinol*. 2012. 1;215:43-9.
 15. Ismayilnajadteymurabadi H, Konukoglu D. The relationship between preptin, Forkhead box protein O1 and mechanistic target of rapamycin levels in prediabetic patients. *J Biol Regul Homeost Agents*. 2017. 31:399-405.
 16. Buchanan CM, Phillips ARJ, Cooper GJS. "Preptin derived from proinsulin-like growth factor II (proIGF-II) is secreted from pancreatic islet β -cells and enhances insulin secretion," *Biochemical Journal*, 2001. vol.360, part 2, pp. 431-439.
 17. Celik O, Celik N, Hascalik S, Sahin I, Aydin S, Ozerol E. "An appraisal of serum preptin levels in PCOS," *Fertility and Sterility*, 2011. vol. 95, no. 1, pp. 314-316.
 18. Hoog A, Hu W, Abdel-Halim SM, Falkmer S, Qing L, Grimelius L. "Ultrastructural localization of insulin-like growth factor-2 (IGF-2) to the secretory granules of insulin cells: a study in normal and diabetic (GK) rats," *Ultrastructural Pathology*, 1997. vol. 21, no. 5, pp.457-466.
 19. Canoy D, Buchan I. "Challenges in obesity epidemiology," *Obesity Reviews*, 2007. vol. 8, supplement 1, pp.1-11.
 20. Hoppener J, Lips C. Role of islet amyloid in type 2 diabetes mellitus. *The international journal of biochemistry & cell biology*, 2006. Vol.38, P:726-736.
 21. Koning D, Bodkin EJ, Hansen NL, Clark A. Diabetes mellitus in *Macaca mulatta* monkeys is characterised by islet amyloidosis and reduction in beta cell population. *Diabetologia*, 1993. Vol. 36, P: 378- 384.
 22. Konarkowska B, Aitken JF, Kistler J, Zhang S, Cooper GJ. The aggregation potential of human amylin determines its toxicity towards islet beta cells. *FEBS, J.*, 2006. Vol. 273, P: 3614- 3624.
 23. Janson J, Ashly RH, Harrison D, McIntyre S, Butler PC. The mechanism of islet amyloid polypeptide toxicity is membrane disruption by intermediate-sized toxic amyloid particles. *Diabetes*, 1999. Vol. 48, P:491-498.
 24. Janciauskiene S, Ahren B. Fibrillar IAPP differentially affects oxidative mechanisms and lipoprotein uptake in correlation with cytotoxicity in two insulin producing cell lines. *Biochem., Biophys., Res., Commun.*, 2000. Vol. 267, No. 2, P:619- 625.
 25. Kahn S, Andrikopoulos S, Vercher C. Islet amyloid along-recognized but underappreciated pathological feature of type 2 diabetes. *Diabetes*, 1999. Vol.48 P: 241-253.
 26. Leighton B, Cooper G. Pancreatic amylin and calcitonin gene related peptide cause resistance to insulin in skeletal muscle in vitro. *Nature*.1988. Vol.335,P: 632- 635.
 27. Yang G, Li L, Chen W, Liu H, Boden G, Li K. Circulating preptin levels in normal, impaired glucose tolerance, and type 2 diabetic subjects. *Ann Med*; 2009. 41:52-6.
 28. Aslan M, Celik O, Karsavuran N, Celik N, Dogan DG, Botan E. Maternal serum and cord blood preptin levels in gestationaldiabetes mellitus. *J Perinatol*; 2011. 31:350-5.
 29. Mierzwicka A, Kuliczowska-Plaksej J, Kolačkov K, Bolanowski M. Preptin in women with polycystic ovary syndrome. *Gynecol Endocrinol*; 2018. 27:1-6.
 30. Celik O, Celik N, Hascalik S, Sahin I, Aydin S, Ozerol E. An appraisal of serum preptin levels in PCOS. *FertilSteril*; 2011. 95:314 6.
 31. Yang G, Li L, Chen W, Liu H, Boden G, Li K. Circulating preptin levels in normal, impaired glucose tolerance, and type 2 diabetic subjects, *Ann Med*, 2009. 41(1):52-56.
 32. Anjali G, Siddhrth K, Padmavathi B, Rajan S, Mamatha G, Sandeep K, Sayak R, Mohit S. "Elevation of correlation of blood glucose and salivary glucose level in known diabetic patients" *Journal of clinical and diagnostic research*, 2015. 9, 106-109.
 33. El-Eshmawy M, Abdel Aal I. Relationships between preptin andosteocalcin in obese, overweight, and normal weight adults. *Appl Physiol Nutr Metab*; 2015. 40:218-22.

Clinical Evaluation of Retention of Metallic Versus Thermoplastic Resin Frameworks in Maxillary Distal Extension Cases

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Abstract

Background and Objective: Acetal resin has been introduced as an esthetic partial denture material. However, the retention of this material when compared to cobalt-chromium (Co-cr) frame works still unclear when applied clinically.

Purpose: To evaluate the retention of (acetal resin) as compared to (Co-cr) frame works and clasps.

Materials and Method: The present study is a randomized controlled trial that included 24 healthy patients with Kennedy class I partially edentulous maxilla and dentulous mandibles. The patients were selected from the out-patient clinic (Dep. of Prosthetic Dentistry, Minia University) and divided randomly into two equal groups according to the used denture base material; **Group 1** received maxillary partial denture with (Co-cr) clasps and frameworks. **Group 2** received maxillary partial denture with acetal resin clasps and frameworks. Retention of the prosthesis was evaluated at partial denture insertion, after 3, 6 and 12 months. Paired t-test was used at $p \leq 0.05$ to assess the changes in the above parameter in each group. Student t-test was used to compare between the two groups.

Results: Retentive force mean values of thermoplastic group were significantly lower than metallic group at denture insertion and at all follow up intervals.

Conclusion: Acetal resin frameworks and clasps provide lesser retention values when compared to chrome cobalt.

Clinical Implications: Although there was lesser retention power of acetal resin than Co-cr, further study has to be done regarding various thicknesses and designs of clasps and framework for its successful dental application.

Keywords: Cobalt-chromium, Removal partial denture, Retention, Acetal resin.

Introduction

Fabricating an esthetically pleasing removable partial denture presented a challenge to dentists. Among

different solutions; acetal resin clasps may be used as a simple and effective means, of improving removable partial denture esthetics.¹

Lack of retention and poor esthetics are main reasons for not wearing partial dentures. Traditional metal alloy clasps have been shown to exert forces on abutment teeth that exceed those capable of producing tooth movement. In addition, metal display on anterior teeth is often unacceptable.²

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The thermoplastic resin materials were reported to have superior flexibility and exerted less force than the metals on the abutment teeth. These forces fell within the physiological range of those abutments and considered safe for use. This coupled with their pleasing esthetics made them suitable for use on periodontally compromised teeth, those with deep undercuts and on anterior teeth.³⁻⁴

Acetal resin is being marketed for the construction of retentive and supportive components of removable partial dentures. The material has a flexural modulus lower than that of polymethylmethacrylate and is sufficiently rigid to be used as a supporting element for partial dentures. Acetal resin clasps may be resilient enough to engage undercuts for the retention of removable partial dentures but the low flexural modulus requires that the resin be used in greater cross-sectional area than metal alloys in order to gain useful retention.⁵

The periodontal conditions of the teeth adjacent to the dentures were poorer than around those not directly involved in its construction due to food stagnation and difficult oral hygiene caused by the removable partial denture components.^{6,7} In addition, removable partial denture might sink into the soft tissues causing bone resorption; and bars and clasps might impinge the gingiva.⁸

In this study we tried to evaluate the retention of acetal resin frame work and clasps as compared to cobalt-chromium frame works and clasps.

Patients and Method

Twenty four partially edentulous male patients were selected from the outpatient clinic of the Prosthodontics Department; Faculty of Dentistry, Minia University. **The inclusion criteria** included: patients exhibiting maxillary bilateral distal extension ridge with edentulous area starting from premolar teeth, Dentate mandible or fully restored by fixed restorations, Age: 45-55 years, Angle's class I maxillo-mandibular relationship with sufficient interarch space, The remaining teeth have no, and no previous prosthetic management in the maxillary arch. **The exclusion criteria** included: clenching habits and bruxism, active periodontal diseases or extensive caries, tempo-mandibular disorders, any systemic or debilitating diseases affecting bone metabolism and any intraoral soft or hard tissue abnormality.

All individuals were examined clinically and

radiographically. Periapical radiographs were made for all abutment teeth and for the edentulous alveolar ridge. Occlusal analysis was also done to detect any premature contact or over-eruption, which was corrected by selective grinding.

Clinical examination of the maxillary partial denture abutments showed that it was free from caries, gingival inflammation, periodontal pockets, and there was no tooth mobility and by X-ray evaluation the partial denture abutments were free from periapical or periodontal pathosis.

Full mouth scaling and root planning were performed to all patients, and they were instructed for proper oral hygiene and home care using toothbrush and dental floss.

Patient grouping: The patients were randomly divided into two equal groups, twelve in each.

Group 1: The patients received maxillary partial denture with metallic cobalt-chromium frameworks and cobalt-chromium clasps (**Wiront Pellets Co-64%, Cr-28.65%, Si, Mn, Ctrace Bego, GmbH & Co. KG, Germany**)cingulum rest on the canine and mesial rest in first premolar in each side joined to the saddle by antro-posterior palatalstraps.

Group 2: Patients received maxillary removable partial denture with thermoplastic frameworks and acetal resin clasps (**Bidentaplast Cartridges Acetal resin (Poly-Oxymethylene) Bredent, GmbH & Co. KG, Germany**) with the same design of group 1.

Construction of the removable partial denture: Study casts prepared from alginate impressions were surveyed, proximal surfaces of the abutment teeth were prepared parallel to the path of insertion to act as guiding planes. Following mouth preparation, final impressions were made using rubber base impression material in a custom tray Master casts were surveyed, modified and duplicated.

For the first group, wax pattern & casting was completed in the conventional.manner. For the second group,the master casts were duplicated for constructing the wax pattern of the acetal resin frame work and retentive arm direct retainers in conventional manner. Wax pattern of acetal resin direct retainer were made in a special muffle. After the wax pattern was eliminated, the acetal resin material was softened at 260 degree

centigrade & injected into the mold with a special injection gun. Pressure was maintained till the material cools, finished & polished, then seated on the master cast.

The metallic and thermoplastic frameworks were tried for both groups. Maxillo-mandibular relation was recorded, setting up of teeth & denture was tried in the patient's mouth. Lastly at insertion, stress the oral & hygienic measures.

Steps for retention measurement procedure:

Identification of the geometric center: The relative geometric center of the partial denture was identified first; Undercuts in the fitting surface of the partial dentures were blocked by wax. Then a mix of stone was poured in the fitting surface of the partial denture to obtain a cast. The centers of the maxillary tuberosities and the midline were marked on the partial denture. A cardboard was cut so as to connect these markings, thereby forming a triangle. The intersection of the three lines bisecting the three angles of the triangle was considered as the geometric center (Fig.1). The geometric center of the triangle was then identified based on scientific grounds.

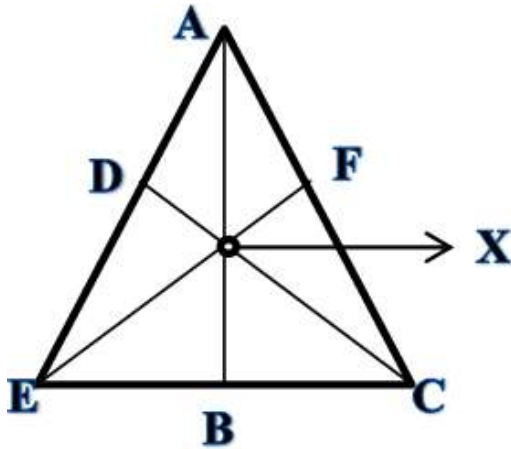


Fig (1): The geometric center of this triangle would be pint X (intersection of AB. CD and EF)

A pin was passed through the cardboard at the geometric center downwards to mark it on the cast. A plastic rod was then fixed to the cast and suspended upwards from the marked point to maintain the location of the predetermined center. Then, three holes were made at the palatal margin of the major connector at the points of emergence of each bisector line of the predetermined triangle. These holes were created 2-3 mm away from the palatal margin to resist fracture. Also, these holes were used to assist the passage of wires to resist dislodgement during the retention measurement procedures (Fig 2).



Fig (2): Thermoplastic RPD attached with wires and loop

The wrought wires were 1mm in diameter to resist deformation during testing procedures. The wires were adjusted to run 2cm below the occlusal plane. The end of the 3 wires was bent to form a loop, to be engaged by the forcemeter hook and allow lifting of the denture. With his mouth open and the lips relaxed, the palate and the maxillary ridge were at nearly 45 degree to the floor (Fig. 3).

The hook of force meter was inserted in the hole of frameworks loop then the peak button was turned on and the zero button of the device was pressed when the device screen showed zero reading; measurement was started immediately. A Pulling force was then gradually applied until the framework was dislodged.

Retention force was measured as the maximum force needed to completely dislodge the partial denture. The measuring procedures were repeated 5 times at 5 minute intervals and the average value was recorded (Fig. 3). Measurements of retention were carried out after denture inspection (zero level) and 3,6,9,12 months later.



Fig (3): Digital force gauge device attached to the maxillary partial denture

Results

Measurements of retention were carried out after denture inspection (zero level) and 3,6,9,12 months later using a digital force measurement gauge. Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 20. Quantitative data were presented as mean, standard deviations and ranges. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following: ($P > 0.05$: Non significant, $P < 0.05$: Significant and $P < 0.01$: Highly significant). Paired t-test was used at $p \leq 0.05$ to assess the retention values within each group.

Table (1), presents the comparison between the two groups regarding retentive force in Newton. The recorded retentive forces with group I at delivery were more than double that recorded with group II (48.9 ± 4.98 vs 22.1 ± 3.57 N). The results showed that retentive force mean values were significantly lower in thermoplastic group; compared to metallic group, at denture insertion and at all follow up intervals (3, 6, 9 and 12 months post insertion) ($P \leq 0.01$). In group (I), significant reduction in retentive force mean values was noticed at 6, 9 and 12 months of denture insertion to end with 41.1 N that is 84% of the original values. However, a nonsignificant reduction was observed in retentive force values in group (II) along with follow up intervals to end with 19.7 N that is almost 90% of the original values.

Table (1): Comparison between groups regarding retentive force in Newton.

Retentive Force (Newton)	Groups				P. value (Sig.)
	Group (I) Metallic (n=12)		Group (II) Thermoplastic (n=12)		
	Mean	SD	Mean	SD	
At denture insertion	48.9 ^a	4.98	22.1	3.57	<0.01**
3 Months	46.5 ^{ab}	5.41	21.5	3.14	<0.01**
6 Months	45.4 ^b	4.74	21.4	3.71	<0.01**
9 Months	43.9 ^c	5.37	20.5	3.91	<0.01**
12 Months	41.1 ^c	4.96	19.7	4.18	<0.01**

Independent T-test was used to compare between groups. Paired T-test was used within each group at partial denture insertion, 3, 6, 9 and 12 months from insertion, a, b, c Means in the same column with different superscripts are significantly different ($P \leq 0.05$), ** Significant ($P \leq 0.01$).

Discussion

The possible use of polyacetal resin as a denture base material was considered by Smith over 40 year's ago 30 and was promoted primarily on the basis of superior esthetics, which allowed the clasp to better match the color of the abutment tooth.⁹ Acetal as a homo-polymer has good short term mechanical properties, but as a co-polymer has better long-term stability. Acetal resin is very strong, resists wear and fracturing, and is quite flexible. These characteristics make it an ideal material for pre-formed clasps for partial dentures, single pressed unilateral partial dentures, partial denture frameworks, provisional bridges, occlusal splints, and even implant abutments.^{10,11}

Retentive clasp arms must be capable of flexing and returning to their original form and should retain an RPD satisfactorily. The tooth should not be unduly stressed or permanently distorted during service and should provide

esthetic results. acetal resin have a sufficiently high resilience and modulus of elasticity to allow its use in the manufacture of retentive clasps.^{12,13}

The retentive force is dictated by tooth shape and by clasp design. Tooth shape influences retention by determining the depth of undercut available for clasping.¹¹ The results of this study showed that retentive force mean values were significantly lower in Thermoplastic group in comparison with metallic group at denture insertion and at all follow up intervals. It is worth mentioning that the retentive values of clasps of group I (metallic) was more than double of that of group II (thermoplastic) even at the end of follow up period. This is due to the excessive rigidity of metallic clasps in comparison of the thermoformed ones.

Group (I) showed significant reduction in retentive force values at 6, 9 and 12 months of denture insertion. However, a slight non-significant reduction was observed

in retentive force values in group (II) along with follow up intervals. This is in accordance with the results of¹⁴ that simulated a 36-month clinical use of RPD clasps made of acetal resin and assessed their retentive force and deformation by comparison with similar clasps cast of Co-Cr. The result showed no deformation for the acetal resin clasp after 36 months of simulated clinical use unlike the Co-Cr clasp which presented an increase in the distance between the tips. Their results also showed that the acetal resin clasps require less force for insertion and removal than Co-Cr clasps.

The fact that the thermoformed resin clasp is more flexible than the metallic one; have driven several authors to recommend shorter and thicker resin clasp engaging deeper undercut to produce acceptable clinical retention. This is due to the relatively low rigidity of the thermoplastic resin (elastic modulus; 2.36 GPa for POM as compared to 240 GPa for CoCr alloy.¹⁵ For this reason, thicker acet al resin clasps were used for comparison in this study. A more recent study found essentially the same results as the current study in regards to denture retention.¹⁶ They concluded that; the cobalt chromium clasp has superior retentive forces than the acetyl resin due to significantly higher flexibility of the acetal resin. They recommended its use in deeper undercuts when an aesthetic demand or periodontal health is a primary concern.

Conclusion

Acetal resin provides less retention compared to chrome cobalt. However patients did not complain from retention with thermoformed removable partial dentures. So, further study has to be done regarding various thicknesses and designs of clasps and framework for its successful dental application.

Conflict of Interest: Nil

Source of Funding: Self-funding.

Ethical Clearance: All patients participated in the study were informed about the nature of the study and its purpose, agreed to take part in it and write an informed consent reviewed and approved by the research ethics committee of the Faculty of Dentistry Minia University which is conducted in accordance of Helisinki.

References

1. Lekha K, Savitha N P, Roseline M, Nadiger RK. Acetal resin as an esthetic clasp material. J

- Interdiscip Dentistry, 2012;2:11-4.
2. Preshaw PM, Walls AW, Jakubovics NS, MoynihanPJ, Jepson NJ, Loewy Z Association of removable partialdenture use with oral and systemic health. J Dent, 2011; 39: 711-719.
3. Faten AA, Ibrahim RE, Mohamed ME, Shereen A. Patient Satisfaction and Radiographical Evaluation of Acetal Resin Retentive Clasp Arm versus Conventional Clasp on Abutment Teeth in Upper Unilateral Removable Partial Dentures. Journal of American Science, 2013;9(5) 425-431.
4. Ucar Y, Akova T & Aysan I. Mechanical properties of polyamide versus different PMMA denture base materials, JOP, 2012; 21: 173-176.
5. Vojdani M & Giti R. Polyamide as a Denture Base Material: A Literature Review. JOD SUMS, 2015; 16: 1-9.
6. Takabayashi Y. Characteristics of denture thermoplastic resins for non metal clasp dentures. Dent Mater J, 2010; 29:353-61.
7. Janaina HJ, Cristiane CC, Carlos EV, Ana LM, Ana CP and Eunice TG. Clinical evaluation of failures in removable partial dentures. Journal of Oral Science, 2012; 54(4): 337-342.
8. Jorge JH, Giampaolo ET, Vergani CE, Machado AL, Pavarina AC, Cardoso de Oliveira MR. Clinical evaluation of abutment teeth of removable partial denture by means of the Periotest method. JOral Rehabil, 2007; 34: 222-227.
9. Kohli S & Bhatia S. Polyamides in dentistry. IJSS, 2013;1: 20-25.
10. Thakral G, Aeran H, Yadav B, Thakral R. Flexible Partial Dentures-A hope for the Challenged Mouth. People's Journal of Scientific Research, 2012; Vol. 5(2): 55-59.
11. Davenport JC, Basker RM, Heath JR, Ralph JP, and Glantz PO. Retention. Br Dent J, 2000; 189:646-57.
12. Tarek M, Osama A, Magdy M. Comparison between Acetal Resin and Cobalt-chromium Removable Partial Denture Clasps: Effect on Abutment Teeth Supporting Structures International Journal of Prosthodontics and Restorative Dentistry, 2011; 13:147-154
13. Phoenix RD, Mansueto MA, Ackerman NA, and Jones RE. Evaluation of mechanical and thermal properties of commonly used denture base resins. J Prosthodont, 2004; 13:17-27.

14. Arda T, Arikani A. An in vitro comparison of retentive force and deformation of acetal resin and cobalt–chromium clasps. *J Prosthet Dent*, 2005; 94:267–74.
15. Turner JW, Radford DR, Sherriff M. Flexural properties and surface finishing of acetal resin denture clasps. *J Prosthodont*, 1999; 8:188–95.
16. Meenakshi A, Gupta R, Bharti V, Sriramprabu G, and Prabhakar R. An Evaluation of Retentive Ability and Deformation of Acetal Resin and Cobalt-Chromium Clasps *J Clin Diagn Res*, 2016 Jan; 10(1): 37–4

E-Ways (Early Warning System): A Literature Study of Smartphone Application-Based Stroke Early Detection

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Abstract

Stroke is one of the highest causes of catastrophic death in Indonesia. Lack of knowledge and public awareness about stroke caused the delay of health care and post-disease recovery. So that, they impacted on death or disease complications and even disability. There were needs for prevention efforts and early detection that could be done at home. Today, the early detection was carried out by health workers in health care facilities through skrinning. The use of smartphones could minimize the delay of health care. This would be an opportunity to develop smart phone applications as media for stroke early detection because most people used smartphones in their daily lives. This study aimed to identify the use of smart phones as media for stroke early detection. Comprehensive literature analysis through Google Scholar, Proquest, and EBSCO in the last 5 years, with keywords: *stroke early detection*, *sourceinformation*, *smartphone application*. Inclusion criteria were smartphone application and stroke articles in the past 5 years. Data were analyzed in a table consisted of title, author, year, and result. A total of 21 articles had showed the use of smartphones might provide sign assessment and mild stroke symptoms experienced by individuals effectively and efficiently. These media had been globally used for early detection and information sources about strokes. Smartphone applications became innovative media that could help individuals to carry out early detection and obtain practical information about stroke and be accountable. The results of this literature study could be used as references to determine the form of appropriate intervention ormedia as support toward the efforts of stroke case prevention in Indonesia.

Keywords: *Smartphone application, early detection, stroke.*

Introduction

Indonesia is faced with a triple burden disease situation, where control of infectious diseases has not been resolved but the trend of an increase in non-communicable diseases occurs every year, especially catastrophic diseases. The period of January-June 2014 had increased in the number of cases and the cost of treating catastrophic diseases such as vascular disease (heart disease, stroke), diabetes mellitus, kidney disease, cancer, thalassemia, and hemophilia⁽¹⁾. The management of catastrophic diseases requires higher cost because the numbers of cases have increased and made various kinds of complications and even death. The government

needed to design appropriate programs and policies through the management of risk factors and calculate disease financing⁽²⁾. One of catastrophic diseases that could be minimized through risk factor management was stroke.

Stroke is non-communicable disease that contributes for the highest mortality after heart disease and cancer and is the first cause of serious and permanent disability. This could be prevented through appropriate treatment considering on the risk factors⁽³⁾. A total of 15 million people worldwide suffered from strokes, 5 million people die from strokes, and 10 million other people survived with permanent disability. This permanent disability

resulted dependence on others⁽⁴⁾. The numbers of stroke cases in Indonesia was 2,137,941 (12.1%) cases. This number have increased 3.8% from the previous year, so that, Indonesia was currently as the country with the highest number of stroke cases in Asia⁽¹⁾.

Stroke stands for *Cerebro Vascular Accident (CVA)* is neurological disorder that occurs due to disruption of blood circulation to the brain for 24 hours or more and tends to be permanent. Clinical symptoms occurred suddenly and progressively, they resulted acute brain damage in focal or global⁽⁵⁾. A total of 87% people had ischemic stroke caused by the blockage of blood flow to the brain and the rest occurred hemorrhagic strokes⁽⁶⁾. Stroke attacks could affect anyone due to unhealthy and instantaneous lifestyle at this time⁽⁷⁾. One of the efforts was early detection of symptoms or the risk of stroke.

Currently, early detection was not only implemented conventionally but also in modern way through the advances of health information technology. *E-health* appeared as a form of existence in the health sector that referred to the delivery of information and the provision of internet-based health services and technology. This was supported by the development of smartphone use among communities included in Indonesia from time to time. The numbers of internet users in Indonesia until 2014 reached 88 million people⁽⁸⁾ (explained that 67.6% used smartphones to access the internet and social media, 87.3% accessed the internet and social media sites for 20-50 hours per week).

Previous research had proven the success of smartphones as accessible media, improved medication compliance, immunization schedule reminders⁽⁹⁾. Monitoring system consisted of website-based server applications and Android-based client applications could help monitor the compliance and development of CD4 (clients' HIV/AIDS ARV) in order to succeed the implementation of ARV therapy⁽¹⁰⁾. The *Girl Talk* application increased the knowledge significantly from the baseline level (35.3% vs. 94.1%; $p < 0.001$)⁽¹¹⁾. At present, there was no study on the implementation and impact of using smartphone applications as media of information and early detection of stroke in Indonesia.

Based on this phenomena, there was a need for literature review on the use of smartphone technology as efforts to provide information and early detection of stroke in various countries. The results of this study were expected to be used as references in the development

of smartphone application-based stroke early detection media. This study aimed to identify research articles that described the use of smartphones as media of information and early detection of stroke.

Research Method

The strategy of searching research articles carried out comprehensively through the databases of Google Scholar, Proquest and EBSCO research journals in the last 5 years, it was obtained 21 articles. The keywords used in the searching for research articles were *stroke early detection, source information, smartphone application*. Searched articles using punctuation "AND" so that the writing "*stroke early detection and smartphone application*" and "*source information for stroke and smartphone application*".

Result

The utilization of smartphone applications in various countries as media for early detection and stroke prevention based on the analysis of 21 articles. The application functioned as screening for clients with risk of stroke, information sources of stroke, detection of abnormalities in the use of walking patterns, routine blood pressure checks, detection of heart problems, stop smoking, checking cholesterol and blood sugar, regular physical activity, and low salt diets.

The results of literature review showed smartphones that were used as media for early detection and prevention of stroke, namely ARM Strokes, FAST-ED (*Field Assessment Stroke Triage for Emergency Destination*), Stroke 119, and mSTOPES. Study result showed that 86 doctors (74%) used the application for patient care process, either for personal use or recommending to patients⁽¹²⁾. Doctors used the application to manage stroke risk factors (25%) all of the time. 77% of doctors stated their interests in using the application because it could help their patients managing their risks. 90% of doctors agreed that this application was useful if provided patient care.

The *e-wars* prototype provided additional features about information to reduce the risk of stroke, it consisted of checking routinely blood pressure, detection of heart problems, stop smoking, checking cholesterol and blood sugar (DM clients), regular physical activity, low sodium diet (low salt) (Erawantini et al., 2018). The mSTOPES application was able to identify and improve the AF screening method for stroke prevention. The results of

this trial also provided greater knowledge of arithmetic characteristics (eg frequency, duration, average, and time of day) that associated with symptoms of AF⁽¹³⁾.

The ARMStrokes application was developed on iPhone using the *built-in* iPhone sensor (accelerometer, gyroscope, and device orientation sensor) to identify movement speed and user position information (eg *pitch*, *roll*, and *yaw* values) during training. Clients were enthusiastic about using ARMStrokes in their daily lives because the given feedback was right after training⁽¹⁴⁾. In addition, the FAST-ED (*Field Assessment Stroke Triage for Emergency Destination*) application provided information through short questions to identify age, anticoagulants use, final normal values, motion weakness, visual impairment, and aphasia; stroke center database that provided endovascular care; and *Global Positioning System* to calculate the feasibility of clients of endovascular care and the distance/time of transportation to emergency health care centers⁽¹⁵⁾. Based on the results of these studies, smartphone applications could help individuals to detect and obtain stroke information easily and practically because it might be accessed anywhere and anytime.

Discussion

Stroke is one of eight types of catastrophic diseases that is included in the National Health Insurance (JKN) financing. This was due to the high cost of treatment, various complications emerged and threatened life. The magnitude of the threat of stroke required prevention and early detection. One of the preventive actions was through the use of information technology in the form of smartphone applications as *early warning system* (e-ways). Based on the literature review of 21 research articles showed various innovations had been developed as media for early detection and prevention of stroke.

Treskes et al through his research on 200 clients by applying *mobile-AF* application in the form of *The Kardia Mobile* for early detection of AF (*Atrial Fibrillation*) and TIA as the cause of cryptogenic stroke. The result showed that *The Kardia Mobile* was non-invasive validated device that was easy to use, low cost and could be used by clients independently⁽¹⁶⁾. This application had the potential to improve the detection of AF and TIA in cryptogenic stroke populations and prevention of recurrent strokes. Similar study was conducted, through “Stroke 119” application was able to perform stroke screening and information about the

nearest hospital. This application provided information about symptoms of stroke, thrombolytic treatment, and action plans for clients at risk of stroke⁽¹⁷⁾. A study through the development of *stroke mobile pre-detection* application showed that most clients believed this application could increase their awareness of stroke and help them to detect early symptoms of mild stroke⁽¹⁸⁾.

Other studies also showed the effectiveness of smartphone applications, among others: “Stroke Riskometer TM” application which was able to detect stroke risk factors. Risk factors for stroke included age, sex, systolic blood pressure, and waist circumference (>89 for men and women)⁽¹⁹⁾. “Stroke Riskometer TM” application was an easy to use tool because individuals could assess stroke risk independently and comfortably, anytime and anywhere. “Stroke Riskometer” application and showed the results “this could calculate the risk of stroke for normal individuals⁽²⁰⁾.

The benefits of smartphone applications showed that there was a need to develop smartphone-based application interventions that could be used extensively in the health sector, especially in managing catastrophic diseases. Various problems in health services such as access to service centers, lack of health care providers, long treatment times, and high costs or needs of health care providers both clients and government, made health problems become complex and needed to get solution for designing participatory services⁽²¹⁾. The World Health Organization (WHO) stated that digital technology (*mHealth*) was intended to improve the quality and coverage of care, improved access to health information, services and skills, and promoted positive changes in health behavior to prevent catastrophic diseases⁽²²⁾.

The benefits of smartphone use were also suggested, *mHealth* which was an element of eHealth played important roles in creating health services that were easily accessed through smart telephone communication such as providing health information as efforts to prevent health problems, collect health data and monitor clients⁽²³⁾. The *mHealth* (ex: *smartphone*) application facilitated communication among users and the health care systems, monitoring, and access to information regarding medical records and developments⁽²⁴⁾. A number of *mHealth* trials on stroke problems had shown greater benefits from the use of smartphones as *early warning system* (e-ways) in the early detection and strokes prevention, complications and stroke recurrence prevention. Through this literature review, it was

expected to provide views on the development of health technologies, especially the development of *mHealth* in chronic diseases and catastrophic.

Conclusion and Suggestion

The use of smart phone as an early warning system (e-ways) presented opportunities to reach the wider communities in the effort of early detection and prevention of stroke. In addition, the use of *e-ways* was also able to prevent the recurrence of stroke. Most of the Indonesian people had used smartphone applications, this was enable the development of smart phone applications in health services, especially in the prevention of stroke.

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Reference

1. Kementerian Kesehatan RI. Profil Kesehatan Indonesia 2015. 2016. 403 p.
2. Kementerian Kesehatan RI. Rawat inap peserta jamkesmas di rumah sakit studi di 10 rumah sakit milik kementerian kesehatan (Expense of INA CBG S Claim and Real Expense of Catastrophic Diseases Health Hospital of January to March 2012). 2012;2012.
3. Powers WJ, Derdeyn CP, Biller J, Coffey CS, Hoh BL, Jauch EC, et al. AHA/ASA Guideline 2015 AHA/ASA Focused Update of the 2013 American Heart Association Stroke Council. 2015. 1-47 p.
4. Wong MM, Poh M, Chu DW, Siu C. a Primary Care Setting Global burden of stroke. :51.. 2016;1-7.
5. Lingga L. All about stroke hidup sebelum dan pasca stroke. Jakarta: Elex Media Komputindo; 2013.
6. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al. AHA Statistical Update Heart Disease and Stroke Statistics — 2016 Update A Report From the American Heart Association WRITING GROUP MEMBERS. 2016. 38-360 p.
7. Pudiastuti RD. Penyakit pemicu stroke. Yogyakarta: Nuha Medika; 2011.
8. Patel V V., Masyukova M, Sutton D, Horvath KJ. Social Media Use and HIV-Related Risk Behaviors in Young Black and Latino Gay and Bi Men and Transgender Individuals in New York City: Implications for Online Interventions. J Urban Heal. 2016;93(2):388-99.
9. Soepomo P. Penerapan Sistem Monitoring Terapi Arv (Antiretroviral) Dengan Metode Client Server Berbasis Smartphone Pada Rsup Dr . Sardjito. 2014;2:982-93.
10. Cecil K, Regina KR, Human I, Virus I, Acquired HI V, Deficiency i. Effect of social viability intervention on the social support of people living. 2015;8(1).
11. Brayboy LM, Schultz L, Mills BSL, Sepolen A, Mezoian T, Wheeler C, et al. Education to Adolescent Girls. 2017;30(1):23-8.
12. Halket D, Singer J, Balucani C, Stefanov D, Levine SR. Mobile Applications for Stroke Prevention: A Survey of Physicians' Perspectives. J Mob Technol Med [Internet]. 2017;6(3):7-13. Available from: <http://www.journalmtm.com/2017/mobile-applications-for-stroke-prevention-a-survey-of-physicians-perspectives/>
13. Steinhubl SR, Mehta RR, Ebner GS, Ballesteros MM, Waalen J, Steinberg G, et al. Rationale and design of a home-based trial using wearable sensors to detect asymptomatic atrial fibrillation in a targeted population: The mHealth Screening to Prevent Strokes (mSToPS) trial. Am Heart J [Internet]. The Authors; 2016;175:77-85. Available from: <http://dx.doi.org/10.1016/j.ahj.2016.02.011>
14. Nogueira RG, Silva GS, Lima FO, Yeh Y, Fleming C, Branco D, et al. The FAST-ED App: A Smartphone Platform for the Field Triage of Patients With Stroke. 2017;1-8.
15. Guo J, Smith T, Messing D, Tang Z, Lawson S, Feng JH. ARMStrokes: A Mobile App for Everyday Stroke Rehabilitation. 2014;1:429-30.
16. Treskes RW, Gielen W, Wermer MJ, Grauss RW, van Alem AP, Dehnavi RA, et al. Mobile phones in cryptogenic strOke patients Bringing sIngle Lead ECGs for Atrial Fibrillation detection (MOBILE-AF): Study protocol for a randomised controlled trial. Trials. 2017;18(1):1-9.

17. Nam HS, Heo J, Kim J, Kim YD, Song TJ, Park E, et al. Development of Smartphone Application That Aids Stroke Screening and Identifying Nearby Acute Stroke Care Hospitals. 2014;55(1):25–9.
18. Foong O, Sulaiman S, Iskandar BS, Rohaya D, Rambli A. Mobile health awareness in pre-detection of mild stroke symptoms MOBILE HEALTH AWARENESS IN PRE-DETECTION OF MILD STROKE SYMPTOMS. 2014;(September 2015).
19. Parmar P, Krishnamurthi R, Ikram MA, Hofman A, Mirza SS, Varakin Y, et al. The Stroke RiskometerTMApp: Validation of a data collection tool and stroke risk predictor. *Int J Stroke*. 2015;10(2):231–44.
20. Zhang MWB, Ho CM. Smartphone Applications Providing Information about Stroke: Are We Missing Stroke Risk Computation Preventive Applications? 2017;19(1):115–6.
21. Montoya JL, Georges S, Poquette A, Depp CA, Atkinson JH, Moore DJ, et al. Refining a personalized mHealth intervention to promote medication adherence among HIV plus methamphetamine users. *Aids Care-Psychological Socio-Medical Asp Aids/Hiv*. 2014;26(12):1477-81.
22. Hightow-Weidman L, Muessig K, Knudtson K, Srivatsa M, Lawrence E, LeGrand S, et al. A gamified smartphone app to support engagement in care and medication adherence for HIV-positive young men who have sex with men (AllyQuest): Development and pilot study. *J Med Internet Res*. 2018;20(4):1–18.
23. Kayyali R, Peletidi A, Ismail M, Hashim Z, Bandeira P, Bonnah J. Awareness and Use of mHealth Apps: A Study from England. 2017;
24. Swendeman D, Ramanathan N, Baetscher L, Medich M, Scheffler A, Comulada WS, et al. Smartphone Self-Monitoring to support self-management among people living with HIV: Perceived benefits and theory of change from a mixed-method randomized pilot study. *J Acquir Immune Defic Syndr*. 2015;69(0 1):S80–91.

Prognostic Impact of Regulatory T-cells in Predicting Response and Prognosis in Primary Breast Cancer

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Abstract

Background: The role of tumor-infiltrating lymphocytes (TILs) in breast cancer has been extensively studied over the last decade; it is now believed that they have predictive and prognostic roles in breast cancer.

Materials and Method: We identified 70 patients with primary breast cancers receiving neoadjuvant chemotherapy (NAC); we analyzed pre- and post-treatment tumor-infiltrating immune cells (CD3, CD8) by immunohistochemistry. Immune cell profiles were analyzed and correlated with response and survival.

Results: We identified two tumor-infiltrating immune cell profiles, which were able to predict pathological complete response (pCR) to NAC. A higher infiltration by CD8 and CD3 lymphocytes was associated with occurrence of pCR. Analysis of the immune infiltrate in post-chemotherapy treatment identified a profile of high CD8 and low CD3 infiltration associated with better disease free survival.

Conclusions: Tumor lymphocytic infiltrates play a predictive role for detecting pCR and a prognostic role in detecting the outcome. Further understanding of the mechanisms underlying the distribution of immune cells and their changes after chemotherapy may contribute to the development of new immune-targeted therapies for breast cancer.

Keywords: Tumor lymphocytic; chemotherapy; neoadjuvant.

Introduction

Neoadjuvant chemotherapy (NAC) is the standard of care for breast cancer and increases the options for breast-conserving surgery.⁽¹⁾

Pathological complete response (pCR) after NAC is considered as an indicator of good outcome, especially in triple-negative breast cancer (TNBC) and human epidermal growth factor receptor 2 (HER2) breast cancer.⁽²⁾ Residual cancer cells after NAC may be more aggressive or have poor outcome.⁽³⁾ However, some patients who fail to achieve pCR after NAC have a relatively good outcome. Therefore, new prognostic markers in residual tumors are needed to identify high-risk patients.

Nowadays, the importance of the immune tumor microenvironment has been reported to play

an important role in predicting outcomes.⁽⁴⁾ Various cells of the immune system can play varying roles in tumor progression; for example, cytotoxic T cells (CD8+ T cells), natural killer cells, dendritic cells and macrophages are associated with improved clinical outcomes, whereas regulatory T (Treg) cells and myeloid-derived suppressor cells suppress antitumor immunity. Specific TIL subsets, such as CD3+, CD8+ and forkhead box protein 3 (FOXP3)-positive TILs, has been reported to be clinically significant and reliable in predicting treatment response.⁽⁵⁾

Chemotherapy enhances the immune activity or the reversal of immunosuppression. Some studies revealed that changes in the levels of CD8+ or CD3+ TILs induced by chemotherapy can be used as a prognostic marker in aggressive breast cancer subtypes, such as TNBC and HER 2 breast cancer.⁽⁶⁾

However, the predictive value of changes in lymphocytic subpopulations after NAC in all breast cancer subtypes has not been discussed sufficiently.

The current study investigated the clinical significance and value of changes in the levels of CD8+ TILs and CD3+ TILs before and after NAC in all breast cancer subtypes.

Patients and Method

Patient Background: A total of 70 patients with stage II and III primary infiltrating ductal breast cancer that were treated with NAC at period from January 2015 till May 2016 follow up period extended till May 2019 was done. Tumor staging were stratified based on the TNM Classification of Malignant Tumors, The Union for International Cancer Control Seventh Edition.⁽⁷⁾

Tumors were classified into subtypes according to the immunohistochemical expression of estrogen receptor (ER), progesterone receptor (PgR), HER2 and Ki-67.

Clinical evaluation included physical examination chest X-ray, mammography, ultrasound breast exam, breast magnetic resonance imaging (MRI) and core biopsy.

In locally advanced tumors bone scintigraphy and body computed tomography were added to the staging workup. For chemotherapy response evaluation, dynamic breast MRI was performed prior to surgery.

Pathology Assessment: Pre-treatment estrogen (ER) and progesterone receptors (PR) status was assessed by immunohistochemistry (IHC), and HER2 status was assessed by either fluorescent in situ hybridization (SICH) or a validated IHC method. Ki67 proliferation index was calculated and 14% was taken as a cutoff point. pCR was defined as the absence of invasive carcinoma both in the breast and the axilla, regardless of the presence of carcinoma in situ.

Tumor-infiltrating lymphocytes assessment: Pre-and post-NCT samples was built after selection of predominantly tumor areas by a pathologist (ACB).

Adequate controls (tonsil and normal breast) were included. For immunohistochemistry, 4 µm sections were cut deparaffinated, rehydrated and processed with standard method using an automatized stainer (Ventana Bench mark, Roch, Germany). Staining was performed

simultaneously in all slides to avoid intersection variability. For TIL study, the following antibodies were used: CD8 (Clone C8/144B, Dako), CD3 (Clone DF-T1, Dako).

Microscopic evaluation of CD3+ and CD8+TILs: Scoring of immune stained positive TILs was done by the pathologist. CD3+ and CD8+ TILs were counted in five randomly selected high power fields at 40X magnification and the counts were averaged. Initially TIL count was recorded as: +(1-25 cells), ++ (26-50 cells), +++ (≥51 cells) in the tumor and the stroma separately. Positive TILs up to 25 cells were considered as low TIL count and more than 25 cells were considered as high TIL count.

Results are expressed as TIL count/mm². For each subpopulation, chemotherapy-related relative variation was determined and expressed as a percentage. Tumor lymphocytic infiltrate detected classified into low and high according to cut off point 10%.

Neoadjuvant therapy regimen and surgery: All patients received a TC protocol consisting of six courses of Docetaxel (75 mg/m²) and (600 mg/m²) cyclophosphamide every 3 weeks.⁽⁸⁾

Clinical end points

Therapeutic antitumor effects were assessed according to the Response Evaluation Criteria in Solid Tumors criteria.⁽⁹⁾ The pCR was defined as the complete disappearance of the invasive compartment of the lesion with or without intraductal components, including the lymph nodes.⁽¹⁰⁾

DFS was defined as the time from surgery to death, locoregional recurrence or distant recurrence.

Statistical Method: The collected data were coded, tabulated, and statistically analyzed using SPSS program (Statistical Package for Social Sciences) software version 25.

The level of significance was taken at (P value < 0.05).

Results

The clinicopathological characteristics of the 70 breast cancer patients were recorded as shown in [Table 1]. The patient's age ranged from 27 to 70 years, 45(64.3%) were premenopausal and 23(35.7%)

were postmenopausal. All patients were invasive duct carcinoma. Patients with grade II carcinoma were 92% while grade III carcinoma was 8%. Patients were of clinical tumor size T2 31.4%, 48.6% of patients were of T3, and 18.6% were of T4. Patients with positive axillary LN metastasis were 71.4%. ER was positive in 68.6%, PR was positive in 55.7%, and Her 2 was positive in 18.7%, and Ki-67 was 14 or more in 82% of patients. Tumor lymphocytic infiltrate presented as 19 (27.1%) cases were CD3 T lymphocyte high and 27 (38.6%) cases were CD8 T lymphocyte high (Figure 1).

Ten out of seventy patients achieved pCR (14.3%), 5 patients were TNBC, 4 patients were HER2 and one patient was Luminal B.

Table 1: Showing clinicopathological characteristics N=70

Age	Range Mean ± SD	(27-70) 46.4±10.6
Age Group	Premenopausal Postmenopausal	45(64.3%) 25(35.7%)
T	T2 T3 T4	22(31.4%) 34(48.6%) 13(18.6%)
N	N0 N1 N2 N3	20(28.6%) 48(68.6%) 0(0%) 2(2.9%)
ER	+ve -ve	48(68.6%) 22(31.4%)
PR	+ve -ve	39(55.7%) 31(44.3%)

TILs analysis: The 70 patients were categorized into those with low and high TILs grades based on the analysis of pre and post treatment tumor specimens (Fig. 1–2). The degrees of CD8 and CD3 positive TILs were evaluated immunohistochemically.

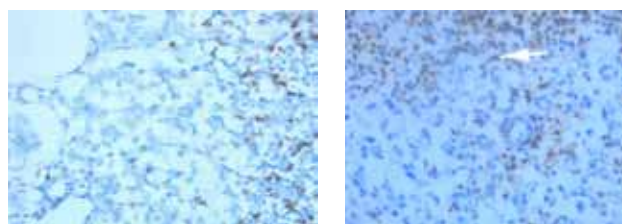


Figure 1: High CD8 and CD3 pre

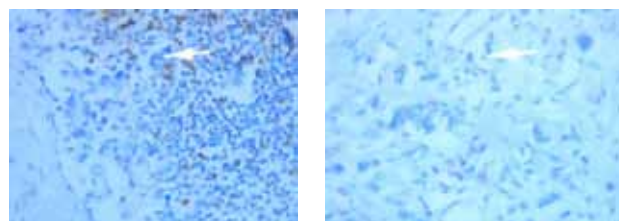


Figure 2: High CD8 and low CD3 post

Predictive value of TIL: Nine of 27 (38.6%) from high CD8 patients and 10 of 19 (27.1%) from high CD3 achieved a pCR (Table 2).

The distribution of TILs grades in the pCR and non-pCR groups is presented in Table 2. The rate of pCR was correlated significantly with TILs grade. The pCR rate in patients with high CD8 TILs grade was 90%, which was significantly higher than that in those with low CD8 TILs grade (1%) ($P = 0.001$) and also the pCR rate in patients with high CD3 was (100%) which was significant than those with low CD3 (0%) ($P = <0.001$).

Table 2: Correlation between CD8 and CD3 with pCR

		PCR		P value
		Non pCR N=60	pCR N=10	
CD8	Low	42(70%)	1(10%)	0.001*
	High	18(30%)	9(90%)	
CD3	Low	51(85%)	0(82.9%)	<0.001*
	High	9(15%)	10(100%)	

Prognostic value of TIL

At a median follow-up of 36 months, 30 recurrences (42.9%) were observed after standard NAC and curative surgery.

Tables (3 & 4) illustrates disease free survival (DFS) according to TILs (high and low levels) post-operative proved to have significant prognostic value.

Table 3: Shows High CD8 TIL in post-operative specimens associated with prolonged survival with statistical significance

Means for Survival Time					Overall comparisons	
TIL CD8 post	Estimate	Std. Error	95% CI		X ²	P value
			Lower Bound	Upper Bound		
Low	122.6	9.7	103.5	141.7	5.83	0.016*
High	149.6	9.8	130.4	168.8		

Table (4): Shows Low CD3 in post treatment specimens associated with prolonged survival with statistical significance

Means for Survival Time					Overall comparisons	
TLI CD3 post	Estimate	Std. Error	95% CI		X ²	P value
			Lower Bound	Upper Bound		
Low	149.8	7.2	135.8	163.9	8.45	0.004*
High	102	13.5	75.4	128.5		

Discussion

The current study detects the role of TILs grade in breast cancer revealed that a high TILs grade in the primary tumor was associated with a significantly higher pCR rate and better outcome especially in HER2 and TNBC. Also, the high CD8 TILs grade in the residual tumor who did not achieve pCR was also associated with a significantly better prognosis, compared with the residual tumors with a low CD8 TILs grade.

Denkert *et al.*⁽¹¹⁾ detected that pathological response rate after preoperative drug treatment was associated with TILs grade in HER2-positive breast cancer. Specifically, they found that the pCR rate was significantly higher in the group with high TILs expression than that with low TILs expression in HER2-positive patients with NAC.

The role of TILs in different subtypes of breast cancer is still unknown. We analyzed the predictive roles of TILs in different subtypes of breast cancer. These results indicated that high TILs detected in pre-treatment biopsy indicated pCR rate increase in triple negative and HER2 positive breast cancer patients, but not higher pCR rate in ER positive patients. Previous studies have mostly supported our results. Ono *et al.*⁽¹²⁾ found a significant association between pCR and the TILs number in triple-negative patients, but not in other breast cancer subtypes. TILs subset in breast cancer, primarily CD3+, CD8 lymphocytes, has also been studied in the relationship of the pCR rate. Since TILs subset have been shown to change after NAC, we found

that higher level of CD8+, CD3+ in pre-treatment biopsy were correlated with the pCR rate and these results were similar to meta-analysis that a high number of TILs is a significant predictor of the pCR rate in response to NAC.⁽¹³⁾

Several studies suggested that TILs expression in residual tumors following preoperative chemotherapy might be an important factor in evaluating the sensitivity of cancer to chemotherapeutic agents. In 2014, Dieci *et al.*⁽¹⁴⁾ compared the TILs expression levels before and after NAC among patients who did not achieve pCR and reported significantly better prognosis in the group with high TILs expression in residual tumors than in the group with low TILs expression.

Our results showed that post-NAC TILs are able to prognostically classify patients with good outcome who did not achieve pCR high CD8 and low CD3 in post treatment was found to be of favorable prognostic value for DFS. Many studies stated that high TLI was associated with better DFS and this was similar to our results in high CD8 as Mahmoud *et al.*⁽¹⁵⁾ and Tsiatas *et al.*⁽¹⁶⁾ but high CD3 in post treatment was not associated with better DFS in our results and this was differ with Castaneda *et al.*⁽¹⁷⁾ but similar to García-Martínez *et al.*⁽¹⁸⁾ and Hamy *et al.*⁽¹⁹⁾.

The identification of these high-risk patients, especially in the group with burden residual disease, might lead to adjuvant immune treatments. Our data might be seen as opposite that of a recent report by Dieci

et al. showing those high TILs in post-NAC residual triple negative breast tumor is a predictor of good prognosis⁽¹⁴⁾. However, given the sample size and the high pCR of TNBC primary tumor in our series, we only identified four patients where TNBC with residual tumor and high TILs infiltration.

Our work has some limitations, the main one being the limited sample size. This fact precluded a more extensive analysis of the interactions between the immune response profile and the tumor subtype. However, other work has shown that prediction of pCR by immune-related signatures is probably not confined to HER2 or TNBC and may also be reliable in luminal breast cancer⁽²⁰⁾.

Also second limitations is that TILs have many variables we only detect CD3 and CD8 types still there is a lot of variables to be detected as CD4, CD68, FOXP3.

Third limitation is that we did not use trastuzumab in NAC or adjuvant setting in HER2 breast cancer patients and this may affect pCR and DFS.

Conclusions

Despite the above limitations, our findings suggest that TILs could serve as an important marker for predicting the pCR rate to NAC, especially in HER2 positive and TNBC patients.

Also it can be used as prognostic marker for those who did not achieve pCR in detecting their outcome, but still we need more characterization and understanding TILs.

Ethics: This study was conducted at Minia university hospital and Minia Oncology Center. All patients were informed of the investigational nature of this study and provided their written informed consent.

Conflict and Interest: None

Disclosure: The authors report no conflicts of interest in this work.

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References

1. Chen AM, Meric-Bernstam F, Hunt KK, et al. Breast conservation after neoadjuvant chemotherapy: the MD Anderson cancer center experience. *J Clin Oncol* 2004;22:2303–12.
2. Cortazar P, Zhang L, Untch M, et al. Pathological complete response and long-term clinical benefit in breast cancer: the CTNeoBC pooled analysis. *Lancet* 2014;384:164–72.
3. De Larco JE, Wuertz BR, Manivel JC, et al. Progression and enhancement of metastatic potential after exposure of tumor cells to chemotherapeutic agents. *Cancer Res* 2001;61:2857–61.
4. Fridman WH, Pages F, Sautes-Fridman C, et al. The immune contexture in human tumours: impact on clinical outcome. *Nat Rev Cancer* 2012;12:298–306.
5. Seo AN, Lee HJ, Kim EJ, et al. Tumour-infiltrating CD8+ lymphocytes as an independent predictive factor for pathological complete response to primary systemic therapy in breast cancer. *Br J Cancer* 2013;109:2705–13.
6. Miyashita M, Sasano H, Tamaki K, et al. Tumor-infiltrating CD8+ and FOXP3+ lymphocytes in triple-negative breast cancer: its correlation with pathological complete response to neoadjuvant chemotherapy. *Breast Cancer Res Treat* 2014;148:525–34.
7. Greene FL, Sobin LH. A worldwide approach to the TNM staging system: collaborative efforts of the AJCC and UICC. *J Surg Oncol* 2009;99:269–72.
8. Mieog JS, van der Hage JA, van de Velde CJ. Preoperative chemotherapy for women with operable breast cancer. *Cochrane Database Syst Rev* 2007:CD005002.
9. Eisenhauer EA, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). *Eur J Cancer* 2009;45:228–47.
10. Symmans WF, Peintinger F, Hatzis C et al. Measurement of residual breast cancer burden to predict survival after neoadjuvant chemotherapy. *J Clin Oncol* 2007; 25(28): 4414–4422.
11. Denkert, C. et al. Tumor-infiltrating lymphocytes and response to neoadjuvant chemotherapy with or without carboplatin in human epidermal growth factor receptor 2-positive and triple-negative primary breast cancers. *J Clin Oncol.* 33, 983–991 (2015).
12. Ono M, Tsuda H, Shimizu C, Yamamoto S, Shibata T, et al. (2012) Tumor-infiltrating lymphocytes are correlated with response to neoadjuvant

- chemotherapy in triple-negative breast cancer. *Breast Cancer Res Treat* 132(3): 793–805.
13. Mao Y, Qu Q, Zhang Y, Liu J, Chen X, et al. (2014) The Value of Tumor Infiltrating Lymphocytes (TILs) for Predicting Response to Neoadjuvant Chemotherapy in Breast Cancer: A Systematic Review and Meta-Analysis. *PLoS ONE* 9(12): e115103. doi:10.1371/journal.pone. 0115103 plos metaanalysis.
 14. Dieci MV, Criscitiello C, Goubar A, Viale G, Conte P, Guarneri V, Ficarra G, Mathieu MC, Delalogue S, Curigliano G, Andre F: Prognostic value of tumor infiltrating lymphocytes on residual disease after primary chemotherapy for triple-negative breast cancer: a retrospective multicenter study. *Ann Oncol* 2014, 25:611–618.
 15. Sahar M.A. Mahmoud, Emma Claire Paish, Desmond G. Powe, R. Douglas Macmillan, Matthew J. Grainge, Andrew H.S. Lee, Ian O. Ellis, and Andrew R. Green *J Clin Oncol* 29:1949 1955.
 16. Marinos Tsiatas, Konstantine T. Kalogeras, Kyriaki Manousou, Ralph M. Wirtz, Helen Gogas, Elke Veltrup *Cancer Medicine*. 2018;7:5066–5082.
 17. Carlos A Castaneda, Elizabeth Mittendorf, Sandro Casavilca, Yun Wu, Miluska Castillo, Patricia Arboleda, *World J Clin Oncol* 2016 October 10; 7(5): 387-394 ISSN 2218-4333
 18. García-Martínez E, Gil GL, Benito AC, González-Billalabeitia E, Conesa MA, García García T, García-Garre E, Vicente V, Ayala de la Peña F. Tumor-infiltrating immune cell profiles and their change after neoadjuvant chemotherapy predict response and prognosis of breast cancer. *Breast Cancer Res* 2014; 16: 488
 19. A.-S. Hamy, J.-Y. Pierga, A. Sabaila, E. Laas, H. Bonsang-Kitzis, C. Laurent, A. Vincent-Salomon, P. Cottu, F. Lerebours, R. Rouzier, M. Lae & F. Reyrol *Annals of Oncology* 28: 2233–2240, 2017 doi:10.1093/annonc/mdx309
 20. Sota Y, Naoi Y, Tsunashima R, Kagara N, Shimazu K, Maruyama N, Shimomura A, Shimoda M, Kishi K, Baba Y, Kim SJ, Noguchi S: Construction of novel immune-related signature for prediction of pathological complete response to neoadjuvant chemotherapy in human breast cancer. *Ann Oncol* 2014, 25:100–106.

The Detection of Escherichiacoli O157: H7 Infections in Children Less than Five Years with Acute Diarrhea

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Abstract

Background: Diarrhea is a leading cause of morbidity and mortality in children aged less than five years. Escherichia coli O157: H7 is a highly pathogenic subgroup of Shiga toxin-producing E. coli (STEC) that causes severe human bloody diarrhea and hemolytic uremic syndrome.

Objectives: To determine the rates of detection of E. coli O157: H7 infections in children less than five years of age and to assess the clinical and laboratory criteria of E. coli O157: H7 associated diarrhea.

Patients and Method: Across sectional prospective, hospital-based study was carried out on children with acute diarrhea visiting the outpatientclinics at Children Welfare Teaching Hospital, AL-Kadhymia Pediatric Hospital and AL-Elweya Pediatric Hospital in Baghdad during the period from Sep. to Dec. 2015. E.coli O157: H7 antigen in fecal samples taken from children with acute diarrhea were detected by immunochromatographic assay (ICA).

Results: Escherichia coli O157: H7 antigen was detected in 43/94(45.7%) of fecal samples for children with diarrhea. 55.8% of children with positive stool samples were females and 44.2% were males with a female to male ratio of 1.3:1. Children with acute diarrhea due to E. coli O157: H7 were younger (mean age 17.19 ± 9.572 months) than those without E. coli O157: H7 infection (mean age 30.63 ± 19.815 months) and the difference is highly significant. Fever and vomiting were symptoms shared by all the studied children regardless of their E.coli O157: H7 infections. Significant associations between bloody diarrhea, pus and red blood cells in stools and E. coli O157: H7 infections were noted.

Conclusions: E. coli O157: H7 infection was a common cause of gastroenteritis in children less than five years in Baghdad. Mainly among infants and young children who presented with acute bloody diarrhea, microscopic pus and red blood cells in their stools.

Keywords: Children, Escherichia coli O157: H7, Acute enteritis, immunochromatographic assay.

Introduction

In developing countries, diarrheal diseases are among the most common causes of morbidity and mortality of young children.⁽¹⁾ Two types of E. coli are recognized among isolates from stool samples; diarrheagenic and non-diarrheagenic E. coli. Regarding diarrheagenic E. coli, these pathogens cannot be distinguished on

bases of colony morphology or biochemical testing.⁽²⁾ Genotypic determination is therefore necessary for the identification of these pathogenic strains and for such purposes, various highly sensitive and specific multiplex PCR method have been developed.^(3,4,5) On the basis of distinct epidemiological and clinical features, specific genetic virulence determinants, and

association with certain serotypes, diarrheagenic strains of *E. coli* have been recognized into six main categories; Shiga toxin-producing *E. coli* (STEC) formerly called Enterohemorrhagic *E. coli* (EPEC), Enterotoxigenic *E. coli* (ETEC), Enteroinvasive *E. coli* (EIEC), Enteroaggregative *E. coli* (EAEC), and diffusely adherent *E. coli* (DAEC). Cytotoxic distending toxin-producing *E. coli* (CDT-EC) are also considered one of the diarrheal *E. coli* group.⁽⁶⁾ Shiga toxin-producing *E. coli* (STEC) strains are important foodborne-zoonotic pathogens of global public health concern, where sheep and their products are important reservoirs for STEC.^(7,8) In 1982, *E. coli*O157:H7 was first recognized as a cause of food-borne outbreak of severe bloody diarrhea and since then in a number of large food and water-borne intestinal disease outbreaks in humans were reported.^(9,10) In human, *E. coli*O157:H7 strains are recognized as highly pathogenic subgroup of STEC that can cause severe outbreaks of gastrointestinal illness, ranging from diarrhea and hemorrhagic colitis to the life-threatening hemolytic uremic syndrome, where most of these outbreaks as well as sporadic cases have been frequently attributed to the STEC O157: H7 strains.^(11,12,13,14,15) Specificity of the causative diarrheal pathogens as well as their epidemiology is critical for implementation of their specific interventional strategies. This study was proposed to unravel the rate of *Escherichia coli* O157:H7 infection in children up to five years of age as well as assessing the clinical and laboratorial criteria of their associated diarrhea in children attending tertiary pediatric hospitals in Baghdad.

Patients and Method

This cross sectional prospective hospital-based study was carried out on 94 children less than 5 years presented with acute diarrhea visiting the outpatient clinics at Children Welfare Teaching Hospital, AL-Kadhymia Pediatric Hospital and AL-Elweya Pediatric Hospital in Baghdad in the period from Sep. to Dec. 2015. Their age ranged from one month to five years. Children with protozoal or parasitic infestations were excluded from the study. Following microscopical and microscopical laboratory examinations of the stool samples, an immunochromatographic assay (ICA) (CerTest Company, Spain) for the detection of *E. coli* O157:H7 antigen which was applied according to the instructions of the manufacturing company. Regarding *E. coli* O157:H7 antigen detection, approximately 0.1 gm or 100 microliters of each stool sample was taken in specified collecting tube that contained a diluent. Then

100 microliters of the diluted mixture were dispensed in the (S)-labelled circular window in the card and to wait for 10 minutes for the appearance of red and green-colored bands. This qualitative immunochromatographic assay was done for determination *E. coli* O157:H7 antigen in fecal samples, where mouse monoclonal antibodies were reacting with *E. coli* O157:H7 antigens present on the pre-coated test band region. According to the capillary action, the stool samples were allowed to move upward across the membrane to react with the colored conjugate (pre-coated with mouse monoclonal anti-*E. coli* O157:H7 antigen antibodies-red microspheres which was pre-dried on the specified test region) so as a red colored line then being visible. This mixture again moves upward to another immobilized antibody placed in the control band region to produce a green-colored band, validating then a qualified procedure. Negative results was indicated as an appearance of only one green band (control line) while a total absence of control band, irrespective to other results, was regarded as an invalid result. The T test, Fischer exact and Chi square tests were applied for the analysis of the obtained results using SPSS program (version-20).

Results

From Sep. to Dec. 2015, 94 children with acute diarrhea attended the consultation clinics at three major tertiary pediatric hospitals in Baghdad were tested for the detection of *E. coli* O157:H7 antigen in their stools. Their age ranged from 1-60 months with a mean age of 24.48 ± 17.257 months. The *E. coli* O157:H7 antigen was detected in of 43/94(45.7%) of the fecal samples. Children with acute diarrhea due to *E. coli* O157:H7 were younger (mean age 17.19 ± 9.572 months) than those without *E. coli* O157:H7 infection (mean age 30.63 ± 19.815 months) and the difference in mean age in relation to *E. coli* O157:H7 infection was highly significant $P= 0.001$. Among the studied children, 51 females and 43 were males, with female to male ratio of 1.2:1. The female to male ratio among those with *E. coli* O157:H7 infection was 1.3:1. Although the gender of studied children with *E. coli* O157:H7 infection was in favor of female predominance (55.8% of those children who have *E. coli* O157:H7 antigen-positive diarrhea were females and 44.2% were males), yet the statistical association between *E. coli* O157:H7 infection and gender was not scored as seen in table-1. Regarding the relationship between clinical features and stool *E. coli* O157:H7 antigen detection; all studied children with and without *E. coli* O157:H7 infections presented with

vomiting. However, there was a significant association between bloody diarrhea and *E. coli* O175:H7 infections as all the children with acute diarrhea and positive fecal specimens for *E. coli* O175:H7 antigen had bloody diarrhea compared to 43.1% of those without *E. coli* O175:H7 antigen. Children with fecal specimens positive to *E. coli* O175:H7 had more nausea than those without *E. coli* O175:H7 antigen (79.1% versus 76.5%), but the association between nausea and *E. coli* O175:H7 infection was not achieved. All the children with acute diarrhea and positive fecal specimens for *E. coli* O175:H7 antigen had fever while 96% of those without *E. coli* O175:H7 antigen were febrile, and a statistical association between fever and *E. coli* O175:H7 infection

was not scored. Children with abdominal pain and fecal specimens positive to *E. coli* O175:H7 antigen were 62.8% while those without *E. coli* O175:H7 antigen were 66.7%, thus no significant association was detected between abdominal pain and *E. coli* O175:H7 infection. Similarly, each of gross fecal pus and mucus scored no significant association with *E. coli* O175:H7 infections as seen in table-2. Regarding the associations between the stool laboratorial findings and *E. coli* O175:H7 antigen findings; the stool color, the presence of pus and red blood cells in stools were significantly associated with *E. coli* O175:H7 infection. While stool consistency, fat drops, and candida in stool were not significantly associated with *E. coli* O175:H7 infection as seen in table-3.

Table 1: The association between demographic characteristics and *E. coli* O175 infection in children

Characteristics		E.coli O175 No (%)	Non-E. coli O175 No. (%)	Total No. (%)	P value
Gender	Male	19 (44.2)	25 (49)	44 (46.8)	0.6
	Female	24 (55.8)	26 (51)	50 (53.2)	
Age mo.	1-12	14 (53.8)	12 (46.2)	26 (27.7)	0.001
	13-36	29 (65.9)	15 (34.1)	44 (46.8)	
	< 36	0 (0.0)	24 (100)	24 (25.5)	

Table 2: The association between clinical features and *E. coli* O175 infection in children

Clinical Features		E.coli O175 No (%)	Non-E.coli O175 No. (%)	Total	P. value
Fever	Yes	43 (100)	49 (96)	92 (79.9)	0.3
	No	0	2 (4)	2 (2.1)	
Nausea	Yes	34 (79.1)	39 (76.5)	73 (77.7)	0.9
	No	9 (20.9)	12 (23.5)	21 (22.3)	
Abdominal pain	Yes	27 (62.8)	34 (66.7)	61 (64.9)	0.5
	No	16 (37.2)	17 (33.3)	33 (35.1)	
Bloody diarrhea	Yes	43 (100)	22 (43.1)	65 (69.1)	0.001
	No	0	29 (56.9)	29 (30.9)	
Gross pus in stool	Yes	8 (18.6)	7 (13.7)	15 (15.9)	0.5
	No	35 (81.4)	44 (86.3)	79 (84.1)	
Gross mucous in stool	Yes	35 (81.4)	43 (84.3)	78 (83)	0.7
	No	8 (18.6)	8 (15.7)	16 (17)	

Table 3: The association between laboratory stool findings and *E. coli* O175 infection in children

Laboratory stool findings		E.coli O175 No (%)	Non-E.coli O175 No. (%)	Total	P. value
Color	Brown	18 (46.2)	23 (45.1)	41 (43.6)	0.001
	Green	20 (51.3)	15 (29.4)	35 (37.2)	
	Yellow	5 (2.6)	13 (25.5)	18 (19.2)	
Consistency	Loose	10 (23.3)	13 (25.5)	23 (24.5)	0.8
	Watery	33 (76.7)	38 (74.5)	71 (75.5)	

Laboratory stool findings		E.coli O175 No (%)	Non-E.coli O175 No. (%)	Total	P. value
Fat Drops	Yes	14 (32.6)	25 (49.0)	29 (41.5)	0.1
	No	31 (72.1)	26 (51.0)	55 (58.5)	
Pus cells	Yes	43 (100)	28 (54.9)	71 (75.5)	0.001
	No	0	23 (45.1)	23 (24.5)	
RBC	Yes	43 (100)	24 (47.1)	67 (71.3)	0.001
	No	0	27 (52.9)	27 (28.7)	
Candida	Yes	2 (4.7)	0	2(2.1)	0.1
	No	41(95.3)	51 (100)	92 (97.9)	

Discussion

In developing countries, diarrheagenic *E. coli* is recognized as an important cause of infantile and young childhood diarrhea. However, in different studies, their incidence have varied from more than 40% as in Bangladesh to less than 30% as in Jordan.^(16,17) Furthermore in the last two decades, infection with *E. coli* O157:H7 has become a significant public health problem in the developed countries.⁽¹⁸⁾ However, data on the etiology of diarrhea in Iraq are scarce.⁽¹⁹⁾ In his study Immunochromatographic assay (ICA) for the detection of *E. coli* O157:H7 antigen was applied. It is considered as a rapid, sensitive and specific detection method to specify the infection by this pathogenic O157:H7 serotype of *E. coli* from other counterpart serotypes that have similar cultural as well as biochemical characteristics. The results showed that *E. coli* O157:H7 antigen was detected in 45.7% of the examined fecal samples. These results are higher than many other Iraqi studies, such as those reported by Al-Awwadi *et al.*(2012)⁽²⁰⁾ who serotyped *E. coli* O157:H7 in 4%, Al-Dawmy *et al.*(2013)⁽⁸⁾ in 4.8%, Mohammed *et al.* (2011)⁽²¹⁾ in 5.7% and Shebib *et al.* (2003)⁽²²⁾ in 11%. Other studies conducted by Elaine *et al* (2012)⁽²³⁾ and Vally *et al.* (2013)⁽²⁴⁾ have also recorded very low rates of infection with *E. coli* O157:H7 in diarrheal children in Australia and USA, respectively. Different rates in different studies might be attributed to different tests used in each of them. However, by using multiplex PCR, Arif *et al.* (2010)⁽¹⁾ detected target genes of diarrheagenic *E. coli* in 38% diarrheal stools specimens from children in Sulaimani and Karkuk, Iraq.

In the present study, children with acute diarrhea due to *E. coli* O157:H7 were significantly younger than those without *E. coli* O157:H7 infection and the frequency of *E. coli* O157:H7 infection had increased

with advancing age towards 36 months and declined after 36 months of age (Table-1). These findings are in agreement with Tozzi A.E study⁽²⁵⁾ where the frequency of STEC O157:H7 infections was found to increase with age. Also Ali in 2004⁽²⁶⁾ found that the *E. coli* O157:H7 infection rate was higher among children <2 years of age than other age groups, however, the frequency of such infections has begun to decrease in 10-12 years age group, representing a decline curve of this infection in relation to age. Another Iraqi study by Al-Dawmy and Yousif (2013)⁽⁸⁾ revealed that most of the *E. coli* O157:H7 diarrheal cases occurred from first month to 5 years. Delignette *et al* study (2008)⁽²⁷⁾ revealed that children less than 5 years are 5 times more susceptible to *E. coli* O157:H7 infection than those more than 5 years.

Our results showed high prevalence of *E. coli* O157:H7 infections among females than males as well as in children less than 36 months. While Ali (2004)⁽²⁶⁾ in Basrah, Iraq, reported that males were more prone to the infection than females. Al-Wgaa and Alwan. (2017)⁽²⁸⁾ found 3.5% of isolates of human urine samples were *E. coli* O157:H7 positive and two third of them were females. The age-specific differences could belong to that infants have an immature immune systems as well as are exposed either to contaminated milk formula, foods and environment, which might increase the probability of the infection among children less than 3 years age.⁽²⁹⁾ In addition, thumbs sucking, dropped dummies or toys, and under supervised hand was hinge may increase the risks of infants and toddlers for such infection. Moreover, family of infants with diarrhea are more likely to seek medical care and to have stool being cultured than older children.⁽⁸⁾

In the present study, each of gross fecal pus and mucus showed no significant association with *E. coli* O157:H7 infections. However, there was a significant association

between bloody diarrhea and *E. coli* O157:H7 infections as all (100%) of the children with acute diarrhea and positive fecal specimens for *E. coli* O157:H7 antigen had bloody diarrhea compared to 43.1% of those without *E. coli* O157:H7 antigen. An association has been identified between certain host-specific factors and progression risk of enteric *E. coli* O157:H7 infection, where up to 15% of gastrointestinal cases progressed to the hemolytic uremic syndrome (HUS).⁽¹⁹⁾ The onset of HUS was most frequently follow an episode of gastroenteritis that often accompanied by bloody diarrhea.⁽³⁰⁾ In addition, *E. coli* O157:H7 infected patients who were at time of presentation have elevated white blood cell counts, fever, or bloody stools have also been noted to have a higher risk of progression to HUS than their counterpart patients without these findings.^(31,32,33) Regarding results of bloody diarrhea observed in the present study, the clinical illness caused by *E. coli* O157:H7 was similar to that noticed previously by Karmali *et al.* and Hughes *et al.* studies.^(34,35) However, bloody diarrhea was not an invariable finding in Ali (2004) study⁽²⁶⁾ where 44% of the patients had non-bloody diarrhea. Children with acute diarrhea whose fecal specimens were positive to *E. coli* O157 antigen did relatively develop fever as those without *E. coli* O157:H7 antigen. In contrast, Ali (2004)⁽²⁶⁾ in Basrah, noted that this agent causes bloody diarrhea with mild clinical presentation and could be distinguished by the lack of fever. In addition, AL-Musawiet *al.* (2018)⁽³⁶⁾ provided an evidence of the spread of *E. coli* O104:H4 in Iraq, via the stool and urine of children under 15 year, that causes an illness similar to infection with *E. coli* O157:H7. In conclusion, this study has highlighted the importance of *E. coli* O157:H7, in infecting and causing severe intestinal tract infection in Iraqi children aged less than five years and provided useful information on the clinical and laboratorial criteria of their associated diarrhea.

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References

1. Arif SK, Salih LIF. Identification of Different Categories of Diarrheagenic *Escherichia coli* in Stool Samples by Using Multiplex PCR Technique. *Asian Journal of Medical Sciences* 2010; 2(5): 237-243.
2. Kalnauwakul S, Phengmak M, Kongmuang U, Nakaguchi Y, Nishibuchi M. Examination of diarrheal stools in Hat Yai city, South Thailand, for *Escherichia coli* O157 and other diarrheagenic *Escherichia coli* using Immunomagnetic Separation and PCR Method. *Southeast Asian J. Trop. Med. Public Health* 2007; 38(5): 871-880.
3. Prere MF, Fayet O. A new genetic test for the rapid identification of shiga-toxines producing (STEC), Enteropathogenic (EPEC) *E. coli* isolates from children. *Pathol. Biol.* 2005; 53: 466-469.
4. Vidal M, Kruger E, Uran CD *et al.* Single multiplex PCR assay to identify stimulatingly the six categories of diarrheagenic *E. coli* associated with enteric infections. *J. Clin. Microbiol.* 2005; 43: 4362-5365.
5. Nessa K, Ahmed D, Islam J, Kabir FL, Hossain M.A. Usefulness of a multiplex PCR for detection of diarrheagenic *Escherichia coli* in a diagnostic microbiology laboratory setting. *Bangladesh J. Med. Microbiol.* 2007; 1(2): 38-42.
6. Torres AG, Zhou X, Kaper JB. Adherence of diarrheagenic *Escherichia coli* strains to epithelial cells. *Infect. Immun.* 2005; 73: 18-29.
7. Sharaf E, Shabana I. Prevalence and molecular characterization of Shiga toxin-producing *Escherichia coli* isolates from human and sheep in Al-Madinah Al-Munawarah. *Infect.* 2017; 21(2): 81-87.
8. Al-Dawmy FAA, Yousif AA. Prevalence of *E. coli* O157:H7 in intestinal and Urinary tract infection in children. *International Journal of Advanced Research* 2013; 1(8): 111-120.
9. Riley LW, Remis RS, Helgerson SD *et al.* Hemorrhagic colitis associated with a rare *Escherichia coli* serotype. *N Engl J Med.* 1983; 308: 681-5.
10. Ogden ID, Hepburn NF, Mac Rae M *et al.* Long-term survival of *Escherichia coli* O157 on pasture following an outbreak associated with sheep at a scout camp. *Lett Appl Microbiol.* 2002; 34: 100-104.

11. Rabinovitz BC, Gerhardt E, Tironi Farinati C et al. Vaccination of pregnant cows with EspA, EspB, Y-intimin, and Shiga toxin 2 proteins from *Escherichia coli* O157:H7 induces high levels of specific colostral antibodies that are transferred to newborn calves. *J Dairy Sci.* 2012; 95:3318–3326.
12. Karch H, Tarr PI, Bielaszewska M. Enterohaemorrhagic *Escherichia coli* in human medicine. *Int J Med Microbiol.* 2005; 295:405-18.
13. Amézquita-López BA, Quiñones B, Cooley MB et al. Genotypic analyses of Shiga toxin-producing *Escherichia coli* O157 and non-O157 recovered from feces of domestic animals on rural farms in Mexico. *PLoS ONE.* 2012; 7:e51565.
14. Ateba, Bezuidenhout. Characterisation of *Escherichia coli* O157 strains from humans, cattle and pigs in the North-West Province, South Africa. *Int J Food Microbiol.* 2008; 128:181-8.
15. Tarr PI, Gordon CA, Chandler WL. Shiga-toxin-producing *Escherichia coli* and haemolytic-uraemic syndrome. *Lancet.* 2005; 365: 1073–86.
16. Albert MJ, Faruque SM, Faruque AS et al. Controlled study of *Escherichia coli* diarrheal infections in Bangladeshi children. *J. Clin. Microbiol.* 1995; 33(4): 973-977.
17. Shehabi, AA, Bulos NK, KG Hajjaj. Characterization of diarrheagenic *Escherichia coli* isolates in Jordanian children. *Scand J. Infect. Dis.* 2003; 35: 368-371.
18. Dundas S, Todd WTA, Stewart AI, Murdoch PS, Chaudhuri AKR, Hutchinson SJ. *E. coli* O157:H7 Infection and HUS. *Clinical Infectious Diseases* 2001; 33:923–31.
19. Tawfeek HI, Najim NH, Al-Mashikhi S. Studies on diarrhoeal illness among hospitalized children under 5 years of age in Baghdad during 1990-1997. *Eastern Mediterranean Health J.* 2002; 8(1): 12-19.
20. Al Awwadi N, Alshimary A, Al kafaji H, Al badry H, Wanys Z. The detection of shiga toxin producing *E. coli* (O157: H7) infection in children diarrhea in Nasseriya city. *GJPAST* 2013; 3 (1): 1-6.
21. Mohammed H, Awatif H, Issa L. Detection of rfbO157 and fliCH7 Genes in *Escherichia coli* isolated from Human and Sheep in Basrah Province. *Raf. J. Sci.* 2012; 23 (1): 19-33.
22. Shebib ZA, Abdul Ghani ZG, Mahdi LKh. First report of *Escherichia coli* O157 among Iraqi children. *East Mediterr Health J.* 2003 Jan-Mar; 9(1-2):159-66.
23. Elaine S, Barbara EM, Robert MH, Patricia MG. Estimates of Illnesses, Hospitalizations and Deaths Caused by Major Bacterial Enteric Pathogens in Young Children in the United States. *The Pediatric infectious disease journal* 2013; 32(3):217-21.
24. Vally H, Hall G, Dyda A, Desmarchelier J. Epidemiology of Shiga toxin producing *Escherichia coli* in Australia, 2000-2010. *BMC Public Health* 2012; 12:63.
25. Tozzi AE. *Emerging Infectious Diseases: DISPATCHES* January 2003; 9(1):106-108.
26. Ali NH. *Escherichia coli* O157:H7 Infection and Hemolytic Uremic syndrome among Iraqi Diarrheal Children. *Bahrain Med Bull* 2004; 26(2):1-7.
27. Delignette-Muller M L, Cornu M. AFSSA STEC study group. Quantitative risk assessment for *Escherichia coli* O157:H7 in frozen ground beef patties consumed by young children in French households. *Int J Food Microbiol.* 2008; 30; 128(1):158-64.
28. Al-wgaa AA and Alwan MJ. Study the prevalence of *Escherichia coli* O157:H7 isolated from humans and sheep with histopathological Study. *Journal of Entomology and Zoology Studies* 2017; 5(6): 2074-2080.
29. Akbar SA. A study of *Escherichia coli* isolated from children with diarrhea in Kalar, M.S. Thesis, College of Education-Kalar, University of Sulaimani, Sulaimaniah, Iraq, 2008.
30. Gerber A, Karch H, Allerberger F, Verweyen HM, and Zimmerhackl LB. Clinical Course and the Role of Shiga Toxin-Producing *Escherichia coli* Infection in the Hemolytic-Uremic Syndrome in Pediatric Patients, 1997–2000, in Germany and Austria: A Prospective Study. *The Journal of Infectious Diseases* 2002; 186:493–500.
31. Pavia AT, Nichols CR, Green DP, et al. Hemolytic-uremic syndrome during an outbreak of *Escherichia coli* O157:H7 infections in institutions for mentally retarded persons: clinical and epidemiologic observations. *J Pediatr.* 1990; 116:544–551.
32. Carter AO, Borczyk AA, Carlson JAK, et al. A severe outbreak of *Escherichia coli* O157:H7-associated hemorrhagic colitis in a nursing home. *N Engl J Med.* 1987; 317:1496–1500

33. Akashi S, Joh K, Tsuji A, et al. A severe outbreak of haemorrhagic colitis and haemolyticuraemic syndrome associated with *Escherichia coli* O157:H7 in Japan. *Eur J Pediatr.* 1994; 153:65–655.
34. Karmali MA, Petric M, Corazon L. et al. The association between idiopathic hemolytic uremic syndrome and infection by verotoxin-producing *Escherichia coli*. *J Infect Dis* 1985; 151:775-82.
35. Hughes DA, Beattie TJ, Murphy AV. Hemolytic uremic syndrome: 17 years experience in a Scottish pediatric renal unit. *Scott Med J* 1991; 36:009-12.
36. AL-Musawi MT, AL-Jobori KM, Al-Musawi AT, Ali SH. *Escherichia coli* O104:H4: a New Challenge in Iraq. *J. Pharm. Sci. & Res.* 2018; 10(5):1118-1121.

The Impact of Healthy Educational Curriculum for Harmonized Exercises in the Development of Some Defense Skills in Handball

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Abstract

The importance of research to provide of the learner by best level of performance skills defensive hand reel through the integration of interoperability exercises with the educational units of an educational curriculum. The study aimed to identify the impact of the educational curriculum for exercises interoperability in the development of some defensive skills reel hand to sample individuals. The study was used in the study of the experimental method of designing the two groups of pre-tribal and post-test to suit the nature of the problem and the objectives of the research. This study was applied to the students of the third stage in the Faculty of Physical Education and Sports Sciences, University of Maysan for the academic year 2017-2018 of 40 students, Such as the control sample, (19) students such as experimental research sample, two students were dismissed for health reasons. Appropriate method, tools and tests were used, and after the results were obtained from the tests, they were processed statistically by using the statistical bag (SPSS). The study concluded with the most important conclusions: The educational curriculum of the combative exercises has a positive effect on the development of the performance of defense skills (interview, coverage, wall block and handover, receipt) for the students of the research sample. In addition, the educational curriculum for the exercises of compatibility achieved a better effect than the traditional curriculum followed by the teacher on the students of the research sample.

Keyword: *Experimental, Control, Smooth, Speed, Central nervous system.*

Introduction

Learning is a process that is inherent to life, that is, the person is in continuous learning as long as he is alive. Everyone knows that the educational process is affected by many factors, including what is related to the learner himself, others are related to the teacher and the type of learning and the surrounding circumstances them. Some of the special learner genetic factors that have a significant role in the success of learning associated with the type of material educated as possible developed, and thus we get a positive impact in achieving the goal of the educational instruction process, and among these factors kinetic compatibility that significantly affects the performance of many of the motor skills. In most of the skills of different sports, including handball skills, and thus whenever the motor compatibility, which is owned learner by a high level whenever the learner was able to reach the best performance of the motor skills. Compatibility means “the player’s ability to integrate

the types of movements in one template is characterized by Streamline and good performance”. In other words, the motor⁽¹⁾.

Compatibility depends mainly on the integrity of the central nervous system, which sends nerve signals to several muscles working simultaneously to perform the motor duty. Thus, whenever increase the higher the accuracy of the sent signals, whenever the higher the motor compatibility, which in turn it is a positive return in the performance of defensive skills in handball that requires a great deal of motor compatibility. Therefore, have to attention it and develop it and here lies the importance of research to deliver the learner to the best level of performance skills defensive handball through the integration of interoperability exercises with the educational units of an educational curriculum.

The students in the Faculty of Physical Education and Sports Sciences must learn the defensive skills of

handball so that they can perform their defense duties during the application of defensive formations; we often notice that they have difficulty learning and not reaching the required level of performance. Although they have no difficulty or problem in receiving information while explaining the skill learned by the teacher of the material.

In an effort to find a solution to this problem, we decided to study the harmonic exercises because of its significant role in the motor performance of the most successful sports skills through application in a curriculum prepared by the researchers⁽²⁾.

The research aims to identify the impact of the educational curriculum for exercises interoperability in the development of some defensive skills handball to sample individuals.

Research methodology and field procedures: The experimental approach was used to design the two sets of equal and for tests Pre and post the suitability of the nature of research.

The Data: The research community represents the students of the fourth stage in the Faculty of Physical Education and Sports Sciences-University of Maysan for the academic year (2017-2018) and it is scientific, theoretical, and applied branches of the number (40) students.

Students were selected to represent the branches of the research sample, the lot fell on the branch of the theoretical science to represent the control group by 19 students, and a branch of Applied Sciences to represent the experimental group of (19) students was excluded two students for health reasons.

Method and tools used in research:

- Method of data collection (Arab and foreign sources, observation, tests, data dump form for research tests).
- Tools and devices used (handball stadium legal, balls hand number (5), Poling number (10), whistle type (fox40) (2), colored adhesive tapes width (5 cm), video camera type (Sony), Laptop Acer.

Identify the studied skills and tests: It has been identified some defensive skills hand reel that will be studied, namely, (interview, coverage, wall block, handover) were determined. The tests were based on the evaluation of the performance of the skills through their

portrayal and presentation to the evaluators to be the evaluation of (10) degrees.

Pre tests: Pre-tests for the research sample in skill tests understudy on Monday, 19/2/2018 at exactly half-past eight o'clock in the morning in the sports hall for the College of Physical Education and Sports Sciences, University of Maysan with Note the following:

1. Give the sample sufficient time to warm up with all supplies.
2. Provide a detailed explanation for members of the research sample how the tests are performed.
3. View each test before it is started by the members of the research sample.

Curriculum for harmonized exercises: To achieve the objectives of the research, the units were prepared for harmonized exercises and included (8) educational units, the duration of the unit (90) minutes divided as follows:

Preparatory section: Duration (25) minutes, including (introduction, warm-up and private warm-up).

Main section: Duration (60) minutes and includes two parts:

- A. The educational part: In this part, the defense formations of the handball are explained. The duration of this section is 15 minutes.
- B. The applied part: In this part, the defense formations of the handball are applied, interspersed with the implementation of consensual exercises. The duration of this part is 45 minutes.

The final section: Duration (15) minutes, including exercises to calm, relax, and greet the departure.

Application of the curriculum: After the completion of the implementation of the curriculum was conducted post-tests for the research sample in skill tests defense understudy on Thursday 12/4/2018 At exactly half-past eight o'clock in the morning in the sports hall for the Faculty of Physical Education and Sports Science-Maysan University. Was subject to conditions and the requirements in which the pretest took place.

Statistical method: The statistical bag (SPSS) was used to derive (arithmetic mean, standard deviation, t-test for the corresponding samples, t-test for asymmetric samples).

Results and Discussions

View the results of the differences between the two measures the pre and post in skills tests for the control group.

Table 1: It shows means and standard deviations and test (t) of the results of skill tests and pre-post control group

tests	Unit	Pre		Post		(t)	Sig	Type of significance
		M	SD	M	SD			
Interview	M	5.79	1.2	6.12	0.76	2.34	0.03	Sig
Coverage	M	5.12	1.17	5.66	0.97	1.12	0.07	not sig
Wall block	M	4.77	2.1	5.33	1.87	1.26	0.07	not sig
Handover	M	4.56	1.43	5.96	1.23	2.44	0.00	sig

* At degree of freedom (18) and probability of error ratio (0.05).

Through the table analysis (1) above, showing the results of the differences between the two measurements pre and post group research control in the test interview and the handover. Have made significant differences in favor of the post-test because of the level of significance value of less than (0.05). While did not show significant differences for test coverage and wall block the probability that the value of the significance level is greater than (0.05).

Discuss the results of the pre and post-tests of the control group: It shows through the presentation and analysis of the results of skill tests under the two measurements pre and post research group control which explained in the table (1). the development of the skills of the interview and the handover, and attributed the reason for this development as a result of its performance repeatedly through the application of formations defense in the educational units of the curriculum of education followed by the teacher.

Present the results of the differences between the pre and post measurements in the experimental tests of the experimental group and analyze them.

Table 2: It shows means and standard deviations and test (t) of the results of skill tests pre and post-experimental group.

tests	Unit	Pre		Post		(t)	Sig	Type of significance
		M	SD	M	SD			
Interview	M	5.79	1.07	7.17	0.73	3.27	0.00	Sig
Coverage	M	4.88	1.18	6.64	1.12	3.34	0.00	not sig
Wall block	M	5.17	1.67	6.73	0.97	2.45	0.00	not sig
Handover	M	4.34	1.41	6.37	1.1	3.32	0.00	sig

* At degree of freedom (18) and probability of error ratio (0.05).

Through the analysis of the table (2) above, the results show that the differences between the two measurements pre and post experimental research group in all skill tests achieved significant differences in favor of the posttest because the level of significance value of less than (0.05).

Discussion the results of the pre and post-testing of the experimental group: Shows through the presentation and analysis of the results of skill tests under the two measurements pre and post-experimental research group that is explained in the table (2).The curriculum of the harmonic exercises and prepared by the

researchers have a positive impact on the development of defensive skills (interview, coverage, wall block, handover), and this is consistent with the imposition of the first search.

This is because the educational curriculum includes harmonized exercises that have a great role in the development of defensive skills in handball (studied). As motor compatibility whenever the good of the individual whenever enables sports movements perform

better and a high level, and this was confirmed by (3) as stated, “The higher the accuracy of the implementation of the motor performance indicates that the high level of compatibility. “As well as the nature of the exercises used in the educational curriculum, as given students enough time to repeat the exercise, has pointed out (4) that imposed on the teachers and trainers encourage learners to the greatest possible number of attempts to exercise performance.

Presenting the results of the differences between the control and experimental groups in the post measures of the skills tests and their analysis.

Table 3: It shows means and standard deviations and test (t) of the results of skill tests pre and post-experimental group and control

Tests	Unit	Pre		Post		(t)	Sig	Type of significance
		M	SD	M	SD			
Interview	M	6.12	0.76	7.17	0.73	3.27	0.00	Sig
Coverage	M	5.66	0.97	6.64	1.12	2.93	0.00	sig
Wall block	M	5.33	1.87	6.73	0.97	3.65	0.00	sig
Handover	M	5.96	1.23	6.37	1.1	2.75	0.00	sig

* The degree of freedom (36) and the probability of error ratio (0.05).

Through the analysis of the table (3) above, showing the results of the differences between the measurement of the post between control and experimental groups in all skill tests achieved significant differences in favor of the experimental group because of the level of significance value of less than (0.05).

Discussion the results of the post-test of the control and experimental groups: As shown in Table (3) above, the experimental group exceeds the control group in learning the studied skills, thus achieving the second hypothesis of the research.

The researchers attributed the reason to the fact that the curriculum is more effective than the traditional method followed by the subject teacher, which includes exercises harmonized and have a significant role in the treatment of the problem of excessive arousal of muscle aggregates and non-performance linked, which shows the lack of flow of movement. This contributed significantly to show moral differences, Compatibility motor is linked to the central nervous system, which in turn receives various information on all the positions and movements of the body through sensory neurons

and take the decision to issue only commands to the core muscles responsible for motor performance by motor neurons. In addition to the harmonic exercises that have been applied marked by a factor of thrill and excitement, which led to a state of interaction between the teacher and the student and therefore a positive sign by the students during the educational unit. as it confirms (5) that learn any skill by practicing various exercises must To be done through the proper practice of skill and focus on the accuracy of performance by using the optimum time and practice of high efficiency.

In addition, that the training exercises positive yield in the development of the skill and mobility in the students, as the performance skill requires (use the entire body to perform the movement with the utmost proficiency with the ability to change direction and speed in a sound and smooth. In addition, need to be a fitness and compatibility to try to succeed in the integration of several basic skills in one framework or change from skill to another or change of speed and direction. In other words, skill performance is tightly related to motor compatibility, which reflects the level of performance. (Learner initially when he performs defensive duties

that require compatibility, the involvements of muscle groups are not required in the performance of movements, causing unrest and lack of skill performance consistency), and the important things that should be referred to in the events of evolution is the quality of the harmonic exercises that have been implemented and their suitability to the level of the sample in terms of the level of difficulty and consistency that the sample students, (the amount of learning spent by the learner in the exercise is not effective only in the development of learning only, but the quality of the exercise is also within the period specified. As a result, the experimental group students have excelled in the performance of the students of the control group.

Conclusions

Through what was shown from the results we reached the following conclusions:

- The curriculum for the harmonic exercises a positive impact on the development of the performance of defensive skills (interview, cover, block wall and handover) for the students of the research sample.
- The curriculum for the harmonic exercises achieved a favorable influence of the traditional curriculum followed by the teacher on the student's research sample.

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References

1. Abu El-Ela Ahmed Abdel-Fattah: Sports Training (physiological foundations), print One, (Cairo: Dar al-Fikr al-Arabi, 1997).
2. Osama KamelRateb: Psychological preparation for the training of youth, a guide for trainers and parents, print 1, (Cairo: Dar al-Fikr al-Arabi, 1997).
3. Hanafi Mahmoud Mukhtar: The Scientific Basis in the Training of Football, (Cairo: Dar Al-Fikr Al-Arabi, 1997).
4. Kamal Darwish et al.: Defense in handball, 1st, (Cairo: Book Center for Publishing, 1999).
5. Wissam Salah Abdel-Hussein and Samer Yousef Meteb: motor Learning and its Applications in Physical and Sports Education, 1st Floor, (Beirut: Scientific Books House, 2014).
6. Craig N. Wrisberg Richard A. Schmidt; motor Learning and performance; (Human kinetics 2000).

The Effect of Different Doses of Green Tea Extract on Hematological and Biochemical Parameters in Adult Male Rats

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Abstract

This investigates the effects of various concentrations of continuous drinking of green tea in rats. (24) male rats are randomly categorized into four groups: control, which does not receive green tea, GTE5, GTE10 and GTE20 (receive 5g, 10g and 20g GTE, respectively). In hematological parameters analysis, there are no significant variation ($p > 0.05$) in the RBC, MCHC and platelet among all groups. Furthermore, Control group presented a considerable decrease ($p < 0.05$) in HB, HTC, MCV and MCH as compared with GTE5, GTE10 and GTE20. The biochemical analysis, control and GTE5 groups had high significant decrease ($p < 0.05$) in glucose level as compared with GTE10 and GTE20 groups. Analysis of albumin and globulin, control and GTE5 groups had a significant decrease ($p < 0.05$) higher than that of GTE10 and GTE20 groups. On the other hand, GTE20 group revealed a highly significant increase variation ($p < 0.05$) in total protein than the control, GTE5 and GTE10 groups. In the control group showed a significant increase ($p < 0.05$) in values of AST, ALT and ALK as compared with other groups. Therefore, it is recommended that using green tea for a long period leads to inhibition of the free oxygen radical damages in the liver and erythrocyte.

Keywords: Green tea, Liver enzymes, Glucose, total protein.

Introduction

The liver in animals, as well as human, is considered to be the site that is continuously subject to various ingested and inhaled chemical substances that might have toxic or non-toxic effects depending upon the uptake of their amounts^{1,2}. The ability of herbal plants to render the effects of poisons and microbial infections is well documented recently^{3,4,5}. Green tea is among the most common herbal plants that contain xanthine analogues, such as caffeine, theophylline, theobromine, glutamide subordinate and theanine which have direct effects on the immune system⁶. The consumption of green tea might enhance weight loss, promote metabolism, fat burning, reduce cholesterol, protect the heart and arteries and prevent cancer⁶. In addition, green tea acts as hepatoprotective and as antioxidant due to its high content of catechins (e.g., epigallocatechin, epicatechin gallate, epicatechin and epigallocatechin gallate), vitamins E and C which function like co-factor^{7,8}. The present study highlights the effect of green tea on some biochemical and hematological parameters in rats.

Materials and Method

Sample investigation: Green tea is made in Turkey and purchased from a local market in Konya governorate, Turkey. Different concentration solutions of green tea (5-10-20 gram) were excreted by boiling each solution in one liter of distilled water. After cooling, the solutions were passed through a piece of gauze and then supplied to rats in their sole wellspring of drinking water^{9,10,11}.

Animals: Twenty-four healthy adult male (15 week age) of Sprague Dawley albino rats of (250-300 g) weight were housed in the polypropylene cages, 12/12 light/dark, at 23-25 °C at College of Veterinary, University of Kirkuk. They were provided with standard rats diet. After seven days, the rats were classified into 4 groups as follows:

Group 1: Provided with normal distilled water for one month (control, n=6).

Group 2: Provided with a prepared solution of 5g green tea/1L of distilled water for one month (GTE5, n=6).

Group 3: Provided with a prepared solution of 10g green tea/1L of distilled water for one month (GTE10, n=6).

Group 4: Provided with a prepared solution of 20g green tea/1L of distilled water for one month (GTE5, n=6).

Collection of blood samples: After completing the experiment, under ether anesthesia, the blood samples were taken legitimately from the heart by utilizing 5 cc syringes with two types of blood collection tube:-

1. EDTA for hematological analysis.
2. Non-coagulant tube for liver enzymes and some biochemical analysis.

The samples were centrifuged at 5000 rpm for 15 minutes, and the serum was collected and kept freezing at -20°C for evaluating the liver enzymes, hematological and some biochemical parameters.

Liver Enzymes parameters: The parameters Aspartate amino-transferase (AST), Alanine amino-transferase (ALT) and alkaline-phosphatase (ALK) were estimated using reagent kits manufacturer’s instructions, which were purchased from RanDox (United Kingdom).

Hematological parameters: Total Erythrocyte Count (RBC), Hemoglobin HB, Hematocrit (HTC), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), Total leukocyte count (WBC) and platelets were estimated using Animal blood counter -ABC vet device (Horiba ABX- France).

Biochemical parameters: Glucose was estimated using reagent kits manufacturer’s instructions, which were purchased from Ran Dox (United Kingdom). Albumin, globulin, and total protein were measured using reagent kits manufacturer’s instructions, which were purchased from biochemical Biolab (USA).

Data Analysis: Statistical analysis was done using a PC program, (SPSS, 23) and one-way (ANOVA) for each parameter.

Results

Impacts of green tea extracts on liver enzymes: As listed in Table 1, the control group presented a considerable increase (p <0.05) in AST, ALT and ALK (p <0.05) in comparison to other groups (GTE5, GTE10 and GTE20).

Table 1: Comparative evolution of liver enzyme between control, green tea 5% (GTE5), green tea 10% (GTE10) and green tea 20% (GTE20) groups.

Parameters	Groups			
	Control (n=6)	GTE5 (n=6)	GTE10 (n=6)	GTE20 (n=6)
ALT	41.00±1.63 ^a	40.75±1.25 ^b	39.75±3.30 ^b	38.00±0.81 ^b
AST	43.50±2.08 ^a	39.75±2.06 ^b	39.50±2.16 ^b	39.00±2.16 ^b
ALK	383.75±189.82 ^a	381.00±32.88 ^b	380.75±21.74 ^b	381.25±16.35 ^b

a and b: indicate the significant difference among the groups in the same parameter (p <0.05).

Effects of green tea on hematological parameters: Based on results shown in Table 2, although there is a variation among groups in the RBC count, MCHC and platelet, there was no statistically significant variation among them. The control group has a significant increase

(p <0.05) in the level of HB, HTC, MCV and MCH in comparison to the GTE5, GTE10, and GTE20 groups. On the other hand, Control, GTE5, and GTE10 groups have WBC level lower than that of GTE20.

Table 2: Comparative evolution of hematological parameters between control, green tea 5% (GTE5), green tea 10% (GTE10) and green tea 20% (GTE20) groups.

Parameters	Groups			
	Control (n=6)	GTE5 (n=6)	GTE10 (n=6)	GTE20 (n=6)
RBC	6.79±0.46 ^a	6.49±0.64 ^a	6.16±0.29 ^a	6.09±0.31 ^a
HB	14.52±0.66 ^a	13.00±1.44 ^b	13.26±0.65 ^b	13.27±0.60 ^b

Parameters	Groups			
	Control (n=6)	GTE5 (n=6)	GTE10 (n=6)	GTE20 (n=6)
HTC	38.82±1.38 ^a	34.80±3.11 ^b	35.27±1.18 ^b	34.82±1.43 ^b
MCV	57.27±2.00 ^a	52.87±0.46 ^b	53.42±0.68 ^b	52.80±0.58 ^b
MCH	22.40±0.50 ^a	20.03±0.26 ^b	20.82±0.05 ^b	20.12±0.25 ^b
MCHC	37.42±0.45 ^a	37.82±0.77 ^a	37.52±0.54 ^a	38.00±0.16 ^a
WBC	8.95±1.09 ^b	9.03±3.43 ^b	8.90±2.57 ^b	14.76±1.60 ^a
Platelets	801.50±72.13 ^a	801.00±213.49 ^a	802.00±25.13 ^a	802.34±128.90 ^a

a and b: indicate the significant difference among the groups in the same parameter (p <0.05).

Impacts of green tea extracts on some blood biochemical parameters: As presented in Table 3, control and GTE5 groups demonstrated a highly significant decrease (p <0.05) in glucose level in comparison to GTE10 and GTE20 groups. Furthermore, control and GTE5 groups showed a significant decrease (p <0.05) in albumin and globulin as compared to GTE10

and GTE20 groups. Moreover, GTE20 group showed a significant increase (p <0.05) in total protein level as compared with control, GTE5 and GTE10 groups. On the other hand, a significant decrease (p <0.05) was revealed in the the control group as compared to other groups (GTE5, GTE10 and GTE20). There was no significant variation between GTE5 and GTE10 groups.

Table 3: Comparative evolution of Some biochemical blood parameter between control, green tea 5% (GTE5), green tea 10% (GTE10) & green tea 20% (GTE20) groups.

Parameters	Groups			
	Control (n=6)	GTE5 (n=6)	GTE10 (n=6)	GTE20 (n=6)
Glucose	146.00±14.14 ^b	146.25±8.57 ^b	148.95±4.50 ^a	149.50±7.59 ^a
Albumen	33.05±0.61 ^b	33.50±0.53 ^b	35.10±3.20 ^a	34.95±0.40 ^a
Globulin	40.87±2.46 ^b	44.87±1.56 ^a	43.13±9.84 ^a	43.24±1.74 ^a
Total protein	70.90±2.06 ^c	78.27±1.37 ^b	77.92±6.83 ^b	85.82±1.34 ^a

a and b: indicate the significant difference among the groups in the same parameter (p <0.05).

Discussion

Green tea refers to a kind of tea made from buds and leaves of *C. Sinensis*. It has not gone through the same process of oxidation employed in making other types of tea like oolong and black. Green tea has emerged in China. Its generation and assembling have extended to various nations in Asia. Though there are significant studies on the conceivable health impacts of consuming green tea normally, only a few numbers of them have proved that drinking green tea has no effects on health¹¹.

Epidemiological and research center examinations have announced that green tea presents assorted valuable wellbeing impacts including hematological, biochemical parameters and liver enzymes¹², anti-hyperglycemic, hepatoprotective¹³.

The significant increase of liver enzyme function observed in the present study is quite similar to that reported by^{13,14,15}. This is possibly attributed partially to that the antioxidant components of green tea could decrease the oxidative stress in liver cells. The free radicals are known to cause damage to the liver cell structures and their organelles which lead to release these enzymes from cytoplasm and mitochondria of the hepatocytes to the blood¹⁵.

The evidence presented in this paper concerning the relative absence of significant changes in RBC count, MCHC and platelets suggests that the polyphenols may interfere with absorption of both heme and nonheme by these cells although polyphenol is considered as one of the most important constituents of green tea^{16,17}. These results are parallel to those reported by^{12,18,19}. The

significant decrease in hematological parameters (HTC, HB, MCH and MCV) and low variation in white blood cell counts are related well with reports of^{20,21,22,23}.

The free radicals could act on oxidation of the unsaturated fatty acid to produce malondialdehyde, which causes liver toxicity. Green tea, on the other hand, contains catechins compounds which may prevent the growth of bacteria and certain kinds of viruses in the body²⁴. The high significant decrease in glucose level among groups is in agreement with results of^{13,25,26}. This result could explain the ability of catechins to repress some digestive enzymes, for example, intestinal-sucrase, salivary-amylase and α -glucosidase, which may lead to lowering the level of blood glucoses. Other authors reported that some chemical substance of green tea, such as epigallocatechin gallate, increase the regeneration of pancreatic β -cells. This, in turn, inhibits the gluconeogenesis by inhibition of phosphoenolpyruvate-kinase^{27,28}.

Also, effects on albumin, globulin and total protein are in agreement with previous reports^{25,29}. The hyperalbuminemia and hypoalbuminemia depend on the toxicity level in the body. Hypoalbuminemia is observed to be brought about by a few factors, for example, decreased combination brought about by liver infections, expanded catabolism because of aggravation or tissue harm^{30,31}.

Conclusion

This article demonstrated that the administration of drinking green tea to the rats for a long period might result in protecting cell ingredients, such as proteins and lipids, decreasing and inhibiting the effect of free oxygen radicals in the liver. Additionally, the administration may also show the useful impact of green tea on common blood cells and plasma compounds.

Conflict of Interest: None of the authors has any conflicts of interest to declare.

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Ethical Clearance: The project was approved by the local ethical committee (College of Veterinary, University of Kirkuk, Kirkuk, Iraq)

References

1. Shohsin OMA, Kececi T. The Effects of Nigella sativa on some Antioxidant System Parameters at Experimental Broiler Chicken Exposed to Acute Heat Stress Master thesis. Selcuk University Institute of Health Sciences.2015.
2. Khan N, Afaq F, Mukhtar H. Cancer chemoprevention through dietary antioxidants: progress and promise. *Antioxid Redox Signal*, 2008. 10: 475–510.
3. Khan N, Mukhtar H. Tea and health: studies in humans. *Current Pharmaceutical Design (Literature Review)*, 2013.19 (34): 6141–7.
4. Stangl V, Lorenz M, Stangl K. The role of tea and tea flavonoids in cardiovascular health. *Mol, Nutr Food Res*, 2006.50: 218–28.
5. Feng WY. Metabolism of green tea catechins: an overview. *Curr Drug Metab*, 2006.7:755–809.
6. Vaidyanathan JB, Walle T. Glucuronidation and sulfation of the tea flavonoid (–)-epicatechin by the human and rat enzymes. *Drug Metab Dispos*, 2002.30: 897–903.
7. Henning SM, Choo JJ, Heber D. Nongallated compared with gallated flavan-3-ols in green and black tea are more bioavailable. *J Nutr*, 2008.138:1529S–34S.
8. Yang B, Arai K, Kusu F. Determination of catechins in human urine subsequent to tea ingestion by high-performance liquid chromatography with electrochemical detection. *Anal Biochem*, 2000.283: 77–82.
9. Abolfathi AA, Mohajeri D, Rezaie A, Nazeri M. Protective Effects of Green Tea Extract against Hepatic Tissue Injury in Streptozotocin-Induced Diabetic Rats. Hindawi Publishing Corporation Evidence-Based Complementary and Alternative Medicine. Article ID 2012.740671, 10 pages.
10. Gad SB, Zaghoul DM. Beneficial effects of green tea extract on liver and kidney functions, ultrastructure, lipid profile and hematological parameters in aged male rats. *Global Veterinaria*, 2013. 11(2): 191-205.
11. Ahmida MH, Abuzogaya MH. The effects of oral administration of green tea and ginger extracts on serum and hepatic lipid content in rats fed a hyperlipidemic diet. *Journal article : Der Pharmacia Lettre*, 2009. 1(1): 56-64 ref.24.

12. Elsayed ASI, Hegazi MA. Ameliorative effects of curcumin and green tea against gasoline- inhalation hematotoxicity. *International Journal of Applied Biology and Pharmaceutical Technology*, 2016. 7(1): 1-18.
13. Bakr EH, Header EA. Effect of aqueous extract of green tea (*Camellia sinensis*) on obesity and liver status in experimental rats. *Int. J. Pure Appl. Sci. Technol.*, 2014. 21(2): 53-63.
14. Hasanein AM, Gawad HAS, El-Megeid AAA. Effect of water extract prepared from green tea, black tea and cinnamon on obese rats suffering from diabetes. *World Applied Sciences Journal*, 2012;20(7): 976-987.
15. Hussein AM. Effect of green tea aqueous extract on body weight and biochemical parameters of male mice, *Journal of Missan Researches*, 2011: 14(7): 26-28.
16. Kim EY, Ham SK, Shigenaga MK, Han O. Bioactive dietary polyphenolic compounds reduce nonheme iron transport across human intestinal cell monolayers. *J. Nutr.*, 2008.138: 1647–1651.
17. Zijp IM, Korver O, Tijburg LB. Effect of tea and other dietary factors on iron absorption. *Crit. Rev. Food Sci. Nutr.*, 2000.40: 371–398.
18. Al-Shawi NN. Impacts of different concentrations of aqueous green tea extract administered during methotrexate treatment on some selected blood indices in rats. *Int. J. Pharm Sci*, 2014. 6(9): 175-178.
19. El-Kott AF, Bin-Meferiji MM. Influence of green tea haematological and lung histological disorders induced by malathion in rats. *Research Journal of Environmental Toxicology*, 2008.2(2): 85-91.
20. RadwanAO, Zayed AA, Mikhail ZA. Effect of green tea (*Camellia sinensis* L.) aqueous extract and L-carnitine supplements on some hormonal levels and some haematological parameters in obese male rats. *Bioscience Research*, 2019.16(2): 1126-1131.
21. Elkirdasy A, Shousha S, Alrohaimi AH, Arshad MF. Hematological and immunobiochemical study of green tea and ginger extracts in experimentally induced diabetic rabbits. *Acta Poloniae Pharmaceutica-Drug Research*, 2015. 72(3): 497-506.
22. SinghN, Rani P, Gupta M, Tandan N. Role of green tea on cadmium toxicity on haematological profile of albino rats. *American Journal of Phytomedicine and Clinical Therapeutics*, 2013.5: 537-542.
23. Zapora E, Holub M, WaszkiewiczE, Dabrowska M, Skrzydlewska E. Green tea effect on antioxidant status of erythrocytes and on haematological parameters in rats. *Bull Vet Inst Pulawy*, 2009.53: 139-145.
24. Ma Q, Kim EY, Lindsay EA, Han O. Bioactive dietary polyphenols inhibit heme iron absorption in a dose-dependent manner in human intestinal Caco-2 cells. *J. Food Sci.*, 2011.76: H143–H150.
25. Al-Samarrae WH, Alobeidi YA. Effect of the Addition of Green Tea to the Awassi Lambs Rations on Some Blood Standards. *Plant Archives*, 2019.19: 1288-1290.
26. Suzuki T, Takagi A, Takahashi M. Catechin-rich green tea extract increases serum cholesterol levels in normal diet- and high fat diet-fed rats, *BMC Proc*, 2012.6(13): 47.
27. Chemler JA, Lock LT, Koffas MA. Standardized biosynthesis of flavan-3-ols with effects on pancreatic b-cell insulin secretion, *Appl. Microbiol. Biotechnol*, 2007. 77: 797-807.
28. Aazami MH, Tahmasbi AM, Ghaffari MH, Naserian AA, Valizadeh R, Ghaffari AH. Effects of saponins on rumen fermentation, nutrients digestibility, performance, and plasma metabolites in sheep and goat kids. *Annual Rev Res Biol*, 2013:3(4): 596-607.
29. Wolfram S, Wang Y, Thielecke F. Anti-obesity effects of green tea, *Molecular Nutrition & Food Research*, 2006. 50(2): 176-187.
30. Bede EN. Effects of regular intake of green tea on nutrient absorption serum albumin and organ sizes of alloxan- induced diabetic rats. *International Journal of Nutrition and Food Sciences*, 2015.4(5): 535-540.
31. Nicholson JP, Wolmarans MR, Park GR. The role of albumin in critical illness. *British Journal of Anaesthesia*, 2000.85: 599–610.

Clinical and Radiographic Evaluation of WaveOne Gold Single-File System in Pulpectomy of Primary Molars: A Randomized Clinical Trial

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Abstract

Purpose: The current study evaluates the reciprocal WaveOne Gold single-file system regarding clinical and radiographic outcomes in root canal treatment of primary molars.

Method: This randomized clinical trial was carried out on 70 primary molars on 60 children in the age group from 4 to 7 years. The teeth selected for this study were randomly assigned into 2 groups according to the used endodontic preparation system. Group I: 35 primary molars were instrumented with WaveOne Gold reciprocating single-file system. Group II: 35 primary molars were instrumented with stainless steel K-files. All teeth were evaluated clinically and radiographically for 12 months with periodic recall at 3, 6 and 12 months.

Results: WaveOne Gold single-file system exhibited higher overall success rate over manual instrumentation, however, the difference between groups was not statistically significant ($P > 0.05$).

Conclusion: Single-file systems are promising instruments that have the power to be an alternative for manual instrumentation in primary molar pulpectomies.

Keywords: WaveOne Gold, Single-file endodontics, Pulpectomy, Pediatric dentistry

Introduction

One of the fundamental objectives of pediatric dentistry is conservation of primary teeth in form and function until their normal exfoliation. Premature loss of primary teeth with irreversible pulp pathosis has the potential to destabilize the developing occlusion with space loss, arch collapse, and premature, delayed or ectopic eruption of the permanent successors.⁽¹⁾

When advanced pulpal degeneration affects a primary tooth, two possible treatment options are

available: pulpectomy or extraction. However, the success of pulpectomies in primary teeth has led to a shift in the paradigm of treating pulpally involved teeth.⁽²⁻⁵⁾

Negotiation and thorough instrumentation of bizarre and tortuous canals encased in roots programed for physiological resorption are the main challenges for pulpectomy.⁽⁶⁾

A practical endodontic treatment for primary teeth should provide short treatment time, effective debridement, and minimal complications. Since most hand preparation techniques are time consuming, and may lead to iatrogenic errors, much attention has been directed toward the use of rotary instrumentation in primary teeth.^(7,8)

In the bygone decade, all rotary systems were based on the use of a series of files to complete shaping of root canals. Recently, the concept of single-file system has been introduced. This concept requires a minimum

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or no glide path, reduces the working time, prevents cross-contamination, and improves safety of the shaping procedures.⁽⁹⁾

Aim of the study: To the utmost of our knowledge, there are no published RCTs about the clinical and radiographic success of primary tooth pulpectomy using the reciprocal single file system; WaveOne Gold (Dentsply Maillefer, Ballaigues, Switzerland). Therefore, the current study was conducted to validate this novel single-file system.

Method

This investigation was a double-blind randomized controlled clinical trial which was designed, analyzed & interpreted according to the Consolidated Standards of Reporting Trials (CONSORT) statement.⁽¹⁰⁾ The sample size was calculated to be 70 teeth (35 teeth for each group) with a power of 80% and type I error of 5% based on a pilot study conducted for 6 months.

Settings and study subjects: The study was conducted on patients who attended outpatient clinic of Pediatric Dentistry Department, Faculty of Dentistry, Minia University. Out of 105 children, 60 patients with 70 necrotic primary second molars indicated for pulpectomy, were enrolled in the study. Their age ranged from 4 to 7 years old.

Inclusion criteria⁽¹¹⁾:

- **Clinical:** History of dull toothache over an extended period of time, history of spontaneous pain or pain at night, swelling adjacent to tooth with or without a sinus tract, abnormal tooth mobility, presence of necrotic pulp tissue or purulent discharge when the pulp chamber was accessed.
- **Radiographic:** Interruption of lamina dura or thickening of PDL space and/or presence of furcation or periapical radiolucency.

Exclusion criteria⁽¹²⁾:

- **Clinical:** Systemic diseases that adversely affect or contraindicate pulp therapy, teeth with non-restorable crowns, tooth with a mechanical or carious perforation of the pulpal floor.
- **Radiographic:** Root canal obliteration, internal or external root resorption, peri-radicular lesion involving the crypt of the developing permanent successor, or presence of underlying dentigerous or follicular cysts.

Randomization and allocation: The selected mandibular second primary molars were randomly assigned to one of two treatment groups by block randomization method using a computer generated sequence. The allocation was done using serially numbered opaque and concealed envelopes opened just after access preparation (allocation ratio was 1:1). The participants and outcome assessor were blinded about the instrumentation technique used.

Clinical procedures: All procedures were performed by the same operator in a standardized treatment protocol regarding: Topical & local anesthesia, isolation using rubber dam and saliva ejector, removal of caries, access preparation & removal of pulp remnants and radiographic working length determination which was maintained at 2 mm short of the root apex.

Then, patients were randomly assigned to one of the study groups.

- **Group I** comprised 35 molars treated with Primary WaveOne Gold (Dentsply Maillefer, Ballaigues, Switzerland) single reciprocating file system in a slow brushing motion according to the manufacturer's instructions.
- **Group II** consisted of 35 molars instrumented with stainless steel K-files (MANI Inc., Tochigi, Japan) with 2% taper in a sequential manner up to size 30 using a quarter-turn-pull technique.

During canal preparation in all groups, EDTA gel 17%, cautious irrigation with 10 ml of 1% NaOCl using side vented needles, a final flush with 5 ml of saline were carried out. Then canal dryness using sterile paper points and Metapex (Meta Biomed Co. Ltd. Chungbuk, Korea) obturation using pressure syringe technique were performed. After root canal obturation, radiographs were taken to determine whether the root canals were completely filled. If not, they were refilled. Finally, all teeth were restored with stainless steel crowns.

Evaluation: All teeth received independent clinical and radiographic evaluations at 3, 6 and 12 months postoperatively by another investigator who was blinded to the instrumentation technique used in each tooth.

Outcome assessment criteria⁽¹³⁾: The pulpectomy treatment was judged as successful if there was none of the following clinical or radiographic criteria:(1) Absence of pain, tenderness to palpation or percussion and abnormal mobility. (2) Presence of healthy soft

tissue (defined as the absence of swelling, redness, sinus tract, or purulent exudate expressed from the gingival margin. (3) Absence of pathological root resorption. (4) Arrest or reduction of bone rarefaction up to 6-12 mm postoperatively. (5) Absence of new periapical or furcational radiolucency postoperatively.

Statistical analysis: Statistical analysis was performed using IBM SPSS, version 23 (SPSS Inc., Chicago, IL, USA). Categorical data was displayed as number and percent and analyzed statistically using Chi-

squared test where indicated. Probability of less than 0.05 was used as a cut off point for all significant tests.

Results

Seventy necrotic second primary molars in children aged between 4 and 7 years were randomly selected and provided with treatment in this clinical trial. All patients were followed up, with no dropouts, at the 3, 6 and 12 month recall visits. The baseline demographic, clinical and radiographic observations of the selected patients are presented in Table 1.

Table 1: Baseline demographic, clinical and radiographic characteristics of study groups.

Group	Age (Years) Mean±(SD)	Gender		Clinical Signs or Symptoms		Peri-radicular Radiolucency	
		Male N(%)	Female N(%)	Present N(%)	Absent N(%)	Present N(%)	Absent N(%)
WaveOne Gold	5.0±0.55	16(45.7)	19(54.3)	26(74.3)	9(25.7)	21(60)	14(40)
K-File	4.9±0.63	15(42.9)	20(57.1)	25(71.4)	10(28.6)	19(54.3)	16(45.7)
p-value*	0.735	0.969		1.000		1.000	

* p>0.05 indicates no significant difference.

The clinical, radiographic and overall success rates of the 2 groups at 3, 6 and 12 months are presented in Table 2. The overall success rates were 85.7% and 80% for WaveOne Gold and K-file groups, respectively, at 12 months.

Although WaveOne Gold group exhibited higher overall success rate, the intergroup comparison didn't

reveal any statistically significant difference at 3, 6, or 12 months (p> 0.05).

Taking into consideration different factors that might have affected the treatment results, the overall success was influenced by presence of preoperative clinical signs & symptoms and pre-operative radiolucency, especially in the k-file group, but without any statistical significance (Table 3).

Table 2: Clinical and radiographic outcomes of the studied groups through the follow up period.

Follow up	Outcome	WaveOne Gold (G I)		K-file (G II)		(p- value)*
		Success N (%)	Failure N (%)	Success N (%)	Failure N (%)	
3 months	Clinical	35(100)	0(0.0)	35(100)	0(0.0)	p: 1.000
	Radiographic	34(97.1)	1(2.9)	34(97.1)	1(2.9)	
	Overall	34(97.1)	1(2.9)	34(97.1)	1(2.9)	
6 months	Clinical	33(94.3)	2(5.7)	33(94.3)	2(5.7)	p: 0.698
	Radiographic	32(91.4)	3(8.6)	31(88.6)	4(11.4)	
	Overall	32(91.4)	3(8.6)	31(88.6)	4(11.4)	
12 months	Clinical	32(91.4)	3(8.6)	31(88.6)	4(11.4)	p: 0.530
	Radiographic	30(85.7)	5(14.3)	28(80)	7(20)	
	Overall	30(85.7)	5(14.3)	28(80)	7(20)	

*p>0.05 indicates no significant difference.

Table 3: Effect of preoperative clinical and radiographic characteristics on overall pulpectomy outcome after 12 months.

Variable		WaveOne Gold			K-File		
		Success N= 30	Failure N= 5	Total N= 35	Success N= 28	Failure N= 7	Total N= 35
Clinical signs / symptoms	Present	22(84.6%)	4	26	19(76%)	6	25
	Absent	8(88.9%)	1	9	9(90%)	1	10
<i>P</i> value*		0.431			0.356		
Peri-radicular radiolucency	Present	17(80.9%)	4	21	14(73.7%)	5	19
	Absent	13(92.6%)	1	14	14(87.5%)	2	16
<i>P</i> value*		0.341			0.316		

* $p > 0.05$ indicates no significant difference.

Discussion

Biomechanical preparation is one of the most important phases of pulpectomy in primary teeth which is mainly aimed at debridement of the canals.⁽¹²⁾ Conventionally, root canal preparation was done with endodontic broaches and hand files. However, the current literature reflects a trend towards the use of nickel-titanium (NiTi) automated file systems in pediatric endodontics.⁽¹⁴⁻¹⁷⁾

The concept of single-file system was recently introduced in endodontics, and its applicability in contemporary endodontic treatment in primary teeth has now been debated.⁽¹⁸⁻²⁰⁾ Thus, the current study was conducted to compare a reciprocal single-filesystem, WaveOne Gold, with manual K-file regarding clinical and radiographic outcomes of endodontically treated primary molars.

WaveOne Gold (Dentsply Maillefer, Ballaigues, Switzerland) is one of the reciprocal single-file systems which is available in four different sizes (small, primary, medium and large) in lengths of 21mm, 25mm, and 31mm. These variabilities allow the clinician to prepare a wide range of apical diameters and root canal anatomies.⁽⁹⁾

Furthermore, this system is supplied in sterilized packs for single use only which increase safety margin and reduce risk of cross-contamination. With all these facts considered, WaveOne Gold single file system was selected for our study.

To eliminate discrepancies, all clinical procedures were performed by the same operator. Endodontic instrumentation, root canal filling and placement of

stainless steel crown were performed in one visit for all patients to avoid contamination from the loss of temporary restorations.^(11,21)

The overall pulpectomy success rates, for WaveOne Gold and K-file groups, observed in our investigation were similar to previous studies.^(11,21-23) This proves the validity of the used methodology. WaveOne Gold group exhibited higher overall success rates, which may be attributed to the file design providing more efficient cleaning.

The overall success rate for root canals prepared with K-files was 80% by the end of the 12 month follow up period. This result came in conformity with those obtained by Mani et al.⁽²²⁾, Barr et al.⁽²⁴⁾ and Barcelos et al.⁽²⁵⁾ who revealed overall success rates of 83.3%, 79.5% and 82.3% respectively.

To the best of our knowledge, this is the first randomized controlled clinical trial to report the application of WaveOne Gold single-file system in endodontic treatment of primary molars. Therefore, there is nothing similar in the literature with which to compare the present results. Thus, the overall outcome was compared with that observed in earlier studies using other engine-driven nickel–titanium instruments.

The 12 month overall success rate obtained for WaveOne Gold, 85.7%, was comparable to those of Kuo et al.⁽²⁶⁾, Guler et al.⁽²⁷⁾ and Vieyra and Enriquez⁽²⁸⁾. Moreover, the overall success was influenced by presence of preoperative clinical signs or symptoms and radiographic radiolucency especially in the K-file group but without any statistical significance. This finding goes in accordance with earlier studies of Coll and Sadrian⁽²⁾, Moskovitz et al.⁽³⁾ and Barcelos et al.⁽²⁵⁾

This finding might confirm that necrotic pulps are more difficult to treat^(3,25) as well as superiority of reciprocal single file systems over manual instrumentation in cleaning and shaping of primary teeth.

Conclusions

WaveOne Gold single-file system demonstrated favorable clinical and radiographic outcomes in pulpectomy of human primary molar teeth over a 12-month follow up period. Additionally, WaveOne Gold was superior to manual stainless steel K-files, regarding treatment of necrotic primary teeth with preoperative clinical signs & symptoms, or peri-radicular radiolucency.

Financial Support: Nil.

Conflicts of Interest: There are no conflicts of interest.

Ethical Clearance: The study was reviewed and approved by Research Ethics Committee, Faculty of Dentistry, Minia University, Egypt (approval number: 42/183/11/2016), in accordance with Helsinki Declaration of 1975, as revised in 2000.

All patients who fulfilled the eligibility criteria, their legal guardian was asked to sign an informed consent after receiving a complete explanation about the objectives of the study, clinical procedures, treatment outcomes and possible complications.

References

1. Zou J, Meng M, Law CS, Rao Y, Zhou X. Common dental diseases in children and malocclusion. *Int J Oral Sci.* 2018;10(1):1-7.
2. Coll JA, Sadrian R. Predicting pulpectomy success and its relationship to exfoliation and succedaneous dentition. *Pediatr Dent.* 1996;18(1):57-63.
3. Moskovitz M, Sammara E, Holan G. Success rate of root canal treatment in primary molars. *J Dent.* 2005;33(1):41-7.
4. Rodd HD, Waterhouse PJ, Fuks AB, Fayle SA, Moffat MA; British Society of Paediatric Dentistry. Pulp therapy for primary molars. *Int J Paediatr Dent.* 2006;16 (Suppl. 1):15-23.
5. Tannure PN, Azevedo CP, Barcelos R, Gleiser R, Primo LG. Long-term outcomes of primary tooth pulpectomy with and without smear layer removal: a randomized split-mouth clinical trial. *Pediatr Dent.* 2011;33(4):316-20.
6. Ahmed HM. Anatomical challenges, electronic working length determination and current developments in root canal preparation of primary molar teeth. *Int Endod J.* 2013;46(11):1011-22.
7. Ahmed HM. Pulpectomy procedures in primary molar teeth. *Eur J Gen Dent.* 2014;3(1):3-10.
8. George S, Anandaraj S, Issac JS, John SA, Harris A. Rotary endodontics in primary teeth - A review. *Saudi Dent J.* 2016;28(1):12-7.
9. Gavini G, Santos MD, Caldeira CL, Machado MEL, Freire LG, Iglecias EF, Peters OA, Candeiro GTM. Nickel-titanium instruments in endodontics: a concise review of the state of the art. *Braz Oral Res.* 2018;32(suppl.1)44:65.
10. Schulz KF, Altman DG, Moher D; CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMJ.* 2010;340:e332.
11. Trairatvorakul C, Chunlasikaiwan S. Success of pulpectomy with zinc oxide-eugenol vs calcium hydroxide/iodoform paste in primary molars: a clinical study. *Pediatr Dent.* 2008;30(4):303-8.
12. Moskovitz M, Tickotsky N. Pulpectomy and Root Canal Treatment (RCT) in Primary Teeth: Techniques and Materials. In Fuks AB, Peretz B, editors. *Pediatric Endodontics: Current Concepts in Pulp Therapy for Primary and Young Permanent Teeth.* 1st ed. Switzerland: Springer International Publishing; 2016.p.71-101.
13. American Academy of Pediatric Dentistry, Clinical Affairs Committee and Pulp Therapy Subcommittee. Guideline on pulp therapy for primary and immature permanent teeth. *Pediatr Dent.* 2017;39(6): 325-33.
14. Barr ES, Kleier DJ, Barr NV. Use of nickel-titanium rotary files for root canal preparation in primary teeth. *Pediatr Dent.* 2000;22(1):77-8.
15. Crespo S, Cortes O, Garcia C, Perez L. Comparison between rotary and manual instrumentation in primary teeth. *J Clin Pediatr Dent.* 2008;32(4):295-8.
16. Ochoa-Romero T, Mendez-Gonzalez V, Flores-Reyes H, Pozos-Guillen AJ. Comparison between rotary and manual techniques on duration of instrumentation and obturation times in primary teeth. *J Clin Pediatr Dent.* 2011;35(4):359-63.

17. Morankar R, Goyal A, Gauba K, Kapur A, Bhatia SK. Manual versus rotary instrumentation for primary molar pulpectomies- A 24 months randomized clinical trial. *Ped Dent J.* 2018; 28(2):96-102.
18. Prabhakar AR, Yavagal C, Dixit K, Naik SV. Reciprocating vs Rotary Instrumentation in Pediatric Endodontics: Cone Beam Computed Tomographic Analysis of Deciduous Root Canals using Two Single-file Systems. *Int J Clin Pediatr Dent.* 2016;9(1):45-9.
19. Jeevanandan G, Govindaraju L. Clinical comparison of Kedo-S paediatric rotary files vs manual instrumentation for root canal preparation in primary molars: a double blinded randomised clinical trial. *Eur Arch Paediatr Dent.* 2018;19(4):273-8.
20. Moraes RDR, Santos TMPD, Marceliano-Alves MF, Pintor AVB, Lopes RT, Primo LG, Neves AA. Reciprocating instrumentation in a maxillary primary central incisor: A protocol tested in a 3D printed prototype. *Int J Paediatr Dent.* 2019;29(1):50-7.
21. Pramila R, Muthu MS, Deepa G, Farzan JM, Rodrigues SJ. Pulpectomies in primary mandibular molars: a comparison of outcomes using three root filling materials. *Int Endod J.* 2016;49(5):413-21.
22. Mani SA, Chawla HS, Tewari A, Goyal A. Evaluation of calcium hydroxide and zinc oxide eugenol as root canal filling materials in primary teeth. *ASDC J Dent Child.* 2000;67(2):142-7.
23. Cassol DV, Duarte ML, Pintor AVB, Barcelos R, Primo LG. Iodoform Vs Calcium Hydroxide/ Zinc Oxide based pastes: 12-month findings of a Randomized Controlled Trial. *Braz Oral Res.* 2019;33:e002.
24. Barr ES, Flatiz CM, Hicks MJ. A retrospective radiographic evaluation of primary molar pulpectomies. *Pediatr Dent.* 1991;13(1):4-9.
25. Barcelos R, Tannure PN, Gleiser R, Luiz RR, Primo LG. The influence of smear layer removal on primary tooth pulpectomy outcome: a 24-month, double-blind, randomized, and controlled clinical trial evaluation. *Int J Paediatr Dent.* 2012;22(5):369-81.
26. Kuo C, Wang Y, Chang H, Huang G, Lin C, Li U, et al. Application of Ni-Ti rotary files for pulpectomy in primary molars. *J Dent Sci.* 2006;1(1):10-15.
27. Guler C, Gurbuz T, Yilmaz Y. The clinical success of different root canal treatments in primary molars. *Cumhuriyet Dent J.* 2013;16(1):31-39
28. Vieyra JP, Enriquez FJ. Instrumentation time efficiency of rotary and hand instrumentation performed on vital and necrotic human primary teeth: A Randomized Clinical Trial. *Dentistry.* 2014;4(4):1-5.

Intrapartum Translabial Ultrasound to Predict Successful Vaginal Birth in Ladies with Previous Caesarean Section

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Abstract

Objective: To evaluate the role of intrapartum translabial ultrasound to predict successful vaginal birth in ladies with previous caesarean section.

Patients and Method: 200 pregnant women with previous caesarean section admitted during the active phase of the first stage of labor.

Results: At a cut-off value 2.5mm the sensitivity of the progression distance was 89.3% and 71.4% specificity in prediction of vaginal delivery. Using 100.5 degree as a cut-off value for the angle of progression to identify patients who deliver vaginally gives 88.5% sensitivity and 74.3% specificity.

Conclusion: Intrapartum translabial ultrasound is a useful tool to predict occurrence of vaginal delivery in women with previous caesarean.

Keywords: VBAC, intrapartum ultrasound, translabial ultrasound, progression distance, angle of progression.

Introduction

Witnessing a dramatically increasing rates of CS deliveries mainly due to the practice of defensive medicine⁽¹⁾, repeat CS is central to that practice.

Although being the 'gold standard' in obstetric practice, the digital transvaginal examination is a subjective evaluation and has several limitations⁽²⁾.

A growing body of knowledge is accumulating regarding intrapartum ultrasound as a relatively new application of ultrasound. Intrapartum ultrasonography can provide objective information on the dynamics of different stages of labor⁽³⁾, and may also be used to

assess labor progression, predict labor outcome and to predict the prognosis for operative vaginal delivery⁽⁴⁾.

Translabial ultrasound was used to demonstrate pelvic floor structures, it was shown to be fast, safe, reliable, easy to learn and readily available tool⁽⁵⁾.

Aim of the work: To assess the ability of intrapartum translabial ultrasound to objectively predict the progress of labor and the occurrence of successful vaginal birth in ladies with previous CS attempting for VBAC at term pregnancy.

Patients and Method

This study included 200 pregnant women, All with previous CS. The same operator performed all ultrasound studies, The managing obstetricians were blinded to the ultrasound results.

Inclusion criteria: Full term(37:41weeks) singleton pregnancy, and Spontaneous onset of the active phase of 1st stage of labor as evidenced by regular uterine contractions and dilatation of the internal cervical OS ≥ 4 cm.

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Exclusion criteria: Abnormal fetal presentations, congenital fetal malformations, abnormalities of the amniotic fluid or placenta, maternal spine or pelvic disease or fractures, and complicated pregnancies.

Full history and complete clinical examination were undertaken for all participants.

This approach was to reveal anatomical structures in the ‘infrapubic plane’: The symphysis pubis, the lowermost parts of fetal skull, and the dorsal part of the birth canal. For standardization the transducer was placed so that the symphysis will be in a horizontal position. In this plane, the progression distance was measured. Described as the minimal distance [c] (in mm) from a line [b] placed vertical to the central axis of the symphysis pubis [a], placed through the infero-posterior symphyseal margin, and the leading edge of the fetal skull. (fig. 1 a)

In the same plane, the angle of progression of the fetal head was measured, described as the angle[b] between a line through the midline of the pubic symphysis [a] and a line from the inferior apex of the symphysis to the leading part of the fetal skull [c] (fig.1 b).

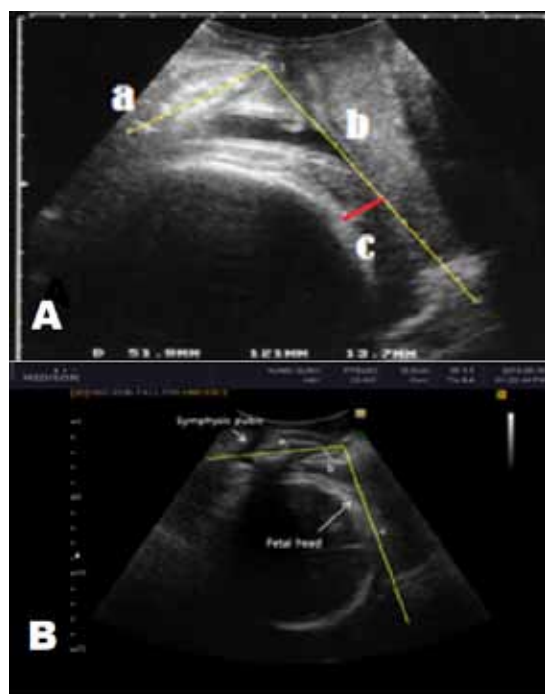


Fig. 1A: Head progression distance⁽⁶⁾, B: Angle of progression of fetal head⁽³⁾

Results

Mean patient age was 28.2 ± 4.5. Gravity was ranging from 2:4. The mean gestational age was 38.2 ±

0.8 weeks. By PV digital examination, the mean cervical dilatation was 4.56 ± 0.87 cm (from 4-8 cm), 19% of cases had their membranes spontaneously ruptured at time of examination. 5.5% of patients had trial of VBAC under epidural analgesia.

49 cases had vaginal delivery, 3 of them delivered by vacuum to shorten the 2nd stage

TOLAC ended by CS delivery in 75.5% of cases, 72.84% of them had a CS for non-progressive labor. Failure to progress was stated according to the definition of the American College of Obstetricians and Gynecologists (ACOG)⁽⁷⁾.

Intrapartum bleeding reported in one case and delivery was by CS, it was found to have dehiscence uterine scar during CS.

Fetal head position was detected by transabdominal US in 100% of cases. Whilst PV examination failed to detect head position in 16%, No significant agreement between head position detected by US and By TV examination (r=0.123).

The mean PD was 2.9±6.0 mm, ranging from -15:18mm. It differ significantly between the vaginal and the CS groups (p=0.0005), and in turn there was significant difference among CS indicated by failure to progress and CS due to other causes (p< 0.001).(tab1)

Table 1: Values of tested parameters in different groups

Group		PD	AoP
Vaginal delivery	Spontaneous	6.10±6.1 (-13 : 13)	105.9±6.1 (89:115)
	Vontose	-2.33±6.0 (-10 : 2)	103.6±5.5 (99:108)
CS	Failed progress	-9.40±5.1 (-17 : -4)	96.6±7.4 (86:105)
	Other indications	-3.85±5.3 (-15 : 8)	100.4±6.7 (98:112)

In 89.8% of vaginal deliveries, the measured PD was ≥ 2.5 mm while it was ≤ 2.5 mm in 71.5% of CS cases. At a cut-off value of 2.5mm the sensitivity was 89.3% and 71.4% specificity in prediction of vaginal delivery.

At a significant statistical value (AUC=0.833, p<0.001) the same cut off value, the sensitivity and specificity of the PD for detection of “failure to progress” was 91.3% and 78% respectively (fig.2).

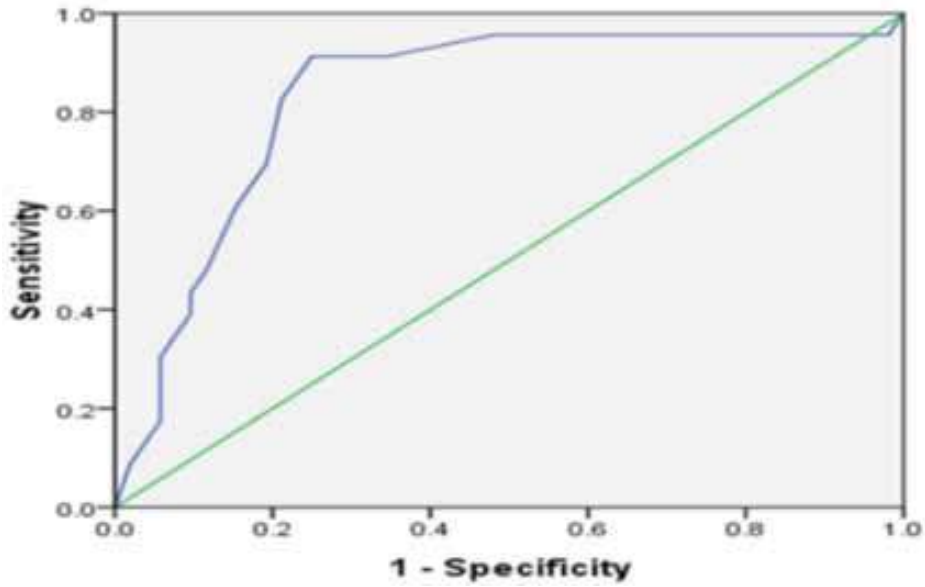


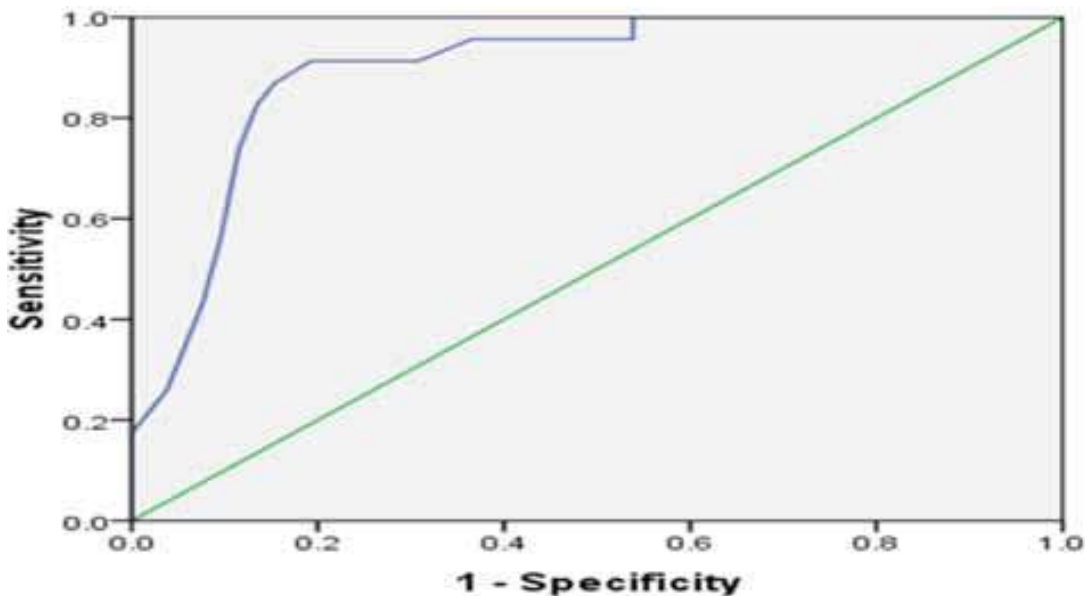
Fig.2: ROC curve PD in the subgroup of “failure to progress”

The mean AoP was $100.8 \pm 6.97^\circ$, ranging from 86 to 115. In women with spontaneous vaginal delivery the mean AoP was $105.0 \pm 5.99^\circ$, while in women with CS it was $98.4 \pm 6.7^\circ$, the difference was found to be of good significance ($p < 0.001$)

A cut-off value of 100.5° , showed the best statistical significance ($p < 0.001$), such value will have a sensitivity of 80.3% and specificity of 85.6% in detecting the engagement of the fetal head compared to digital PV examination.

The AoP was measured ≥ 100 in 87.7% of patients who had VBAC while it was < 100 in 73.5% of cases who delivered by CS. At a statistically significant level ($P = 0.001$) using 100.5° as a cut-off value to identify patients who deliver vaginally gives 88.5% sensitivity and 74.3% specificity.

In the subgroup of “ failed progression”, the same cut off value, gives higher sensitivity (91.3%) and specificity (80.8%) at a statistically significant level ($AUC = 0.896, P < 0.001$).



(Fig 3): ROC curve showing the ability of the AoP in predicting failure of progression

There was noticed significant correlation between both wider AoP and longer PD with shorter interval to delivery ($p < 0.001$, $p < 0.05$ respectively).

Time to delivery was 6 hours+31 min when AoP was

below 99° , 5 hours+30 min when AoP between 100 and 109, and 4 hours+45 min with angle ≥ 110 . longer PD was found to have similar effect (5 hours+54 min with PD less than 0 mm, 5 hours+24 min if PD is ≥ 0 mm).

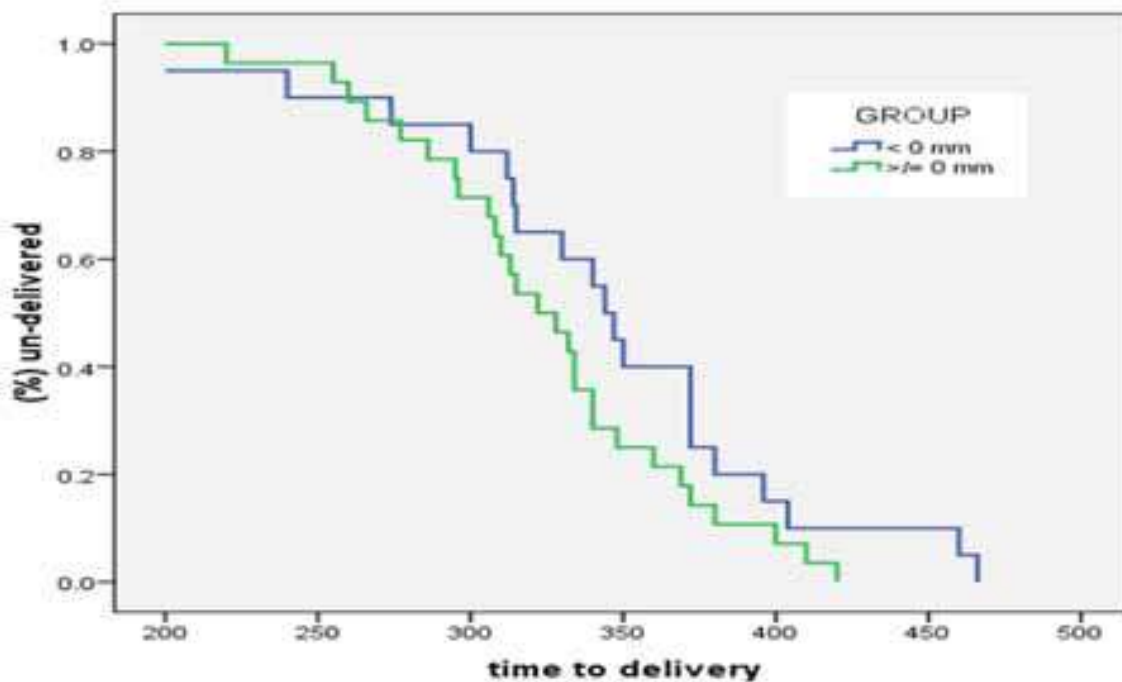


Fig.4: Kaplan-Meier curve of time to delivery in 2 sub-groups according to PD.

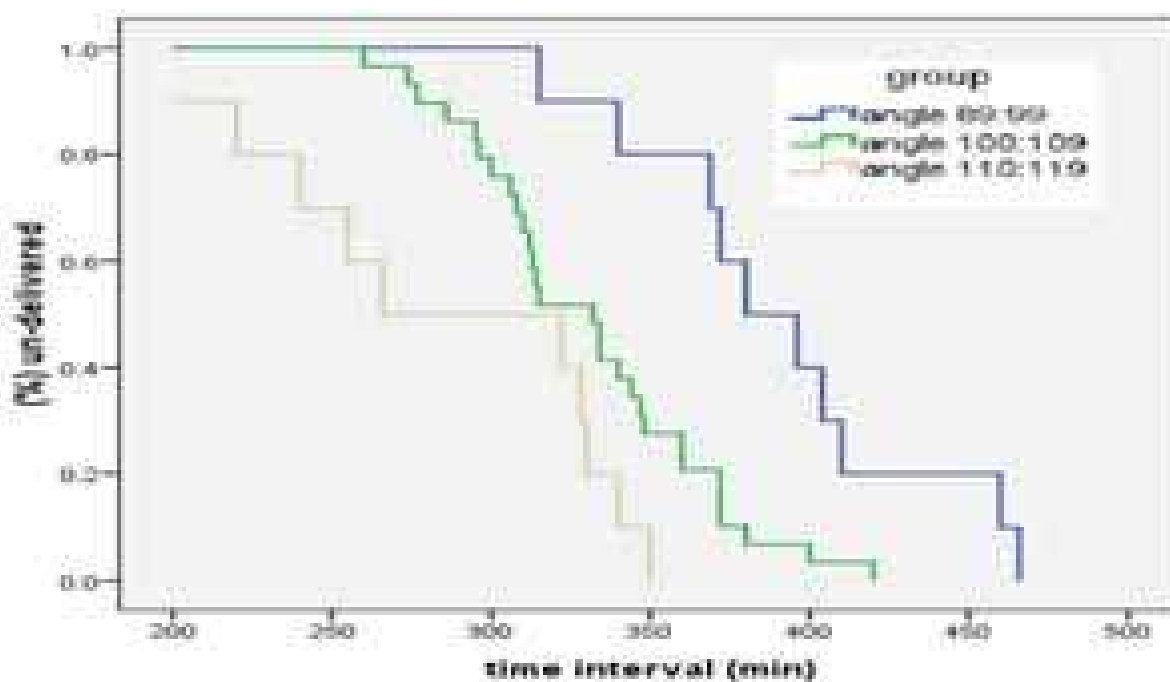


Fig.5: Kaplan-Meier curve of time to delivery in 3 sub-groups according to AoP

Discussion

The identification of the fetal head position by PV was not possible in 16% of cases, no significant agreement was found between the ultrasound and PV examination findings ($r=0.123$). Many studies observed transvaginal digital examination as being less accurate than ultrasonography for determining the fetal head position during the first stage of labor. With high rate of error^(8,9). In a study by Usman et al., Fetal head position was recorded in 99.7% of US and 51.5% on vaginal examination ($p<.0001$)⁽¹⁰⁾. Some studies even recommended the routine use of ultrasound in early first stage of labor or prior to instrumental delivery for accurate detection of fetal head position⁽¹¹⁾.

Several studies have shown that digital determination of fetal head station in laboring women is imprecise even in the hands of experienced examiners⁽¹²⁾.

One of the most studied ultrasound parameters to detect fetal head engagement to predict mode of delivery is the angle of progression of fetal head⁽¹³⁾. In the current work we tested a relatively new parameter - the progression distance - in addition for the main purpose.

Dietz et al. first described the PD of the fetal head. They provided evidence that the PD was correlated well with the fetal head station⁽⁶⁾.

The studied PD differ significantly among different reports, due to different methodology used in PD measurement and different population groups, also most of the reports focus on PD in prolonged 2nd stage of labor⁽¹⁴⁾.

Our mean PD (-2.9 ± 6.0 mm.) was near to that from the original work of Dietz et al. They reported a mean of -6.7 mm. Taking in consideration that their study was on nonlabouring women, it may explain our shorter PD.

The ability of the PD at a cut-off value of 2.5mm to predict VBACK, has sensitivity of 89.3% and specificity of 71.4%. It was raised to 91.3% and 78% respectively when used more specifically to predict unsatisfactory labor progress.

These findings are in agreement with Henrich et al.⁽¹⁵⁾ they used 3D-CT reconstruction of pelvimetric measurements of normal female pelvis in correlation with intrapartum US and confirmed that the infrapubic plane lies cranial to the level of the ischial spines and hence the plane of fetal head engagement.

In a study by Erik et al.⁽¹⁶⁾ PD was found to be significantly longer ($p=0.01$) in women who delivered vaginally compared to those who had CS for obstructed labor. But due to lack of standardization of the used measurement method, their values were far from ours (2.51 ± 1.71 cm and 1.48 ± 1.9 cm).

The mean value of the 'AoP' was $105.0 \pm 5.99^\circ$ in cases who delivered vaginally, a lower value was found in cases delivered by CS ($98.4 \pm 6.7^\circ$). This difference was of high statistical significance ($p < 0.001$).

The same angle was studied by Omar et al. they found similar difference between both groups (104 ± 16.6 and 88.3 ± 14)⁽¹⁷⁾. Also Lavy et al. found a narrower angle in patients who went for CS (90 vs 104). But the later study was conducted on patients who are not in active labor⁽¹⁸⁾.

The AoP value obtained by this study to identify head engagement (100.5) is apparently lower than the 123 reported by Chan et al.⁽¹⁹⁾, and the 116 reported by Tutschek et al. (8) It is, however, closer to the 101 obtained by Yaw et al.⁽²⁰⁾. However, these studies all agree on station 0 typically corresponding to an AoP above 99.

Using the same cut-off value to predict occurrence of vaginal delivery, it gives 88.5% sensitivity and 74.3% specificity at a statistically significant level ($P=0.001$). and to predict slow labor progress, it gave higher sensitivity(91.3%) and specificity (80.8%).

Some consecutive studies have shown that AoP is more accurate than digital examination in predicting vaginal delivery in nulliparous women with prolonged first stage of labor^(21,22).

Several studies with conflicting results have attempted to solve the issue of the correlation between a specific AoP and fetal head station within the birth canal. A MRI study by Bamberg et al.⁽²³⁾ found that an AOP of 120° corresponded to a fetal head station of 0. In another study by Barbera et al.⁽²⁴⁾ developed a geometric model from CT images and from TLUS. they concluded that a TLUS angle of 100° correlated with zero station of the fetal head.

The results of the current study agreed with the work done by Barbera et al. as the cut-off for the prediction of fetal head engagement was above 99° . Moreover, cases who delivered vaginally had the mean values above 99° unlike those who delivered by CS⁽²⁴⁾.

It was noticed that wider AoP were associated with significantly decreased time to delivery. This is in agreement with Ghi et al, ⁽²⁵⁾, and Bianca et al. ⁽²⁶⁾, however, the later reported that the impact on clinical practice seems low.

Conclusion

TLUS is a useful feasible acceptable and safe adjunctive assessment tool in the evaluation of laboring women trying to have vaginal delivery with a prior CS.

Disclosure of Interest: The authors declare that they have no competing interests.

Declaration of Authorship: All authors have directly participated in the planning, execution, analysis or reporting of this research paper. All authors have read and approved the final version of the manuscript.

Conflict of Interest: None

Financial: None

References

1. Wells CE. Vaginal birth after cesarean delivery: views from the private practitioner. *Semin Perinatol.* 2010;34(5):345-350.
2. Buchman E, Libhaber E. Interobserver agreement in intra-partum estimation of fetal head station. *Int J Gynaecol Obstet.* 2008; 101(3):285–289
3. Ki Hoon Ahn, Min-Jeong O. Intrapartum ultrasound: A useful method for evaluating labor progress and predicting operative vaginal delivery. *Obstet Gynecol Sci.* 2014; 57(6): 427–435.
4. Helene Ingeberg, Anna Miskova, Diana Andzane. Intrapartum ultrasound to predict vaginal labor: a prospective cohort study. *Int J Reprod Contracept Obstet Gynecol.* 2017;6(11):4778-4781
5. Kim K, Cheng J, Shen J, Wagner H, Staack A. Translabial Ultrasound Evaluation of Pelvic Floor Structures and Mesh in the Urology Office and Intraoperative Setting. *Urology.* 2018;120:267
6. Dietz HP, Lanzarone V. Measuring engagement of the fetal head: validity and reproducibility of a new ultrasound technique. *Ultrasound Obstet Gynecol.* 2005; 25: 165–168.
7. Spong CY, Berghella V, Wenstrom KD, et al. Preventing the first cesarean delivery: summary of a joint Eunice Kennedy Shriver National Institute of Child Health and Human Development, Society for Maternal-Fetal Medicine, and American College of Obstetricians and Gynecologists Workshop. *Obstet Gynecol* 2012; 120:1181.
8. Tutschek B, Torkildsen EA, Eggebø TM. Comparison between ultrasound parameters and clinical examination to assess fetal head station in labor. *Ultrasound Obstet Gynecol.* 2013;41(4):425-9.
9. Bellussi F, Ghi T, Youssef A, Salsi G, Giorgetta F, Parma D, Simonazzi G, Pilu G. The use of intrapartum ultrasound to diagnose malpositions and cephalic malpresentations. *Am J Obstet Gynecol.* 2017;217(6):633-641.
10. Usman S, Wilkinson M, Barton H, Lees C. The feasibility and accuracy of ultrasound assessment in the labor room. *J Matern Fetal Neonatal Med.* 2018;30:1-10.
11. Adam G, Sirbu O, Voicu C, Dominic D, Tudorache S, Cernea N. Intrapartum ultrasound assessment of fetal head position, tip the scale: natural or instrumental delivery? *Curr Health Sci J.* 2014;40(1):18-22.
12. Dupuis O, Silveira R, Zentner A, Dittmar A, Gaucherand P, Cucherat M, Redarce T, Rudigoz RC. Birth simulator: reliability of transvaginal assessment of fetal head station as defined by the American College of Obstetricians and Gynecologists classification. *Am J Obstet Gynecol.* 2005; 192: 868–874.
13. Tutschek B, Braun T, Chantraine F, Henrich W. A study of progress of labour using intrapartum translabial ultrasound, assessing head station, direction, and angle of descent. *BJOG.* 2011; 118: 62–69.
14. Gilboa Y., Kivilevitch Z., Spira M., Kedem A., Katorza E., Moran O., Achiron R. Head progression distance in prolonged second stage of labor: relationship with mode of delivery and fetal head station. *Ultrasound Obstet Gynecol.* 2013 Apr;41(4):436-41.
15. Henrich W, Dudenhausen J, Fuchs I, Kamena A, Tutschek B (2006) Intrapartum translabial ultrasound (ITU): sonographic landmarks and correlation with successful vacuum extraction. *Ultrasound Obstet Gynecol.* 28(6):753–760.
16. Erlik U, Weissmann-Brenner A, Kivilevitch Z, Moran O, Kees S, Karp H, Perlman S, Achiron R,

- Gilboa. Head progression distance during the first stage of labor as a predictor for delivery outcome. *J Maternal-Fetal Neonatal Medicine*.2018; 1:1-5.
17. Omar Khalil, Elsayed Elbadawi, Mahmoud Abdelnaby, Louay Hassan Zayed. Assessment of the progress of labor by the use of intrapartum ultrasound. *Alexandria Journal of Medicine*. 2012; 48, 295–301
 18. Levy R. Barak O. Flidel O. Zaks S. Gillor M. Hagay Z. Vaisbuch E. The Routine Use of Intrapartum Ultrasound in Clinical Decision-Making during the Second Stage of Labor - Does It Have Any Impact on Delivery Outcomes?. *Gynecol Obstet Invest* 2018;83:9-14.
 19. Chan YT, Ng VK, Yung WK, et al. Relationship between intrapartum transperineal ultrasound measurement of angle of progression and head–perineum distance with correlation to conventional clinical parameters of labor progress and time to delivery. *J Matern Fetal Neonatal Med*. 2015; 28: 1476–1481.
 20. Yaw A Wiafe, Bill Whitehead, Heather Venables and Alexander T Odoi. Sonographic parameters for diagnosing fetal head engagement during labour. *Ultrasound*. 2018;26(1) 16–21
 21. Eggebø TM, Wilhelm-Benartzi C, Hassan WA, Usman S, Salvesen KA, Lees CC. A model to predict vaginal delivery in nulliparous women based on maternal characteristics and intrapartum ultrasound. *Am J Obstet Gynecol* .2015; 213: 362. e1–6.
 22. Ghi T, Eggebø T, Lees C, Kalache K, Rozenberg P, Youssef A, Salomon J, Tutschek B. ISUOG Practice Guidelines: intrapartum ultrasound. *Ultrasound Obstet Gynecol*, 2018; 52: 128–139
 23. Bamberg C, Scheuermann S, Slowinski T, Duckelmann AM, Vogt M, Nguyen-Dobinsky TN, Streitparth F, Teichgraber U, Henrich W, Dudenhausen JW, Kalache KD. Relationship between fetal head station established using an open magnetic resonance imaging scanner and the angle of progression determined by transperineal ultrasound. *Ultrasound Obstet Gynecol*, 2011; 37: 712–716.
 24. Barbera A, IF, Becker T, et al. Anatomic relationship between the pubic symphysis and ischial spines and its clinical significance in the assessment of fetal head engagement and station during labor. *Ultrasound Obstet Gynecol*. 2009;33(3):320–5.
 25. Ghi T, Maroni E, Youssef A, Morselli-Labate AM, Paccapelo A, Montaguti E, Rizzo N, Pilu G. Sonographic pattern of fetal head descent: relationship with duration of active second stage of labor and occiput position at delivery. *Ultrasound Obstet Gynecol*. 2014 Jul;44(1):82-9.
 26. Bianca Masturzo, Annalisa Piazzese, Sara Paracchini, Maria S Quezada, Tullia Todros, Antonio Farina. Time remaining in labor and probability of vaginal delivery as a function of the angle of progression in a low risk population with a normal first stage of labor. *Minerva Ginecologica*. 2018; 70 (1): 35-43.

The Effect of Isotonic Training Method for the Development of Healthy Muscular Ability and Accuracy of the Performance of Volleyball Skill for Young Players

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Abstract

The aim of this research is to develop the muscular ability and its effect on the performance of volleyball and the development of isotonic training method (movement), and the researchers supposed that the impact of the method in the development of muscle capacity and accuracy of the performance of the skill of transmission, they used the experimental method, Al-Muqdadiya Youth Sports Club in Diyala Governorate (15) players were chosen in a deliberate manner. The method was prepared by the researchers and the candidate tests were used. The results were processed using the statistics. The most important recommendations are the use of the isotonic training method to develop the muscular ability of all practitioners of the game. Whether students or professional or amateur, taking into account that the level and the ability of the sample as well as the need to emphasize the conduct of continuous and regular tests to test the physical and skill capabilities of the players to know their level and try to develop them to the best.

Keywords: *Isotonic, Healthy Ability, Performance.*

Introduction

Explosive power is “one of the most important motor skills in volleyball. It depends on two components: muscle strength and speed. The combination of these two components together and their explosive output is evidence of the individual’s ability to exercise” [1]. Muscle power plays an important and essential role in the performance of skills in the game of volleyball and vary in importance in varying degrees between skill and other and increasingly important in the offensive skills of the game being critical in achieving the points that require the performance of the maximum force and speed possible any force characteristic of speed or explosive force, and these skills sending and beating Which is characterized by this type of performance where the player uses all his physical and skill to achieve the best achievement of the point, and thus emerged the importance of research in the application of a method designed to train the Isotonic skills to develop muscle and accuracy of the performance of the skill of volleyball for the youth.

Research Problems: Through the observation

and the field experience of the researchers as teachers and practitioners of volleyball, noted the weakness of the skill performance of the players, especially in the performance of sending muscle strength and speed, as well as accuracy in performance and the reason for this gap in the educational and training method used for the development of force and their association with other physical qualities that serve the skill performance and one of these gaps is the muscle capacity (explosive power or speed characteristic).

Research Objectives:

1. Preparation of a training method includes the Isotonic training (movement), as a method for the sample of the research.
2. To recognize the impact of isotonic training in the development of muscle strength and accuracy of the performance of the skill of the volleyball for young players.
3. Identify the development of muscle strength and its impact on the performance of volleyball for young people.

Hypothesis of the Research: Isotonic training affects the development of muscle capacity and accuracy of the performance of the volleyball for young people.

Research Areas:

1. **Population:** Muqdadiya players in the junior volleyball class.
2. **Time:** 1/4/2018 up to 1/9/2018
3. **Place:** Al-Muqdadiyah Sports Club Stadium in Diyala.

Research Methodology: The researchers used the two-group experimental approach (experimental design with pre and post control) to suit the research and its objectives.

Sample of The Research: The sample of the research was among the youth players of the Muqdadiya Sports Club in Diyala Province, who were chosen by the deliberate method of (17) players, two players were excluded so the sample became (15) players.

Means, tools and devices used in the research:

Data collection method: Arab and foreign scientific sources, observation and experimentation, testing and measurement.

Tools and devices used: (1 kg, 2 kg, 3 kg, 4 kg, 5 kg), non-stretchable colour stripe, stained-glass wall, chairs, colourful chairs, various wooden benches, Swedish seats, rubber ropes, Iron bar with different weights.

Identification of Variables: The variables of the research were determined by looking at many scientific sources and previous related studies. The variables that were determined are as follows:

1. Muscle Strength Test,
2. The accuracy of the skill of transmission from the top.

Identification of Research Tests: Test the strength of the arm (push the medicine ball of (3) kg by hands in the sitting position).

Purpose of the test: Measure the strength of the arms.

Required tools: Flat space area, medical balls weighing 3 kg, chair, measuring tape, wide belt.

Performance description: The trainee sits on the chair holding the medical ball with hands so that the ball is in front of the chest and below the chin level as the trunk should be attached to the edge of the chair. A belt is placed around the lab's chest so that it is held from the back by an airway. This is to prevent the movement of the trainee forward while throwing the ball in the hands from the top of the head. The movement is done using hands only and as far as possible the trainee is given two attempts and the best is calculated. When the trainee vibrates or moves on the chair while performing one of the attempts. The result is not counted and another attempt is given instead, with a measuring tape to measure the distance of the ball.

Recording: The distance in meters and the distance from the inner edge of the firing line and the closest to the medical ball are measured by the line and the best two attempts are measured by meters and centimetres.

Figure (1) shows the test of throwing the medical ball weighing (3) kg

Test the accuracy of transmission from the top: In the second half of the stadium two parallel lines are drawn to the first side line, four feet from the side line, and the second six feet from the first line (10 feet from the front line). Side) Write in the first rectangle (10), in the second rectangle (5) and in the third rectangle (1) where these numbers represent the trainees cores if the ball falls in any of these three areas as shown in Fig.

Performance Specifications: The trainee stands in the transmission area and performs the transmission skill to the half of the corresponding field. The ball passes the net (without touching it) and tries to drop it in the rectangle in which it is written (10).

Conditions: 1. The type of transmission used shall be agreed in advance. 2. Each individual has ten attempts on the test (consecutive) 3. The trainee shall receive (0) in case of contact with the net whether it falls on or off the field.

Registration: The player gets 10 points if the ball falls in the designated area (the first rectangle next to the side line) and on (5) if the ball falls into the third rectangle (1). If the ball falls on one of the fair lines of the two rectangles inside the lines of the stadium is within the target measures and the final grade represents the set of degrees of the trainee in its ten attempts, i.e.: the final grade of these tests is (10) degrees.

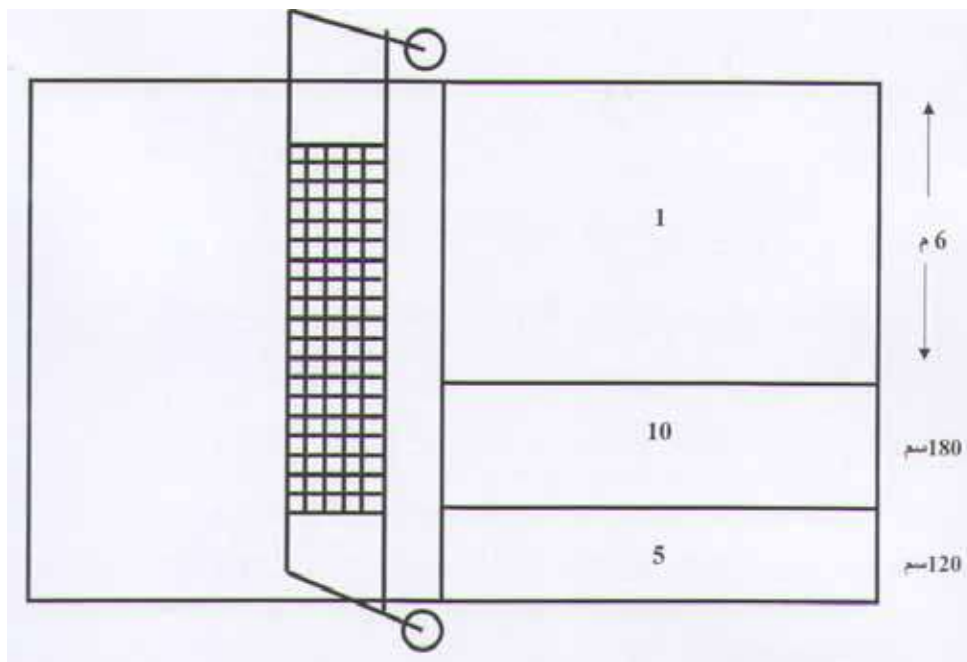


Figure (1): Shows the transmission skill test from the top

Pilot experiment for the two tests:

Exploration Experience: The researchers carried out the pilot test for muscle strength test and transmitter skill test on 26/4/2018 at the Shahrban Sports Club. The researchers applied the test to a sample of 12 players.

The scientific basis for the tests:

Honesty: Is that the test is designed to measure what was put to measure, the field or phenomenon studied (1) was the credibility of the virtual presentation of technical tests to the experts and specialists, as it was agreed by all experts and specialists.

Consistence: The test is the same that gives the same results are close if the test is applied in the same circumstances. The test was applied on 26/4/2018 and returned after seven days on 3/5/2018 and on the same sample to know the stability of the test, the researchers used Pearson correlation coefficient between the results of the first and the second test, and the results showed a “significant” correlation between them.

Pre-Tests: The muscle strength test and the precision test of the skill of the transmitter were conducted on (8/5/2018) on the research sample (15) players and the conditions of the pre-tests were recorded and the possibility of applying them in the post tests.

Implementation of the main experiment: The results of the training course prepared by the team’s own trainer, from the remaining vocabulary and time of the training module, were applied to the training module, from 10/5/2018 to 5/7/2018. (8) Weeks and three training units per week as the training time (120 d) was the main part. 80 d). The researchers used a ripple load (2-1) and two high units Low unit (gradient Balhdd) ranging Alhdd in the exercise used (65-100%).

Post-tests: After the completion of the exercises, the tests of the research sample were carried out on 7/7/2018, taking into consideration the temporal and spatial conditions and the means used in the pre-tests and the same auxiliary team.

Statistical Method: Researchers used SPSS to process data.

Presentation, analysis and discussion of the results of physical: To determine the significance of the differences in the results of the physical and psychological the pre and post-tests of the sample, the researchers used the t-test of the sample as shown in Table (1).

Table (1): Shows the mean, standard deviations and the value of (T) of the research sample in the pre and post-tests of the physical and skill tests:

Sr.	Physical & Skilful tests	Pre-Test		Post Test		T-test	level of significance	Type of Significance
		Mean	Standard Deviation	Mean	Standard Deviation			
1	Muscle strength test	6.152	0.705	6.509	0380	2.202	0.03	Significant
2	accuracy of transmissions from the top	7.521	10.986	8.802	8.928	3.201	0.01	Significant

Below the degree of (14) and the level of significance (0.05): From the table above we find that the value of the mean and the standard deviation of the test of throw a ball weighing 3 kg in two hands over the head from the position of sitting on the chair in the pre-test was the value of the arithmetic mean and standard deviation, respectively (6.152), (0.705) (0.509), (0.380), and (t) (2.202) and freedom level (14) below the level of significance (0.05), indicating that there are significant differences in favour of the post-test. The results of the test of accuracy of the transmissions, the value of the mean and the standard deviation respectively are (7,521), (10.986) and for the post test are (8.802), (8.928), the value of t (3,201) and the degree of freedom (41) 0.05), indicating significant differences in favour of post-test.

Discussion

The results show that there are significant differences between the pre and post-tests and for the post-researchers which emphasize that it is not necessary to improve the level of strength and speed to increase the level of accuracy, but that occurred and the practice of Isotonic development of muscle capacity of the arms and trunk, which contributed to generate additional strength of the muscles working and accelerate the movement of the strike arm for the ball allowing the player to hit the ball from the highest point in the air and from the upper corner, thus leading to full control of the direction of hitting the ball and then increase the accuracy of the direction of the ball to the desired location and this is confirmed by DhaferHashim, “that muscle strength For the purpose of performing the transmitter skill requires increasing the horizontal or vertical momentum of the force generated by the body, which increases the hitting of the ball quickly when performing the skill of transmission “.

Conclusions

There are Significant differences in the pre and post-tests for the muscle strength test (using isotonic training (movement) and the volleyball performance skill for the players of the Muqdadiyah Club for young people.

Recommendations:

1. The researchers recommend using the isotonic training to develop the muscular ability of all the practitioners of the game, whether students, professional or amateur, taking into account the method level and the ability of the player.
2. The need to emphasize the conduct of continuous and regular tests to test the physical and skill capabilities of the players to recognize their abilities and try to develop them to the best level.
3. Conduct a similar study using the training method and linking other variables as well as the physical and skill variables under study whether functional variables or biomechanical variables.

Source of Funding: Self

Ethical Clearance: Not required

Conflict of Interest: None

References:

1. DhaferHashim: The technical and planning numbers in tennis, I 2, the university house for printing, publishing and translation, Ministry of Higher Education, 2002.
2. Ali Hamid Ali; the impact of special exercises in the development of the determination of the strength of the arms and some basic skills of volleyball players of the team of education Diyala aged 13-15 years,

- (unpublished doctoral thesis, Faculty of Basic Education, University of Diyala, 2017).
3. Kazem Karim Reza Al-Jabri; *Research Method in Education and Psychology, I 1*, (Baghdad, Al-Nuaimi Printing and Reproduction Office, 2011), p. 217.
 4. Kamal Darwish, Mohamed Sobhi Hassanein: *The New in Circular Training*, The Book Centre for Printing and Publishing, Cairo, 1999.
 5. Mohammed Wahib Mahdi; *Effect of Explosive Force Training in the Water Centre for the Development of Some Volleyball Skills for Youngsters* (Master Thesis, Diyala University, Faculty of Basic Education, 2011).

The Effect of Use Healthy Acupuncture in Odynolysis Chronic Pain of the Biceps Femoral Muscle of Taekwondo Players

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Abstract

The importance of the research lies in the use of acupuncture for the spastic muscle (biceps femoral) of taekwondo players in the clubs of Al Najaf Al Ashraf province.

The problem of research is the dealing mistakes with these injuries as many of injured resort to do massage and deep massage, which increases the case of injury in addition to the muscle rupture cases.

The study objectives to achieve, the researchers used the experimental methodology of one group to suit the nature of the problem, the research population identified as taekwondo players with muscle spasms of the femoral biceps muscle, the researchers used acupuncture to relieve muscle spasm and odynolysis the degree of pain caused by a specialist, where tests were conducted on the Taekwondo hall in AL Najaf Al Ashraf Club and after getting of results were treated statistically by using statistical bag spss, and reached the following conclusions result of acupuncture clearly on odynolysis the degree of pain caused by muscle spasm, therefore enable the sample of the research to perform muscle contractions properly and in the light of the obtained results by the researchers, they recommend with the need of acupuncture in of muscle spasm cases.

Keywords: *Acupuncture, Odynolysis, Chronic Pain.*

Introduction

Interest of sports activity in developed and developing societies alike has become an essential aspect of human resources in order to improve human health. Sport has become a common feature in doctors' advice to diseases prevention that may infect humans at different stages of life.

Injuries related to high effort, poor physical fitness and body building are muscle injuries and muscle spasm, as well as for taekwondo and karate players, this injury is caused by pain, the posterior femoral muscles and connective muscles, and this movement is closely related to the integrity of the ligaments, muscles and in the femoral articulation.

Muscle injuries of all kinds occur in martial artists as most practitioners complain of pain in the connective muscles and the biceps femoral due to the pressure caused by the use of rotational movements during the performance of basic exercises, these pains are usually

caused by acute or chronic infect their structures in the articulations or some (cartilages, bones, ligaments, muscles and nerves).

The therapeutic exercises are the main axis and the common factor in the treatment of injuries and is one of the most important ways in removing dysfunction cases of muscles and articulations, as well as interest in understanding (biomechanical) the body movements and healthy body through performing exercises to develop the muscle strength and articulation flexibility and the degree of neurological compatibility to restore normal state.

Acupuncture is one of the physiotherapy method used to restore the balance and internal stability in the human body and way to induce the nervous system responsible for causing pain and where acupuncture play important and effective role in gr rid of pain through the theory of control of pain gate (closing the pain gate), and secretion of stored natural chemicals materials in the

body called (blood opioids), which lead to stop the pain and thus significantly reduce dependence on external analgesics with its harmful effects.

Hence the importance of research in the use of acupuncture in relieving spasm in the biceps femoral muscle of Taekwondo players.

The Research Problem: Taekwondo is one of the games that require great effort and high flexibility for muscles and articulations where these games need fast movements and a high level of muscle flexibility, through the researchers note that the martial artists frequent muscle exposure of biceps femoral muscle to the muscle spasms, and this promoted the researchers to use acupuncture to odynolysis the muscle spasm.

Objectives:

The research aim to:

1. Using the acupuncture in odynolysis the spasm of biceps femoral muscle of Taekwondo players.
2. Identify the effect of acupuncture in odynolysis muscle spasm.

Hypothesis: There is a positive effect of acupuncture in odynolysis the spasm of the biceps femoral muscle of taekwondo players.

Methodology: The researchers used the experimental approach of one-group as the most appropriate method to solve the research problem.

Research Population and Sample: The research population was identified as the injured players of the Taekwondo game in Najaf sports clubs, and the number of 8 injured, representing the research population.

Means of collect information, devices and tools used: The researchers used more than one method that can help him to reach the facts, as they use many different research tools to ensure obtaining accurate and correct data to implement the requirements of the research, including:

Means of collect information:

- Foreign and Arabic Sources
- Observation and experimentation.
- Testing and measurement.

Used devices and tools:

- Chinese needles.

- Dynamometer
- Tape measure.

Determination of Research Tests:

First, measure the strength of the biceps femoral muscle and the pain level:

The aim of test: Measuring the maximum strength of the biceps femoral muscle of the affected muscle.

Test Description: From the prone position, the laboratory pulls the dynamometer fixed horizontally with the affected muscle and raises the foot to back with angle of 90 (rear kilometer) and with maximum force, give each experimenter two attempts to calculate the best attempt.

Recording Method: The force is recorded in Newton with the pain level indicated by the player himself according to the pain level test shown in the figure below.

Pre-tests: Researchers conducted the pre-tests of the research sample on Saturday (17/11/2018) at two o'clock in the Taekwondo Hall in Najaf Sports Club.

Main Experience: The researchers used acupuncture by a specialist in physiotherapy and acupuncture of three sessions a week for two weeks (6 sessions) for the purpose of odynolysis the spasm in the muscle of the biceps femoral resulting from high stress on the muscle as the prick muscle affected by spasticity especially from the large measurement for the purpose of reaching the depth of the muscle and in the specified areas for tingling away from the nerve feeding the muscle and the duration of stimulation acupuncture for (5) minutes with manual stimulation and not electrical activity has been used stimulation two method are the method of (lifting and pushing–turnover method) this was effective in odynolysis the pain of infected.

The post- tests: The researchers conducted the post-test for the members of the research sample on Friday (30/11/2018) at exactly 2:00 pm in the hall of Najaf Club also in the same manner of pre- tests.

Statistical method used in the research: The researchers used the spss statistical program and the following Laws.

- Arithmetic mean.
- Standard deviation.
- T test for correlated samples.

Presentation, analysis and discussion of results:

Presentation and analysis of differences between pre and post-tests:

Table (1): The differences between pre- and post-tests in the searched variables of the control group

Sr.	variables	pre		post		T Calculated Value	Sig Value	Significance
		s	h	s	h			
1	The maximum strength of the affected muscle	125.33	10.09	166.75	12.44	11.86	0.00	moral
2	Pain Degree	6.55	0.83	2.5	1.08	7.36	0.01	moral

This indicates that the results of the research showed a significant change in reducing the pain degree of the players, which clearly affected the amounts of muscle strength of the infected muscles, application of therapeutic exercises with acupuncture has a clear effect in improving the effectiveness of the injured muscle because acupuncture play an important role in odynolysis, which is reflected positively on the motor extent, this result is consistent with what (Peter E. Baldry 2005)^[1] said that various physical therapies means, including motor rehabilitation (therapeutic exercises), odynolysis spontaneously and significantly affect the reduction of muscle pain besides acupuncture at near and far energy points and leads to Better results, as (70%) of patients suffering from muscles pain and articulations and subject to acupuncture sessions and continuously had a significant impact in odynolysis, increase the flexibility of the joint, increase electrical activity of muscles, and acupuncture is a property in closing the gate of pain, which helps the injured to do the exercises well and properly without pain. This was confirmed by ^[2].

The results of the ^[3]study confirm that acupuncture on the anatomical points of the energy pathways in the body leads to an improvement in the electrical activity of the muscles working on this track and improved the functional efficiency of these muscles.

As confirmed by ^[4]and^[5] that there is evidence of the effectiveness of acupuncture on reducing the degree of pain, and the nerve tissue is considered a bundle of thick and thin sizes. The thin size that transmits the sensation of pain while the thicker transmits other sensations such as touch and can prevent traversal of thin tissues, this is done during the closure of the pain gate, which is in specific neurons in the spine and tingling needles stop the pain by secreting chemicals materials

called (Opioids) leads to stop the pain. It was possible to follow the progress of the acupuncture alert from the body contour to the cerebral cortex and record the inhibitory effect of pain by tingling and alerting some points in several areas of the body.

These results are consistent with ^[1] that acupuncture works to reduce muscle tension, where the muscles within the body have continuous and imperceptible contractions to maintain their mobility in treatment these symptoms not only in the implant area but on continuous inhibition effect of pain sensation of (Contineam Inhibition) There is a reaction similar to pass the pain sensation comes from the mechanical and thermal receptors in the skin affected by the presence of acupuncture that occur mechanical and thermal effect and occur effectively change to any pain sensation comes from the spinal parts of the brain where it is sent continuous nerve signals to discourage pain sensation ^[6].

As stated by^[7] and^[8] that on the excruciating pain expresses a deficiency in the natural control system, where new therapeutic method have emerged depend on nervous induction to enhance this control the pain-resistant chemicals are entered, which are natural types of morphine are secreted by neurons during acupuncture, which leads to less pain sensation.

Source of Funding: Self

Ethical Clearance: Not required

Conflict of Interest: None

References

1. Mohamed Adel: Physiotherapy and the explosion of pain points, first edition, Al Ma'areef facility, Alexandria, 2015, p. 141.

4. Samiaa Khalil Mohammed: athletes injuries and physical therapy method, Cairo, 2008, p. 57.
3. Marwan Al-Jabban: Principles and Foundations of Acupuncture, Dar Al Bashaer for Printing and publishing, Damascus, 1992, p. 30.
4. Fathi Sayed Nasr: Acupuncture Chinese illusion or fact, Atlas Press, Cairo, 1991, p. 17.
5. Abdul Hadi Abdul Rahman:, Acupuncture Dar El Hwar for publishing and distribution, Lattakia Syria, 1988, pp. 85-86.
6. Paul Shoshar: Translation, Hala Murad, The Pain, Dar Al Mustaqbal Al Arabi, Cairo, 1992, p. 113.
7. Peter e. Baldry :Acupuncture Trigger Points and Musculoskeletal Pain, British Library Congress Cataloguing in Publication Data, USA,2005,p. 251-219.
8. Elizabeth, Tough :There is Little Effect of Acupuncture on the Electrical Activity of Muscle Electromyography (EMG), University of Plymouth, UK.2006.P.200.

Fate of Dysfunctional Bladder after Pediatric Renal Transplantation

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Abstract

Introduction: Graft function on long term into patients with LUTD is still a myth, So, we aimed know the natural history of LUTD and graft function into patient with abnormal lower urinary tract.

Patient and Method: The study was conducted by retrospective review of 129 files of pediatric live renal transplant patients; Patients in either group had clinical evaluation of lower urinary tract function and assessment of graft functions at least one year after RT.

Results: On evaluation the magnitude of change of cystometric variables we found 57% improvement of incidence of urodynamic detrusor overactivity and 48% improvement in patient categorized as poor/ decreased compliance. There was 90% increase in the number of patients with adequate capacity. Patients showed 55.5% decrease in the number of patient with high PVR.

Conclusion: Live donor renal transplant into pediatric patients with LUTD due to organic or neurogenic lower urinary tract pathology showed high serum creatinine on long term follow up.

Keywords: ESRD - Follow up - Serum creatinine.

Introduction

Recent advances in surgical techniques in pediatric renal transplantation, preoperative and postoperative care, as well as immunosuppressive therapy have contributed to increase patient and graft survival for this population. However, important differences in the

pediatric transplantation compared with adult especially for children who have lower urinary tract dysfunction LUTD which represents chronic problem in the context of renal transplantation.⁽¹⁾

Data about the renal allograft function in cases with LUTD is limited and also, results of pediatric renal transplant patients with abnormal bladder have been conflicting. Some showed that these patients are poor candidates for renal transplant with poor graft and patient outcome. In contrast, other studies have shown that renal transplant is a safe and effective treatment for end-stage renal disease in children with lower urinary tract abnormalities. ⁽²⁾We aimed at assessing the impact of lower urinary tract dysfunction on renal allograft function, graft survival and related morbidities.

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Patient and Method

Our study included a retrospective cohort of 129 ESRD patient received live related donor renal allograft in the period between 2010 and 2016 at Aboul-Riche pediatric University Hospital. Patient was diagnosed for LUTD due to underlying different clinical conditions including PUV (39 patients), primary VUR (32 patients) and neurogenic bladder (20 patients) and urethral stricture disease (1 cases) remaining cases had no obvious LUTD.

Long term assessment of serum creatinine and clinically significant lower urinary tract manifestations were examined. Also, we studied the effect of pre, intra and post-operative variables together with lower tract parameters on last serum creatinine as a mirror of graft functions.

Results

Mean age of live donor was 38 years most of them were mother of the child with ESRD in 61.5%. Mean recipient age at transplantation was 9 years with a mean weight at operation 26.5 Kg. (See table 1)

On comparing magnitude of change of cystometric variables in each group we found 57% of incidence of urodynamic detrusor overactivity and 48% improvement in patient categorized as poor/decreased compliance. There was 90% increase in the number of patients with adequate capacity. Group B patients showed 55.5% decrease in the number of patient with high PVR.

Mean serum creatinine in last follow up was 1.3 with no graft failure or deaths. (See table 2)

Donor and recipient criteria in both study groups

Table 1: 61.5% of recipients were males with mean age at transplantation of 9.2 years

Parameter		Group B NO. (129)
Donor age	Mean ± SD	38.1 ± 8.5
Donor sex	Male	15 (38.5%)
	Female	24 (61.5%)
Recipient sex (%)	Males	24 (61.5%)
	Females	15 (38.5%)
Age at renal transplantation	Mean ± SD	9.2 ± 4.1
Weight at renal transplantation	Mean ± SD	26.5 ± 9.9

Graft function outcome in both study groups in the end of the study:

Table 2: Mean serum creatinine at the last follow up was 1.3 mg/dl in 3.6 to 7.8 years of follow up duration (median follow up 6 years).

Parameter		Group B NO.(39)
Last Creatinine (mg/dl)	Mean ± SD	1.3 ± 0.9

Discussion

Our study in considered an a follow up of a second study was done on 123 pediatric renal transplant patient to compare the outcome of renal graft and related complication between two groups; control group of patient with non-urological cause of ESRD and group of patient who developed ESRD due to urological causes including mainly patients with LUTD. However, the above study did not report whether LUTD changes affects graft outcome.

Many studies reported 62.5% live related donors versus 37.5% cadaveric donor, while in our studies only live donor was accepted by law. (4-13)

Mean age donor in the studies described before was calculated to be 35.4 years versus 38 year in our study which was similar to us. (4-13)

In our series, donor gender distribution between two groups showed no statistically significant difference where most of donor were female (70.5%) of total donors (See table 1). However in some studies; males (46.6%) were nearly equal female donors (53.4%) of 296 total donors reported. This difference could be attributed to presence of more cadaveric donor in the mentioned studies and more live related donor in our study where mother is the main donor. (4-13)

There were different means of age at transplantation of some of studies ranged from 4.8 to 13.7 years. (4-13) similar to our study where mean age at operation in group A was 9 years in our study reflecting that patient with LUTD usually had more time of till development of ESRD more than renal group. But without statistical significance (See table 1).

Most of our study patients were males in 71% with no statistically significant difference between study groups. Similar to our study, other studies; males

represented 64% of total cases reported. Also,, mean weight at transplantation of our study cases was 26.5 Kg. Only two studies among those described in table 1 reported weight at transplantation with no statistically significant difference between their groups. (5-6)

In our study, cases showed statistically significant differences on the baseline and final urodynamic parameters which forced us to study the magnitude of changes, on comparing the change of cystometric variables in each group. We found 57% improvement of incidence of urodynamic detrusor overactivity. Patients categorized as poor/decreased compliance showed 48% improvement associated with 44.9% significant increase in mean mL needed to rise detrusor pressure one unit i.e. compliance. There was 90% rise in the number of patients with adequate capacity which was reflected as 63.8% increase in the mean of mL needed to reach MCC. Patients showed 55.5% decrease in the number of patient with high PVR which was associated with 79.9% increase in the mean volume of PVR.

All cases in our study has negative panel reactive antibodies PRA according to standard protocol of the institute. The most common HLA crossmatch pattern in each group was 3 out of 6 with no significant difference in the distribution of different grades of HLA crossmatch between study groups. In a single cohort of pediatric renal transplant recipient done in the same institute of us, median number of HLA crossmatch was 4 out of 6 crossmatch (39% of HLA crossmatch). Also, 42% of HLA cross match was 3 out of 6 HLA pairs similar to us. (3) Also, another comparative study reported no significant difference between the distributions of the number of HLA crossmatch in between both groups of patients, one of them included recipient with LUTD, (13)

Luke et al., 2003 reported increase in mean cystometric capacity by 63% from mean CC at baseline (186 ml). Also, there was a reduction in the mean of detrusor pressure before RT from 40 to 19 cmH₂O after RT. (13)

High PVR was estimated in 45 out of 129 cases, there was no significant change in the mean of PVR from baseline towards the post-transplant follow up. In addition, voiding difficulties were expressed in additional (7) non-CIC Non toilet trained patients associated with 33% increase in the need for assisted voiding e.g. CIC after RT

After RT, need for urinary diversion appeared in 8 cases with LUTD reported in studies described in table 1, only 5 patients needed Mitrofanoff procedure mainly due to development of urethral stricture in CIC dependent patients and non-compliance and inadequate urethral drainage in patients with urogenital sinus as mentioned. (6-12) Vesicostomy was needed in two cases one of them was due to urethral stricture development in CIC patient.

Mean UTIs episodes of our cases was 5-6 UTIs episodes yearly occurred ranging from 1 to 11 episode.

Three studies described a significant difference in the incidence of UTIs as for the favor of high UTIs occurrence in LUTD patients. (4, 7, 12) Only 2 studies reported non-significant difference between their study and control group regarding UTIs incidence. (3, 5)

In another study, comparing between pediatric transplant patients with nephrology versus urologic cause for ESRD. There was no significant difference between percentages of patient with UTIs between study groups before renal transplantation but after receiving graft the percentage of UTIs in the urologic group was markedly higher with high statistical significance. Which was similar to what was interpreted in our study that there was increase in the mean of UTIs episode in renal transplant patient with dysfunctional bladder against those with normal LUT. (14)

Serum creatinine at last follow up was high with a mean of 1.3 mg/dl. Only one study by Aki et al., 2015 reported significant difference between its groups regarding last serum creatinine (1.3 vs. 0.9 in LUTD+ve and LUTD-ve group respectively). (7) Despite that remaining studies did not describe a statistically significant difference regarding serum creatinine or eGFR in between their groups, serum creatinine or eGFR usually higher in groups with LUTD. (4-13)

High serum creatinine at the last follow up forced us to seek for predictors of serum creatinine, UTIs was responsible for 45% of last serum creatinine changes. Thus incident UTIs results in 20% change of serum creatinine.

In previous study, results of multiple regression analysis for factors affecting graft function showed that underlying urological pathology have a significant risk for graft function and postoperative complication (OR = 0.2, p= 0.05). (5)

Conclusions

Live donor renal transplant into pediatric patients with LUTD due to organic or neurogenic lower urinary tract pathology showed worse serum creatinine in patients with pathological LUTD. Comparing the effect of different LUT parameters on the net result of serum creatinine we found that UTIs account for 45% of serum creatinine result on the long term after receiving live donor transplantation.

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Ethical Consideration: All procedures performed were in accordance with the ethical standards of our local institutional research ethical committee of the faculty of Medicine, Minia Univ., Egypt. also in agreement with Helsinki Declaration as well as the Declaration of Istanbul 2008.

References

1. United States Renal Data System. NAPRTCS 2011 Annual report. Chapter 8: pediatric end-stage renal disease [cited 1 April 2013]. Available from: http://www.usrds.org/2011/pdf/v2_ch08_11.pdf
2. Knight, S. R., Morris, P. J., Schneeberger, S. and Pengel, L. H. (2016), Trial design and endpoints in clinical transplant research. *Transpl Int*, 29: 870-879. doi:10.1111/tri.12743.
3. Kim, J. J., & Marks, S. D. (2014). Long-term outcomes of children after solid organ transplantation. *Clinics (Sao Paulo, Brazil)*, 69 Suppl 1(Suppl 1), 28–38. doi:10.6061/clinics/2014(sup01)06.
4. Ismail R. Saad, Enmar Habib, Mohammed S. Elsheemy, Mahmoud Abdel-Hakim, Mostafa Sheba, Aziz Mosleh, Doaa M. Salah*, Hafez Bazaraa*, Fatina I. Fadel*, Hany A. Morsi And Hesham Badawy. Outcomes Of Living Donor Renal Transplantation In Children With Lower Urinary Tract Dysfunction: A Comparative Retrospective Study. *BJU Int* 2016; 118: 320–326
5. Hussein AA, Shoukry AI, Fadel F, Morsi HA-R, Hussein HA, Sheba M, Et Al. Outcome Of Pediatric Renal Transplantation In Urological Versus Non-Urological Causes Of End Stage Renal Disease: Does It Matter? *Journal Of Pediatric Urology*. 2018;14(2):166. E1-. E7.
6. Sierralta MC, González G, Nome C, Pinilla C, Correa R, Mansilla J, Et Al. Kidney Transplant In Pediatric Patients With Severe Bladder Pathology. *Pediatric Transplantation*. 2015;19(7):675-83.
7. Aki F, Aydin A, Dogan H, Donmez M, Erkan I, Duzova A, Et Al., Editors. Does Lower Urinary Tract Status Affect Renal Transplantation Outcomes In Children? *Transplantation Proceedings*; 2015: Elsevier.
8. Morita K, Iwami D, Hotta K, Shimoda N, Miura M, Watarai Y, Et Al. Pediatric Kidney Transplantation Is Safe And Available For Patients With Urological Anomalies As Well As Those With Primary Renal Diseases. *Pediatric Transplantation*. 2009;13(2):200-5.
9. Bilginer Y, Aki FT, Topaloglu R, Tekgul S, Demirkaya E, Düzova A, Et Al. Renal Transplantation In Children With Lower Urinary Tract Dysfunction Of Different Origin: A Single-Center Experience. *Transplantation Proceedings*. 2008;40(1):85-6.
10. Mendizabal S, Estornell F, Zamora I, Sabater A, Ibarra FG, Simon J. Renal Transplantation In Children With Severe Bladder Dysfunction. *The Journal Of Urology*. 2005;173(1):226-9.
11. Ali-El-Dein B, Abol-Enein H, El-Husseini A, Osman Y, El-Din AS, Ghoneim M, Editors. Renal Transplantation In Children With Abnormal Lower Urinary Tract. *Transplantation Proceedings*; 2004: Elsevier.
12. Adams J, Mehls O, Wiesel M. Pediatric Renal Transplantation And The Dysfunctional Bladder. *Transplant International*. 2004;17(10):596-602.
13. Luke PP, Herz DB, Bellinger MF, Chakrabarti P, Vivas CA, Scantlebury VP, Et Al. Long-Term Results Of Pediatric Renal Transplantation Into A Dysfunctional Lower Urinary Tract. *Transplantation*. 2003;76(11):1578-82.
14. Silva, A., Rodig, N., Passerotti, C. P., Recabal, P., Borer, J. G., Retik, A. B., & Nguyen, H. T. (2010). Risk Factors For Urinary Tract Infection After Renal Transplantation And Its Impact On Graft Function In Children And Young Adults. *The Journal Of Urology*, 184(4), 1462-1468.

15. Van der Weide MJA et al. (2006) Lower urinary tract symptoms after renal transplantation in children. *J Urol* 175: 297–302.
16. Song M, Park J, Kim YH, Han DJ, Song SH, Choo MS, Hong B. Bladder capacity in kidney transplant patients with end-stage renal disease. *International urology and nephrology*. 2015 Jan 1;47(1):101-6.
17. Flechner SM: Donor and Recipient selection. *Therapy of renal diseases and related disorders* 1998; 64: 1079.

Updated Review on Revascularization in ST-elevation Myocardial Infarction (STEMI)

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Abstract

Effective and in time reperfusion of the infarct-related coronary artery is essential to optimal treatment for ST-elevation myocardial infarction (STEMI). Now it is established the benefit of primary percutaneous intervention (PPCI) in STEMI over fibrinolysis. While intervention of the non-infarct related artery still a large area of debate with no definite consensus. Here in this review we will highlight the different reperfusion strategies and different ways to reach optimal reperfusion and debate about non-IRA in different situations.

Keywords: STEMI, Revascularization, primary PCI.

Introduction

Effective and in time reperfusion of the infarct-related coronary artery is essential to optimal treatment for acute coronary syndrome (ACS). In comparison with fibrinolysis, primary percutaneous coronary intervention (PCI) establishes more consistent and predictable epicardial artery recanalization, significantly lowers the risk of intracranial hemorrhage and stroke, reduces recurrent ischemia and reinfarction, and improves survival^(1,2).

Early angiography followed by revascularization when appropriate also improves clinical outcomes with the greatest benefits realized in the highest risk patients. Because epicardial artery reperfusion does not guarantee myocardial reperfusion, strategies for cardioprotection and optimization of tissue level reperfusion are also essential⁽³⁾.

Here we will highlight different reperfusion strategies to achieve faster and more effective epicardial vessel and micro vascular reperfusion in patients with STEMI as well as temporal and logistic factors that may affect treatment outcomes.

Reperfusion in STEMI: Early reperfusion therapy is the most important issue in the management of STEMI. The greatest amount of infarction occurs in the first few hours after coronary occlusion⁽⁴⁾. A recent analysis of 12 675 STEMI patients in the FITT-STEMI trial confirmed the strong impact of time delays on mortality, particularly in STEMI patients with cardiogenic shock or out-of-hospital cardiac arrest.⁽⁵⁾

Given this association between shorter time to reperfusion and survival, Door to Ballone (D2B) time became the focus of regional and national quality improvement initiatives.^(6,7) Several strategies were developed, tested, and formally incorporated into clinical guidelines to shorten D2B times.⁽⁸⁾ By using such evidence-based strategies, there have been significant improvements in D2B times across the country and across different types of hospitals.⁽⁹⁾

Which Reperfusion Method: Primary PCI, defined as percutaneous catheter intervention in the setting of STEMI without previous fibrinolysis, is

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the preferred reperfusion strategy⁽¹⁰⁾. It has replaced fibrinolysis in patients with STEMI, provided it can be performed in a timely manner in high-volume PCI centers with experienced operators and 24 h/7 days week catheterization laboratory activation⁽¹¹⁾.

In settings where primary PCI cannot be performed in a timely fashion, fibrinolysis should be administered as soon as possible. If first medical contact (FMC) is out-of-hospital, lysis should be implemented pre-hospital (e.g. in the ambulance)⁽¹²⁾.

It should be followed by transfer to PCI-capable centers for routine coronary angiography in all patients, and should be performed without delay for rescue PCI in the case of unsuccessful fibrinolysis or within 2–24 h after bolus administration.⁽¹³⁾

Primary PCI: Primary PCI is the preferred reperfusion strategy if a skilled interventional cardiologist and catheterization laboratory is available and if the procedure can be performed within 90 minutes after initial medical contact with the patient.⁽¹⁴⁻¹⁸⁾

The TRANSFER-AMI study further tested the pharmacoinvasive strategy concept in high-risk STEMI patients. Patients who had at least 1 high-risk feature [greater than or equal to 2 mm of ST-segment elevation in 2 anterior leads, systolic blood pressure less than 100 mm Hg, heart rate higher than 100 bpm, Killip class II to III, 2 mm or more of ST-segment depression in the anterior leads⁽¹⁹⁾, or 1 mm or more of ST elevation in right-sided lead V4 indicative of right ventricular involvement for inferior MIs⁽²⁰⁾.

Management of Non-infarct Stenosis during Primary PCI: Multi-vessel disease is seen in up to 60% of patients presenting with STEMI and has a worse prognosis compared with patients with STEMI with single-vessel disease.⁽²¹⁾

Previous observational and nonrandomized studies and metaanalyses supporting the strategy of IRA-only PPCI recommended by the 2013 AHA/ACC guidelines⁽²²⁾.

However, then emerging data suggested that PCI of non-IRA in patients with STEMI may be superior to the standard approach of IRA-only PCI. As a result, a focused update on primary PCI was published in 2015 by the ACC/AHA, suggesting that PCI of non-IRAs may be considered in select patients⁽²³⁾.

Four major randomized trials-PRAMI (Preventive Angioplasty in Acute Myocardial Infarction, CvLPRIT (Complete Versus LesionOnly Primary PCI trial),⁽²⁴⁾ DANAMI-3-PRIMULTI (The Third DANish Study of Optimal Acute Treatment of Patients with STsegment Elevation Myocardial Infarction: PRImary PCI in MULTIVessel Disease, and Compare-ACUTE have consistently shown a benefit of complete revascularization (performed immediately or staged) as compared with IRA-only PCI in patients with STEMI and multivessel disease⁽²⁵⁾

While in another meta analysis by Elgendy et al. showed that the risk of all-cause mortality and spontaneous reinfarction is not different among the various revascularization strategies for multivessel disease. Complete revascularization at the index procedure or as a staged procedure (either during the hospitalization or after discharge) was associated with a reduction of MACE due to reduction in urgent revascularization with no difference between these 3 strategies.⁽²⁶⁾

Functional Assessment of Non-Ira Lesions: Recently DANAMI- 3-PRIMULTI trial studied the clinical outcomes by comparing the fractional flow reserve (FFR) guided by complete revascularization with IRA-only PCI in STEMI, and found that the composite rate of all-cause mortality, nonfatal reinfarction, and repeat revascularization was significantly lower in the complete revascularization group, which was mainly driven by a reduction in repeat revascularization and More recently, another randomized trial (COMPAREACUTE) revealed that FFR-guided complete revascularization of non-IRA arteries in an acute setting was associated with a lower risk of the composite cardiovascular outcome⁽²⁵⁾.

So, updated ACC/AHA guidelines recommended that complete revascularization can be considered either at the time of primary PCI or after the index procedure as a staged procedure. The 2017 European Society of Cardiology guidelines recommended a class IIa recommendation for complete revascularization STEMI patients with MVD.⁽¹¹⁾

Recently, the results of COMPLETE trial were released. At a median of three years, complete revascularization reduced the risk of the composite of cardiovascular mortality or MI (HR = 0.74, 95% CI: 0.60-0.91, P = 0.0004) driven by a reduction in the risk of MI (HR = 0.68, 95% CI: 0.53-0.86). Complete

revascularization also reduced the risk of the composite of cardiovascular mortality, MI or ischemia-driven revascularization (HR = 0.51, 95% CI: 0.43-0.61, P < 0.0001). ± 2.7).⁽²⁷⁾

Table (1) Characteristics of the major trials comparing complete revascularization with IRA only revascularization⁽²⁷⁾

Trial	Year	N	Complete revascularization approach	Major adverse cardiac events	All-cause mortality	Re-infarction	Urgent revascularization
PRAMI	2013	234/231	Index	21/53	12/16	7/20	16/46
CvLPRIT	2015	150/146	Index (67%), staged prior to hospital discharge (33%)	15/31	2/6	0/2	7/12
DANAMI-3-PRIMULTI	2015	314/313	Staged 2 days after index PCI	40/68	15/11	15/16	17/52
COMPARE-ACUTE	2017	295/590	Index (83%), staged prior to hospital discharge (17%)	23/121	4/10	7/28	18/103
COMPLETE	2019	2016/2025	Staged: 64% prior to discharge (median 1 day), 36% after discharge (median 23 days)	179/339	96/106	109/160	29/160

Management of Non-IRA in the setting of cardiogenic shock: Cardiogenic shock (CS) in the setting of acute myocardial infarction (AMI) is associated with significant morbidity and mortality⁽¹¹⁾

For the treatment of patients with multi-vessel disease, current European guidelines for the management of acute ST-segment elevation myocardial infarction recommend immediate percutaneous coronary intervention (PCI) of both culprit and non-culprit lesions⁽¹¹⁾

However, the 30-day results of the Culprit Lesion Only PCI versus Multi-vessel PCI in Cardiogenic Shock (CULPRIT-SHOCK) trial⁽²⁵⁾ showed that the risk of a composite of death from any cause or severe renal failure leading to renal-replacement therapy was lower with culprit lesion- only PCI than with immediate multi-vessel PCI, thus challenging the guideline recommendations. On the basis of these results, the European revascularization guidelines have now downgraded immediate multi-vessel PCI in cardiogenic shock to a class III B recommendation (i.e., a recommendation that the procedure is not useful and may be harmful, according to evidence from a single randomized trial⁽¹⁹⁾).

In light of the short-term results of the CULPRITSHOCK trial, the use of multi-vessel PCI in patients with cardiogenic shock is now controversial.⁽¹¹⁾

Conclusion: The benefit of primary percutaneous intervention (PPCI) in STEMI over fibrinolysis was established, and after small non-randomized studies concluded the advantages of IRA only strategy in STEMI, multiple large trials recently declared the advantage of total revascularization in decreasing the short and long term adverse outcomes, and large randomized trials now are needed to create agreement about the best time for revascularization of residual lesions after dealing with IRA.

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References

1. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet*. 2003;361:13–20.
2. Stone GW. Angioplasty strategies in ST-segment-elevation myocardial infarction: part I: primary percutaneous coronary intervention. *Circulation*. 2008;118:538–551.
3. Fox KA, Clayton TC, Damman P, Pocock SJ, de Winter RJ, Tijssen JG, Lagerqvist B, Wallentin L; FIR Collaboration. Long-term outcome of a routine versus selective invasive strategy in patients with non-ST-segment elevation acute coronary syndrome: a meta-analysis of individual patient data. *J Am Coll Cardiol*. 2010;55:2435–2445.
4. Gersh BJ, Stone GW, White HD, Holmes DR Jr. Pharmacological facilitation of primary percutaneous coronary intervention for acute myocardial infarction: is the slope of the curve the shape of the future? *JAMA*. 2005;293:979–986.
5. Scholz KH, Maier SKG, Maier LS, Lengenfelder B, Jacobshagen C, Jung J, Fleischmann C, Werner GS, Olbrich HG, Ott R, Mudra H, Seidl K, Schulze PC, Weiss C, Haimerl J, Friede T, Meyer T. Impact of treatment delay on mortality in ST-segment elevation myocardial infarction (STEMI) patients presenting with and without haemodynamic instability: Results from the German prospective, multicentre FITT-STEMI trial. *Eur Heart J* 2018;39:1065–1074.
6. Jacobs AK, Antman EM, Ellrodt G, Faxon DP, Gregory T, Mensah GA, Moyer P, Ornato J, Peterson ED, Sadwin L, Smith SC; American Heart Association's Acute Myocardial Infarction Advisory Working Group. Recommendation to develop strategies to increase the number of ST-segment-elevation myocardial infarction patients with timely access to primary percutaneous coronary intervention. *Circulation*. 2006;113:2152–2163.
7. Jollis JG, Al-Khalidi HR, Monk L, Roettig ML, Garvey JL, Aluko AO, Wilson BH, Applegate RJ, Mears G, Corbett CC, Granger CB; Regional Approach to Cardiovascular Emergencies (RACE) Investigators. Expansion of a regional ST-segment-elevation myocardial infarction system to an entire state. *Circulation*. 2012;126:189–195.
8. O'Gara PT, Kushner FG, Ascheim DD, et al; American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2013;127:e362–e425.
9. Krumholz HM, Herrin J, Miller LE, Drye EE, Ling SM, Han LF, Rapp MT, Bradley EH, Nallamothu BK, Nsa W, Bratzler DW, Curtis JP. Improvements in door-to-balloon time in the United States, 2005 to 2010. *Circulation*. 2011;124:1038–1045.
10. Menees DS, Peterson ED, Wang Y, Curtis JP, Messenger JC, Rumsfeld JS, Gurm HS. Door-to-balloon time and mortality among patients undergoing primary PCI. *N Engl J Med*. 2013;369:901–909.
11. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, Caforio ALP, Crea F, Goudevenos JA, Halvorsen S, Hindricks G, Kastrati A, Lenzen MJ, Prescott E, Roffi M, Valgimigli M, Varenhorst C, Vranckx P, Widimsky P, Group ESCSD. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2018;39:119–177. *Eur Heart J* 2018; 39: 119-77
12. Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert Y, Sulimov V, Rosell Ortiz F, Ostojic M, Welsh RC, Carvalho AC, Nanas J, Arntz HR, Halvorsen S, Huber K, Grajek S, Fresco C, Bluhmki E, Regelin A, Vandenberghe K, Bogaerts K, Van de Werf F; STZREAM Investigative Team. Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. *N Engl J Med* 2013;368:1379–1387.
13. Cantor WJ, Fitchett D, Borgundvaag B, Ducas J, Heffernan M, Cohen EA, Morrison LJ, Langer A, Dzavik V, Mehta SR, Lazzam C, Schwartz B,

- Casanova A, Goodman SG; TRANSFER-AMI Trial Investigators. Routine early angioplasty after fibrinolysis for acute myocardial infarction. *N Engl J Med*. 2009;360:2705–2718.
14. Byrne RA, Serruys PW, Baumbach A, Escaned J, Fajadet J, James S, Joner M, Oktay S, Juni P, Kastrati A, Sianos G, Stefanini GG, Wijns W, Windecker S. Report of a European Society of Cardiology-European Association of Percutaneous Cardiovascular Interventions task force on the evaluation of coronary stents in Europe: Executive summary. *Eur Heart J* 2015;36:2608–2620.
 15. Bona KH, Mannsverk J, Wiseth R, Aaberge L, Myreng Y, Nygard O, Nilsen DW, Klow NE, Uchto M, Trovik T, Bendz B, Stavnes S, Bjornerheim R, Larsen AI, Slette M, Steigen T, Jakobsen OJ, Bleie O, Fossum E, Hanssen TA, Dahl-Eriksen O, Njolstad I, Rasmussen K, Wilsgaard T, Nordrehaug JE; NORSTENT Investigators. Drug-eluting or bare-metal stents for coronary artery disease. *N Engl J Med* 2016;375:1242–1252.
 16. Varenne O, Cook S, Sideris G, Kedev S, Cuisset T, Carrie D, Hovasse T, Garot P, El Mahmoud R, Spaulding C, Helft G, Diaz Fernandez JF, Brugaletta S, Pinar-Bermudez E, Mauri Ferre J, Commeau P, Teiger E, Bogaerts K, Sabate M, Morice MC, Sinnaeve PR; SENIOR Investigators. Drug-eluting stents in elderly patients with coronary artery disease (SENIOR): A randomised single-blind trial. *Lancet* 2018;391:41–50.
 17. Neumann FJ, Kastrati A, Pogatsa-Murray G, Mehilli J, Bollwein H, Bestehorn HP, Schmitt C, Seyfarth M, Dirschinger J, Schömig A. Evaluation of prolonged antithrombotic pretreatment (“cooling-off” strategy) before intervention in patients with unstable coronary syndromes: a randomized controlled trial. *JAMA*. 2003;290:1593–1599.
 18. Sorrentino S, Giustino G, Mehran R, Kini AS, Sharma SK, Faggioni M, Farhan S, Vogel B, Indolfi C, Dangas GD. Everolimus-eluting bioresorbable scaffolds versus everolimus-eluting metallic stents. *J Am Coll Cardiol* 2017;69:3055–3066.
 19. Van de Werf F, Bax J, Betriu A, et al; ESC Committee for Practice Guidelines (CPG). Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation: the task force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology. *Eur Heart J*. 2008;29:2909–2945.
 20. Andrés M. Pineda, MD,* Nikita Carvalho, MD,* Saqib A. Gowani, MD,* Kavita A. Desouza, MD,* Orlando Santana, MD,* Christos G. Mihos, DO,* Gregg W. Stone, MD,† and Nirat Beohar, MD*, Managing Multivessel Coronary Artery Disease in Patients With ST-Elevation Myocardial Infarction A Comprehensive Review, *Cardiology in Review* 2017;25: 179–188 2013;127:e362–e425.
 21. Levine GN, Bates ER, Blankenship JC, et al. ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. *Circulation*. 2015;124:e574–e651.
 22. Gershlick AH, Khan JN, Kelly DJ, Greenwood JP, Sasikaran T, Curzen N, Blackman DJ, Dalby M, Fairbrother KL, Banya W, Wang D, Flather M, Hetherington SL, Kelion AD, Talwar S, Gunning M, Hall R, Swanton H, McCann GP. Randomized trial of complete versus lesion-only revascularization in patients undergoing primary percutaneous coronary intervention for STEMI and multivessel disease: the CvLPRIT trial. *J Am Coll Cardiol* 2015;65:963–972.
 23. Smits PC, Abdel-Wahab M, Neumann F-J, Boxma-de Klerk BM, Lunde K, Schotborgh CE, Piroth Z, Horak D, Wlodarczak A, Ong PJ, Hambrecht R, Angerås O, Richardt G, Omerovic E, Compare-Acute I. Fractional flow reserve-guided multivessel angioplasty in myocardial infarction. *N Engl J Med* 2017;376:1234–1244.
 24. Elgendy IY, Mahmoud AN, Kumbhani DJ, Bhatt DL, Bavry AA. Complete or culprit-only revascularization for patients with multivessel coronary artery disease undergoing percutaneous coronary intervention: a pairwise and network meta-analysis of randomized trials. *JACC Cardiovasc Interv* 2017; 10:315–324
 25. Mehta SR, Granger CB, Boden WE, et al; TIMACS Investigators. Early versus delayed invasive

intervention in acute coronary syndromes. *N Engl J Med.* 2009;360:2165–2175.

26. Thiele H, Desch S, Piek JJ, et al. Multivessel versus culprit lesiononly percutaneous revascularization plus potential staged revascularizationin patients with acute myocardial infarction complicated by cardiogenic shock: design and rationale of CULPRIT-SHOCK trial. *Am Heart J* 2016; 172: 160-9.
27. Zaman, Muhammad O., Mohammad K. Mojadidi, and Islam Y. Elgendy. “Revascularization Strategies for Patients with Myocardial Infarction and Multi-Vessel Disease: A Critical Appraisal of the Current Evidence.” *Journal of geriatric cardiology: JGC* 16, no. 9 (2019): 717-23

MCP-1 Serum Levels were Higher in Patient with Diabetic Nephropathy among Balinese

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Abstract

Background and Aim: Diabetic nephropathy is a complication of diabetes mellitus which can lead to kidney failure. Monocyte Chemoattractant Protein-1 (MCP-1) is a protein that is expected to be a biomarker of diabetic nephropathy. The purpose of this study was to examine the relationship of MCP-1 with diabetic nephropathy in Indonesia, especially in Bali therefore the accuracy in detecting diabetic nephropathy can be assessed.

Method: One hundred and sixteen patients with type 2 diabetes mellitus with diabetic nephropathy (n = 37) and without diabetic nephropathy (n = 79) were included in this study. MCP-1 serum was examined using the enzyme-linked immunosorbent assay (ELISA) method.

Result: MCP-1 serum levels were significantly higher in patients with diabetic nephropathy (p <0.001). Analysis of receiver operating characteristic (ROC) curve for diabetic nephropathy detection showed that cut-off point of MCP-1 serum was 436 pg/ml with a sensitivity of 83.7% and 84.8% specificity.

Conclusion: It can be concluded that MCP-1 serum can be considered as a biomarker for detection of diabetic nephropathy.

Keywords: MCP-1 serum, diabetic nephropathy, biomarker.

Introduction

Diabetes mellitus (DM) is a series of metabolic diseases characterized by hyperglycemia due to defects in the secretion or action of insulin. The prevalence of this disease is increasing rapidly throughout the world and becoming one of the major health problems. In 2013, 382 million DM cases were estimated worldwide and

will increase to 592 million in 2035¹. Complications in diabetes are microvascular and macrovascular complication. One of the complications is diabetic nephropathy (DN). Diabetic nephropathy can occur in 30-40% of patients with type 1 and type 2 diabetes mellitus².

Various factors have been described to be involved in the pathophysiology of DN, such as hemodynamic and metabolic changes, oxidative stress, activation of the renin-angiotensin system and most recently the role of the inflammatory process that can cause disease progression towards DN^{2,3}. The mechanism underlying the regulation of cytokines in the kidney of DM patients is still unclear. Cytokines and chemokines which increase their expression (production) during the inflammatory process in the glomerular membrane of mice with

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diabetes are CC-chemokine ligand 2 (CCL2)/monocyte chemoattractant protein (MCP-1), Interleukin 1, 6, 18, TNF- α , TGF- β 1, TF, Smads, adhesion molecules and adipokines².

Monocyte Chemoattractant Protein-1 (MCP-1) is a protein produced by kidney cells in response to proinflammatory stimuli that specifically attract monocytes and macrophages⁴. High glucose levels can stimulate MCP-1 production in rat and human mesangial cells⁵. Interaction between MCP-1 and its receptor, CCR2 causes an inflammatory process that leads to mesangial cell fibrosis in the kidney⁴.

Renal epithelial cells including glomerular podocyte and tubular cells also produce MCP-1 in response to increased blood glucose^{6,7}. MCP-1 is a chemokine that attracts monocytes from the blood into the kidneys and triggers macrophage activation and releases ROS, proinflammatory cytokines (IL1, TNF alpha) and proinflammatory growth factor. The MCP-1 signal through CCR2 in mesangial cells activates the NF- κ B transcription factor and produces TGF- β 1 thereby inducing fibronectin mRNA which acts to induce the occurrence of fibrotic response in glomerular mesangial cells^{4,8}. TGF- β 1 stimulates the expression of MCP-1 in mesangial cells and allows the amplification of MCP-1⁸.

In some previous studies there was controversy in the results of MCP-1 serum. MCP-1 serum can be increased in diabetic patients. It has been found that MCP-1 serum has a significant relationship to macroalbuminuria⁹ in mice, while other studies suggest an insignificant relationship¹⁰ in Japan's populations. Researchers would like to examine the relationship of MCP-1 with diabetic nephropathy in populations in Indonesia, especially in Bali to assess its accuracy in detecting diabetic nephropathy.

Materials and Method

Patients and sample selection: This study used a cross-sectional analytical study design in patients with type 2 diabetes mellitus at the Tabanan General Hospital and Sanjiwani Gianyar General Hospital, Bali. A total of 116 subjects were included in this study. Patients were selected by consecutive sampling method with regard to the following inclusion criteria: patients with type 2 diabetes mellitus, had type 2 diabetes mellitus for at least 3 years, patients were excluded if the patient had other kidney disease (based on clinical or laboratory evidence), and patients with hematuria.

Laboratory assessments: Subjects were examined clinically and their blood drawn for blood chemistry levels, including blood urea nitrogen (BUN), serum creatinine (SC), total cholesterol and triglycerides at the laboratory of Sanjiwani Hospital and Tabanan Hospital. The patient's body weight and height were used to calculate body mass index (BMI), while serum creatinine, age, sex and body weight were used to calculate eGFR based on the formula from CKD-EPI.

Microalbuminuria examination was done by measuring the urine creatinine albumin ratio. Urine sampling was carried out in the morning as much as 10 ml and then the urine albumin level was analyzed by the immunoturbidometry method, whereas urine creatinine levels were measured by the kinetic method on the integra analyzer (Roche, Basel, Switzerland). Microalbuminuria examination was carried out at the Prodia Clinics Laboratory in Tabanan and Gianyar. The condition of diabetic nephropathy was determined by the ratio of albumin-creatinine in urine (uACR) of more than 30 mg/g.

Examination of MCP-1 serum levels was carried out at the Biochemistry Laboratory of Gadjah Mada University by R & D ELISA kit reagent. The examination was carried out according to the instructions on the ELISA kit. The collected data were analyzed statistically using independent t-test and chi square to analyze bivariately. Multivariate analysis was done by binomial logistic regression.

Results

This study involved 116 subjects with type 2 diabetes mellitus with and without diabetic nephropathy with an average age of 59.2 (9.16) years, period of diabetes 9.2 (6.04) years, and BMI of 24.9 (3, 75) kg/m². This can be seen as in table 1.

Table 1: Characteristic of Study Subject

Characteristic	N= 116
Gender (% Males)	55.2%
History of Hypertension (yes/no)	58.6%
Current Hypertension (%)	36.2%
Age in years (mean \pm sd)	59.2 \pm 9.16
Period of DM in years (mean \pm sd)	9.2 \pm 6.04
BMI (kg/m ²) (mean \pm sd)	27.2 \pm 23.99
Triglycerides (mean \pm sd)	138.8 \pm 83.08
Total Cholesterol (mean \pm sd)	190.3 \pm 46.51
eGFR ml/min/1,73 m ² (mean \pm sd)	57.2 \pm 36.84
MCP-1 (pg/ml) (mean \pm sd)	403.1 \pm 176.05

Subjects experiencing nephropathy and non-nephropathy were determined based on uACR values. UACR value ≥ 30 mg/g was considered as diabetic nephropathy (DN) while uACR<30 mg/g as non-DN. After being analyzed bivariately, several variables

showed significant results when compared between the diabetic nephropathy and non-nephropathy groups. As shown in table 2, gender, history of hypertension, current hypertension, total cholesterol, eGFR and MCP-1 serum levels have a statistically significant differences.

Table 2. Bivariate analysis of categorical and numerical variables in diabetic nephropathy

	DN (37)	Non-DN (79)	p-value
Gender			
Male (freq)	27	37	0.008*
Female (freq)	10	42	
History of Hypertension			
Yes (freq)	35	33	<0.001*
No (freq)	2	46	
Current Hypertension			
Yes (freq)	19	23	0.020*
No (freq)	18	56	
Age in years (mean ± sd)	57.4 ± 10.18	60.1 ± 8.57	0.140
Period of DM in years (mean ± sd)	10.5 ± 5.28	8.5 ± 6.31	0.099
BMI (kg/m ²) (mean ± sd)	25.6 ± 3.66	27.9 ± 28.99	0.633
Triglycerides (mean ± sd)	142.0 ± 88.51	137.7 ± 81.70	0.818
Total Cholesterol	168.0 ± 42.94	197.9 ± 45.46	0.003*
eGFR ml/min/1.73 m ² (mean ± sd)	19.0 ± 18.88	75.2 ± 28.56	<0.001*
MCP-1 (pg/ml) (mean ± sd)	556.9 ± 153.41	331.1 ± 135.51	<0.001*

Table 3 showed the results of multivariate analysis with binomial logistic regression. After the process of analyzing the model with backward elimination, a final model with two independent variables was obtained, which was eGFR and MCP-1 serum therefore these two variables is a strong predictors for diabetic nephropathy. The last model is shown in table 4.

Table 3. Results of multivariate logistic regression analysis of DN variables

	Variable	Coefficient	p	OR
Step 1 ^a	MCP-1	.026	.008	1.027
	eGFR	-.220	.013	.803
	Total Cholesterol	-.008	.684	.992
	Hypertension (Yes)	-3.797	.221	.022
	his_hyp (Yes)	1.930	.247	6.892
	Gender (Male)	1.639	.306	5.148
	Constant	-.771	.877	.463

Table 4. Final models of MCP-1 and eGFR

	Variable	Coefficient	p	OR
Step 5 ^a	MCP-1	.021	.001	1.021
	eGFR	-.176	.001	.839
	Constant	-1.069	.538	.343

Table 4 also showed that after adjusting eGFR, there was a significant association between MCP-1 and diabetic nephropathy, where each 10 unit increase of MCP-1, the likelihood of becoming nephropathy increased by 21 percent. The formula that can be drawn from the analysis above is:

$$\text{Odd Ratio Nephropathy} = e^{0.021 \text{ MCP-1} - 0.176 \text{ eGFR} - 1.069}$$

Hosmer Lemeshow of the model indicates that observed and predictive probabilities are in line (p = 0.852) which means that the model provides a good fit/prediction.

In Figure 1, it showed that the MCP-1 serum has an area under curve (AUC) of 0.886. This value was classified as very good diagnostic accuracy. These results were followed by determining the cut off point and cross tabulation analysis. Cross tab based on MCP-1 serum cut-off point 436, ie if the MCP-1 serum value was less or equal to 436 then there was no risk

of diabetic nephropathy, whereas more than 436 was risky. If the MCP-1 serum variable was supplemented with eGFR and both were included in the diagnostic test model, both of these variables cause an increase in sensitivity and specificity towards the diagnosis of diabetic nephropathy (Table 5.)

Table 5. Diagnostic indicators of MCP-1 serum compared to MCP-1 serum and eGFR for detecting diabetic nephropathy

Cut-off value	Sensitivity	Specificity	PPV	NPV	AUC
MCP-1 >436 pg/ml	83.7%	84.8%	72%	91.7%	0.886
MCP-1+eGFR > 0.500	91.9%	98.7%	97.1%	96.3%	0.989

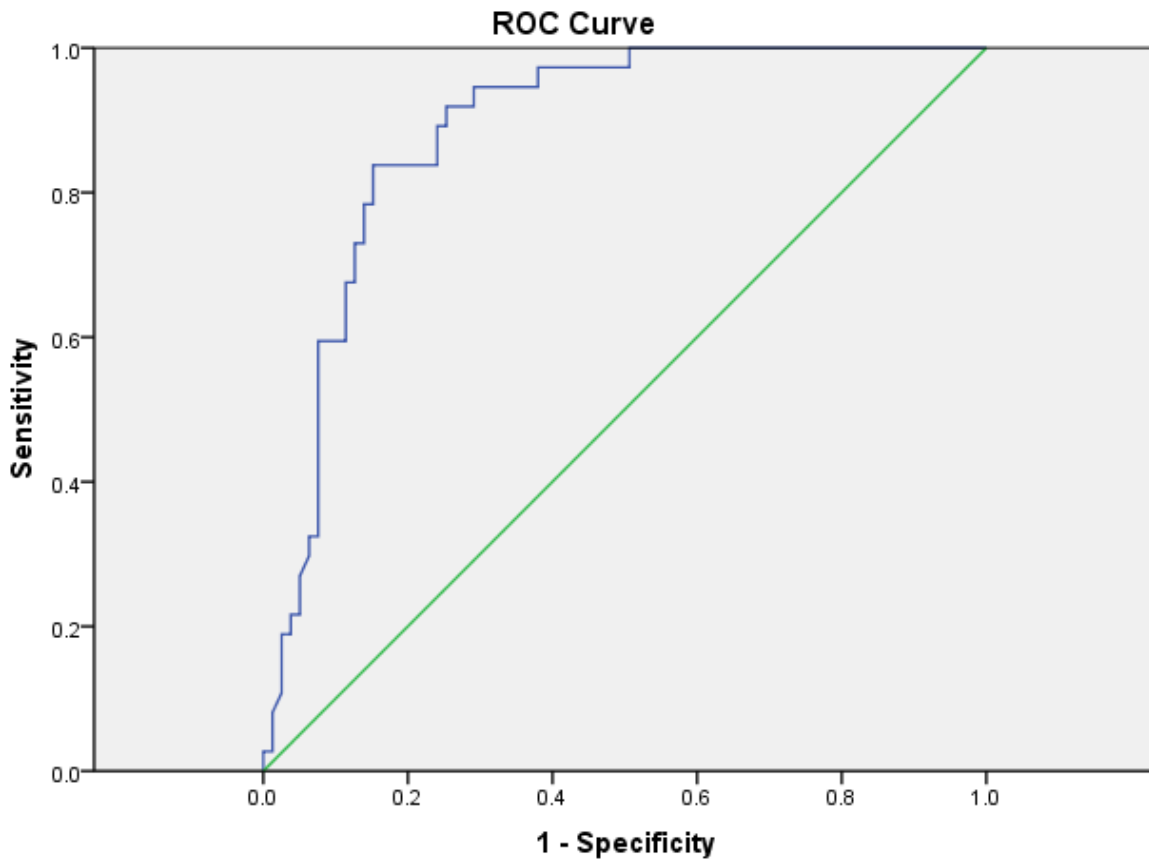


Figure 1: Receiver-operator characteristic (ROC) curves for the prediction model of MCP-1 serum in diabetic nephropathy

Discussion

CCL2/MCP-1 is expressed by various cell types. Large amounts of MCP-1 are found in endothelial cells, fibroblasts and mononuclear cells. In the kidney,

MCP-1 is produced by tubular cells, smooth muscle cells, mesangial cells, podocytes, eosinophils and mast cells. MCP-1 is produced in the kidney in response to inflammation¹¹. The released MCP-1 has the main effect of attracting other inflammatory cells. In vitro, MCP-1

concentrations can induce chemotaxis from monocytes and attract T cells and natural killer cells. In monocytes, MCP-1 induces not only chemotaxis, but also respiration bursts, rapid induction of arachidonic acid release and changes in calcium concentration. One study found that MCP-1 can reduce the survival of graft by improving the pro-inflammatory environment or MCP-1 itself can be a marker for damaged graft¹².

Diabetic nephropathy is a complication of diabetes mellitus, one of which is associated with inflammation. Several recent studies have shown that the progression of diabetic nephropathy in the affected kidney can be characterized by infiltration of inflammatory cells such as monocytes and macrophages. The macrophage infiltration releases enzymes lysozyme, NO, reactive oxygen intermediates, and TGF-beta which have been reported to play an important role in kidney damage¹³.

In this study, it was found that MCP-1 serum was a strong predictor of diabetic nephropathy, which is in line with the results of research from Takebayashi et al. in 2006 which found that MCP-1 in circulation was significantly different in subjects with macroalbuminuria compared to normoalbuminuria⁹. Although it cannot be explained, it is likely because of the expression of MCP-1 in renal macrophages can lead to an increase in systemic levels of MCP-1 which is proportional to the inflammatory and nephropathic stages. Another possibility is that MCP-1 serum levels increase in patients with early nephropathy as a result of activation of dysregulation of systemic leukocytes, although several studies showed deviant production of cytokines and inflammatory chemokines by monocytes and circulating lymphocytes in type 2 DM patients with nephropathy¹⁴.

This study found that MCP-1 serum levels could be a candidate biomarker that could further strengthen the diagnosis of diabetic nephropathy by becoming an additional examination after eGFR. eGFR which is the result of calculation of serum creatinine levels, body weight and age, has often been used to determine the stage of chronic kidney disease, but is less sensitive in predicting diabetic nephropathy, which could be the beginning of chronic kidney disease. These results are in line with research from Sinkala (2017) which found that serum creatinine, urea and microalbuminuria are biomarkers that can still be used to predict acute kidney injury and chronic kidney disease¹⁵.

Several studies have shown that MCP-1 serum levels were not significantly different from kidney

function^{16,17}. This can be caused by the number of samples in previous studies was greater and the classification of microalbuminuria into 3 groups including normoalbuminuria, microalbuminuria, and macroalbuminuria, while in this study only divided into two groups which were normoalbuminuria and albuminuria (micro and macroalbuminuria). The result differences can also be caused by the different population that used so that there were roles of ethnic, dietary and activity factors that affect metabolism in the pathophysiology of diabetic nephropathy in this study.

In conclusion, MCP-1 serum levels were significantly higher in patients with diabetic nephropathy than those without diabetic nephropathy. Additionally, MCP-1 serum correlates with uACR levels so that it can predict diabetic nephropathy in patients with type 2 diabetes mellitus. The accuracy of diagnosis and cut-off points of MCP-1 serum for detection of diabetic nephropathy has been assessed and compared with eGFR. The result showed that MCP-1 serum can be considered as a diagnostic biomarker for the detection of diabetic nephropathy and will be more accurate when supplemented with eGFR results.

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Conflict of Interest: The authors declare that there is no conflict of interests.

References

1. Nazir N, Siddiqui K, Qasim SA, Naqeb DA. Meta-analysis of diabetic nephropathy associated genetic variants in inflammation and angiogenesis involved in different biochemical pathways. *BMC Medical Genetics*. 2014;15:103-11.
2. Salgado MBD, Guerra AFR. Diabetic nephropathy and inflammation. *World J Diabetes*. 2014;5(3):393-8.
3. Ahluwalia TS, Khullar M, Ahuja M, Kohli HS, Bhansali A, Mohan V, et al. Common variants of inflammatory cytokine genes are associated with

- risk of nephropathy in type 2 diabetes among Asian Indians. *PLoS ONE*. 2009;4(4): e5168.
4. Tesch GH. MCP-1/CCL2: a new diagnostic marker and therapeutic target for progressive renal injury in diabetic nephropathy. *Am J Physiol Renal Physiol*. 2008;94:697-701.
 5. Zhang Z, Yuan W, Sun L, Szeto FL, Wong KE, Li X, et al. 1,25 Dihydroxyvitamin D3 targeting of NF- κ B suppresses high glucose-induced MCP-1 expression in mesangial cells. *Kidney International*. 2007;72:193-201.
 6. Wada T, Yokoyama H, Matsushima K, Kobayashi K. Monocyte Chemoattractant Protein-1: Does It Play A Role In Diabetic Nephropathy?. *Nephrol Dial Transplant*. 2003;18: 457-9.
 7. Hafez AAE. Microinflammation as a candidate for diabetic nephropathy. *El Mednifico Journal*. 2014;2(3):251-8.
 8. Singh V, Srivastava N, Srivastava P, Mittal RD. Impact of CCL2 and Its Receptor CCR2 Gen Polymorphism in North Indian Population: A Comparative Study in Different Ethnic Groups Worldwide. *Ind J Clin Biochem*. 2013;28(3):259-64.
 9. Takebayashi K, Matsumoto S, Aso Y, Inukai T. Association between circulating monocyte chemoattractant protein-1 and urinary albumin excretion in non-obese Type 2 diabetic patients. *J Diabetes Complications*. 2006;20:98-104.
 10. Wada T, Furuichi K, Sakai N, Iwata Y, Yoshimoto K, Shimizu M, et al. Up-regulation of monocyte chemoattractant protein-1 in tubulointerstitial lesions of human diabetic nephropathy. *Kidney Int*. 2000;58:1492-9.
 11. Haller ABH, Nadrowitz F, Menne J. Monocyte chemoattractant protein-1 and the kidney. *Curr Opin Nephrol Hypertens*. 2016;25:42-9.
 12. Ogliari AC, Caldara R, Socci C, Sordi V, Cagni N, Moretti MP et al. High levels of donor CCL2/MCP-1 predict graft-related complications and poor graft survival after kidney-pancreas transplantation. *Am J Transplant*. 2008;8:1303-11.
 13. Banba N, Nakamura T, Matsumura M, Kuroda H, Hattori Y, and Kasai K. Possible relationship of monocyte chemoattractant protein-1 with diabetic nephropathy. *Kidney International*. 2000;58:684-90.
 14. Wong CK, Ho AW, Tong PC, Yeung CY, Kong AP, Lun SW, et al. Aberrant activation profile of cytokines and mitogen-activated protein kinases in type 2 diabetic patients with nephropathy. *Clin Exp Immunol*. 2007;149:123-31.
 15. Sinkala M, Zulu M, Kaile T, Simakando M, Chileshe C, Kafita D, et al. Performance characteristics of kidney injury molecule-1 in relation to creatinine, urea, and microalbuminuria in the diagnosis of kidney disease. *Int J App Basic Med Res*. 2017;7:94-9.
 16. Niewczas MA, Ficociello LH, Johnson AC, Walker W, Rosolowsky ET, Roshan B, et al. Serum concentrations of markers of TNF α and Fas-mediated pathways and renal function in nonproteinuric patients with type 1 diabetes. *Clin J Am Soc Nephrol*. 2009;4:62-70.
 17. Murea M, Register TC, Divers J, Bowden DW, Carr JJ, Hightower, et al. Relationships between MCP-1 serum and subclinical kidney disease: African American-Diabetes Heart Study. *BMC Nephrol*. 2012;13:148.

Optimizing Bone Wound Healing Using BMP2 with BDNF in Osteoporotic Rats: Histological Evaluation

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Abstract

Background: Bone is a high vascular tissue and resilient organ with intuitive healing ability. Bone tissue contains multipotent stromal cells which have the ability to differentiate into different specialized cells. Induced stem cells have been developed by various growth factors. Using of biomaterial and growth factor is one of the most commonly used as new tissue engineering strategies.

Aim of the study: To evaluate the effect of application of a combination bone morphogenic protein 2 (BMP-2) with brain-derived neurotrophic factor (BDNF) as biomaterial to enhance bone healing in osteoporotic rat .

Materials and Method: Twenty female Wistar rat(10 normal rat and other 10 induced osteoporotic rat). Bone defects (3mm)was created in femur of each rat,one in the left side that left to heal spontaneously without any application,while the right side with application of a combination of 0.5 µl of BMP2 and 1µl of BDNF .Evaluation of histological changes includes bone cell counting and scoring of inflammation were estimated at different periods .

Results: Histological examination of Bone healing with application of BMP2 & BDNF for normal and osteoporotic rat shows formation of woven bone and bone trabeculae that filled most of bone hole with minimal inflammatory response and with a significant differences value in comparism to inapplicable bone .

Conclusion: The study concludes that application of the combination of BMP-2 & BDNF enhanced bone repair in osteoporotic rat.

Keywords: BMP-2, osteoporosis, bone defect, bone healing, BDNF, bone cells.

Introduction

Bone healing is a proliferative physiological process in which new bone formation was illustrated to fill the hole or the fracture site.^[1,2]

Three stages involved in bone healing include

1. Inflammatory phase in which blood starts to clot and forms a fracture hematoma

2. Repairing phase represents by formation of spongy bone called trabecular bone that replace the defect.
3. Bone remodeling.

Osteoporosis is one of the most common metabolic bone disorder leading to bone fractures. It is also, thought to delay or impair the regenerative response^[3,4] osteoporotic fractures remain challenging to treat that needs for new treatment protocol to increase bone regeneration capacity. Among other major risk factors, decreased expression of morphogenetic proteins has been identified for impaired fracture healing in osteoporosis^[5,6]. Studies on osteoporotic animals show atrophy of dental tissue and that this atrophy was accompanied by a reduction in the pool of osteoprogenitor cells that associated with significantly slower wound healing^[7,8].

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Combining of biomaterials such as bone morphogenetic protein 2 (BMP2) with growth factor was implicated in many advanced bone healing studies. Bone morphogenetic proteins BMPs are group of bone-inducing growth factors that used to enhance osseous repair.^[9,10]

Brain-derived neurotrophic factor (BDNF) has an influence on the establishment of the bone innervation, and might have morphogenetic effects includes modulating the proliferation or differentiation of developing bone cells^[11]. In addition, they have also been shown to act as an osteogenic and angiogenic factor, and this neurotrophin can also enhance expression of the other factor, like BMP-2, as well as the major angiogenic factor, VEGF, to promote bone formation, vascularization, and healing of the injury site.^[12]

The objective of this study was to evaluate the effect of application of a combining BMP-2 and BDNF in facilitating of bone healing in osteoporotic rat.

Materials and Method

Animals: Twenty female Wistar rats, weighting (0.25–0.30 kg), aged 4-5 months were used and kept in the animal department of (National Center of Drug Control and Research/Iraq) at a constant humidity and temperature of 23°C according to the National Council's guide for the care of laboratory animals. After 2 weeks of acclimatization, rats were randomly allocated to 4 groups (No.5 for each group), include:

Control Group includes

A: Normal rats with bone defect left to heal spontaneously .

B: Induced osteoporotic rats with bone defect left to heal spontaneously

Experimental group includes

C: Normal rats with bone defect that healed with application of BMP-2 & BDNF.

D: Induced osteoporotic rats with bone defect that healed with application of BMP-2 & BDNF .

Materials

- Recombinant bone morphogenic protein-2(rhBMP-2) Medtronic Sofamor Danek, TN/USA.
- Lyophilised BDNF protein 10µg (ab9794)/

Abcam, the protein was reconstituted in water to a concentration of 0.01mg/ml and used for experimental group

Method

Experiment on rats

Induction of osteoporosis: Ten rats were induced for osteoporosis by bilateral ovariectomy, and after 2 weeks postoperatively, the animals were received a systemic daily I.M injection of methylprednisolone hemisuccinate (MPH) at dose (1 mg/kg) for 4 consecutive week.

Surgical procedure: Six weeks after ovariectomy, rats were anaesthetized generally with a mixture of ketamine (50 mg/kg) with xylazine (2.5 mg/kg). Surgical technique was performed in rat femur to prepare two drill-holebone defects (3mm). The left femur was considered for the control group(A & B) of normal and osteoporotic .The holes were left to heal spontaneously without any application, just washed by normal saline and dried gently by air and closed the overlying tissue while the right side was considered for the experimental group(C & D).The holes were restored as previously described but with application of a combination of 0.5 µl of BMP2 and 1 µl of BDNF, using micro-pipette, allowed for one minute before closing.

Note: Determination of effective dose for BMP2/BDNF depends on previous studies.^[13,14]

Histopathological preparation and analysis:

The animals were sacrificed by an overdose of carbon dioxide gas after surgical operation at the periods (7th & 28th day).

Specimen retrieval: Bone hole along with their surrounding bone were excised with a surgical saw right away following the euthanasia. The excess tissue was dissected and the specimens were removed with a margin of surrounding bone of about 5–10 mm. The specimens were immediately put into the 10% formaldehyde solution.

Sample preparation for embedding: The specimens were decalcified, washed and then dehydrated in the ascending graded ethanol solution. Specimens were embedded in wax block and trimmed, the first undefined slice was removed from the saw blade of the sliding microtome (RM2255, Leica Biosystems, Wetzlar, Germany) and the desired serial sections 5-µm

thickness were selected. Mounting and staining of slides by hematoxylin and Eosin (H & E). The stained sections were blindly evaluated by a trained investigator who was previously calibrated with an experienced pathologist. Under a light microscope (Olympus BX53, Olympus, Tokyo, Japan), all samples were evaluated and scored in terms of:

- 1) inflammatory cell infiltration, 2) bone cells

According to Mestreneur et al (2003)^[15], the quantitation of intensity of inflammatory response at 7th day was evaluated by counting them in visual field (X10, X20, X40) with subsequent of arithmetic mean for each specimen as follow:

Intensity of inflammatory reaction

- I. Absent or very few inflammatory cell.
- II. Mild average number less than 10 inflammatory cells.
- III. Moderate average number 10-25 inflammatory cells.
- IV. Severe average number greater than 25 or necrosis.

Counting No. Of bone cells (osteoblast, osteocyte and osteoclast) for the periods (7th & 28th day) was done too.

Statistical method: Mean values and standard deviations were calculated for the number of bone cells at different groups and periods with multiple Comparisons by (LSD Method) among all pairs of effect's Parameters. Frequency and percentage of inflammatory response in different groups was recorded. P value <0.05 was considered significant.

Findings

Histological findings revealed the followings: Bone healing for **normal rat (control)** shows bone trabeculae and osteoid tissue at 7th day, and at 28th day shows bone trabeculae filled 2/3 of bone defect. Figure, 1(A & B).

Bone healing for **normal rat with application of BMP2 & BDNF (experimental)** shows formation of woven bone, bone trabeculae surrounds by active osteoblast at 7th day, and at 28th day shows bone

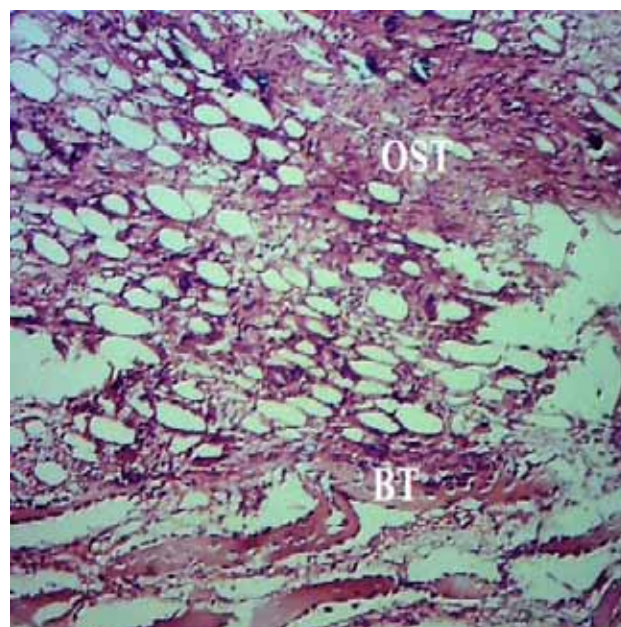
trabeculae filled approximately the whole bone defect coalesce with basal bone. Figure, 2(A, B & C).

Bone healing for **osteoporotic rat (control)** shows resorptive bone with osteoclast cells with presences of inflammatory cell at 7th day, and at 28th day a thin sparse bone trabeculae with fibrous tissue was illustrated in figure, 3(A & B).

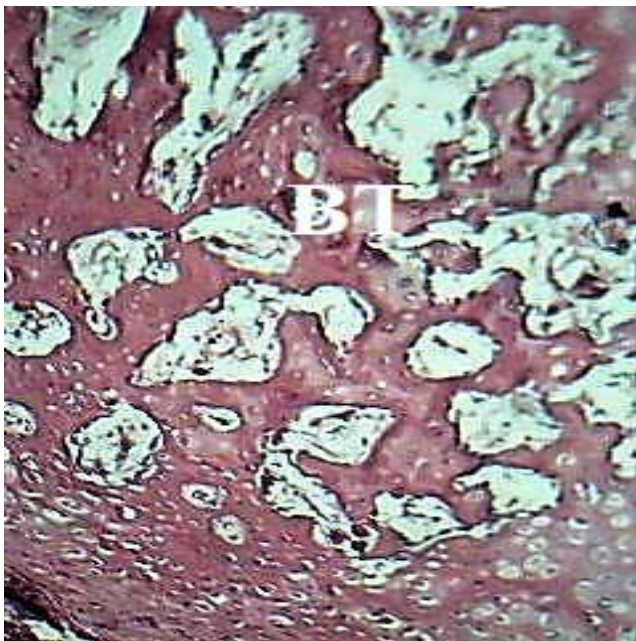
Bone healing for **osteoporotic rat with application of BMP2 & BDNF (experimental)** shows bone trabeculae, woven bone with osteoblast and osteocyte at 7th day, and at 28th day a thin bone trabeculae filled approximately 1/2 of bone defect. Figure, 4(A & B).

Statistical analysis revealed a high significant difference for bone cell count in comparison of normal with osteoporotic, while a non significant difference was recorded between the normal control and the osteoporotic experimental. On other hand, number of whole cells at 7th and 28th day show a significant differences in comparison of normal with osteoporotic. Table (1).

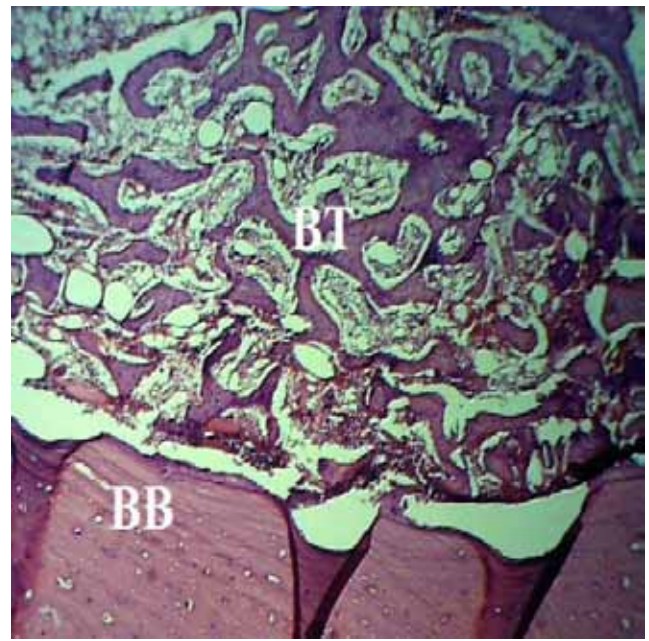
Frequency and percentage of inflammatory response in different groups at 7th day shows a significant to high significant difference values in comparison of normal and osteoporotic in control and experimental, respectively. Table (2).



A

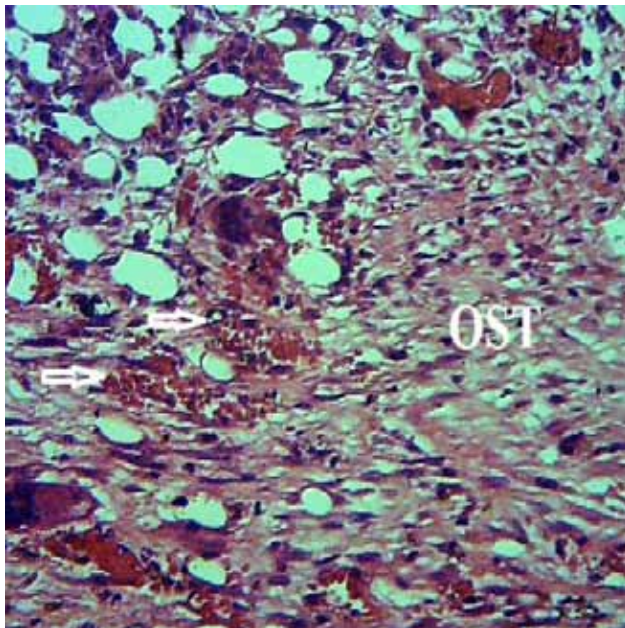


B

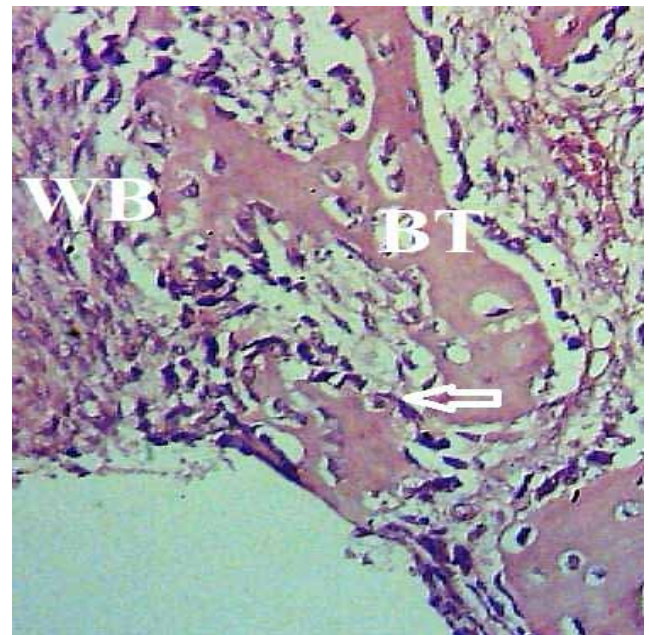


B

Figure 1: Bone healing for normal rat (control) without any application for 7 & 28 day
A. View for bone healing at 7 day shows bone trabeculae (BT), and osteoid tissue (OST) formation. H & Ex4
B. View for bone healing at 28 day shows bone trabeculae (BT) filled 2/3 of bone defect. H & Ex10

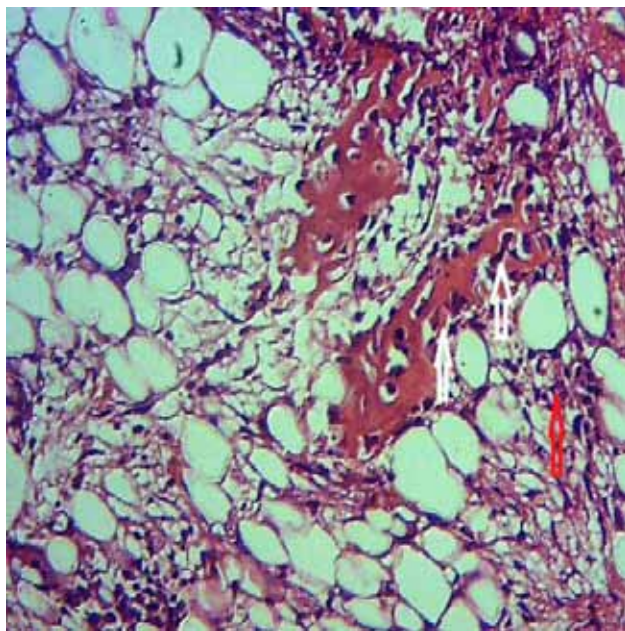


A

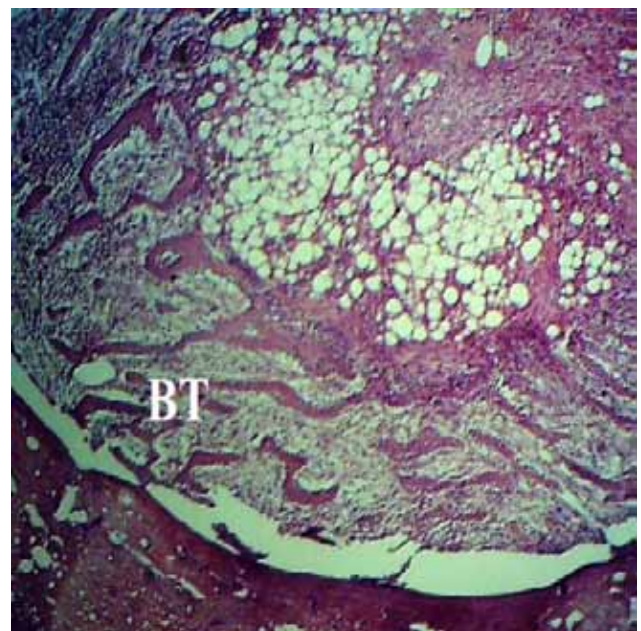


C

Figure (2): Bone healing for normal rat with application of BMP2 & BDNF for 7,28 day period
A. View for bone healing at 7 day shows osteoid formation (OST) with newly blood vessels (arrows). H & Ex10
B. Other view shows formation of woven bone (WB), bone trabeculae (BT) surrounded by osteoblast (arrow). H & Ex20
C. View for bone healing at 28 day shows bone trabeculae (BT) filled approximately the whole bone defect coalesce with basal bone (BB) around. H & Ex4



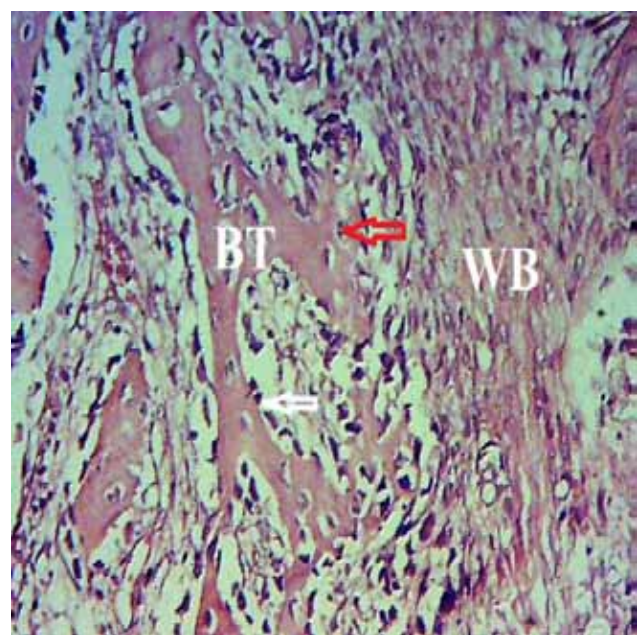
A



A



B



B

Figure(3): Bone healing for osteoporotic rat without any application for 7,28 day periods A.View for bone healing at 7day shows resorptive bone with osteoclast (white arrow), inflammatory cells(red arrow). H & Ex10 B.View for bone healing at 28 day shows thin sparse bone trabeculae (BT) and fibrous tissue (FT).H & Ex4

Figure(4)Bone healing for osteoporotic rat with application of BMP2 & BDNF for 7,28 day period A.View for bone healing at 7 day shows bone trabeculae(BT),osteoblast(white arrow),osteocyte(red arrow) and woven bone(WB).H & Ex10 B.View for bone healing at 28 day shows thin bone trabeculae (BT) filled approximately 1/2 of bone defect.H & Ex4

Table (1): Statistic analysis of the number of bone cells with multiple Comparisons by (LSD Method)at different groups and periods

Types of Bone cells at diff. Periods	Groups	No.	Mean	Std. Dev.	Std. Error	95% C. I. for Mean		Min.	Max.
						Lower Bound	Upper Bound		
Osteoblast 7th day	Control normal	5	7.00	0.63	0.26	6.34	7.66	6	8
	Normal (with BMP2 & BDNF)	5	14.67	1.06	1.47	13.31	15.02	13	16
	Control osteoporosis	5	4.33	1.08	1.07	3.05	4.62	3	5
	Osteoporosis (with BMP2 & BDNF)	5	8.83	1.33	0.54	7.44	9.23	7	10
Osteoblast-28th day	Control normal	5	13.7	0.82	0.33	11.81	14.52	12	15
	Normal (with BMP2 & BDNF)	5	18.50	1.52	0.64	16.91	19.09	17	20
	Control osteoporosis	5	3.17	0.33	0.54	2.77	3.56	3	4
	Osteoporosis (with BMP2 & BDNF)	5	9.83	0.97	0.40	7.80	9.87	8	10
Osteocyte-7th day	Control normal	5	4.50	0.54	0.34	3.62	5.38	4	6
	Normal (with BMP2 & BDNF)	5	7.00	1.10	0.86	6.80	8.20	6	9
	Control osteoporosis	5	2.17	0.62	0.33	1.81	3.52	1	4
	Osteoporosis (with BMP2 & BDNF)	5	5.83	0.73	0.54	4.44	6.23	5	7
Osteocyte-28th day	Control normal	5	7.50	0.84	0.34	5.62	8.38	5	9
	Normal (with BMP2 & BDNF)	5	9.83	1.40	0.98	7.31	10.35	7	11
	Control osteoporosis	5	2.33	0.43	0.42	1.25	3.42	1	4
	Osteoporosis (with BMP2 & BDNF)	5	6.67	0.71	0.49	5.40	7.94	5	8
Osteoclast-7th day	Control normal	5	0.50	0.03	0.02	0.5	1.5	0	1
	Normal (with BMP2 & BDNF)	5	1.33	0.52	0.21	0.79	1.88	1	2
	Control osteoporosis	5	2.50	0.53	0.22	1	2.78	1	3
	Osteoporosis (with BMP2 & BDNF)	5	1.17	0.05	0.11	0.75	1.88	1	2
Osteoclast-28th day	Control normal	5	0.33	0.02	0.01	0.22	1.88	0	2
	Normal (with BMP2 & BDNF)	5	0.27	0.02	0.10	0.19	0.88	0	1
	Control osteoporosis	5	2.33	0.52	0.21	1.33	2.98	1	3
	Osteoporosis (with BMP2 & BDNF)	5	0.8	0.12	0.11	0.44	1.88	0	2

Factors Bone Cells No. in groups LSD test			Sig. (*)	C.S.
Groups	Control normal	Normal with (BMP2 & BDNF)	0	**HS
		Control osteoporosis	0	**HS
		Osteoporosis (with BMP2 & BDNF)	0.98	NS
	Normal (with BMP2 & BDNF)	Control osteoporosis	0	**HS
		Osteoporosis (with BMP2 & BDNF)	0	**HS
	Control osteoporosis	Osteoporosis (with BMP2 & BDNF)	0	**HS
Periods	No. of cells Day 7	Normal/osteoporotic	0	**HS
	No. Of cells Day 28	Normal/osteoporotic	0.049	*S

**P<0.01High significant (HS), *P<0.05 significant (S)

Table (2): Frequency and percentage of inflammatory response in different groups at 7th day

Groups	Inflammatory score				X2	Likelihood ratio	d.f.	P-value
	I	II	III	IV				
Control normal	2(40%)	2(40%)	1(20%)	0(0%)	10	11.77	3	*0.04(S)
Normal with BMP2 & BDNF	4(80%)	1(20%)	0(0%)	0(0%)				
Control osteoporosis	0(0%)	1(20%)	2(40%)	2(40%)	7.6	10.7	3	**0.001(HS)
Osteoporosis with BMP2 & BDNF	2(40%)	2(40%)	1(20%)	0(0%)				

**P<0.01High significant (HS), *P<0.05 significant (S)

Discussion

The present results show that application of a combination of BMP-2 and BDNF as biomaterial for bone defect induce new differentiation of osteogenic stem cell into osteoblast cell that apposed woven bone with enhancement of process of minerlization .Bone trabeculae was found to fill approximately the whole bone defect for the normal and about 1/2 of bone hole in osteoporotic rats.

Many studies found that BMP-2 provides a strong signal for differentiation of osteoblastsand an over expression of BMP2 can promote fracture healing and osteogenic ability in senile osteoporotic fractures through activating the BMP/Smad signaling pathway^[16,17].

Animal studies related to post-menopausal estrogen deficient osteoporosis had shown healing to be prolonged with decreased levels of mesenchymal stem cells (MSCs) and decreased levels of angiogenesis^[18,19,20].

In present study application of neurotrophin (BDNF) effects on vascular endothelial growth factor VEGF that enhances vascularization and promotes bone formation

The application of combination of BMP-2 & BDNF illustrates that many events has been affected including the recruitment and differentiation of (MSCs) to osteoblast cell andenhancement of angiogenesis with new blood vessels formationin the early bone healing with minimal inflammatory responseand finally formation bone that filled the defect.^[21,22]

The present study records frequency and percentage of inflammatory response at 7th day that shows a significant difference value in comparism of normal with osteoporotic,and furthermore,in exp.osteoporotic rat illustrates a decrease in inflammatory cell score in response to presence of BMP-2 & BDNF in bone defect.

Conclusions:The present findings implied that application of combination of BMP-2 & BDNFin osteoporotic bone healing,act as inductive agent that initiates the differentiation of osteoblast cell and formation of new bone and could be taken into consideration when designing a biomaterial for inducing osteogenic tissue engineering.Further researchers should focus on this important topic and provide more data in this field in order to enable a sound clinical use of these materials in osteoporotic subjects.

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Conflict of Interest: Nil

Source of Funding: By ours

Ethical Clearance: All work of this study had done according to the National Council's guide for the care of laboratory animals.

References

1. Cheng G, Yin C, Tu H, Jiang S, Wang Q, Zhou X, Xing X, Xie C, Shi X, Du Y, Deng H, Li Z. Controlled Co-delivery of Growth Factors through Layer-by-Layer Assembly of Core-Shell Nanofibers for Improving Bone Regeneration. *ACS Nano*. 2019 Jun 25;13(6):6372-6382.
2. Li F, Yu F, Liao X, Wu C, Wang Y, Li C, Lou F, Li B, Yin B, Wang C, Ye L.Efficacy of Recombinant Human BMP2 and PDGF-BB in Orofacial Bone Regeneration: A Systematic Review and Meta-analysis.*Sci Rep*. 2019 May 30;9(1):8073.
3. Mathavan N, Turunen MJ, Guizar-Sicairos M, Bech M, Schaff F, Tägil M, Isaksson H. The compositional and nano-structural basis of fracture healing in healthy & osteoporotic bone. *Sci Rep*. 2018 Jan 25;8(1):1591.
4. Van Lieshout EM, Alt V.Bone graft substitutes and bone morphogenetic proteins for osteoporotic fractures: what is the evidence? *Injury*. 2016 Jan;47 Suppl 1:S43-6.
5. Chen CH, Wang L, Serdar Tulu U, Arioka M, Moghim MM, Salmon B, Chen CT, Hoffmann W, Gilgenbach J, Brunski JB, Helms JA.An osteopenic/osteoporotic phenotype delays alveolar bone repair. *Bone*. 2018 Jul;112:212-219.
6. Iizuka T, Miller SC, Marks SC .Alveolar bone remodeling after tooth extraction in normal and osteopetrotic (ia) rats. *Jr.J Oral Pathol Med*. 1992 Apr; 21(4):150-5.
7. Arioka M, Zhang X, Li Z, Tulu US, Liu Y, Wang L, Yuan X, Helms JA.Osteoporotic Changes in the Periodontium Impair Alveolar Bone Healing.*J Dent Res*. 2019 Apr; 98(4):450-458. Epub 2019 Jan 9.
8. Bykova NI, Sirak SV, Kobylkina TL, Odolsky AV, Bykov IM, Arutyunov AV. [Optimization

- of reparative dentinogenesis in experimental osteoporosis]. *Stomatologia (Mosk)*. 2017;96(6):4-8.
9. Wang X, Matthews BG, Yu J, Novak S, Grcevic D, Sanjay A, Kalajzic I. PDGF Modulates BMP2-Induced Osteogenesis in Periosteal Progenitor Cells. *JBMR Plus*. 2019 Jan 15;3(5):e10127.
 10. Durham EL, Howie RN, Hall S, Larson N, Oakes B, Houck R, Grey Z, Steed M, LaRue AC, Muise-Helmericks R, Cray J. Optimizing bone wound healing using BMP2 with absorbable collagen sponge and Talymed nanofiber scaffold. *J Transl Med*. 2018 Nov 21;16(1):321.
 11. Skaper SD. The biology of neurotrophins, signalling pathways, and functional peptide mimetics of neurotrophins and their receptors. *CNS Neurol Disord Drug Targets*. 2008; 7(1):46-62.
 12. Al hijazi A, Ali M, Hasan D, Al shamma A. Pulp response capped by BDNF. *Indian Journal of Public Health Research & Development*, January 2019;10(1):740-745.
 13. Al hijazi A, Al-Mahammadawy A, Al rifae E, et al. Association of application of BMP4 with expression of BMP7 in rat bone repair. *Indian Journal of Public Health Research & Development*, March 2019;10(3):359-363.
 14. Al hijazi A, Al rifae E, Akram Z, Kaka L. Acceleration of Socket Healing by Using Placental Collagen with BDNF: Radiological and Histological Studies. *Indian Journal of Public Health Research & Development*, July 2019, 10(7);740-745.
 15. Mestreneur, SR., Holland, R., Dezan, E. Influence of age on the behavior of dental pulp of dog teeth capping of adhesive system. *Dental Traumatology* 2003;19(5):255-61.
 16. Cho, YD., Yoon, WJ., Woo, KM., Baek, JH., Park, JC., Ryoo, HM. The canonical BMP signaling pathway plays a crucial part in stimulation of dentin sialophosphoprotein expression by BMP-2. *J Biol Chem*. 2010;285(47):36369-76.
 17. Ariffin, SH., Manogaran, T., Abidin, IZ., Wahab, RM, Senafi, S. A Perspective on Stem Cells as Biological Systems that Produce Differentiated Osteoblasts and Odontoblasts. *Curr Stem Cell Res Ther*. 2017;12(3):247-259.
 18. Cheung WH, Miclau T, Chow SK, Yang FF, Alt V. Fracture healing in osteoporotic bone. *Injury*, 2016;47 Suppl 2:S21-6.
 19. Huang K, Wu G, Zou J, Peng S. Combination therapy with BMP-2 and psoralen enhances fracture healing in ovariectomized mice. *Exp. Ther. Med*. 2018;16(3):1655-1662.
 20. Wu, J., Wang, Q., Han, Q., Zhu, H., Li, M., Fang, Y., Wang, X. (2019) Effects of Nel-like molecule-1 and bone morphogenetic protein 2 combination on rat pulp repair. *J Mol Histol*. 2019;50(3):253-261.
 21. Harada S, Rodan GA. Control of osteoblast function and regulation of bone mass. *Nature*. 2003;423:349-355.
 22. Ralston SH, de Crombrughe B. Genetic regulation of bone mass and susceptibility to osteoporosis. *Genes & Development*. 2006;20:2492-2506.

Macronutrients Analysis in *Ipomoea Batatas L. Poiret* as an Alternative Food in Improving Nutritional Adequacy of Pregnant Women

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Abstract

Background: Adequacy of nutritional intake in pregnant women is needed in order to deliver healthy babies. Inability to provide nutritional needs due to financial problems is a common issue. Diversification of cheap and affordable food is needed for pregnant women so they will be avoided for various pregnancy complications. The objectives of this study are conducting a nutritional content analysis of *Ipomoea batatas L. poiret* as an alternative food to improve the nutritional status of pregnant women as well as examine the pattern of macronutrient consumption during pregnancy with the growth of the pregnancy.

Method: There are two designs used in this study (1) a field quantitative with completely randomized design, a laboratory experimental design, and (2) retrospective correlational design with cross-sectional study. The study samples are *Ipomoea batatas* and pregnant women in the second and third trimester with simple random sampling. Data analyses used in this study are proximate analysis in *Ipomoea batatas* and chi-square in pregnant women.

Results: The macronutrients content of 100 gr dry *Ipomoea batatas* are 84.08 carbohydrates, 1.00 gr proteins, and 2.22gr fats. Macronutrient consumption analysis obtained p-value 0.03 for carbohydrates, 0.02 for proteins, and 0.14 for fats which means that there is a correlation between carbohydrates, proteins, and fats with an increase of body mass index in pregnant women.

Conclusion: *Ipomoea batatas* can be an alternative macronutrient source for mother's needs during pregnancy.

Keywords: *Ipomoea batatas*, nutrition, pregnant women.

Introduction

Issues in nutrition are still a major public health problem in Indonesia⁽¹⁾⁽²⁾. Malnutrition in mothers and babies has contributed to around 3.5 million deaths annually and approximately 11% of disease globally as well as reaching 30% of the total world population⁽³⁾⁽⁴⁾. According to Ethiopian Demographic and Health Survey

(EDHS) for developing countries, the malnutrition problem in Kerala (India) is around 19%, while same number of 34% in Bangladesh and the slums area of Dhaka⁽⁵⁾. Anemia during pregnancy and chronic energy deficiency (CED) are an impact of malnutrition and can increase the risk of born prematurely and low birth weight babies⁽⁴⁾⁽⁶⁾.

Basic health research (riskesdas) in Indonesia (2013) showed that CED is still the main problem in pregnant women since there is a 7.2% increase in the prevalence from 31.3% in 2010 to 38.5% in 2013⁽⁷⁾⁽⁸⁾. The main cause of chronic energy deficiency in pregnant women is an unbalance between the need for food during pregnancy and food intake in sufficient quantities⁽⁹⁾⁽¹⁰⁾

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with several indirect factors are socioeconomic, short birth interval, parity or number of babies born, early age of first pregnancy, and low education⁽¹¹⁾.

Mothers need adequate nutrition during pregnancy. Diversification of cheap and affordable food is needed to avoid various pregnancy complications⁽¹⁰⁾⁽¹²⁾. Nutritional needs that must be fulfilled include energy, protein, vitamins, folic acid, calcium, iron, iodine, zinc, flour, and its amounts must be adjusted to the gestational age⁽¹²⁾⁽¹³⁾.

Rice consumption standards according to Food and Agriculture Organisation is 60-65 kg/capita/year⁽⁵⁾⁽¹⁴⁾⁽¹⁵⁾. The national social-economic survey by the Indonesian central bureau of statistics (2017) reported that Indonesian people consume 114.6 kg/capita/year of rice from 2002 to 2017, that is why Indonesia is categorized as Asia's number one consumption of rice as a staple food. This number needs to be reduced by decreasing the dependence on rice consumption through diversifying food consumption⁽⁴⁾⁽¹⁵⁾.

Ipomoea batatas is one of the main sources of carbohydrates and has an important role in providing an alternative food and opportunity to replace rice as the main foodstuff of Indonesian people⁽¹⁶⁾⁽¹⁷⁾. The concept of food source substitution will have an important role in food diversification and can be processed into a variety of products that can encourage the development of agro-industry⁽¹⁸⁾⁽¹²⁾. One of the benefits of products made from *Ipomoea batatas* is improving the nutritional adequacy of pregnant women since it contains vitamin A, C, E, betacarotene, magnesium, potassium and antioxidants⁽¹⁹⁾.

This study aims to conduct a nutritional content analysis of *Ipomoea batatas L. poiret* as an alternative food to improve the nutritional status of pregnant women as well as examine the pattern of macronutrient consumption during pregnancy with the growth of the pregnancy.

Material and Method

a. Study design and setting: There are two designs used in this study (1) a field quantitative with completely randomized design, a laboratory experimental design to identify macronutrients content in *Ipomoea batatas*, (2) retrospective correlational design with cross-sectional study to assess macronutrients consumption habits in

pregnant women by food frequency questionnaire (FFQ) for 3 months related to pregnancy growth through body mass index (BMI).

b. Sample: The main sample in this study was *Ipomoea batatas* with two times of test in a fresh and dried condition in the form of flour.

1. Materials and tools to analyze macronutrient contents in *Ipomoea batatas*.

The materials used in this study were local *Ipomoea batatas* which have been washed with tap water. The chemicals used were HCl (Merck), NaOH (Merck), aquadest, H₂SO₄ (Merck), Na₂SO₄ (Merck), K₂SO₄ (Merck) and n-Hexan (Merck). Tools used in this study were scales, knives, plastic containers, slicers, abrasion peeler, dryer cabinet, 80 mesh sifter, freeze dryer, and oven. The tools for physic and chemical identification were analytic scale, spectrophotometer UV-VIS 200S, and HPLC waters e2695 separations module.

2. **Women pregnancy:** Macronutrients consumption habits assessment in pregnant women were those in the second and third trimester with the criteria including the mothers do not experience with hyperemesis, chronic infections, and willing to join assessment program for daily nutritional consumption for the last 3 months. The sampling technique used in this study was simple random with the number of participants were 100 pregnant women in the district of Jember-Indonesia.

c. Data collection and instrument: Data collection techniques are carried out using a structured interview form and questionnaire about sociodemographic characteristics, pregnancy history, and food consumption during pregnancy. Daily macronutrient consumption habits collected using FFQ which was modified to assess eating habits in the last 3 months. BMI of mothers obtained through weight and height measurement.

d. Data analysis:

1. **Analysis of *Ipomoea batatas* for laboratory experimental design** Laboratory testing is carried out using proximate analysis in *Ipomoea batatas* to identify macronutrient content.

2. **Analysis of micronutrients consumption in pregnant women** Statistical analysis used in this

study is chi-square to assess the consumption habits of macronutrients in pregnant women with a BMI.

Findings

- 1. Study result in Ipomoea batatas:** Proximate analysis in this study used to identify carbohydrate, protein, and fat content in 100 gram *Ipomoea batatas L.*

Table 1. Macronutrients composition in 100 grams *Ipomoea batatas* by proximate analysis

No	Macronutrient content	Fresh <i>Ipomoea batatas</i>			Dry <i>Ipomoea batatas</i>		
		UI 1	UI 2	Rata2	UI 1	UI 2	Rata 2
1	Carbohydrate (gr)	25.80	25.18	25.49	84.00	84.16	84.08
2	Fat (gr)	0.4	0.6	0.5	0.94	1.07	1.00
3	Protein (gr)	0.70	0.90	0.80	2.31	2.14	2.22

Ipomoea batatas also has macronutrients such as carbohydrates, protein, and fats which needed to help the growth of the fetus. Based on proximate laboratory tests it was found that the highest carbohydrate content was found in dried *Ipomoea batatas* with an average rate of 84.08 grams. While the fat composition of about 1% in dried *Ipomoea batatas* and 2.22 grams of dried *Ipomoea batatas* protein content.

2. Study result in pregnant women

a. Respondent characteristics

Table 2. Respondent characteristic based on age, education level, occupation of mother, and pregnant status (n=100)

Variables	n	Percentage
Age of mothers		
< 20 years old	24	24
20-30 years old	57	57
> 30	19	19

Variables	n	Percentage
Education level		
Elementary school	17	17
Junior high school	47	47
Senior high school	23	23
College	3	3
Occupation		
Housewife	65	65
Private sector	16	16
Labor	19	19
Pregnant status		
Primigravida	49	49
Multigravida	51	51

Based on the frequency data, it was found that most of the pregnant women were 20-30 years of age, junior high school education and were not working.

b. Macronutrient consumption analysis with the growth of pregnancy

Table 3. Carbohydrate consumption with body mass index (n=100)

BMI	Carbohydrate consumption		Total	OR95% CI	P value
	Not fulfilled	Fulfilled			
Not appropriate	75	25	100	4.286	0.03
Appropriate	41.2	58.8	100	1.683-10.9127	
Total	52	48	100		

There is a relationship between carbohydrate consumption with BMI of pregnant women with OR 4.286 that means the mothers whose carbohydrate

consumption patterns are not fulfilled have a 4.286 times chance of having an appropriate BMI.

Table 4. Fat consumption with body mass index (n=100)

BMI	Fat consumption		Total	OR95% CI	P value
	Not fulfilled	Fulfilled			
Not appropriate	46.9	53.1	100	3.403	0.14
Appropriate	20.6	79.4	100	1.370-8.453	
Total	29	71	100		

There is a relationship between fat consumption with BMI in pregnant women and OR analysis found that mothers whose fat consumption was not fullfiled had a 3.403 times chance of having an appropriate BMI.

Table 5. Protein consumption with body mass index (n=100)

BMI	Protein consumption		Total	OR95% CI	P value
	Not fulfilled	Fulfilled			
Not appropriate	45,1	54,9	100	4,371	0,02
Appropriate	19,6	80,4	100	1,76 - 10,857	
Total	29	71	100		

There is a relationship between protein consumption with BMI and OR analysis found that mothers whose protein consumption was not fulfilled had the opportunity to have 4.37 times appropriate BMI.

Discussion

Macronutrients are substances needed by the body in large numbers to provide direct energy⁽²⁰⁾⁽²¹⁾. In pregnant and lactating women, intake of macronutrients acts as forming organs and fetal cells⁽¹⁴⁾⁽²¹⁾. The results of this study about macronutrient consumption habits in mothers showed an association with pregnancy growth as measured by BMI⁽²²⁾⁽²³⁾. Macronutrients are very important in pregnant women to get balanced nutrition and growth of the fetus⁽²⁴⁾⁽²⁵⁾. Rice is the number one consumption of Indonesian people as a staple food, even though there are many cheaper and have complete nutritional content from other sources of macronutrients.

Ipomoea batatas is one of Indonesia’s agricultural products which has high carbohydrate content to provide the nutritional needs of pregnant women⁽¹⁸⁾⁽¹⁶⁾. Mothers need additional 300 kcal of nutrients per day during pregnancy from macro and micronutrients⁽²⁶⁾⁽¹²⁾. Additional macronutrient requirements are 20 gr/day protein, 10 gr/day fat and 40 gr/day carbohydrate.84.08 grams carbohydrate content in 100 grams dry *Ipomoea batatas* is bigger than in fresh one that just 25.49 grams. The increased in macronutrients need during pregnancy is used to provide the need for metabolic changes and fetal growth⁽¹⁵⁾. This result suggests that *Ipomoea*

batatas is very potential to replace rice as a source of food. Carbohydrate has an important role to maintain circulation and protein synthesis during pregnancy⁽¹⁹⁾⁽²⁷⁾. Anemia during pregnancy and CED can increase the risk of born prematurely and low birth weight babies⁽²⁸⁾⁽⁴⁾.

Ipomoea batatas also has protein content that needed for fetal growth as well as a source of calories, synthesis of enzymes and hormones, muscles and other body tissues, blood cell formation, growth of the placenta and brain development⁽⁶⁾⁽¹²⁾. The result of proximate analysis showed that dry *Ipomoea batatas* has 2.22 grams/100 gram protein content which can help to provide 15% of protein needs. Indicator for the maternal protein adequacy assessment can be measured through maternal weight and fetal growth⁽²⁹⁾. Chronic energy and protein deficiency during pregnancy can reduce the nucleus in both DNA and RNA that affect to disruption of the maternal nutrients transfer to the fetus and lead to low birth weight babies and intra uteri growth retardation (IUGR)⁽⁹⁾⁽²⁹⁾.

Fat, especially omega 3 and 6 are important to increase birth weight and fetal growth as its main role in providing metabolic energy. Saturated and unsaturated fatty acids have resulted from fat metabolism⁽⁹⁾⁽³⁰⁾. Docosahexaenoic acid (DHA) and arachidonic acid (AA) is a long-chain unsaturated fatty acid derived from diffused lipids and useful for the growth and development of the fetus⁽²⁾⁽¹⁵⁾. *Ipomoea batatas* which has an optimal content of fat indicates that this food is safe for pregnant

women daily consumption since the result of proximate analysis is 1 gram/100 grams fat content⁽²⁷⁾⁽¹⁶⁾.

Ipomoea batatas is local food sources that are able to be an alternative food source in providing the adequacy of nutrition in pregnant women⁽⁵⁾. The complete macronutrient content and some of the micronutrient contents in *Ipomoea batatas* make this food feasible and safe for pregnant women to consume and can be a food substitute for rice⁽³¹⁾⁽²⁹⁾.

Conclusion

As a cheap source of carbohydrates, *Ipomoea batatas* have great potential as ingredients that can provide the nutrition of mothers during pregnancy. *Ipomoea batatas* also has macronutrients such as carbohydrates, protein, and fats which needed to help the growth of the fetus.

Statistically showed that there is a significant relationship between macronutrient consumption of pregnant women with fetal growth as measured by BMI.

Conflict of Interest: None

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Ethical Clearance: This study has passed and got an ethic approval (No: 1142/II.3.AU/FIKES/O/2019) from Faculty of Health Science University of Muhammadiyah Jember. To ensure confidentiality, the research sample data is given a code number.

References

1. Khalafallah AA, Dennis AE. Iron deficiency anaemia in pregnancy and postpartum: Pathophysiology and effect of oral versus intravenous iron therapy. *J Pregnancy*. 2012;2012.
2. Who, Chan M. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Geneva, Switz World Heal Organ [Internet]. 2011;1–6. Available from: <http://scholar.google.com/scholar?hl=en & btnG=Search & q=intitle:Haemoglobin+concentrations+for+the+diagnosis+of+anaemia+and+assessment+of+severity#1>
3. Sahu SK, Bhat BV, Sarkar S, Roy G, Joseph N. Malnutrition among under-five children in India. 2015;6(1):18–23.
4. Retni R, Margawati A, Widjanarko B. Pengaruh status gizi & asupan gizi ibu terhadap berat bayi lahir rendah pada kehamilan usia remaja. *J Gizi Indones*. 2017;5(1):14.
5. Yadav S, Chandramouli V. International Journal of Allied Medical Sciences and Clinical Research (IJAMSCR) Prenatal Nutrition: Nutrient recommendations Before, During & After. 2013;1(1):1-7.
6. Desta M, Akibu M, Tadese M, Tesfaye M. Dietary Diversity and Associated Factors among Pregnant Women Attending Antenatal Clinic in Shashemane, Oromia, Central Ethiopia: A Cross-Sectional Study. *J Nutr Metab*. 2019;2019:7–10.
7. Timur J. Kesehatan 13. 2014;
8. Kemenkes. INFO DATIN, Pusat Data Dan Informasi Kementerian Kesehatan RI. 2015.
9. Prawita A, Susanti AI, Sari P. Survei Intervensi Ibu Hamil Kurang Energi Kronik (Kek) Di Kecamatan Jatinangor Tahun 2015. *J Sist Kesehat*. 2017;2(4):186–91.
10. Depkes R. Departemen Kesehatan Republik Indonesia. 2006;
11. Syari, Serudji & M. Peran Asupan Zat Gizi Makronutrien Ibu Hamil terhadap Berat Badan Lahir Bayi di Kota Padang. *J Kesehat Andalas*. 2015;4(3):729–36.
12. Hasyim A, Yusuf M. Diversifikasi Produk Ubi Jalar sebagai Bahan Pangan Substitusi Beras. 2008;(1):3–5.
13. Health Service Executive. CLINICAL PRACTICE GUIDELINE Nutrition for Pregnancy Institute of Obstetricians and Gynaecologists, Royal College of Physicians of Ireland and Directorate of Clinical Strategy and Programmes, Health Service Executive Guideline No . 27 Date of publication. 2016;(27):1–48. Available from: <https://rcpi-live-cdn.s3.amazonaws.com/wp-content/uploads/2016/05/22.-Nutrition-during-Pregnancy.pdf>
14. Chen X, Zhao D, Mao X, Xia Y, Baker PN, Zhang H. Maternal dietary patterns and pregnancy outcome. *Nutrients*. 2016;8(6):1–26.
15. Nagari RK, Nindya TS. Tingkat Kecukupan Energi, Protein Dan Status Ketahanan Pangan Rumah Tangga Berhubungan Dengan Status Gizi Anak Usia 6-8 Tahun Levels Adequacy of Energy and Protein and Household Food Security Status with Nutritional Status of Children Aged 6-8 Years. *Amerta Nutr*. 2017;189–97.

16. Sangrai PC, Santosa I, Winata AP, Sulistiawati E. Kajian Sifat Kimia dan Uji Sensori Tepung Ubi Jalar Putih Hasil. 2016;3:55–60.
17. Hamid Y, Setiawan B, Suhartini. Analisis pola konsumsi pangan rumah tangga (Studi kasus di Kecamatan Tarakan Barat Kota Tarakan Provinsi Kalimantan Timur). *Agrise*. 2013;13(3):175–90.
18. Zuraida N, Supriati Y. Usahatani Ubi Jalar sebagai Bahan Pangan Alternatif dan Diversifikasi Sumber Karbohidrat. *Bul AgroBio*. 2001;4(1):13–23.
19. Nurhalimah L. Kandungan Gizi Dan Daya Terima Makanan Tambahan Ibu Hamil Trimester Pertama. *Food Sci Culin Educ J*. 2012;1(1):16–23.
20. Marangoni F, Cetin I, Verduci E, Canzone G, Giovannini M, Scollo P, et al. Maternal diet and nutrient requirements in pregnancy and breastfeeding. An Italian consensus document. *Nutrients*. 2016;8(10):1–17.
21. Brion MJA, Ness AR, Rogers I, Emmett P, Cribb V, Smith GD, et al. Maternal macronutrient and energy intakes in pregnancy and offspring intake at 10 y: Exploring parental comparisons and prenatal effects. *Am J Clin Nutr*. 2010;91(3):748–56.
22. Zuhairini Y, Kasmanto H, Nugraha GI. Indeks Massa Tubuh Awal Kehamilan Ibu sebagai Indikator yang Paling Berperan terhadap Kenaikan Berat Badan Ibu Selama Hamil. *Maj Kedokt Bandung*. 2016;48(3):171–5.
23. Model P, Pembangunan I. Pengembangan Model Indeks Pembangunan Gizi. *KESMAS - J Kesehat Masy*. 2013;8(2):166–75.
24. Mecacci F, Biagioni S, Ottanelli S, Mello G. Nutrition in pregnancy and lactation: how a healthy infant is born. *Jpnim* [Internet]. 2015;4(2):1–14. Available from: <http://www.jpnim.com/index.php/jpnim/article/view/040236>
25. Warriner S. Pregnancy and body mass index (BMI). *Oxford Univ Hosp*. 2016;50.
26. Mousa A, Naqash A, Lim S. Macronutrient and Micronutrient Intake during Pregnancy: An Overview of Recent Evidence. *Nutrients*. 2019;11(2):1–20.
27. Santiago SE, Park GH, Huffman KJ. Consumption habits of pregnant women and implications for developmental biology: A survey of predominantly Hispanic women in California. *Nutr J* [Internet]. 2013;12(1):1. Available from: *Nutrition Journal*
28. Gebreweld A, Tsegaye A. Prevalence and Factors Associated with Anemia among Pregnant Women Attending Antenatal Clinic at St. Paul’s Hospital Millennium Medical College, Addis Ababa, Ethiopia. *Adv Hematol*. 2018;2018.
29. Wibowo N, Bardosono S, Irwinda R, Syafitri I, Putri AS, Prameswari N. Assessment of the nutrient intake and micronutrient status in the first trimester of pregnant women in Jakarta. *Med J Indones*. 2017;26(2):109–15.
30. Kulkarni B, Christian P, LeClerq SC, Khattry SK. Determinants of compliance to antenatal micronutrient supplementation and women’s perceptions of supplement use in rural Nepal. *Public Heal Nutr*. 2010;13(1):82–90.
31. Knudsen VK, Orozova-Bekkevold IM, Mikkelsen TB, Wolff S, Olsen SF. Major dietary patterns in pregnancy and fetal growth. *Eur J Clin Nutr*. 2008;62(4):463–70.

Association of Prothrombin G20210A Mutation with Unexplained Recurrent Pregnancy Loss

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Abstract

Purpose: To assess the relationship of Prothrombin G20210A gene mutations as a risk factor for idiopathic repeated pregnancy loss. The focus has been on Prothrombin G20210A mutation that may predispose women to microthrombosis during the stages of embryo implantation and placentation.

Method: A total of 70 women with recurrent pregnancy loss, mean age 31.1±4.2 years, were involved in the study. As a control group, 70 women [mean age 32.2±3.3 years with at least two live-born child and no history of abortion] were included. We used real-time polymerase chain reaction (PCR) to determine the frequencies of Prothrombin G20210A genotype.

Results: The frequency of heterozygotes for *F2* was significantly higher in women with repeated pregnancy loss compared to women without abortion ($p = 0.0001$).

Conclusion: In summary we found an association of prothrombin G20210A mutation with recurrent pregnancy loss. We recommend for prothrombin G20210A screening in cases with repeated pregnancy loss so they can start anticoagulant therapy more earlier.

Keywords: Prothrombin G20210A; pregnancy; PCR.

Introduction

Recurrent miscarriage (RM) -defined by ESHRE guideline as ≥ 2 consecutive pregnancy losses before 20 weeks post menstruation affects approximately 1% of couples trying to conceive⁽¹⁾. Current diagnostic procedures can identify etiologic factors in approximately 50% of these couples, such as uterine defects, advanced woman age, parental karyotype abnormalities, embryonic aneuploidies, infections and thrombophilia disorders^(2,3). While the role of acquired thrombophilia

has been accepted as an etiology of RM, the contribution of specific inherited thrombophilic genes to this disorder has remained controversial⁽⁴⁾.

The balance between coagulation and fibrinolysis is an essential part in early pregnancy, and thrombophilia has been postulated to be a contributor to the pathophysiology of recurrent pregnancy loss. Pregnancy is a hypercoagulable state with an increase in procoagulant factors and a decrease in the levels of anticoagulants⁽⁵⁾.

Among the causes of these adverse pregnancy outcomes, three in particular are considered as the major factors of recurrent pregnancy loss and other adverse pregnancy outcomes including: (i) structural and numerical chromosomal abnormalities, (ii) inflammatory and autoimmune disorders, and (iii) allelic polymorphisms of some pro-thrombophilic genes⁽⁶⁾.

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Mutation G20210A in 3' untranslated region of Prothrombin gene is associated with an increase level of plasma Prothrombin and consecutive excessive thrombin generation⁽⁷⁾. The aim of this study was to investigate association of prothrombin G20210A with recurrent pregnancy loss in a group of women of the Egyptian population.

Study Design:

Patients: This study included 70 patients who were selected from the Gynecological and Obstetric Clinic, Faculty of Medicine, Minia University Hospital, Minia, Egypt during the period from December 2018 to June 2019. Patients were further categorized into two Subgroup **Ia**, had the following characters: 23 women with history of two consecutive recurrent pregnancy loss and subgroup **Ib** 47 women with history of more than two times abortions either consecutive or not.

We Included women with two or more recurrent pregnancy loss consecutive or not before 20 weeks gestation and excluded women having Anti phospholipid antibody syndrome, Diabetes mellitus, chronic liver disease, chronic kidney disease, patients with thyroid diseases, dyslipidemia, local uterine abnormalities, patients with polycystic ovary syndrome or luteal phase defect and patients with self-induced abortion.

The control group consisted of 70 apparently healthy women with matched age to the patient group attended to the same institutions for regular follow up. They had normal obstetric history with no history of abortion. All subjects volunteered to participate in the study. They were subjected to thorough history taking, clinical and radiological examination, Routine laboratory investigations included blood count, Prothrombin concentration (PC) and INR, activated partial thromboplastin time (PTT), Special laboratory investigations involved: Lupus anticoagulant screening test (PTT LA), D-Dimer and qualitative analysis of prothrombin gene A20210G.

Method

All participants were screened for antiphospholipid syndrome by sensitive APTT reagent (KACZOR D.A., BICKFORD N.M 1992), The kit was supplied by DIAGNOSTICA STAGO SAS, France. The reading was obtained via (CoaDATA2001, Germany). The principle of the PTT-LA test is based on the measurement of plasma recalcification time in the presence of cephalin

and activator. The presence in the test plasma of lupus anticoagulant prolongs the clotting time. Sensitization of the reagent specially enhances the prolongation of the clotting time due to the LA in the plasma.

All participants were screened for any thrombophilic manifestation or presence of microthrombus through D-Dimer. It was measured by enzyme immunoassay method (EIA) by Humareader plus 3700-1272 Germany. The kit was supplied by Wuhan EIAab Science Co., Ltd, China.

Principle: The micro-titer plate provided in this kit has been pre-coated with an antibody specific to D-Dimer. Standards and samples are then added to the appropriate micro-titer plate wells with a biotin conjugated antibody preparation specific for the target protein. Next, Avidin conjugated to Horseradish Peroxidase (HRP) is added to each microplate well and incubated. Then a TMB substrate solution is added to each well. Only those wells that contain target antigen, biotin-conjugated antibody and enzyme-conjugated Avidin will exhibit a change in color. The enzyme-substrate reaction is terminated by the addition of sulphuric acid solution and the color change is measured spectrophotometrically at a wave length of 450 nm. The concentration of D-Dimer in the samples is then determined by comparing the optical density (O.D.) of the samples to the standard curve.

Molecular study: DNA extraction was performed using PROBA-NA DNA mini kit from DNA-Technology company. One ml in ethylene diamine tetra acetic acid (EDTA) containing tube for genotyping technique. DNA extraction was done from fresh whole blood samples then DNA was stored at -20 °C till amplification by real time PCR.

Real time PCR was performed using TaqMan Gene Expression Assays followed by melting curve analysis, The Kit were supplied by DNA-TECHNOLOGY (catalog no.334-1), Russia.

Procedure: The following were left to thaw, completely re-suspended by doing gentle vortex, then were briefly centrifuged to bring liquid to the bottom of the tube: Taq-AT-polymerase, DNA samples, Probes, PCR buffer. The required number of 0.2 mL PCR-tubes were marked for each mutation to be tested. The PCR master mix was prepared as following:

For each sample, the following were pipetted into a nuclease free 1.5 mL microcentrifuge tube:

- 10×(N+1) µL of PCR-buffer;
- 0.5×(N+1) µL of Taq-AT-polymerase;

N—number of the marked tubes.

20 µL of corresponding PCR-mix were added into the marked tubes . Vortex of the tubes with PCR-buffer and Taq-AT-polymerase were performed for 3-5 seconds, then spinning for 1-3 seconds was done to collect the drops.10 µL of PCR-buffer and Taq-AT-

polymerase mixture was added into each PCR-tube. Then 20 µL of mineral oil were added in each PCR-tube. The tubes were closed tightly .Finally, each tube was opened and 5.0 µL of DNA sample were added into corresponding PCR-tubes, then the tube was closed again before proceeding to the next DNA sample . The tubes were spun for 1–3 seconds to collect the drops.

The tubes were set to Real-time PCR instrument (DNA-TECHNOLOGY, Russia).

Genotypes and melting temperatures (only for DT*lite* or DT*prime* instruments)

Polymorphism	Homozygote Fam/Fam			Homozygote Hex/Hex			Heterozygote		
	Genotype	Fam, °C	Hex, °C	Genotype	Fam, °C	Hex, °C	Genotype	Fam, °C	Hex, °C
F2: 20210 G>A	GG	58.2	46.5	AA	50.0	57.8	GA	57.1	56.3

Content:	
Reagent	Quantity
PCR-mix	
1. F2: 20210 G>A	960 µL 1 tube
2. F5: 1691 G>A (Arg506Gln)	960 µL 1 tube
PCR-buffer	480 µL 2 tubes
Taq-AT-polymerase	48 µL 1 tube
Mineral oil	960 µL 2 tubes

Dye label detection channels corresponding to allelic variants and IC					
PCR -mix	Fam	Hex	Rox	Cy5	Cy5.5
F2: 20210 G>A	G	A	-	IC	-

Prothrombin A20210G genotyping by REAL-TIME PCR

Statistical analysis: The collected data were tabulated and analyzed by Statistical Package for Social Sciences program (SPSS) software version 20. Descriptive statistics were done for numerical variables by mean, standard deviation, median and interquartile range, while they were done for qualitative variables by number and percentage.

Mann-Whitney test was used to determine the statistical difference between the two groups for normally distributed quantitative variables and independent samples **t-test** for not normally distributed quantitative variables. **Fisher’s exact** were used to determine the statistical difference between the two groups for **Prothrombin A20210G gene** variable.

Pearson’s and **Spearman’s** correlation were used

to correlate between different variables. According to (r) ranged from (0±1), the degree of correlation was determined (0-0.24 weak, 0.25-0.49 fair, 0.5-0.74 moderate and ≥0.75 strong). The level of significance was taken at **p value** less than or equal to 0.05 as significant.

Results

All groups in our study showed similar age There was no statistical significant difference between the studied groups as regard age (p=0.08). Frequency of abortion among cases ranged from 2-10 times with mean ± SD 3.6±1.8,while the control group (group II) had no abortion . There was highly statistical significant difference between the studied groups as regarding frequency of abortion (p=0.0001*).

Table (1): Comparison between studied groups regarding HB, WBCs and platelets.

	Group I N=70	Group II N=70	P value
HB: (g/dl)			
Mean ± SD	12.1±0.9	12.4±1.1	0.1
Median	12	12.5	
Range	10-14.8	10-15	
WBCs: (×10³/μl)			
Mean ± SD	6.8±2.1	6.5±1.7	0.4
Median	6.7	6.2	
Range	4-12	4-10.8	
PLT: (×10³/μl)			
Mean ± SD	282.5±60	281.5±62	0.8
Median	279.5	283	
Range	167-400	153-400	

Regarding HB, WBC's and platelet count, there was no statistical significant differences were found between the studied groups (p= 0.1,0.4,0.8 respectively).

Table (2): Comparison between studied groups as regarding PC, INR and aPTT.

	Group I N=70	Group II N=70	P value
PC:%			
Mean ± SD	93.5±8.4	87.1±9	0.0001*
Median	99	88	
Range	72-100	70-100	
INR			
Mean ± SD	1.04±0.05	1.09±0.07	0.0001*
Median	1	1.08	
Range	1-1.17	1-1.25	
aPTT :(Sec)			
Mean ± SD	30.1±5.9	27.3±3.6	0.008*
Median	29.4	27.8	
Range	18.6-41	17.9-38.6	
PTT.LA: (Sec)			
Mean ± SD	32.9±5.1	30.9±3.5	0.01*
Median	33.1	30.9	
Range	21.3-39.5	22.3-37.9	
D.Dimer:(ng/ml)			
Mean ± SD	40.5±83.9	24±24.8	0.03*
Median	9.7	13.5	
Range	5.3-400	5-106	

Prothrombin concentration in group I ranged from 72-100% with mean ± SD93.5±8.4, In group II prothrombin concentration ranged from 70-100% with mean ± SD87.1±9. There was statistically significant difference between the studied groups (p=0.0001).

INR showed statistically significant increase in group II when compared with group I (p=0.0001).

Activated partial thromboplastin time in group I ranged from 18.6 -41 second with mean ± SD 30.1±5.9. In group II it was ranged from 17.9-38.6 second with mean ± SD 27.3±3.6. There was statistically significant increase in group I when compared with group II as regarding the aPTT (p=0.008).

Partial thromboplastin time lupus anticoagulant

in group I ranged from 21.3-39.5 second with mean \pm SD 32.9 \pm 5.1. In group II it was ranged from 22.3-37.9 second with mean \pm SD 30.9 \pm 3.5. Partial thromboplastin time lupus anticoagulant showed statistically significant increase in group I when compared with group II (p=0.01).

D. Dimer in group I ranged from 5.3-400 ng/ml with mean \pm SD 40.5 \pm 83.9, in group II it was ranged from 5-106 ng/ml with mean \pm SD 24 \pm 24.8. There was statistically significant increase in group I when compared with group II as regarding D. Dimer (p=0.03).

Table (3) Comparison between both groups as regarding Prothrombin A20210G expression

	Group I N=70	Group II N=70	p value
Pro thrombin A20210G Wild			
G/G	57 (81.4%)	70 (100%)	0.0001*
Heteromutant A/G	13 (18.6%)	0 (0%)	

The expression of prothrombin A20210G was higher in group I in comparing with group II as 13 cases of group I (18.6%) were heteromutant (A/G) while group II were all wild type (A/A). There was statistically significant increase in the expression of prothrombin A20210G mutation in group I when compared with group II (p=0.0001).

We compared HB, WBCs, platelets, PC., INR., aPTT., PTTLA., and D. Dimer between group I subgroups (Ia and Ib) there were no statistical significant difference between group I subgroups (p= 0.5,0.3,0.5 0.4,0.5,0.2, 0.8,0.1) respectively.

Table (4) Comparison between group I subgroups (Ia and Ib) as regarding Prothrombin A20210G expression .

	Group Ia N = 23	Group Ib N = 47	P value
ProthrombinA20210G Wild			
G/G	23 (100%)	34 (72.3%)	0.003*
Heteromutant A/G	0 (0%)	13 (27.7%)	

ProthrombinA20210G mutation was higher in group Ib when compared with group Ia as 13 cases (27.7%) of group Ib were heteromutant (A/G) while the group Ia were all wild type (A/A). There was statistically significant increase in the expression of prothrombin A20210G mutation in group Ib when compared with group Ia (p=0.003).

Discussion

We examined the relationship between unexplained RPL and thrombophilia gene mutations.

Spiral artery thrombosis and infarction occurs, and as a result of these, uteroplacental insufficiency may be the final common pathophysiologic pathway in RM and

later pregnancy complications associated with inherited thrombophilia become possible^[8].

A central factor of coagulation cascade is coagulation factor II or thrombin coded by prothrombin gene. Its precursor is prothrombin which is cleaved and thus activated through the action of coagulation factor X⁽⁹⁾. It may increase the risk for pregnancy loss but many individuals heterozygous or homozygous for the 20210G>A polymorphism never develop thrombosis, while most heterozygotes who develop thrombotic complications remain asymptomatic until adulthood⁽¹⁰⁾.

In our study we found that the prevalence of ProthrombinA20210G mutation was higher in the studied cases in comparing with the control group

as 13 cases (18.6%) were heteromutant (A/G) while the control group were all wild type (A/A) and it was statistically significant in cases when compared with the control group ($p=0.0001$). Although Sehirali et al. ⁽¹¹⁾ found the association between the F2 20210A allele and pregnancy loss in Turkish women ($p < 0.05$). Also Finanet al. ⁽¹²⁾ reported that 13.64% of women with recurrent pregnancy loss carried the Prothrombin G20210A mutation, compared to 2.99% carrier rates among control group which was statistically significant. Similarly a study made by Pihuschet al. ⁽¹³⁾ reported that heterozygous Prothrombin G20210A mutation is more common in patients with abortions in the first trimester.

In our study prothrombinA20210G mutation was higher in group IB in comparing with group IA as 13 cases (27.7%) were heteromutant (A/G) while the control group were all wild type (A/A). This was in agree with Barut M.U. et al ⁽¹⁴⁾ who reported that when patients with 2 prothrombin G20210A heterozygous abortions and patients with 3 or more abortions were compared.

In the other hand Pickering et al. ⁽¹⁵⁾ reported that the prevalence of the G20210A Prothrombin mutation is not increased in women with recurrent pregnancy loss, although it was only found in women who had suffered early pregnancy losses. Finally, a literature review performed by Ghee et al. ⁽¹⁶⁾ claimed that there is no evidence to support an association of Prothrombin G20210A mutation with RM.

Conclusion

Prevalence of prothrombin gene mutations is significantly increased in patients having recurrent miscarriages.

The Institutional Ethics Committee approved this study of the School of Medicine, Minia University, Egypt, and all patients gave informed consent before participation in this study. The study conducted in accordance with the ethical guidelines of the 1975 Declaration of Helsinki and International Conference on Harmonization Guidelines for Good Clinical Practice.

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References

1. Jauniaux E, Farquharson RG, Christiansen OB,

Ex- alto N. Evidence-based guidelines for the investigation and medical treatment of recurrent miscarriage. *Hum Reprod.* 2006;21:2216-22.

2. Rai R, Regan L. Recurrent miscarriage. *Lancet.* 2006; 368(9535):601-11.

3. Rubio C, Pehlivan T, Rodrigo L, Simón C, Remohí J, Pellicer A. Embryo aneuploidy screening for unexplained recurrent miscarriage: a minireview. *Am J Reprod Immunol.* 2005;53(4):159-65.

4. Bradley LA, Palomaki GR, Bienstock J, Varga E, Scott JA. Can factor V Leiden and prothrombin G20210A testing in women with recurrent pregnancy loss result in improved pregnancy outcomes: Results from a targeted evidence-based review. *Genet Med.* 2012;14(1):39-50.

5. Kyu Ri Hwang, Young Min Choi, Jin Ju Kim, Sung Ki Lee, Kwang Moon Yang, Eun Chan Paik, Hyeon Jeong Jeong. Methylenetetrahydrofolate Reductase Polymorphisms and Risk of Recurrent Pregnancy Loss: a Case-Control Study. *J Korean Med Sci.* 2017 Dec; 32(12): 2029–2034.

6. Vesna Livrinova, Marija Hadzi Lega, Anita Hristova. Factor V Leiden, Prothrombin and MTHFR Mutation in Patients with Preeclampsia, Intrauterine Growth Restriction and Placental Abruption. *Journal of Medical Sciences.* 2015 Dec 15; 3(4):590-594.

7. Nada Aracic, Damir Roje, Ivana Alujevic Jakus. The Impact of Inherited Thrombophilia Types and Low Molecular Weight Heparin Treatment on Pregnancy Complications in Women with Previous Adverse Outcome. *Yonsei Med J.* 2016 Sep 1; 57(5): 1230–1235.

8. Kujovich JL: Thrombophilia and pregnancy complications. *Am J Obstet Gynecol,* 2004 191:412–424.

9. Dizon-Townson D, Miller C, Sibai B. The relationship of factor V Leiden mutation and pregnancy outcomes for mother and fetus. *Obstet Gynecol.* 2005;106:517-24.

10. Bouvier S, Cochery-Nouvellon E, Lavigne-Lissalde G. Comparative incidence of pregnancy outcomes in thrombophilia positive women from the NOH-APS observational study. *Blood.* 2014;123:414.

11. Sehirali S, Inal MM, Yildirim Y, Balim Z, Kosova B, Karamizrak T. Prothrombin G20210A mutation in cases with recurrent miscarriage: A study of the mediterranean population. *Arch Gynecol Obstet*

- 2005;273(3):170-3.
12. Finan RR, Tamim H, Ameen G. Prevalence of factor V G1691A (factor V-Leiden) and prothrombin G20210A gene mutations in a recurrent miscarriage population. *Am J Hematol*; 2002; 71:300–305.
 13. Pihusch R, Buchholz T, Lohse P. Thrombophilic gene mutations and recurrent spontaneous abortion: prothrombin mutation increases the risk in the first trimester. *Am J Reprod Immunol*; 2001, 46:124-131.
 14. Barut M.U. Thrombophilia and recurrent pregnancy loss, 2018; 24: 4288-4294.
 15. Pickering W, Marriott K, Regan L. G20210A prothrombin gene mutation: prevalence in a recurrent miscarriage population. *Clin Appl ThrombHemost*; 2001, 7:25–28.
 16. Ghee CB, Burrows RF. Prothrombin G20210A mutation is not associated with recurrent miscarriages. *Aust N Z J ObstetGynaecol*; 2002, 42:167–169.

The Role of Trust and Social Networking in the Use of Long Term Contraception Method in Kampung KB

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Abstract

The demographic bonus is a nation's challenge that needs to be managed. Data from the Department of Population Control, Women's Empowerment and Child Protection (DP5A) shows in 2016 the new long term contraception method user in Surabaya City reached 7.70%, in 2017 to 5.16%, and 36.29% in 2018 of the total contraception method participants from every year. The data shows that there is an increase of member of long term contraception method. The new member of long term contraception method in 2018 is 63.71%, greater than short term contraception method. Utilize of long term contraception method in 2018 is increase, but it cannot compete with short term contraception method especially injection contraceptive method. This research is a descriptive study using a qualitative approach using a phenomenological study approach. Data collection is held at Kampung KB and non-Kampung KB Tambaksari District of Surabaya City. Informants in this study consisted of key informants and informants. Trust and social networking are used as an effort to improve the family planning program in utilizing a long term contraception method at Kampung KB. While trust and social networking have not been utilized to improve family planning program in utilizing a long term contraception method at non-Kampung KB.

Keywords: *trust, social networking, family planning.*

Introduction

Demographic bonus is a nation's challenge that needs to be managed. Indonesian projected population was estimated at 5% every five years. National Medium-Term Development Plan (RPJM) has a target to be achieved at Population Control Family Planning for five years, which is to realize Balanced Growing Population (PTS) with the achievement of Total Fertility Rate 2,1 in 2019⁽¹⁾. It shows that there is a health-oriented development will be carried out by the government to control population growth. Development as an effort for people's welfare in terms of population growth regulation is manifested in reproductive health, one of which is family planning.

The seventh target of Sustainable Development Goals third objective explains that by 2030 ensuring universal access for sexual and reproductive health services, including for family planning, information,

education, and integrating reproductive health into strategies and national programs⁽²⁾.

Kampung KB is stands for Kampung Keluarga Bencana (Village of family planning), Kampung KB as a forum that can be used to overcome problems that arise related to an area based on studies that have been identified previously. active participation of the community is key to implementing empowerment. The program incorporated in the Kampung KB as an implementation of the integration of existing programs in improving the welfare of the community. The cross-sector role in the concept of health-oriented development is expected to be able to make a positive contribution to the formation of the environment and healthy behavior.

Data of 2017 SDKI about birth planning based on the age of womans giving birth in 2017 is known that the age of womans is 35-39 years who want to have children 75.2% and have children later 6.4%, the age of 40-44

years old womans who want to have children soon 63,4% and have children then 3,5%, womans aged 45-49 years who want to have children 59,0% and have children later 5,5%⁽¹⁾. This shows the desire to have children is still high both who want to have children immediately and who want to have children later. Therefore the need for pregnancy planning so that family planning can be achieved. Long term contraception method as an appropriate contraceptive tool to control pregnancies namely implants and Intra Uterine Device (IUD).

Data from the Department of Population Control, Women's Empowerment and Child Protection (DP5A) shows that in 2016 the new long term contraception user in Surabaya was 7,70%, in 2017 decrease to 5,16%, and in 2018 there were 36,29% of the total contraception method participants from every year. The data shows that there is an increase in new long term contraception user. The new contraception method user in 2018 is still greater in use at short term contraception method, which is 63,71% of contraception method participants⁽³⁾. Participation in the Family Planning Program shows that there needs to be support and further efforts to be able to encourage and improve the achievements of the long term contraception method.

Popularity of the way of work and the effectiveness of the long term contraception method are still lacking compared to short term contraception method. The usage of long term contraception method in 2018 has increased, but it is still less than short term contraception method, especially the method of injection contraception. Based on this background the researchers wanted to described more through about the role of trust and social networking in usage of long term contraception method in Kampung KB of Surabaya City.

Materials and Method

This research is a descriptive study using a qualitative approach using a phenomenological study approach. Place of data collection in Kampung KB and non Kampung KB Tambaksari District Surabaya City. Informants in the study consisted of informants and key informants by taking data through indepth interviews. Data analysis techniques through the process of selection, focusing, simplifying, and abstraction that is done during the research process takes place through the selection of data. So, the data can be more concise and can be classified in one or more patterns. Drawing conclusions through data triangulation in the form of focus group discussion.

Result

Each couples of reproductive age has a person who is trusted in obtaining information about family planning. Couples who use long term contraceptive method believe that the person who provided the information needed. The following are statements from several informants:

"Cadres who understand about family planning have experience here. Initially I consulted about complaints using injection contraception method. Then the cadre suggested giving an IUD. I got an explanation from the cadres. Cadres in this village also did not hesitate to assist couples who wanted to use contraception" (W1).

"Cadres are trusted people who provide information about family planning. Because cadres have experience handling family planning. The cadre assured me not to be afraid to use the implants, and this was an comfort birth control program" (W2).

Most of couples are aware that family planning is needed, especially financial and physical readiness that can affect to their life. Traditions that have been expanded by the generation in the selection of contraception make couples used to be a role model. Couples makes succes of the family planning program by helping people who want to use the long term contraception method as a form of maintaining tolerance.

Short term contraception method informants in non-Kampung KB claimed that the cadre leader had convinced to use long term contraception method in cadre associations only. The informant's fear was because some friends who had been asked about the IUD had failure of that device that caused an unplanned pregnancy. This makes informants not use contraceptives, especially long term contraception method. Other reasons for not using contraception are incompatibility with previous contraceptive device and fear of using other contraceptives. The following supporting quotes are based on discussion forums:

"Sometimes at PKK group meetings there is a information about the installation of contraception is free of charge. Leader of PKK gave that information about free charge of contraception, but rarely gave out information of contraceptive method. I have never known information about family planning" (SK, FGD7).

Trust in long term contraception method in couples can be obtained based on knowledge. Couples knowledge comes from information held through

learning or experience from others. Couples who do not use long term contraception method have no knowledge about long term contraception method. Family planning counselors from DP5A said that popular contraceptive method in the community are pills and injection contraception. Couples feel embarrassed and afraid to use long term contraception method. Challenges in the selection of contraceptives were also conveyed by DP5A Surabaya that indeed the use of contraceptives in the community requires attention. The selection of the right method is promoted through the Kampung KB's program. Following are supporting statements from key informants:

"The main thing is that trust needs to be utilized as a strength in society. Special attention is needed so that people can choose the right method. Most people, carelessly choose the method of contraception. The common ones are injections, pills, that's all. From the data, we can see interest in method for short-term contraception method is more than long-term contraceptive method, especially injection" (HAI).

Community organizations or groups that exist in the Kampung KB are able to provide easy access to all couples regarding long term contraception method. Most informants mentioned that there are community associations that often discuss about family planning at the Posyandu at the Family Empowerment and Welfare Association (PKK: Pemberdayaan dan Kesejahteraan Keluarga). In addition to explaining the choice of contraception, socialization also facilitates the data collection of Couples who want to use the long term contraception method. The following is a supporting statement from informan:

"There is a family empowerment and welfare group, the PKK, and also a Posyandu, usually the leader of the small group of family (RT: RukunTetangga) and their cadres. Every 1 month there is a PKK meeting and it is always announced about family planning. Those involved in the selection of contraceptive method are cadres, leader of medium group of family (RW :RukunWarga), and of course couples who want to use an IUD and implants. Cadres also often collect data door to door at their neighbours and offer couples to use longterm contraception method" (W4).

Whereas community organizations or groups in the non-Kampung KB just giving of information when they need to carried out surveillance of free of charge

of contraception installation. Short term contraception method informants mentioned that they had never used and knew of the failure of family planning in their social networks, so they were not satisfied. Non contraception method participant informants also conveyed the same thing related. Non contraception method participant social network that has experienced a case of family planning failure. Social networks in non-Kampung KB have not been utilized in an effort to increase the use of long term contraception method. The following is a quote that supports the statement:

"Usually during PKK meetings, cadres provide information on who wants to use implantable contraceptive method and IUD. Just like that, so offer installation of contraceptive method. Nothing is explained again" (WA2).

Family planning counselors stated that there were differences in family planning activities. The Kampung KB often gets program exposure. Whereas program in non-Kampung KB is less than the KB family. Following the supporting statements from key informants:

"Indeed different. In the Kampung KB, they have active cadres, the family planning program is indeed focused there. That's why in Kampung KB there is more exposure to the community. Kampung KB receives funds that are used to provide stimulus through a series of activity agendas to solve problems in the village. Many activities carried out in the Kampung KB such as monitoring, meetings, and various cadre support training. This is one of them being used to accelerate the use of long-term contraceptive method in couples" (NIM).

Discussion

The use of long term contraception is an effort to manage pregnancy plan in family planning. Pregnancy planning needs to be done so that pregnancy becomes the desired process and is carried out with good planning. The use of long term contraception method is also like using other contraceptives as a preventive program in family planning so that it can reduce the number of deaths due to problems in pregnancy, childbirth, and unsafe abortion, prevent pregnancy too early, and distance the pregnancy⁽⁴⁾.

Trust as a dimension in social capital has a role in providing the value of mutual trust between community members and the community. Trust is the determinant

of social relations, as the smallest belief needed to start social interaction. The role of trust is decisive in social society.

Couples beliefs in family planning programs related to long term contraception method consist of feelings of identity of trusted people, belief systems, expectations, and performance of people who provide information about family planning. Each couples has a person who is trusted in obtaining information about family planning. Couples in the Kampung KB will seek information about family planning in the cadre. Couples seek information from that person because they are considered to have experience and understand more about family planning. Whereas the non-Kampung KB also has a trusted person, namely the neighbors. Trust can arise by believing that the person can provide the information needed. The role of trust in as a bridge in determining expectations and goals to be achieved is obtaining information.

Other research states that cadres are workers from the community, chosen by the community, and work voluntarily to foster and improve community welfare. The role of family planning cadres is to carry out the processing and guidance of population and family planning programs at the village level or below⁽⁵⁾.

Theory states that trust is a cognitive component of socio psychological factors. Belief in this case is the belief that something is right or wrong. Trust is often rational and irrational. Trust is formed by knowledge, needs, and interests⁽⁶⁾. Other research states that there is a relationship between knowledge and the choice of contraceptive method⁽⁷⁾.

Information obtained with complete confidence can be a reference in choosing a contraceptive method. The trust of cadres in long term contraception method users that the information obtained becomes trusted information. Couples trust is used as a strength in organizing family planning programs in Kampung KB.

The source of the strength of social capital is the ability of a group of people to build associations and the way people in an organization or associations involve themselves in a network of social relations⁽⁴⁾. Social network will strengthen the cooperation of members and benefit from the participation of its members. High levels of community participation in the courage to argue with their leaders and the many residents who use the opportunity to deliver their aspirations⁽⁸⁾.

Couples who use Long term contraception method are satisfied because they feel the benefits gained. While short term contraception method and non used contraception method user were not satisfied with the existence of long term contraception method. Social networks in social capital as a strong source in both Kampung KB and non-Kampung KB. Community activities are known to provide easy access to family planning services, especially long term contraception method. The free long term contraception method program is an effort to bring people closer to becoming acceptors. This access is known by most informants, especially women of reproductive age.

The ability of the community in a group to work together to build a network to achieve common goals. Social capital places more emphasis on group potential and is an important variable in achieving public health⁽⁹⁾. The source of the strength of social capital is the ability of a group of people to build associations and the way people in an organization or associations involve themselves in a network of social relations⁽⁴⁾. Couples who are in Kampung KB know that in village activities such as the family welfare empowerment movement (PKK) and Posyandu they are always informed about free method of implant and IUD. Even cadres did not hesitate to deliver prospective acceptors directly to health services. Whereas the women of fertile age in non-Kampung KB who are better informed through PKK activities or who are cadres can get it from the cadre management association. Whereas in non-Kampung KB the existence of social networks has not been utilized in increasing the use of long term contraception method.

Suggestion: Couples of reproductive age has trust in others about the use of long term contraception method. Trust is influenced by the knowledge possessed. Social networks in the community are resources that can be used for family planning programs, specially the use of long term contraception method. Trust and social networking are used as an effort to improve the family planning program in the use of couples in the Kampung KB. While trust and social networking have not been utilized in improving family planning programs in the use of couples in non Kampung KB.

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References

1. BKKBN. Survey Dasar Kesehatan Indonesia. Jakarta; 2018.
2. SDG. Sustainable Development Goals. 2017.
3. DP5A. Number of participants KB by method of contraception. Surabaya 2019.
4. Glacial A, Gebbie A. Family planning and reproductive health. Jakarta: EGC; 2006.
5. Yuniarso M. Role of the cadre of rural Community institutions (IMP) in the family planning Program (KKB) in Klaten Regency. University of the Open; 2017.
6. Notoatmodjo. Health Behavioral Sciences. Jakarta: Rineka Cipta; 2010.
7. Bowles, Gintis. Social Capital and Community Governance. Econ J. 2002;
8. Putnam R. Democracies in Flux: The Evolution of Social Capital in Contemporary Society. New York: Oxford University Pers, Inc; 2002.
9. Coleman J. Foundations of Social Theory. Cambridge Mass: Harvard University Press; 1990.

Relationship among Cervical Cancer Risk Factors with Pap Smear Results in Medan North Sumatera

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Abstract

Objects: To identify relationship among cervical cancer risk factors with pap smear results in Medan North Sumatera.

Method: The study was a correlative descriptive. The samples were 60 respondents. Data were collected using a questionnaire and analysis using the Chi Square test at an error rate of 0.05.

Results: The result showed that there were no significant correlations among education ($p>0.484$), employment ($p>0.329$), age at first sexual intercourse ($p>0.410$), history of pregnancy ($p>0.204$), and use of vaginal cleansers ($p>0.569$) with the results of pap smears. There was a significant between using contraceptive with pap smear results with p-value 0.00 ($p<0.004$).

Conclusion: It is hoped that women need increase the knowledge about the importance of early detection of pap smear examination in reducing the number morbidity and mortality of cervical cancer in Indonesia.

Keywords: Cervical Cancer, Risk Factors, Pap smear.

Introduction

New cases of cervical cancer are the number one most attacking the reproductive health of women in Indonesia. Cervical cancer ranks second as the leading cause of death due to reproductive age in developing countries. In Indonesia there are 15,000 new cases with 8,000 deaths annually. This cancer is the most common cancer in Indonesian women. This cancer appears without causing symptoms and is very difficult to detect so that the disease is often diagnosed at an advanced stage⁽¹⁾.

In Indonesia, the prevalence of cancer is also very high. The prevalence of tumors/cancer in Indonesia is 1.4 per 1000 population, or around 330,000 people. The highest cancers in Indonesia in women are breast cancer and cervical cancer. The incidence of cervical cancer in Indonesia is 17 per 100,000 women⁽²⁾.

In the early stages, symptoms that arise such as menstrual disorders, vaginal discharge, vaginal bleeding outside the menstrual period, complaints of pain in the lower abdomen, bleeding during sexual intercourse, and infection of the bladder tract. If this continues at a

higher stage, the patient will feel pain in the pelvic area, bleeding that smells fishy, lost appetite, drastic weight loss, and anemia with bleeding⁽³⁾.

To reduce the morbidity and mortality of cervical cancer prevention efforts need to be made, which consists of several stages, namely: 1. Primary prevention carried out at this stage is the promotion, education and vaccination of HPV (Human Papilloma Virus). 2. Secondary prevention is early detection. 3. Tertiary Prevention is treatment for cases that are found in early detection and prevent complications and early death⁽⁴⁾.

The problem of the high incidence of cervical cancer in Indonesia is due to the lack of cervical cancer screening measures, namely cervical cytology and acetic acid reviews, late diagnosis at an advanced stage, general weakness, low socioeconomic status, limited resources, limited facilities and infrastructure, the type of histopathology, and the degree of education involved in determining the patient's prognosis⁽⁵⁾.

Prevention of cervical cancer can be done by minimizing the existing risk factors by familiarizing yourself with a healthy lifestyle, making early detection

by doing a pap smear for women who are sexually active. Therefore the earlier the early symptoms of cervical cancer are known, the easier the treatment and treatment (6). Early detection in Indonesia is done by pap smear tests, colposcopy, ginescopy, cervicography, speculscopy, autoion (IVA) inspection method. Pap smear test coverage is estimated to be less than 5%. To fulfil tmatred screening cytology, liquid based cytology/ thin prep, HPV tests and visual acetate acid inspecthis, an alternative Pap smear test with IVA is sought, which is expected to get wider coverage(7).

Pap smear is a simple and quick examination to determine the presence of abnormal cells in the cervix by taking a smear of cells in the cervix, and then examined under a microscope to see whether or not the cells are abnormal. This examination can be done at any time, except during menstruation. All women who have had sexual intercourse are encouraged to have regular Pap

smears, once a year/at least 3 years. For women who have gone through menopause, a Pap smear can be done until the age of 65 years(8).

Method

This study used a cross sectional study design with a study design by measuring or observing research subjects at the same time or once, measurement of independent variables (education, employment, age at first sexual intercourse, history of pregnancy, use of vaginal cleaners and using contraceptive) and the dependent variable (results of Pap smear) without a repeat visit. This type of research is “descriptive correlative”, which is research that aims to explain the relationship, estimate, test based on existing theories. In this study, researchers used a consecutive sampling technique with a total of 60 respondents. Data were analyzed by using the Independent T Test.

Results

Table 1. Frequency distribution base on variables

Variables	Frequency normal pap smear	%	Frequency abnormal pap smear	%	Frequency sample	%
Educations						
Junior high school	1	1.7	0	0	1	1.7
Senior high school	19	31.7	17	28.3	36	60
College	9	15	14	23.3	23	38.3
Total	29	48.4	31	51.6	60	100
Employment						
Work	4	6.7	8	13.3	12	20
Housewife	23	38.3	25	41.7	48	80
Total	27	45	33	55	60	100
Age at first sexual intercourse						
12-16 years	0	0	1	1.7	1	1.7
17-25 years	20	33.4	24	40	44	73.3
26-35 years	7	11.6	7	11.6	14	23.3
36-45 years	0	0	1	1.7	1	1.7
Total	27	45	33	55	60	100
History of pregnancy						
0	1	1.7	1	1.7	2	3.3
1	2	3.3	4	6.7	6	10
2	10	17.5	11	18.3	21	35
3	8	13.3	11	18.3	19	31.7
4	3	5	3	5	6	10
5	2	3.3	1	1.7	3	5
6	1	1.7	2	3.3	3	5
Total	25	45	35	55	60	100

Variables	Frequency normal pap smear	%	Frequency abnormal pap smear	%	Frequency sample	%
Using contraceptive						
Hormonal	0	0	8	13.4	8	13.4
IUD	1	1.7	5	8.3	6	10
Non Contraceptive	26	43.3	20	33.3	46	76.6
Total	27	45	33	55	60	100
Use of vaginal cleaner						
Yes	6	10	11	18.3	17	28.3
No	22	36.7	21	35	43	71.7
Total	28	46.7	32	53.3	60	100

Table 1. Shows that the majority of samples with a history of high school education were 36 samples (60%) with normal pap smear results of 19 people (31.7%) and abnormal pap smear results of 17 people (28.3%). The majority of samples with work history as housewives were 48 people (80%) with normal pap smear results of 23 people (38.3%) and abnormal pap smear results as many as 25 people (41.7%). The majority of samples with a history of first sexual intercourse, namely the age of 17-25 years were 44 people (73.3%) with normal pap smear results of 20 people (33.3%) and abnormal pap smear results of 24 people (40%). The majority of

samples with a pregnancy history of 2 children were 21 samples (35%) with normal pap smear results of 10 people (17.5%) and abnormal pap smear results of 11 people (18.3%). The majority of samples with a history of using non contraception were 46 samples (76.6%) with normal pap smear results of 26 people (43.3%) and 20 abnormal pap smear results (33.3%). The majority of samples with a history of using vaginal cleaner did not use as many as 43 people (71.7%) with normal pap smear results as many as 22 people (36.7%) and abnormal pap smear results as many as 21 people (35%).

Table 2. Relationship among cervical cancer risk factors with pap smear results

Model	Unstandardized Coefficients		Standardized Coefficients	T	Sig.
	B	Std. Error	Beta		
(Constant)	3.326	1.347		2.469	.017
Education	.037	.108	.051	.341	.734
Employment	-.149	.116	-.301	-1.288	.204
Age at first sexual intercourse	-.121	.145	-.122	-.830	.410
History of pregnancy	.112	.093	.295	1.207	.233
Using contraceptive	-.278	.091	-.395	-3.041	.004
Use of vaginal cleaners	-.082	.143	-.074	-.574	.569

Table 2. Shows that the relationship of education with pap smear results with a t value of 0.705 and Beta value of 0.108 and a significant level of 0.484 means greater than 0.05 ($p > 0.05$) means that there was no significant relationship between education with pap smear examination results. Shows that the relationship of work with Pap smear results with a value of $t = -0.985$ Beta value -0.156 and a significant level of 0.329 means greater than 0.05 ($p > 0.05$) means that there was

no meaningful relationship between pap smear results. Shows that the relationship between age of sexual intercourse with the results of pap smear with a value of $t = -0.830$ Beta value -0.122 and a significant level of 0.410 means greater than 0.05 ($p > 0.05$) meaning that there was no meaningful relationship between age of having sex with pap smear results. Shows that the relationship between pregnancy history and pap smear results with a value of $t = 1.207$ Beta value of

0.295 and significant level of 0.233 means greater than 0.05 ($p > 0.05$) meaning that there was no significant relationship between pregnancy history and pap smear results. Shows that the relationship between the use of vaginal cleansers with Pap smear results with a value of $t = -0.574$ Beta -0.074 value and a significant level of 0.569 means greater than 0.05 ($p > 0.05$) means that there is no significant relationship between the use of vaginal smears with Pap smear results. Shows that the relationship between contraceptive use and pap smear results with a value of $t = -3.041$ Beta value -0.395 and a significant level of 0.004 means greater than 0.05 ($p > 0.05$) means that there is a significant relationship between the use of contraception with pap smear results.

Discussions

The results of this study obtained the majority of educated middle and above so the results obtained that the relationship of education with pap smear results with a significant value of 0.484 means greater than 0.05 ($p > 0.05$) meaning that there is no significant relationship between education with pap smear examination results. Based on supporting theories, research results, and previous research, the researcher believes that the higher the level of formal education, the better the mother's knowledge, especially about pap smears.

The relationship of work with the results of Pap smear with a significant level of 0.329 means greater than 0.05 ($p > 0.05$) meaning that there is no significant relationship between work with Pap smear results. Housewives are light work that is small at risk of cervical cancer, whereas heavy work that is at risk of cervical cancer can be seen from the results of pap smears, where women who work as manual laborers and farmers show a greater chance of developing cervical cancer than women who work light workers like housewives stairs.

The results of this study indicate the majority of samples with a history of age having first sexual intercourse, namely the age of 17-25 years with the majority of pap smear results abnormal. In accordance with the etiology of the infection, women who start sexual intercourse at a young age will increase the risk of cervical cancer because cervical columnar cells are more sensitive to metaplasia during adulthood, women who have sex before the age of 18 will be five times at risk of cervical cancer⁽⁹⁾. At a young age, mucosal cells in the cervix are immature. That is, still vulnerable to stimulation. So it is not ready to accept stimuli from the

outside. Including chemicals carried by sperm. Mucosal cells can change the nature of becoming cancerous where mucosal cells are no longer too susceptible to change⁽¹⁰⁾.

The results of this study indicate the majority of pregnancy history as much as 2 times with a significance level of 0.233 meaning greater than 0.05 ($p > 0.05$) meaning that there is no significant relationship between pregnancy history with pap smear results. A woman who often gives birth (many children) belongs to a high risk group for cervical cancer, the higher the parity of the mother, the less good the endometrium. This is caused by reduced vascularization or atrophic changes in the decidua due to past labor, which can lead to complications in the reproductive organs. With the frequent birth of a mother, it will have an impact on the frequent occurrence of injury to her reproductive organs which ultimately the impact of the injury will facilitate the emergence of Human Papilloma Virus (HPV) as a cause of cervical cancer. In line with the results of Hidayat study, that parity of more than > 3 is 16.03 times at risk of developing cervical cancer than people who have a number of parities < 3 ⁽¹¹⁾.

Women with high parity associated with cervical columnar epithelial eversion during pregnancy which causes new dynamics of immature metaplastic epithelium that can increase the risk of cell transformation and trauma to the cervix making it easier for HPV infection. Dangerous parity is to have children more than 3 or the distance of pregnancy is too close, it is because it can cause changes in abnormal cells in the cervix that can develop into malignancy⁽¹²⁾.

According to ACS women who have experienced 3 or more pregnancies in the full term have an increased risk for cervical cancer. Research has shown that hormonal changes during pregnancy may make women more vulnerable to HPV infection or cancerous growth⁽¹³⁾.

The results of this study indicate that the majority of samples with a history of non-family planning contraceptive use. The use of hormonal contraception for more than 4 or 5 years can increase the risk of cervical cancer 1.5-2.5 times⁽¹⁴⁾.

According to ACS states that the risk of cervical cancer is doubled in women who take birth control pills for more than 5 years, but the risk returns to normal 10 years after they stop. Combined oral contraceptives are a mixture of synthetic estrogens such as ethinylestradiol

and one of several C19 steroids with progesterone activity such as noretindron. This contraception contains a fixed dose of estrogen and progesterone. The use of estrogen can be risky because it stimulates the thickening of the endometrial walls and stimulates endometrial cells so that it changes properties⁽¹³⁾.

The results of this study found a significant level of 0.569 means greater than 0.05 ($p > 0.05$) meaning that there is no significant relationship between the use of vaginal cleansers with pap smear results. A healthy vagina must contain Lactobacillus bacteria, which is a good bacterium to maintain the acidity of the vagina so that germs do not easily infect. The habit of using vaginal fluid (douching) will eradicate the Lactobacillus bacteria, so that the vagina is more susceptible to infection. One of them is a Human Papilloma Virus (HPV) infection, which causes cervical cancer⁽¹⁵⁾.

Pap smear examination should be done routinely and regularly on women who have sexual intercourse, Pap smear examination is the easiest and cheapest way to detect cervical cancer early. This examination can be done in the menstrual cycle, during childbirth or post-miscarriage which can be done at any time and can be done on women with suspected or known STI or HIV/AIDS.

Conclusion

The result showed that there were no significant correlations among education ($p > 0.484$), employment ($p > 0.329$), age at first sexual intercourse ($p > 0.410$), history of pregnancy ($p > 0.204$), and use of vaginal cleansers ($p > 0.569$) with the results of pap smears. There was a significant between using contraceptive with pap smear results with p -value 0.00 ($p < 0.004$).

Suggestions: Increase education and health promotion activities on cervical cancer prevention by holding seminars or examinations of cervical cancer detection in the form of Pap smear examination, IV examination and IHC examination.

Conflict of Interest: Nil

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Ethical Consideration: The Research Ethics Committee from the Commission of Health Research Ethics Faculty of Nursing Universitas Sumatera Utara No. 1171/V/SP/2017.

References

1. WHO. WHO/ICO information Centre on HPV and Cervical Cancer (Information Centre). Human Papillomavirus and related cancer. 2015. Summary Report Update 3 rd edition 2010. Available from : www.who.int/hpvcentre.
2. Riskesdas. 2013. Riset Kesehatan Dasar; RISKESDAS. Jakarta: Balitbang
3. Rappler. Semua yang perlu kamu tahu mengenai kanker serviks [Internet]. 2017. Available from: <https://www.rappler.com/indonesia/data-dan-fakta/172623-data-fakta-penyakit-kanker-serviks>.
4. Adam MMRT, Dharminto, Cahyaningrum F. Age relationship, parity and personal hygiene diagnosis with IVA in Puskesmas Brangsong District 2 Brangsong Kendal. *Jurnal Kebidanan*. 2017; 6(2): 103-107. Available from: doi : 10.26714/jk.6.2.2017.103-107.
5. Arisandi QT, Izzuddin A. Sistem pakar diagnose awal kanker serviks menggunakan metode naive bayes berbasis android. 2016. Available from: <https://ejournal.upm.ac.id/index.php/energy/article/download/147/434/>.
6. Soebachman A. *Awas, 7 Kanker Paling Mematikan*. 2011. Syura Media Utama; Yogyakarta.
7. Nuranna. *Program Pencegahan Kanker Serviks "See and Treat"*. 2011. FK. UI: Jakarta.
8. Rasjidi I. 2007. *Vaksin Human Papilloma Virus dan Eradikasi Kanker Mulut Rahim*. 2007. Sagung Seto: Malang.
9. Rasjidi I. *Manual Prakanker Serviks*, edisi 1. 2014. Sagung Seto: Jakarta.
10. Dugue PA, Rebolj M, Hallas J, Garred P, Lynge E. Risk of cervical cancer in women with autoimmune diseases, in relation with their use of immunosuppressants and screening: population-based cohort study. *Int J Cancer*. 2015; 136(6):711-719. Available from: doi: 10.1002/ijc.29209.
11. Hidayat E, Hasibuan DHS, Fitriyani Y. Hubungan Kejadian Kanker Serviks dengan Jumlah Paritas di RSUD Moewardi Tahun 2013. *Jurnal Kesehatan Komunitas Indonesia*. 2014; 6: 128-136.
12. Jensen KE, Schmiedel S, Norrild B, Frederiksen K, Iftner T, Kjaer SK. Parity as a cofactor for high-grade cervical disease among women with persistent human papillomavirus infection: a 13-year follow-up. *British Journal of Cancer* 2013;

108:234–239.

13. American Cancer Society. Cervical Cancer Prevention and Early Detection. Available from: <http://www.cancer.org/acs/groups/cid/documents/webcontent/003167-pdf.pdf>.
14. Emilia O. Bebas Ancaman Kanker Serviks. 2010. Media Pressindo: Yogyakarta.
15. Paavonen J. Human Papillomavirus Infection and the Development of Cervical Cancer and Related Genital Neoplasia. 2007. *International Journal of Infectious Disease*. 11(2): 5359.

Hair Mercury Exposure and Hypertension among Community Artisanal and Small Scale Gold Mining in Banten, Indonesia

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Abstract

Background: Mercury was a heavy metal that persistent in the environment and harmful to human health and still used by Artisanal Small Scale Gold Mining (ASGM), especially in Indonesia. Cimanggu was one of ASGM in Banten province who still active using mercury and had found high levels of mercury that exceed the threshold in wastewater and human hair. Mercury exposure can affect human health, such as hypertension. This research aimed to determine the levels of hair mercury, hypertension, and individual characteristics such as age, sex, and smoking habits. And also determine the association between hair mercury with hypertension among communities in ASGM.

Material and Method: Design studies in this research using cross-sectional design. The data from BBTKLPP Jakarta datasheet “Analysis of Potential Impact of Risk Factors Environment Based for Disease Outbreaks on Interest Mining Society”. Retrieved data was hair mercury that analyzed in the laboratory BBTKLPP Jakarta using Mercury Analyzer (MA) 3000 with cold pavor method and blood pressure were measured directly two times using sphygmomanometer merk ABN and individual characteristics taken through a questionnaire. Totaling 100 samples analyzed were taken by quota sampling.

Findings: Univariate test showed that most of the respondents had abnormally hair mercury levels (55%), hypertension 29%, woman 78%, smoking 23%, and > 40 years 46%. Chi-square test showed no significant association between hair mercury levels and hypertension (P value=1, OR= 1.01, 95% CI = 0.42-2.40).

Conclusion: Respondents who had normal or abnormally hair mercury levels had the same odds to have hypertension risk. Further research is needed by using a larger sample with high-intensity process mercury use to clarify the association of hair mercury levels with hypertension.

Keywords: *Mercury; hypertension; Artisanal and Small Scale Gold Mining (ASGM).*

Introduction

Mercury emissions in the environment can from human activities such as fossil fuels burning, solid waste burning, and Artisanal Small Scale Gold Mining (ASGM)⁽¹⁾. In the ASGM, mercury used to extract gold

from the seeds by forming an amalgam. The widespread of mercury use in ASGM because simple to use, can be done individually, and relatively quick to separate the gold. Globally around 15 million people, including 3 million women and children participate in ASGM in 70 countries⁽²⁾. Based on the survey results consisting of 800 ASGM in Indonesia with estimated 250,000 miners and 1 million, whereas women and children⁽³⁾. ASGM had an increase in Indonesia. It's in line with many studies have shown that mercury pollution has occurred the sea, sediments, water wells, fishes, plants, and communities have an impact on public health⁽⁴⁻⁶⁾. Such as Hartono research which found mercury exposure in fish in Buyat Bay and Teluk Ratotok which has improved health for people who consume air from the Ratotok River Estuary,

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Buyat River Hulu, and clean water/drinking water storage PT. Newmont Minahasa Raya⁽⁷⁾. The results of a study conducted in ASGM Gorontalo showed that the concentration of hair mercury respondents had exceeded the established standard of 2 with an average concentration of hair mercury in 5.0480 ppm⁽⁸⁾.

ASGM donate 37% of mercury emissions in air and water. Mercury vapor present in the air around ASGM always high and the mercury pollution in water almost exceeds the quality standards by WHO. Continuously exposure can affect the central nervous system, the reproductive system and the cardiovascular system⁽²⁾.

The last few years, the impact of mercury on the cardiovascular system, especially hypertension has become a concern. Hypertension has been proved as a major risk factor for cardiovascular disease triggers. The incidence of hypertension has increased for the last three decades. Besides food consumption which high salt intake and obesity, exposure to mercury in the environment also one important factor driving the incidence of hypertension. Epidemiological and experimental studies showed association between mercury exposure and increased blood pressure. Chronic mercury exposure levels in humans can be determined by examining the hair biomarker are considered most suitable for chronic exposure, easy to collected, and non-invasive⁽⁹⁾. Several studies in the world showed an association between mercury exposure to increased blood pressure among the gold miners who use mercury were found significant increased sistolee blood pressure ($P < 0.01$) correlated with lipid peroxidation and oxidative stress ($P < 0.01$)⁽¹⁰⁾. A case-control study showed the incidence of gold miners who have hypertension 46% greater than the control group. Other studies showed that a significant correlation between hair mercury levels with hypertension⁽¹¹⁾. A study of 251 people in the Brazilian Amazon showed that blood pressure was associated with higher levels of total mercury in the hair where an increased in blood pressure sistolee along with the increased amount of mercury in the hair of $< 10 \text{ lg/g}$ ⁽¹²⁾. In Indonesia research about association between hair mercury exposure with hypertension is still not received attention by researchers.

This research aims to determine the levels of hair mercury, blood pressure as well as individual factor characteristics (age, sex, and smoking habits) and determine the association between hair mercury with hypertension in communities around ASGM Cimanggu,

Pandeglang, Banten Province. Cimanggu was an area of the ASGM who around a residential area that still used mercury to gold processing and has operated for approximately eight years. Balai Besar Teknik Kesehatan Lingkungan dan Pengendalian Penyakit (BBTKLPP) Jakarta in 2017 had found mercury in wastewater in the processing of gold and mercury hair on people living around ASGM above the predetermined quality standards⁽¹³⁾. If it continuously happened could have a negative impact on human health one of hypertension disorders due to exposure to mercury.

Material and Method

This study was conducted using a quantitative method with cross-sectional study design and use secondary data derived from datasheet "Analysist of Potential Impact of Risk Factors Environment Based for Disease Outbreaks on Interest Mining Society" conducted by BBTKLPP Jakarta. This research will describe mercury levels in the hair and it's association with hypertension in community living around ASGM, Cimanggu, Pandeglang, Banten.

The population in this study was communities who live around ASGM in Cimanggu with total of 5442 people, the samples in this study were communities who selected based on inclusion criteria among men or women have equal opportunity to participate, length of stay ≥ 1 year around ASGM, in good health and willing to become respondents signed an informed consent. Calculation of sample size using the formula Lemeshow sought, in order to obtain a maximum sample is 100 sample. Sampling was conducted using quota sampling.

This study will use Univariate analysis to describe Hair mercury level, blood pressure, and individual characteristics respondents, and bivariate analysis used a chi square test to show association between hair mercury with hypertension. Hair mercury analyzed in the laboratory BBTKLPP Jakarta using Mercury Analyzer (MA) 3000 with cold vapor method and blood pressure were measured directly two times using sphygmomanometer merk ABN and individual characteristics taken through a questionnaire.

Findings: Based on Table 1 showed that of the 100 respondents who checked his blood pressure, only 29% who have hypertension, that was systolic ≥ 140 or diastolic pressure ≥ 90 ⁽¹⁴⁾. Respondents who had hair mercury levels above the quality standards that have been established by UNEP (2 ppm) is 55%. Individual

characteristics show that respondents >40 years old only 46%, which was man 22%, and smokers only 23%.

Table 1: Distribution of Hair Mercury, Hypertension, and Individual Characteristics Around ASGM in Cimanggu 2018

Variables	Total	Presentation (%)
Hypertension		
No (<140/90)	71	71
Yes (\geq 140/90)	29	29
Hair Mercury Levels		
Normal (\leq 2ppm)	45	45
Abnormally (> 2ppm)	55	55
Age		
\leq 40 years	54	54
> 40 years	46	46
Gender		
Woman	78	78
Man	22	22
Smoking Status		
Do Not Smoke	77	77
Smoking	23	23

The association showed There is no association between hair mercury levels and hypertension (P-value=1, OR= 1.01, CI 95%= 0.42-2.40). OR=1.01 that means respondents with abnormally hair mercury level have equal odds to have hypertension with normally hair mercury with 95% confidence interval hair mercury respondents between 0.42-2.40 ppm. Mercury exposure in society was measured using hair as a biomarker because can explain mercury levels long term in the body, hair mercury also quite persistent even not lost when washing with shampoo and coloring, and hair mercury levels 250 times in blood⁽¹⁵⁾. Hair will be examined using Mercury Analyzer (MA) 3000 and cold vapor method with the results of measuring parts per million (ppm) with quality standards set by UNEP (2 ppm)⁽¹⁶⁾.

The analysis showed most of the respondents have hair mercury level abnormally. Abnormally hair mercury level in ASGM communities related to their exposure to mercury from combustion processes and the separation of gold which exposes humans through intermediary of water, air, and land for a long time, in additionally the hair shaft grows to combine mercury from the blood⁽¹⁷⁾. This result same with previous studies conducted around ASGM in KruegSabee, Aceh, 90.28% of respondents contains mercury levels above the quality standard value 10 μ g/g set by the WHO. Fillion found 67.9% of the

population living around the Amazon River containing hair mercury levels \geq 10 mg/g⁽¹²⁾.

Hypertension was defined as increasing systolic blood pressure or diastolic after at least 2 times measurement. Hypertension in this study defined as blood pressure that had systole pressure of 140 mmHg or diastolic pressure of 90 mmHg⁽¹⁴⁾. This study showed just a few respondents with hypertension. This result was lower than research conducted by Valera et al. that showed 53.9% of people living around the mining have hypertension⁽¹⁸⁾. And about 46% of miners in Europe have hypertension⁽¹⁰⁾. Many factors can lead to hypertension such as age, sex, smoking, obesity, lack of exercise, excessive salt consumption, and stress⁽¹⁹⁾. And from this research, we can show that most of the respondent had a low risk of hypertension, because most of the respondents were woman, \leq 40 years and do not smoke.

In this study showed no significant association between hair mercury levels and hypertension with OR = 2.072. It's not in line with Bautista et al. where people with high levels of hair mercury was four times more at risk for hypertension (p value= 0.02)⁽¹⁷⁾. The same results also proved by Fillion et al. and Valera who reported a positive association between mercury levels and hypertension^(12,20). In recent years there had increased attention to mercury effects on cardiovascular system like atherosclerosis, cardiac arrhythmia, and renal dysfunction^(21,22). The mechanism of mercury affecting blood pressure cannot be explained with certainty, but the accumulation of mercury can affect endothelial function by inhibiting NO synthesis⁽²³⁾ and increasing oxidative stress, lipid peroxidation, and TNF α and interculin^(17,24,25). Increased oxidative stress from lipid peroxidation and decrease in antioxidants can trigger endothelial and renal dysfunction, which can increase the risk of hypertension and atherosclerosis, and result increase in blood pressure and pulse^(22,23,25).

The same result with this study showed by Rajae who cannot found association between mercury levels with blood pressure around communities ASGM⁽²⁶⁾. The lack of association between hair mercury levels with hypertension because there had many factors causing hypertension behind mercury contaminants such as age, smoking, obesity, alcohol consumption, high sodium consumption, and low physical activities⁽²⁷⁾. Besides that small sample size and low hair mercury levels can effect significance result study. Therefore need further

verification by using a larger sample with high intensity process mercury use. Although statistically there's no association between hair mercury and blood pressure, mercury exposure continuously for a long time can had a negative impact on health, one of them is hypertension, so monitoring of mercury use in ASGM areas should be monitored and conducted routine health monitoring in the community around ASGM.

Conclusion

The study concluded that most of (55%) respondent had abnormally hair mercury level, but only 29% had hypertension with the characteristics age >40 years old 46%, man 22%, and smoking 23%. There's no significant association between hair mercury and hypertension (p value = 1) with OR = 1.01 means respondents with abnormally hair mercury level have equal odds to have hypertension with normally hair mercury.

Conflict of Interest: The authors declare they have no conflict of interest.

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Ethical Clearance: The research protocol was approved by the research and community engagement, the ethical committee of public health faculty of the Universitas Indonesia with number of ethics 95/UN.2.F10/PPM.00.02/2019.

References

1. ATSDR. Toxizine Mercury. Atlanta; 2015.
2. WHO. Mercury Exposure and Health Impacts among Individuals in the Artisanal and Small-Scale Gold Mining (ASGM) Community [Internet]. Geneva; 2013. Available from: http://www.who.int/ipcs/assessment/public_health/mercury_asgm.pdf?ua=1
3. Ismawati, Y., I. Said, I. Nur, W. Selvia and M. Isnaeni. Social and Environmental Production of Suffering: Socio-Economic Impact of Artisanal and Small-Scale Gold Mining in Indonesia, Case Study Palu, Central Sulawesi. 2012;
4. Sofia, Husodo AH. Kontaminasi Merkuri pada Sampel Lingkungan dan Faktor Risiko pada Masyarakat dari Kegiatan Penambangan Emas Skala Kecil Krueng Sabee, Provinsi Aceh. 2016;23(3):310–8.
5. Grishela VV, Tamba E, Kristen U, Wacana K, Korespondensi A, Arjuna J, et al. Artikel Penelitian Gambaran Pencemaran Merkuri terhadap Masalah Kesehatan Penambang dan Masyarakat di Sekitar Aliran Sungai Behe Bulan Juli - Agustus 2016 Mercury Pollution Profiles among Miner and Local Residence at Behe River from July–August 2016. 2017;23(61):48–59.
6. Pratiwi CA, Ariesyady HD. Analisis Risiko Pencemaran Merkuri Terhadap Kesehatan Manusia yang Mengonsumsi Beras di Sekitar Kegiatan Tambang Emas Tradisional (Studi Kasus: Desa Lebaksitu, Kecamatan Lebakgedong, Kabupaten Lebak, Banten). 2012;18:106–14.
7. Hartono B. Distribusi Risiko Kesehatan Logam Merkuri Di Lokasi Pertambangan Emas Kabupaten Minahasa Selatan Provinsi Sulawesi Utara Tahun 2004. Universitas Indonesia; 2006.
8. Singga S, Kementerian P, Kupang K. ANALISIS RISIKO KESEHATAN PAJANAN MERKURI PADA BONE BOLANGO PROVINSI GORONTALO Health Risk Assessment of Mercury Exposure in the Bulawa District Community, Bone Bolango Regency, Gorontalo Province. 2013;21–8.
9. WHO. Concise International Chemical Assessment Document 50 Elemental Mercury and Inorganic Mercury Compounds: Human Health Aspects. Geneva; 2003.
10. Kobal AB, Horvat M, Prezelj M, Briški AS, Krsnik M, Dizdarevič T, et al. The Impact of Long-Term Past Exposure to Elemental Mercury on Antioxidative Capacity and Lipid Peroxidation in Mercury Miners. J Trace Elem Med Biol. 2004;17(4):261–74.
11. Salonen JT, Seppänen K, Lakka TA, Salonen R, Kaplan GA. Mercury Accumulation and Accelerated Progression of Carotid Atherosclerosis: A Population-Based Prospective 4-Year Follow-Up Study in Men in Eastern Finland. Atherosclerosis [Internet]. 2000 Feb 1 [cited 2019 Jan 29];148(2):265–73. Available from: <https://www.sciencedirect.com/science/article/pii/S0021915099002725>
12. Fillion M, Mergler D, Passos CJS, Larribe F, Lemire M, Guimarães JRD. A Preliminary Study of Mercury Exposure and Blood Pressure in the Brazilian Amazon. Environ Heal [Internet].

- 2006 Oct;5(1):29. Available from: <https://doi.org/10.1186/1476-069X-5-29>
13. BBTCLPP Jakarta. Analisis Dampak Faktor Risiko Penyakit KLB Berbasis Lingkungan pada Masyarakat Sekitar Pertambangan Kecamatan Cimanggu, Kabupaten Pandeglang, Provinsi Banten, Tahun 2017. Jakarta; 2017.
 14. JNC VII. The Seventh: Report of Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. 2003.
 15. Chamid dkk. Kajian Tingkat Konsentrasi Merkuri (Hg) Pada Rambut Masyarakat Kota Bandung. Eksata; Bandung (Prosiding SNaPP 2010 Ed Eksata- ISSN). 2010;2089–3582.
 16. UNEP, WHO. Guidance for Identifying Population at Risk From Mercury Exposure. Geneva; 2008.
 17. Bautista LE, Stein JH, Morgan BJ, Stanton N, Young T, Nieto FJ. Association of Blood and Hair Mercury with Blood Pressure and Vascular Reactivity. *WMJ J*. 2015;108(5):250–2.
 18. Valera B, Dewailly É, Poirier P, Counil E, Suhas E. Influence of mercury exposure on blood pressure, resting heart rate and heart rate variability in French Polynesians: A cross-sectional study. *Environ Heal A Glob Access Sci Source [Internet]*. 2011;10(1):99. Available from: <http://www.ehjournal.net/content/10/1/99>
 19. Casey A, Benson H. Menurunkan Tekanan Darah. New York: PT Bhuana Ilmu Populer; 2006.
 20. Valera B, Dewailly É, Poirier P. Environmental Mercury Exposure and Blood Pressure Among Nunavik Inuit Adults. *Hypertension*. 2009;54(5):981–6.
 21. Mass R, Patch S, Sergent K. A Statistical Analysis of Factors Associated With Elevated Hair Mercury Levels in the U.S. Population. An Interim Progress Report. *Unc-ashv Environ Qual Insitute Tech Rep*. 2004;
 22. Salonen JT, K E, Nyysönen K. Intake of mercury from fish, lipid peroxidation, and the risk of myocardial infarction and coronary, cardiovascular, and any death in eastern Finnish men. 1995;91:645-655.
 23. Kishimoto T, Oguri T, Abe M et al. Inhibitory Effect of Methylmercury on Migration and Tube Formation by Cultured Human Vascular Endothelial Cells. *Arch Toxicol*. 1995;69:357–361.
 24. Kim SH, Johnson VJ SR. Mercury Inhibits Nitric Oxide Production But Activates Proinflammatory Cytokine Expression In Murine Macrophage: Differential Modulation Of Nfkappab And P38 MAPK Signaling Pathways. *Nitric Oxide*. 2002;7:67–74.
 25. Pellizzari ED, Fernando R, Cramer GM, Meaburn GM BK. Analysis of Mercury in Hair of EPA Region V Population. *J Expo Anal Env Epidemiol*. 1999;9:393–401.
 26. Rajae M, Sánchez BN, Renne EP, Basu N. An Investigation of Organic and Inorganic Mercury Exposure and Blood Pressure in a Small-Scale Gold Mining Community in Ghana. *Int J Environ Res Public Health*. 2015;10020–38.
 27. WHO. The Atlas of Heart Disease and Stroke. 2010 [cited 2019 Jan 29]; Available from: https://www.who.int/cardiovascular_diseases/resources/atlas/en/

Effect of Aloe Vera Gel on Severity of Radiation Induced Dermatitis among Patients after Mastectomy

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Abstract

Radiation induced dermatitis is a significant adverse effect of radiation therapy occurring in the majority of patients treated with this modality such as mastectomy. No standard treatment has been recommended for the prevention of this side effect. This article is a report of a study evaluating the effect of Aloe Vera gel on severity of radiation induced dermatitis among patients after mastectomy. A time-series nonequivalent quasi-experimental research design was utilized, hence, a convenient sample of 132 adult female patients receiving radiation therapy after mastectomy were equally assigned randomly to either a study or a control group. Data were collected using two tools: 1) Demographic and Medical Data Sheet, and 2) Radiation Induced Skin Reaction Assessment Scale (RISRAS). The study results revealed statistical significant reduction in radiation induced dermatitis severity scores among the study group compared to the control group. It was concluded that the use of Aloe Vera gel is effective in reducing the severity of radiation induced dermatitis among patients after mastectomy.

Keywords: *Aloe Vera Gel; Radiation Therapy; Radiation Induced Dermatitis; Mastectomy.*

Introduction

Radiation therapy is one of the main modalities in the management of breast cancer; along with chemotherapy and surgery to provide maximum damage to tumor cells.¹ Despite new improvements in irradiation skin-sparing techniques, most patients still experience a variety of short-term and long-term side-effects. Radiation induced dermatitis is a prominent clinical problem that affects the majority of patients receiving radiation therapy.²

Radiation induced dermatitis is defined as “an acute or chronic inflammation of the skin caused by exposure to radiation therapy”. This reaction is a result of radiation therapy disrupting the normal process of cell division and regeneration in the basal cell layer of the skin, resulting in cell damage or cell death.³ Acute radiation induced dermatitis exhibit varying degrees of severity, including erythema ranging from mild to severe, followed by dry desquamation which may proceed to moist desquamation and necrosis. These side

effects interfere with quality of life, patient compliance, and may cause treatment cessation.⁴

The severity of the radiation induced dermatitis depends on many factors including; treatment-related and patient-related factors. Treatment-related factors include higher total dose, higher dose per fraction, the use of concurrent chemotherapy and field size, in addition to patient-related factors such as obesity, older age and chronic sun exposure.⁵

The radiation oncology literature contains no evidence for prevention or treatment of radiation induced dermatitis, so that it remains an unsolved problem.⁶ Natural products, especially herbal medicines, have found great attentions in the recent decades to solve this problem as they are assumed to have less adverse effects; it includes chamomile cream, almond ointment, topical vitamin C, calendula cream, corticosteroid cream and Aloe Vera.⁷

Aloe Vera (AV) as a plant-based remedy is cheap, cost-effective and easily available. The pharmacological action of AV gel includes anti-inflammatory, antibacterial, antifungal, antioxidant, immune-boosting and wound healing properties.⁸ It also contains vitamins A, C, E, B12 and folic acid. Vitamin C, which is involved in collagen synthesis, increases concentration of oxygen at the wound site because of dilation of blood vessels. Furthermore, AV penetrates and dilates capillaries going to an injured site, which improves healing.^{9,10}

The findings of this study might help to improve the quality of patient care and establish evidence based data that can promote nursing practice and research. Therefore, the aim of the current study is to evaluate the effect of Aloe Vera gel on severity of radiation induced dermatitis among patients after mastectomy.

Research Hypothesis:

H: There is statistically significant difference between the severity of radiation induced dermatitis mean scores of the study group participants who receive Aloe Vera gel application when compared to the control group who receive the routine hospital care throughout measurement time.

Method

Selection and description of participants:

A convenient sample of 132 adult female patients receiving radiation therapy after mastectomy were included in the current study from the Radiology Unit of a selected university hospital in Cairo, Egypt. Participants were equally randomly assigned to either a study group receiving Aloe Vera gel application or to a control group receiving routine hospital care. All the studied participants didn't receive any medical treatment regimen regarding prevention of radiation induced dermatitis either before or during radiation therapy, except if moist desquamation occurs, then medical ointment was prescribed.

The study sample was calculated based on statistical power analysis; considering $r=1$, α error was 0.05 (one sided), effect size (0.25) and G- power version 3.1.1, the power at 95%, the sample size for each group would be 66 participants.

Inclusion and exclusion criteria: Participants having the following criteria were eligible to participate: (1) Undergo radiation therapy after modified radical

mastectomy through linear accelerator and receiving fractionated dose of 2 Gray, (2) Not sensitive to natural AV gel or its products. While exclusion criteria were: (1) Co-morbid disease as diabetes mellitus, hypertension, infectious diseases, auto-immune diseases, (2) Presence of skin diseases in the radiation area, (3) Anemic patients, (4) Old age (more than 60 years), (5) Previous exposure to radiotherapy on the present irradiated area, or concurrent chemotherapy.

Data Collection tools: Two adapted tools were utilized to collect data pertinent to study variables. The first one was Demographic and Medical Data Sheet; it was designed by the researchers to collect the baseline characteristics of the participants such as age, marital status, education and duration of disease.

The second tool was Radiation Induced Skin Reaction Assessment Scale (RISRAS) to measure radiation induced dermatitis severity.¹¹ Cronbach's alpha of this tool was 0.95. It consisted of two parts: **Part 1:** Signs of radiation induced dermatitis, **Part 2:** Patient symptoms of radiation dermatitis.

Part 1: Health care professional visual assessment (*Radiation induced dermatitis*) scale. This include four observations to measures the extent and severity of erythema, dry desquamation, moist desquamation, and necrosis. The total scores of this part ranged from 0–16. Score zero was assigned for no dermatitis, score $1 \leq 4$ represent mild dermatitis (**Grade 1**), score $5 \leq 8$ represent moderate dermatitis (**Grade 2**), score $9 \leq 12$ represent severe dermatitis (**Grade 3**) and score $13 \leq 16$ represent life threatening condition (**Grade 4**).¹²

Part 2: Patient symptoms scale. It is composed of four questions which focus on skin tenderness, itching, burning, and functional activity with four-point likert scale responses quantifying symptoms reported by patients started from 0-3.

The total scores of this part (2) ranged from **0-12**. Score zero was assigned for no symptoms, score from **1** ≤ 4 indicate mild symptoms, score from **5** ≤ 8 indicate moderate symptoms, and score from **9** ≤ 12 indicate severe symptoms.

Scoring system of Total RISRAS: The summation of health care professional assessment scale scores 0-16, and total patient's symptoms scale scores 0-12 gives the total combined RISRAS severity scores which, can be expressed in the range of 0-28, with 0 representing no

changes, $1 \leq 7$ represent mild severity, $8 \leq 14$ represent moderate severity, $15 \leq 21$ represent severe and score $22 \leq 28$ represent life threatening condition.

Procedure: The designed study intervention was conducted on three phases; preparatory, intervention, and evaluation phase.

Preparatory phase: Participants who met the inclusion criteria for the study were approached by the researchers; individualized interview session was conducted to collect data related to the demographic and medical data.

All participants were scheduled for 20 fractionated dose of external beam radiotherapy through linear accelerator; it was taken 5 fractionated doses per week (in 5 consecutive days in a week with 2 days rest from radiotherapy each week) for 4 weeks.

Intervention phase: The researchers provided each participant in the study group with an adequate amount of fresh AV gel. Written instructions for usage and storage of AV were provided, as following; Wash

the irradiated area by using distilled water and applying AV gel with gentle massage twice daily for 6 weeks starting from first day of radiation session. Aloe Vera gel container should be stored in sterile, dark container in refrigerator for direct use.

Evaluation phase: All participants were followed up for 6 consecutive weeks. Weekly assessment of radiation site was performed using the Radiation Induced Skin Reaction Assessment Scale (RISRAS) for four weeks during radiation therapy and 2 weeks after completion.

Results

Table (1): shows that there were no statistically significant differences at demographic characteristics among the two groups; this means that the two groups of the study were homogenous groups. Furthermore, the highest percentages of both groups were university educated, married, and their age ranged between 40-60 years.

Table (1) Comparison between Study and Control Groups’ Demographic Characteristics (N=132).

Variables	Study (n= 66)		Control (n= 66)		Test	P-value
	No	%	No	%		
Age:						
30 – < 40	13	19.7	15	22.7	t = 0.477	0.634
40 – < 50	22	33.3	19	28.8		
50 – ≤ 60	31	47	32	48.5		
Mean ± SD	48.5 ± 8.34		47.78 ± 8.80			
Marital Status:						
Single	5	7.6	5	7.6	$\chi^2 = 0.36$	0.797
Married	39	59.1	36	54.5		
Widow	13	19.7	14	21.2		
Divorced	9	13.6	11	16.7		
Educational Level:						
Can’t read and write	3	4.5	2	3	$\chi^2 = 3.128$	0.429
Read and write	7	10.6	12	18.2		
Primary	9	13.6	7	10.6		
Preparatory	6	9.1	7	10.6		
Secondary	20	30.3	13	19.7		
University	21	31.8	25	37.9		

*Significant at P value ≤ 0.05

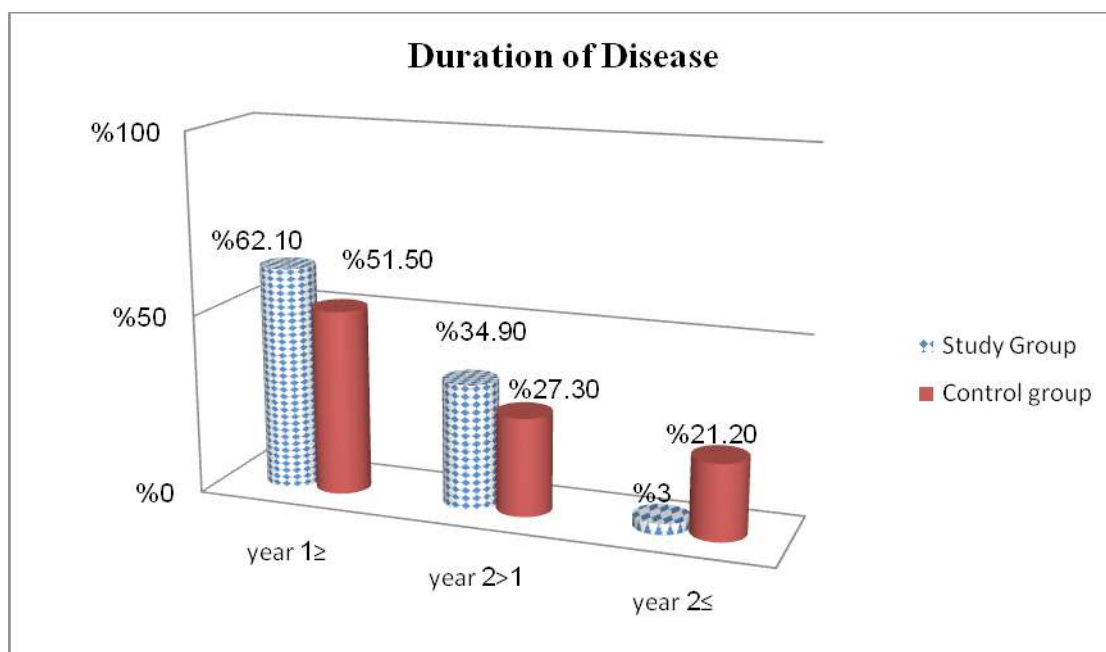


Figure (1): Percentage distribution of Study and Control Groups Regarding duration of Disease (N = 132).

Figure (1) Illustrates that the majority of the participants in the study and control groups have disease duration less than one year.

Table (2) demonstrates statistically significant differences between the study and control groups as regard grades of radiation induced dermatitis by the end of 2nd, 3rd, 4th and 6th weeks of intervention. No dermatitis occurred in the first week in both groups. As can be seen from the table, the highest percentage of

the participants in the study group had Grade 0; also, there is no observable Grades 3 of dermatitis severity in the study group along the study period compared to the control group.

Table (2) Frequency, Percentage distributions and comparison between the Study and Control Groups Regarding Grades of Radiation Induced Dermatitis along the Study Period (N= 132).

Measurement time	Grades of skin reactions (RTOG-Grades)	Study group (n=66)		Control group (n=66)		χ^2	p-value
		No	%	No	%		
1 st week	Grade 0	66	100	66	100	-	-
2 nd Week	Grade 0	66	100	31	47	47.62	0.002*
	Grade 1	0	0	35	53		
3 rd Week	Grade 0	45	68.2	16	24.2	25.6	0.001*
	Grade 1	21	31.8	50	75.8		
4 th Week	Grade 0	31	47	13	19.7	11.26	0.00*
	Grade 1	22	33.3	36	54.5		
	Grade 2	13	19.7	17	25.8		
6 th week	Grade 0	31	47	13	19.7	21.86	0.00*
	Grade 1	19	28.8	14	21.2		
	Grade 2	16	24.2	29	43.9		
	Grade 3	0	0	10	15.2		

*Significant at P value ≤ 0.05

Table (3) demonstrates no symptoms occurred in the first week of intervention in both groups. It also shows that there were highly statistical significant differences between the study and control groups regarding symptoms of radiation induced dermatitis at 2nd, 3rd, 4th & 6th weeks of intervention.

Table (3): Comparison between Study and Control Groups’ Symptoms mean scores of Radiation Induced Dermatitis along Study Period (N = 132).

Variables	Study (n= 66) Mean ± SD	Control (n= 66) Mean ± SD	t-test	P- value
Patient symptoms				
1 st Week	0.00 ±0.00	0.00 ±0.00	-	-
2 nd Week	0.00 ±0.00	1.57 ±1.50	8.48	0.000*
3 rd Week	0.57±0.97	3.15 ±2.51	7.74	0.000*
4 th Week	1.83 ±2.08	4.90 ±3.61	5.98	0.000*
6 th Week	1.50 ±1.83	6.09 ±3.67	9.07	0.000*

*Significant at P- value ≤ 0.05 probability level

Table (4): Comparison between Study and Control groups as regards. Total Mean of Radiation Induced Dermatitis Severity Scores along study period (N=132).

Total Radiation Induced Dermatitis

Study Period	Study Group	Control Group	t-test	P-value
	Mean ± SD	Mean ± SD		
2 nd Week	0.00 ± 0.00	2.30 ± 1.96	9.50	0.000*
3 rd Week	0.95± 1.51	4.75± 3.35	8.39	0.000*
4 th Week	3.34 ± 3.84	7.89± 5.03	6.90	0.000*
6 th Week	3.31 ± 3.78	10.59± 6.23	8.03	0.000*

*Significant at P- value ≤ 0.05 probability level

Discussion

The present study findings revealed that the participants were predominately university educated, married, and had age ranged between 40-60 years. Furthermore, there was statistically significant reduction of the mean severity dermatitis scores among the study group when compared to control group, indicating improvement of the radiation induced dermatitis severity condition in the study group after AV gel application.

This finding is supported by several studies that demonstrates Aloe Vera as an anti-inflammatory, moisturizing in addition to the pharmacological actions which include antibacterial, antioxidant, immune-boosting and wound healing properties.^{9,10,13,15} Also it was founded that the severity of dermatitis was significantly reduced among the study group who applied Aloe Vera gel at the radiation site.^{5,7,13,15}

The results of this study might be interpreted in the light of the fact that the application of Aloe Vera natural gel increases the collagen content of the wound and also alters the collagen composition, increasing the collagen cross linking. It improved wound healing by increasing blood supply and increasing oxygenation, which results in increased fibroblast activity and collagen proliferation. The most important component of AV gel is the polysaccharide acemannan, which reduce opportunistic infections, and stimulates wound healing, and also it has anti-inflammatory action; carboxypeptidase, which inhibits prostaglandin synthesis and arachidonic acid, thus it is a potent anti-inflammatory agent.¹⁵ The moisturizing effect of AV gel appears as result of mixing of water and polysaccharide constitutes. In addition, the antimicrobial effects have been attributed to the plant’s natural anthraquinones; providing analgesic, antibacterial, antifungal and antiviral activity.^{15, 16}

Also, application of Aloe Vera gel; twice daily for six consecutive weeks in the current study allowed sufficient time for interaction, and enhanced much better action and consequently improvement in radiation induced dermatitis severity.

Conclusion and Recommendations

The current study concluded that Aloe Vera gel application could be effective in reducing the severity of radiation induced dermatitis.

The study recommended the following:

- Aloe Vera gel application needs to be endorsed in the nursing management of patients receiving radiotherapy post mastectomy.
- Replication of the research study is recommended with using a larger sample size from different geographical areas in Egypt in order to provide generalization of findings.
- Longitudinal study should be designed to determine the long term effect of AV gel for this group of patients over a long period of time.

Conflict of Interest: The authors declare no conflict of interest.

Source of Funding: it is a self-funding.

Ethical Clearance: A written initial approval was obtained from the ethics and research committee of the Faculty of Nursing - Cairo University. Written informed consent was obtained from each participant after explaining the nature & purpose of the study. Patients were informed that participation in the study was entirely voluntary and anonymity and confidentiality of the data were assured.

References

1. Ryan JL. Ionizing radiation: the good, the bad, and the ugly. *J Invest Dermatology*. 2012; 132, 985-93
2. Ahmadloo N, Kadkhodaei B, Omidvari S, Mosalaei A, Ansari M, & Nasrollahi H. Lack of Prophylactic effect of Aloe Vera gel on radiation dermatitis. *Asian Pacific Journal of Cancer Prevention*. 2017; 18 (4), 1139-1143.
3. Kim JH, Kolozsvary AJ, Jenrow KA & Brown SL. Mechanisms of radiation-induced skin injury and implications for future clinical trials. *International Journal of Radiation Biol*. 2013; 89(5):311–8.
4. Ansari, M., Dehsara, F., & Mosalaei, A. Efficacy of topical alpha ointment (containing natural henna) compared to topical hydrocortisone (1%) in the healing of radiation-induced dermatitis in patients with breast cancer: A randomized controlled clinical trial. *Iran Journal of Medical Science*. 2013; 38,293.
5. Adeyemi OF, Okungbowa GE & Ogbeide, OU. Aloe Vera Prevents Radiation-Induced Dermatitis among the Black Population. *Tropical Journal of Natural Product Research*. 2018; 2(9): 433-437. doi. org/10.26538/v2i9.5
6. Khanna NR, Kumar DP, Laskar SG & Laskar S. Radiation dermatitis: An overview. *Indian Journal of Burns*. 2013; 21 (1),24-31.
7. Chan R, Webster J, Chung B, Marquart L, Ahmed M. & Garantziotis S. Prevention and treatment of acute radiation-induced skin reactions: A systematic review and meta-analysis of randomized controlled trials. *BMC Cancer*. 2014; doi:10.1186/1471-2407-14-53
8. Radha MH & Loxmipriya NP. Evaluation of biological properties and clinical effectiveness of Aloe Vera. A systematic review. *Journal of Traditional and Complementary Medicine*. 2015; 5 (1), 21-26.
9. Revathy J. ‘The plant of immortality’ Aloe Vera, its therapeutic and medicinal uses. *International Journal of Advanced Research in Computer Science and Software Engineering*. 2015; 5(3), 86.
10. Sharma P, Kharkwal H, Abdin M & Varma A. A review on pharmacological properties of Aloe Vera. *International Journal of Pharmaceutical Sciences Review and Research*. 2014; 29(7), 34.
11. Noble-Adams R. Radiation-induced skin reactions 1: An examination of the phenomenon. *British Journal of Nursing*. 1999; 8(17), 1134–1140.
12. Miller AB, Hoogstraten B, Staquet M, Winkler A. Reporting results of cancer treatment. *Cancer* 1981; 47:207–14.
13. Abdel-Hamid AA & Soliman MF. Effect of topical Aloe Vera on process of healing of full-thickness skin burn: A histological and immunohistochemical study. *Journal of Histology and Histopathology*. 2015; 2(3),7.
14. Weheid SM, Riad NA & Elgarhy SM. The effect of skin preparation by using Aloe Vera gel on incidence of skin reactions among breast cancer patients

- undergoing radiation therapy *Journal of Biology, Agriculture and Healthcare*. 2013; Available at: www.iiste.org ISSN 2224-3208 (Paper) ISSN 2225-093X (Online) Vol.3, No.15, 2013
15. Husain S, Alam M, Jahan N, Ahmed Sh & Kauser H. Sibr (Aloe Vera) and its therapeutic efficacy described in Unani Medicine: A review *Journal of Scientific and Innovative Research*. 2014; 3(5):547.
 16. Bhuvanka KB, Hema NG & Patil RT. Review on Aloe Vera. *International Journal of Advanced Research*. 2014; 2(4), 689.

Effect of Lavender Oil Massage on Pain among Patients with Knee Osteoarthritis

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Abstract

Osteoarthritis (OA) is a progressive chronic joint disease with global relevance with up to 250 million people being affected from knee OA worldwide. The aim of this study was to evaluate the effect of Lavender oil massage on pain among patients with knee osteoarthritis. A convenient sample of 60 adult male and female patients who admitted to Rheumatology and Rehabilitation unit affiliated to Cairo University hospital in Egypt with confirmed diagnosis of knee OA divided into experimental (study) and control group. A quasi-experimental Time Series pre-post test nonequivalent interrupted control design was utilized in the current study. Data was collected using Personal and Medical Background Information Form, Pain Numerical Rating Scale and Lequesne Algo Functional Index of Severity. The study findings revealed that there were significant statistical differences of pain intensity score and OA severity between study and control group after application of lavender oil massage.

Conclusion: Lavender oil massage was proved in this study to be effective on pain and OA severity among patients with knee osteoarthritis.

Keywords: Lavender oil massage, pain, Patients with osteoarthritis.

Introduction

Osteoarthritis is one of the most common musculoskeletal diseases, with an estimated prevalence of 12% to 22% worldwide¹. In Egypt OA is the third leading cause of disability just after heart disease and back disorder; 1.6 million people were affected by OA in Egypt². According to the American College of Rheumatology, OA is defined as a group of conditions which are associated with the defective integrity of articular cartilage result in changes in the underlying bone and articular margins³.

Knee OA is divided into two types either idiopathic (primary) or secondary (post-traumatic). The primary

OA is a gene-dependent disease, while secondary OA occurs after a traumatic event. Clinical characteristic of knee OA include pain, swelling, stiffness, crepitation and loss of movement that results in functional limitation, physical disability and reduced health-related quality of life³.

Aromatherapy is one of complementary and alternative therapy (CAT) uses essential oils and herbal essences for improving mental health or relieving physical symptoms. Previous studies have examined the effect of aromatherapy on anxiety, pain and wound healing⁴. As result of its simplicity and affordability, aromatherapy has been used as an optional choice in some medical settings, either alone or together with standard pain control protocol⁵.

Nursing practices for patient with osteoarthritis should be focused on performing regular follow up, training, and determining the most effective symptom management method. Aromatherapy and massage are among the non-pharmacological method which nurses may directly and independently use to control pain

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so they should increase their knowledge and skills regarding aromatherapy massage like recognizing the pharmacological actions of the essential oils and how to apply aromatherapy massage properly⁶.

Method

Aim of the Study: The aim of the current study was to evaluate the effect of Lavender oil massage on pain among patients with knee osteoarthritis. To fulfill the aim of this study the following research hypotheses were tested:

H1: Total mean score of pain of OA patients who receive lavender oil massage will be different from total mean score of pain of OA patients who receive routine protocol of care.

H2: The severity of osteoarthritis in OA patients who receive lavender oil massage will be different from the severity of osteoarthritis in OA patients who receive routine protocol of care.

Research Design: Quasi-experimental time series pre-post test nonequivalent interrupted control design was utilized in the current study.

Sample: A convenient sample of adult male and female patients with confirmed diagnosis of OA of the knee, their age ranged between 18 and 50 years. All patients admitted to rheumatology unit and met the inclusion criteria throughout 6 months from July 2018 to January 2019 were allocated to either study or control group starting with control group.

Setting: The current study was conducted in a selected Rheumatology and Rehabilitation unit, at Cairo university hospital, Egypt.

Data Collection Tools:

1. Personal and Medical Background Information Form (PMBIF): It is consisted of two parts: (a) Personal data sheet (b) Medical data sheet related to disease onset, duration, medical treatment, etc.
2. The pain Numerical Rating Scale (NRS): It is an 11-point scale (0-10). Pain intensity can be classified into mild, moderate, and severe levels based on the NRS score.

3. Lequesne Algo Functional Index of Severity: it is a disease questionnaire related to severity of OA. It consists of three scales with eleven items. Its scoring system 0= none, 1-4 mild, 5-7 moderate, 8-10 severe, 11-13 very severe and ≥ 14 extremely severe

Validity & Reliability: Tools were validated by a panel of five experts in the field of Medical-Surgical Nursing and modifications were carried out. Reliability was tested using Cronbach's alpha with value of 0.98.

Procedure: Patients were randomly divided into study and control group. Participants in the study group were instructed to massage their affected knee joint for 20 min 3 times per week for 3 weeks using 5 ml lavender essential oil diluted in sweet almond oil at a concentration of 3% and continued to receive conventional drugs. While the participants in the control group receive similar conventional drugs described by the rheumatologist.

Results

Section I: Demographic characteristics and medical data of the study and control groups.

The age of 60% of the study group and 56.6% of the control group ranged from 41-60 years old and the mean age was 41.83 ± 6.828 . Female gender constituted 83.3% of both study and control group. 86.7% and 93.4% of study and control group respectively were married. Less than half of study group (40%) and around one third of control group can read and write, 66.6% in both groups were housewives and 73.3% were rural areas' inhabitants.

According to medical data, around two thirds and 63% of study and control group respectively had gradual onset of osteoarthritis. 73% and 77% of study and control group respectively had no chronic diseases. 60% and 43% of study and control group respectively had no family history of osteoarthritis.

Section 2: Delineates hypothesis testing for being supported or not among study and control groups.

Table (1): Comparison between pain intensity score at four time points of both study and control group (N=60).

Pain intensity		Study group		Control group		X ²	P value
		No.	%	No.	%		
Base line	Mild	1	(3.3)	0	(0)	1.355	0.508
	Moderate	5	(16.7)	7	(23.3)		
	Severe	24	(80)	23	(76.7)		
First week	Mild	5	(16.7)	2	(6.7)	5.540	0.063
	Moderate	13	(43.3)	7	(23.3)		
	Severe	12	(40)	21	(70)		
Second week	Mild	11	(36.7)	3	(10)	7.251	*0.027
	Moderate	8	(26.6)	7	(23.3)		
	Severe	11	(36.7)	20	(66.7)		
Third week	Mild	13	(43.3)	3	(10)	9.583	*0.008
	Moderate	7	(23.4)	7	(23.4)		
	Severe	10	(33.3)	20	(66.6)		

*significant at $P \leq 0.05$.

Table (1) denotes that there was significant statistical difference between study and control group along study period.

Table (2) Comparison between levels of algofunctional index score at four time points of both study and control group (N=60).

Disease severity		Study group		Control group		X ²	P value
		No.	%	No.	%		
Base line	Severe	5	(16.7)	3	(10)	.605	0.739
	very severe	7	(23.3)	7	(23.3)		
	extremely severe	18	(60)	20	(66.7)		
First week	mild	1	(3.3)	0	(0)	8.865	0.065
	Moderate	4	(13.3)	0	(0)		
	Severe	11	(36.7)	7	(23.3)		
	very severe	7	(23.4)	8	(26.7)		
	extremely severe	7	(23.3)	15	(50)		
Second week	mild	4	(13.3)	0	(0)	11.910	*0.018
	Moderate	4	(13.3)	0	(0)		
	Severe	10	(33.4)	9	(30)		
	very severe	6	(20)	6	(20)		
	extremely severe	6	(20)	15	(50)		
Third week	mild	5	(16.7)	0	(0)	13.001	*0.011
	Moderate	4	(13.3)	0	(0)		
	Severe	10	(33.3)	9	(30)		
	very severe	5	(16.7)	6	(20)		
	extremely severe	6	(20)	15	(50)		

*significant at $P \leq 0.05$.

Table (2) clarifies that there was significant statistical difference between study and control group along study period.

Figure 1: shows that there was statistical significant difference in pain score among study and control group (ANOVA test: 46.229, p-value: *0.000) respectively along the study period. Also there was a statistical significant difference in pain score between study group when compared to control group in the 1st, 2nd, and 3rd weeks of intervention.

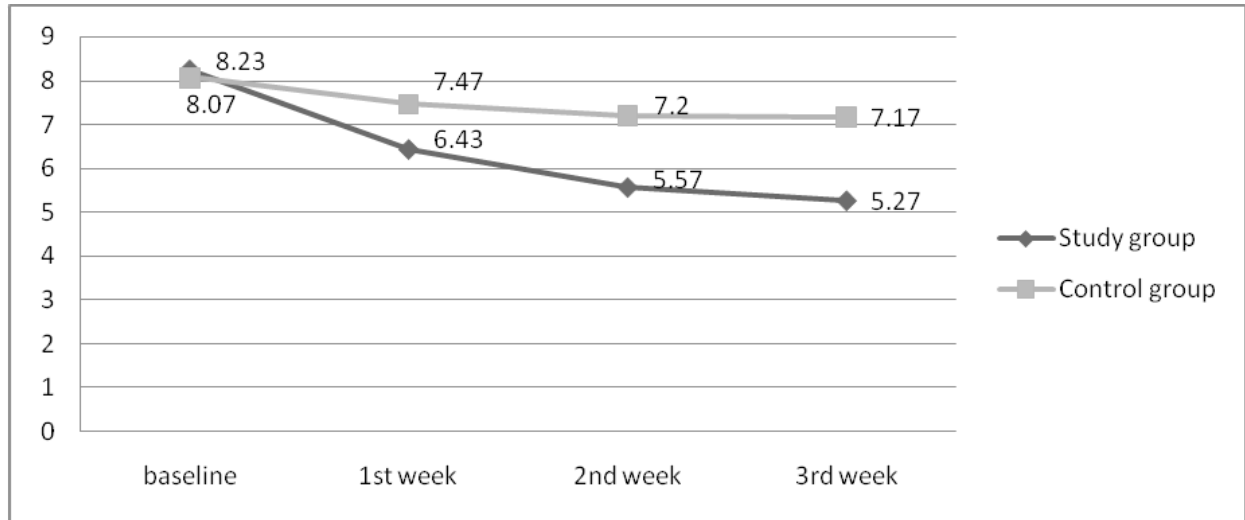


Figure 1: Differences of pain score between study & control group at four time points.

Figure 2: clarifies that there was statistical significant difference in algofunctional index score among study and control group (ANOVA test: 52.260, p-value: *0.000) along the study period. Also there was a statistical significant difference in algofunctional index score between study group when compared to control group in the 1st, 2nd, and 3rd weeks of intervention.

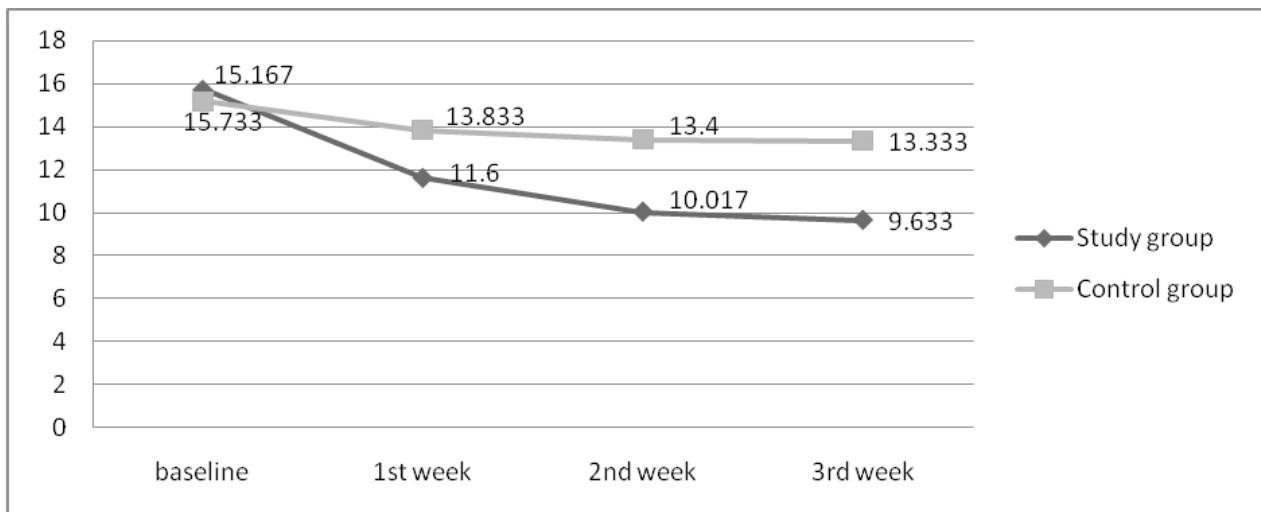


Figure 2: Differences of algofunctional index score between study & control group at four time points.

Discussion

The current study revealed that, the majority of the study participants aged between 41-60 years old with mean and standard deviation of age $41.83 \pm$

6.828. This finding is almost consistent with Arslan, Kutlutürkan and Korkmaz, (2019)⁷, the majority of their study participants were 35-64 years old. The findings can be explained with the fact that OA development

starts much earlier than originally thought, and ranked among the top 20 diseases in the 40–45 years age group.

Regarding gender, more than half of the participants were females. This finding is congruent with the findings of the studies by Nasiri and Mahmodi, (2018); Arslan, Kutlutürkan and Korkmaz (2019) & Pehlivan and Karadakovan, (2019)^{8,7,6} all affirmed that the majority of their study participants were females. In addition, Mahajan and Patni, (2018)⁹ confirmed that OA strikes women more often than men and it increases in prevalence, incidence and severity after menopause. The majority of study participants were housewives. These findings were relatively congruent with Nasiri and Mahmodi, (2018);⁸. The finding that the majority of the participants were housewives could be explained that the majority are females and reside from rural areas.

More than two thirds of study participants had gradual onset of disease. This could be explained with that OA develops slowly and that's why it takes time to induce symptoms that appears gradually starting with pain which worsens overtime. The majority of study participants had no comorbidities as diabetes and hypertension. In contrast Swain et al., (2019)¹⁰ reported that 67% of patients with OA had at least one other chronic condition, being 20% higher than those without OA. In addition, Hawker et al., (2017)¹¹ mentioned that 77% of their study sample had hypertension, added that OA-related difficulty walking was a significant and potentially modifiable risk factor for diabetes complications. The mean age of the current study participants was 41.83 ± 6.828 years old that could be the reason why the majority of study participants had no co morbidities as the prevalence of co morbidities increases with advancing age.

The findings of the present study revealed that a significant reduction in the mean score of pain 5.27 ± 2.083 and OA severity 9.633 ± 5.0085 after application of lavender oil massage on knee joint compared to the control group 7.17 ± 1.802 and 13.333 ± 3.4996 respectively. This finding supports the effectiveness of lavender oil massage on pain and OA severity among patients with osteoarthritis. The findings of the present study are consistent with other study conducted by Nasiri & Mahmodi, (2018); Nasiri et al., (2016)^{8,12}. The findings showed that pain severity reduced significantly in the group undergoing massage with lavender oil compared to control group. This finding could be explained in the light of fact that the direct pharmacological effects

of lavender oil is possibly because of linalyl acetate and linalool, which can effectively decrease pain and inflammation, prevent muscle spasms and reduce tensions, leading to improve pain and physical function.

In this respect, other study conducted by Seda Pehlivan (2018)⁶, reported that there were significant differences in pain score in the aromatherapy group when compared with the massage and control group. Other study done by Arslan et al.'s (2019)⁷ revealed that aromatherapy massage performed in patients with osteoarthritis had positive effect to reduce knee pain scores, morning stiffness, and improve physical functioning status and considered that complementary treatment modalities are useful for nurses who can perform aromatherapy massage for symptom management in OA.

In the current study, there was a statistical significant difference in mean score of pain between study group when compared to control group in the 1st, 2nd, and 3rd weeks of intervention. This findings is consistent with Nasiri and Mahmodi, (2018); Nasiri et al., (2016);^{8,12} who reported that pain severity differed significantly immediately, 1 week, and 4 weeks after the intervention with p value (<0.001) compared with placebo and control groups.

On the same stream, another study findings belongs to Zhang et al., (2018)¹³ revealed that patients with bilateral knee OA has been demonstrated that lavender oil aromatherapy massage, significantly reduced the patients' knee pain, tenderness, and morning stiffness. Furthermore, other study conducted by Won and Chae, (2011)¹⁴, reported that aromatherapy massage could be recommended as an effective intervention to decrease pain and to increase stride length in the elderly with knee osteoarthritis. Atkins and Eichler (2013)¹⁵ added aromatic massage therapy was more beneficial than massage alone among knee OA patients.

Conclusion

Lavender oil massage was proved in this study to be effective on pain among patients with knee osteoarthritis.

Implications: The complementary therapy is useful to healthcare providers who can learn, apply, or recommend aromatherapy massage techniques as a component of care for symptoms management of OA patients.

Recommendations:

- Replication of the study using a larger probability sample selected from different geographical areas in Egypt.
- Longitudinal study should be designed to determine the long term effect of lavender oil massage for this group of patients over a long period of time.

Ethical Clearance: A research approval was obtained from the Research and Ethical committee at Faculty of Nursing - Cairo University and official permission was obtained from the administrators at study setting. Written informed consent was obtained from each patient.

Conflict of Interest: The authors declare that there is no conflict of interest.

Source of Funding: Self-funding.

References

1. Smith T, Hawker G, Hunter D, March L, Boers M, Shea B et al. The OMERACT-OARSI Core Domain Set for Measurement in Clinical Trials of Hip and/or Knee Osteoarthritis. *The Journal of Rheumatology*. 2019;46(8):981-989.
2. Abdel-Magied R, AbdelGawad E, El-Shereef R, Lotfi A, Saedii A. Relationship between serum 25-hydroxy vitamin D levels, knee pain, radiological osteoarthritis, and the Western Ontario and McMaster Universities Osteoarthritis Index in patients with primary osteoarthritis. *Egyptian Rheumatology and Rehabilitation*. 2014;41(2):66.
3. Khuman R, Chavda D, Surbala L, Bhatt U. Reliability and validity of modified western ontario and mcmaster universities osteoarthritis index gujarati version in participants with knee osteoarthritis. *Physiotherapy - The Journal of Indian Association of Physiotherapists*. 2018;12(1):8.
4. Fazlollahpour-Rokni F, Shorofi S, Mousavinasab N, Ghafari R, Esmaeili R. The effect of inhalation aromatherapy with rose essential oil on the anxiety of patients undergoing coronary artery bypass graft surgery. *Complementary Therapies in Clinical Practice*. 2019;34:201-207.
5. Chen S, Wang C, Chan P, Chiang H, Hu T, Tam K et al. Labour pain control by aromatherapy: A meta-analysis of randomised controlled trials. *Women and Birth*. 2019;32(4):327-335.
6. Pehlivan S, Karadakovan A. Effects of aromatherapy massage on pain, functional state, and quality of life in an elderly individual with knee osteoarthritis. *Japan Journal of Nursing Science*. 2019.
7. Efe Arslan D, Kutlutürkan S, Korkmaz M. The Effect of Aromatherapy Massage on Knee Pain and Functional Status in Participants with Osteoarthritis. *Pain Management Nursing*. 2019;20(1):62-69.
8. Nasiri A, Mahmodi M. Aromatherapy massage with lavender essential oil and the prevention of disability in ADL in patients with osteoarthritis of the knee: A randomized controlled clinical trial. *Complementary Therapies in Clinical Practice*. 2018;30:116-121.
9. Mahajan, A., & Patni, R. 2018. Menopause and Osteoarthritis: Any Association?. *Journal of Mid-life Health*. 2018; 9(4), 171.
10. Swain S, Sarmanova A, Coupland C, Doherty M, & Zhang W. Comorbidities in Osteoarthritis: A systematic review and meta-analysis of observational studies. *Arthritis care & research*. 2019.
11. Hawker G, Croxford R, Bierman A, Harvey P, Ravi B, Kendzerska T & Lipscombe L. Osteoarthritis-related difficulty walking and risk for diabetes complications. *Osteoarthritis and cartilage*. 2017; 25(1), 67-75.
12. Nasiri A, Mahmodi M & Nobakht Z. Effect of aromatherapy massage with lavender essential oil on pain in patients with osteoarthritis of the knee: A randomized controlled clinical trial. *Complementary therapies in clinical practice*. 2016;25, 75-80.
13. Zikri E. Evaluation of the effect of aromatherapy in management of knee osteoarthritis patients. *International Journal of Complementary & Alternative Medicine*. 2018;11(2).
14. Won S, & Chae Y. The effects of aromatherapy massage on pain, sleep, and stride length in the elderly with knee osteoarthritis. *Journal of Korean Biological Nursing Science*. 2011;13(2):142-148.
15. Atkins D, & Eichler D. The effects of self-massage on osteoarthritis of the knee: a randomized, controlled trial. *International journal of therapeutic massage & bodywork*. 2013; 6(1), 4

An Empathy of Family for Reducing Stigma on People with HIV/AIDS: A Case Study in North Coastal of Central Java

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Abstract

People living with HIV/AIDS (PLWHA) faces powerless. Those aggravated with social problems from the family and community. Support from family allows them to have greater acceptance related to the disease. The Aimed of study to explore family stigma from PLWHA perspective in the North Coastal of Central Java. Method of research used qualitative with case study approach was conducted at Kudus district. Purposive sampling was applied to recruit participant. In-depth interview with semi-structured questions was attempted to 15 migrant workers also been carried out to families and case manager for triangulation. Thematic of manual content analysis was used. The stigmatization among gender showed different result in the context of family. Families were more tolerance and accepted the males with HIV/AIDS without any stigmatization. The culture of lower class of family have good attitude which potentially to be developed such as skills of understanding, being empathy and willing to care. There are specific programs needed which could encourage family empowerment to develop integrated community-based care for PLWHA.

Keywords: Empathy, Stigma, PLWHA, Reducing Stigma, HIV/AIDS.

Introduction

People living with HIV/AIDS (PLWHA) faces several powerless circumstances related to physical, psychological and social problems. The major social problem in Indonesia are self-stigmatization and difficulty to find someone to share about the disease.¹ Stigma issue is complicated it is not only associated with PLWHA but also impacted to their family.² While PLWHA and close family member (CFM) being stigmatized by others, but CFM also spreads stigmatization to PLWHA.^{3,4}

The stigma becomes the main reason for the global epidemiology among HIV/AIDS. A recent study conducted in Central Java Indonesia by 2017 founded

3.731 PLWHA. Kudus district has a greater increasing number of HIV/AIDS cases compared to the previous years. As many 114 cases, more than half were migrant workers' family. Migrant workers are classified as a high-risk group for HIV.^{5,6}

Stigmatization among PLWHA was still widespread in Indonesia.^{7,8} Stigma has a negative impact on PLWHA and their families.⁹ It contributes for low access of healthcare services, HIV screening test,¹⁰⁻¹² increases the risk of transmission.¹³ 40-51% PLWHA overdue of receiving HIV treatments,¹⁴ poor quality of life.¹⁵ The stigma can eliminate someone's position in the family and community.

The support from a big family is necessary needed in accepting the condition of PLWHA and also willingness to provide care for them,¹⁶ improve their physical and psychological well-being.¹⁷ This study is aimed to explore family stigma from the perspective of PLWHA among migrant workers in the northern coastal of Central Java.

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Method

A qualitative research method with a case study approach was performed in this study.

Sample: Purposive sampling method was applied to recruit the participant with the inclusion criteria: (1) Male and female with HIV positive; (2) Recently worked as a migrant worker or been experiencing in the past; (3) Permanent resident in Kudus district. Amount of 15 migrant workers (12 males, 3 females) participated in this study.

Setting: The research setting is North coastal at Kudus district, Central Java province, Indonesia. The interview takes place at the case manager’s house. The interviewers rapport building with participants along with confidential issues.

Data Collection: Formal written informed consent was provided to the participants along with demographic data. Interviewers also clearly explained that participants

have the right to dismiss the interview process whenever participants feel uncomfortable. In-depth interview method with open semi-structured questions about feeling of PLWHA after they have been diagnosed with HIV/AIDS, perceive about family respond and stigma. Field notes and MP3 recorder were used to perform complete documentation. It was about 45 to 60 minutes. All participants received transportation fee as the amount of IDR 100.000 after fulfilling the interview session.

Data Analysis: Analyse the data used a “thematic analysis”. The descriptive table presented to describe the demographic data. Inductive content analysis was used to analysed narratives contents.

Results

Participants’ Characteristics: 15 PLWHA who identified has experience working as a migrant worker outside of the city or overseas with a range of age 23-70 years old (Table 1).

Table 1: Participants’ demographic data

Demographic Information	n	Range
Gender		
- Male	12	
- Female	3	
Education Degree		
- Low Education	9	
- Middle Education	8	
Occupation, return home period of time dan Income:		
- Construction worker	7	Every 4 to 6 months (IDR 300.000–400.000)
- Household worker	3	Every 2 to 3 years (IDR 10-30 million)
- Inter-city or inter-island driver	5	Every 5 to 7 days (IDR 250.000).
Period of time of recognizing as an HIV sufferer	15	(1 to 4 years)

All participants was married, but 2 participants have divorce status with their spouse because of financial problems. 7 from 15 participants started heading their work to the big city since they were graduate from junior high school, as stated:

I was getting married at my young age, when my child was turning 3 months old, at 2012 I divorced with my husband because of financial problem which cannot afford my our living expense, then I stayed back with my parent and started working overseas at Malaysia through Indonesian Labor Service Company Kendal district branch...(Mrs. R, 23 Years old, Household

worker)

I started working since long time ago when I have graduated from junior high school in the year 1996. I was working as a construction labor at Jakarta. I just followed my friend who has worked before, because in my village it was very difficult to find a job... (Mr. R, 25 years old, construction worker)

Research Themes: Thematic analysis generated four themes, such as:

- a. There was no stigma and discrimination by a big family, as stated:

“My family, nephew, and others also stated that my disease is an ordinary disease which can occur when my wife left me, it’s already happened, just let it flew. (Mr. S, 55 years old, Construction worker)”.

- b. Family showed different responses among gender. Female with HIV/AIDS mostly associated with morality. They also become more introvert with their HIV status, as stated:

“It showed a result that I diagnosed with HIV positive. After that, I was departed back to Indonesia. When a question been asked “who are you having sexual intercourse with?”. “then I was not answering that question..” (Mrs. R, 23 Years old, household worker)

- c. Male are more tolerated to buy sex while they have long hours of working and away from their wives (e.g. when they were leaving their wives working overseas) as stated:

“..when my wife knew that I suffer this disease, she accepted me... she god mad in the beginning and she totally fine if I would like to find a new wife... but now, she totally being acceptance person..” (Mr.E, 37 years old, construction worker).

- d. An Empathy from their family accepted male with HIV/AIDS without stigmatization, they also redefine the meaning of healthy as “back to work as usual” as stated:

“...now the important thing is being healthy and back to work as usual.. (Mr. S, 55 years old, construction worker)”.

Discussion

Families feel ‘suffering’ when they experiencing stigma related to HIV/AIDS on their family members, an interesting phenomenon explored in this study that from all of the participants in Kudus district were not reported any stigmatization and discrimination from a big family.

Stigma is defined as a social process, experience or anticipation, characterized by exclusion, rejection, blame or devaluation which detrimental to a person or group¹⁸. Three main causes of family stigma, such as (a) negative perceptions, attitudes, emotions and avoidance behaviors of among others to family; (b) people’s beliefs that family with HIV/AIDS are dangerous, unhealthy, have a negative effect or have differences from general social norms; and (c) people’s beliefs that family members are

directly or indirectly contaminated by another family member with HIV/AIDS. So it considered dangerous, unhealthy, and have negative effects on others.¹⁹

That stigma occurred due to lack of adequate information related to the diseases, and low education among community,²⁰ Stigma and discrimination have contributed to the breakdown of kinship. Moreover, it also contributed PLWHA did not disclose their HIV status to their sexual partner and dissolution of families in Nigeria.²⁰

Female participants feel embarrassed to express their feeling related to their HIV/AIDS to their big family. Female PLWHA in China also showed higher significant internalization stigma experience than male ($p < 0,001$). There are gender differences in HIV-related stigma especially for internal stigma.²¹ Female PLWHA is mostly associated with cultural value as “bad sexual behavior” and “promiscuity”.²² As many as 77.7% women living with HIV/AIDS in 27 countries experienced stigma by community, regardless of the severity condition of illness.⁸ Study in Nepal discovered there were differences in stigma related to sexual behavior among migrant workers. 43.5% among them had sex with their partner and 26% among them had sex with a prostitute. All of those criteria had an average or high stigmatization.⁵

Male are more tolerated to buy sex while they have long hours of working and away from their wives. Gender inequality and poverty have increase women’s vulnerability to risk behaviour and exposure²³. This is the big problem situation in Indonesia, the highest number of cumulative AIDS sufferers is housewives and the highest percentage of AIDS risk factors from not safely sexual behavior in heterosexual (71%).²⁴

An Empathy from their family accepted male with HIV/AIDS without stigmatization, they also redefine the meaning of healthy as “back to work as usual”. The English Oxford Dictionary mention that empathy means the ability to understand and share the feeling of another. An Empathy helps others to feel the same way that they understand and tend to provide good care,²⁵ eliminate stigma and being acceptance to PLWHA will strongly support care and treatment.

The culture of the lower class of family at North Coastal of Central java have good attitude which potentially to is developed skills. Consistent with previous studies in Nigeria,²⁶ family are willing to care

for a relative with AIDS which goes to show the level of empathy toward PLWHA. Likewise, a study in Nepal found 63% level of stigma about HIV/AIDS among migrant workers.⁵ In Turkey found low prevalence of HIV/AIDS because were almost no stigma from families member. Their cultural value tends to support and become an important facilitator of internal stigma.¹⁷ In Nigeria found higher level of education and those higher wealth index seem to be more compassionate toward PLWHA. More than 70% in the population are willing to care for relative with AIDS.²⁶

People tend to be more empathetic to family members, group members, close friends, and people who have personal needs and problems as the same as their own needs and problems²⁷. Family redefine the meaning of health as “back to work as usual”. Family concerns become an important social attachment which builds the feeling that family has a role and responsibility to accept and care their family members with HIV/AIDS.

Everyone has a role to eliminate the stigma and make meaningful contributions to help to cure someone’s health problems by building self-esteem. It can be successfully done through small changes in the way of thinking, feeling and acting surrounding the home environment. Social support by providing psychological motivation for PLWHA can improve their mental health condition as a necessity for comprehensive health status.²⁸ Social support influence mental health condition and quality of life better.²⁸ The specific participants PLWHA-migrant workers as the limitation in this study. Need more assessments of family stigmatization to other risk group in the community.

Conclusion

This study found good practice family willing to care for relatives toward PLWHA. In order to combat HIV/AIDS epidemic in the region, issues pertaining to stigma and discrimination need to be addressed. The family acceptance of the health condition among their family members with HIV/AIDS is reflecting of the function in carrying out of family health care. It can influence the family system as a morality culture of the community. Overcoming psychosocial needs through family support can help PLWHA overcome the problems of HIV infection and also stress associated with HIV infection properly. An Empathy can be used as an approach in one of the stigma reduction interventions. Finding from this study have implication to develop integrated

community-based care for PLWHA.

Ethical Clearance: The study protocol was approved by the Faculty of Nursing Science of Universitas Islam Sultan Agung Semarang.

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Conflict of Interest: none

References

1. Lindayani L, Chen Y, Wang J. Complex Problems, Care Demands, and Quality of Life Among People Living With HIV in the Antiretroviral Era in Indonesia. *J Assoc Nurses AIDS Care* [Internet]. 2018;29(2):300–9. Available from: <https://doi.org/10.1016/j.jana.2017.10.002>
2. Angula P, Ncama BP. Guidelines for Community-Based HIV/AIDS Stigma Reduction Intervention in a Rural Community. *World J AIDS*. 2016;(March):27–36.
3. Kalembo FW, Kendall GE, Ali M, Chimwaza AF, Tallon MM. Primary caregivers, healthcare workers, teachers and community leaders’ perceptions and experiences of their involvement, practice and challenges of disclosure of HIV status to children living with HIV in Malawi: a qualitative study. 2018;1–17.
4. Pretorius JB, Greeff M, Freeks FE, Kruger A. A HIV stigma reduction intervention for people living with HIV and their families. *Heal SA Gesondheid* [Internet]. 2016;21(018):187–95. Available from: <http://dx.doi.org/10.1016/j.hsag.2015.11.005>
5. Dahal S, Pokharel PK, Yadav BK. HIV/AIDS Related Stigma among Male Labor Migrants in Nepal. 2013;2013(December):305–12.
6. de Vries DH, Koppen L, Lopez AM, Foppen R. The vicious cycle of stigma and disclosure in “Self-management”: A study among the Dutch HIV population. *AIDS Educ Prev*. 2016;
7. Waluyo A, Culbert GJ, Levy J, Norr KF. Understanding HIV-related Stigma Among Indonesian Nurses. *J Assoc Nurses AIDS Care* [Internet]. 2014;1–12. Available from: <http://dx.doi.org/10.1016/j.jana.2014.03.001>
8. Chew BH, Cheong AT. Ethnic groups difference in

- discriminatory attitude towards HIV/AIDS patients among medical students: A cross-sectional study. *Malaysian J Med Heal Sci*. 2014;
9. Ferris FD, Balfour HM, Adv BA, Bowen K, Farley J, Hardwick M, et al. A Model to Guide Patient and Family Care: Based on Nationally Accepted Principles and Norms of Practice. 2002;24(2):106–23.
 10. UNAIDS. UNAIDS data 2018 [Internet]. 2018. Available from: www.unaids.org
 11. Steward WT, Koester KA, Fuller SM. Shaping the Patient-Centered Medical Home to the Needs of HIV Safety Net Patients: The Impact of Stigma and the Need for Trust. *J Assoc Nurses AIDS Care* [Internet]. 2018;1–15. Available from: <https://doi.org/10.1016/j.jana.2018.06.005>
 12. Kemppainen JK, MacKain S, Alexander M, Reid P, Jackson MP. Posttraumatic Stress Disorder and Stressful Life Events Among Rural Women With HIV Disease. *J Assoc Nurses AIDS Care* [Internet]. 2017;28(2):216–25. Available from: <http://dx.doi.org/10.1016/j.jana.2016.06.001>
 13. Golub SA, Gamarel KE. The Impact of Anticipated HIV Stigma on Delays in HIV Testing Behaviors: Findings from a Community-Based Sample of Men Who Have Sex with Men and Transgender Women in New York City. *AIDS Patient Care STDS*. 2013;27(11).
 14. Koirala S, Deuba K, Nampaisan O, Marrone G, Ekstro M. Facilitators and barriers for retention in HIV care between testing and treatment in Asia — 2017;1–20.
 15. Han H, Kim K, Murphy J, Cudjoe J, Wilson P, Sharps P, et al. Community health worker interventions to promote psychosocial outcomes among people living with HIV — A systematic review. 2018;1–18.
 16. Bonnington O, Wamoyi J, Ddaaki W, Bukenya D, Ondenge K, Skovdal M, et al. Changing forms of HIV-related stigma along the HIV care and treatment continuum in sub-Saharan Africa: a temporal analysis. 2017;1–6.
 17. Öktem P. The Role of the Family in Attributing Meaning to Living With HIV and Its Stigma in Turkey. 2015;2016.
 18. Thapa S, Hannes K, Cargo M, Buve A, Aro AR, Mathei C. Building a Conceptual Framework to Study the Effect of HIV Stigma-Reduction Intervention Strategies on HIV Test Uptake: A Scoping Review. *J Assoc Nurses AIDS Care* [Internet]. 2017;28(4):545–60. Available from: <http://dx.doi.org/10.1016/j.jana.2017.04.004>
 19. Park S, Park KS. Family Stigma: A Concept Analysis. *Asian Nurs Res (Korean Soc Nurs Sci)* [Internet]. 2014;8(3):165–71. Available from: <http://dx.doi.org/10.1016/j.anr.2014.02.006>
 20. Fatoki B. AIDS & Clinical Research Understanding the Causes and Effects of Stigma and Discrimination in the Lives of HIV People Living with HIV/AIDS: Qualitative Study. 2016;7(12).
 21. Li Li CL & GJ. Gendered Aspects of Perceived and Internalized HIV-Related Stigma in China. *Women Health*. 2016;0242(October).
 22. Paudel V, Baral KP. Women living with HIV/AIDS (WLHA), battling stigma, discrimination and denial and the role of support groups as a coping strategy: a review of literature. 2015;1–9.
 23. Paudel V, Baral KP. Women living with HIV/AIDS (WLHA), battling stigma, discrimination and denial and the role of support groups as a coping strategy: a review of literature. *Reprod Health* [Internet]. 2015;1–9. Available from: <http://dx.doi.org/10.1186/s12978-015-0032-9>
 24. Kementerian Kesehatan Republik Indonesia DJP dan PP. Laporan Perkembangan HIV-AIDS & Infeksi Menular Seksual (IMS) Triwulan IV Tahun 2017 [Internet]. 2017. Available from: http://siha.depkes.go.id/portal/files_upload/Laporan_HIV_AIDS_TW_4_Tahun_2017__1_.pdf
 25. Akta A, Merdiye Ş, Atav AS. Attitudes towards HIV/AIDS patients and empathic tendencies: A study of Turkish undergraduate nursing students. 2014;34:929–33.
 26. Dahlui M, Azahar N, Bulgiba A, Zaki R, Oche OM, Adekunjo FO, et al. HIV/AIDS related stigma and discrimination against PLWHA in Nigerian population. *PLoS One*. 2015;
 27. Oxley JC. The moral dimensions of empathy: limits and applications in ethical theory and practice. Palgrave Macmillan; 2011. 219 p.
 28. Wu X, Chen J, Huang H, Liu Z, Li X, Wang H. Perceived stigma, medical social support and quality of life among people living with HIV/AIDS in Hunan, China. *Appl Nurs Res* [Internet]. 2014; Available from: <http://dx.doi.org/10.1016/j.apnr.2014.09.011>

Phytochemical Investigation, Antioxidant and Antimicrobial Activities of *Ravenala Madagascariensis* (Sonn.) Family Strelitziaceae Growing in Egypt

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Abstract:

Introduction: *Ravenala madagascariensis* (Sonn.) family Strelitziaceae, commonly called traveler's tree or palm; it is used traditionally in India as tea made from young leaves for treatment of diabetes. On the other hand its seed found to have antiseptic properties.

Objective: Phytochemical investigation and isolation as well as testing the antioxidant and antimicrobial activities of the crude total and different successive fractions.

Material and Method: The leaves total ethanol extract was subjected for phytochemical screening. The *n*-BuOH fraction was fractionated using chromatographic isolation. Total phenolics and flavonoids and antioxidant activity of the crude total ethanol extract as well as *n*-hexane, CH₂Cl₂, EtOAc and *n*-BuOH successive fractions were determined using ABTS assays. On the other hand the antimicrobial of the crude total ethanol was carried out against 13 microorganisms using agar well diffusion method.

Results: Phytochemical screening showed the presence of flavonoids, tannins and sterols. Three phenolic compounds were isolated from the *n*-BuOH fraction and they were identified using different spectroscopic techniques. The different fractions showed high antioxidant activities especially EtOAc fraction that showed 88.96% for ABTS inhibition. Crude total ethanol extract showed selective moderate antimicrobial activity against the tested strains of *Cryptococcus neoformans*, *Bacillus cereus* and *Serratia marcescens*.

Conclusion: The ethyl acetate fraction showed significant antioxidant activity probably due to presence of the flavonoids contents.

Keywords: Antimicrobial, Antioxidant, Flavonoids, Phenolics, *Ravenala*.

Introduction

Replacement of synthetic products with natural products is our aim nowadays for safe life. Free radicals (especially oxygen free radicals) which generated by oxidation reactions of exogenous factors (like protein and lipids) are the cause of start chronic diseases like diabetes and cancer⁽¹⁾. Inhibition of these oxidation reactions by antioxidants is targeted to reduce free radicals and its effects on our bodies. Thus, antioxidants are useful for prevention of harmful diseases caused by

free radicals⁽²⁾. Searching of new source is important because of the increase in antibiotics resistance for developing antimicrobial agent. Due to low level of toxicity of plants, the priority to choose plants for treatment of the infectious diseases⁽³⁾.

Ravenala madagascariensis, commonly called traveler's palm or traveler's tree, is one of nature's most distinctive and remarkable plants for the arrangement of its leaves in a fan shape⁽⁴⁾. The common name is thought to refer to how travelers could be refreshed in

an emergency by drinking the water that has collected in the cup-like leaf bases. The traveler's palm (not a true palm) has been described as being part banana plant and part palm tree. Although it's called a palm, this plant is not a member of the palm family (Arecaceae); it actually belongs to the bird-of-paradise family, Strelitziaceae^(5,6). *Ravenala madagascariensis* is native to Madagascar, the African island renowned for its many endemic plant and animal species. Also present in other tropical countries which it is easily cultivated as an ornamental tree^(7,8). The tested extracts (hexane, carbon tetrachloride, chloroform and aqueous) of the leaves of *R. madagascarinsis* exhibited moderate antimicrobial activity with zone of inhibition ranging from 2.0 to 9.0mm against microbile strains while the crude methanol extract 9.0 mm zone of inhibition against *Escherichia coli*⁽⁹⁾. Beside these tested fractions and methanol extract exhibited significant thrombolytic activity⁽¹⁰⁾. Ethanolic extract was found effective in hypolipidaemic activity and improve the renal morphology and reduce lesions associated with diabetes induced by alloxan^(7, 11). Ethanol extract of the leaves of *R. madagascarinsis* has proved to be effective in inhibiting the growth (i.e. showed a bacteriostatic but not bactericidal at 200 mg/ml) of enteric bacteria such as *Shigella flexneri* ATCC 12022, *Serratia marcescens* ATCC 39006, *Klebsiella pneumoniae* ATCC 13883, *Proteus mirabilis* ATCC 25933, *Serratia marcescens*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Citrobacter freundii* which are among the causative agents of diarrhea⁽⁵⁾.

Material and Method

Plant Material: The leaves of *Ravenala madagascariensis* (Sonn.) were collected from the plants cultivated in El-Orman garden, Egypt, August 2015. The plant was authenticated by Ibrahim Ahmed El-Garf, professor of Botany, department of Botany and Microbiology, Faculty of Science, Cairo University, Giza, Egypt. The leaves were air-dried, powdered, weighed and kept in amber-colored, well-closed glass container, at low temperature for phytochemical and biological studies.

Chemicals: Methanol, gallic acid, sodium carbonate (Na₂CO₃), Folin-Ciocalteu (FC) reagent were obtained from Fluka (Milwaukee, WI, US). Aluminum chloride (AlCl₃), sodium nitrite (NaNO₂), rutin, 2, 2'-azinobis (3-ethylbenzothiazoline-6-sulfonic acid) diammonium salt (ABTS), potassium persulfate, butylated hydroxyanisole (BHA). All chemicals and standards were

provided from Sigma-Aldrich (St Louis, MO, USA).

Preparation of plant extract: The powdered leaves (1.7 kg) were exhaustively extracted with 70% ethanol by maceration, on cold, and at room temperature then concentrated to yield 400g. An aliquot of the ethanol extract (200g) was resuspended in distilled H₂O and successively fractionated with solvent of increasing polarity: *n*-hexane, CH₂Cl₂, EtOAc and *n*-BuOH.

Phytochemical screening: The total ethanolic extract of *R. madagascariensis* leaves was screened for the presence of carbohydrates and/or glycosides, tannins, flavonoids, saponins, sterols and/or triterpenes, alkaloids, anthraquinones and cardiac glycosides. It was carried out in accordance with the method described by Pandith⁽¹²⁾ and Pandey⁽¹³⁾.

Extraction and isolation: The powdered leaves (1.7 kg) were exhaustively extracted with 70% EtOH on cold by maceration at room temperature and concentrated to yield 400g. An aliquot of the ethanol extract (200g) was resuspended in distilled H₂O and successively fractionated with solvent of increasing polarity: *n*-hexane, DCM, EtOAc and finally *n*-BuOH. The *n*-butanol extract (25g) was subjected to a polyamide column (100 × 5 cm, 250 g) chromatography, gradient eluting with MeOH: H₂O in a way of increasing polarity by 10% increment. Fractions (100 mL each) were collected, evaporated under reduced pressure and screened by TLC using different systems. Similar fractions were pooled to yield 12 subfractions. The 1th fraction was chromatographed by a Sephadex LH₂₀ column (38 × 3 cm, 40 g) chromatography, isocratic eluting with saturated *n*-BuOH to give 6 subfractions, from which the 4th subfraction was subjected to a silica gel column (60 × 3 cm, 100 g) chromatography by gradient eluting with DCM: MeOH followed by sephadex LH-20 column (38 × 3 cm, 40 g) chromatography which eluted with 80% MeOH to give (1, 5 mg), (2, 10 mg) and (3, 10 mg).

Hexyl glucose⁽¹⁴⁾, ¹H-NMR (400 MHz, MeOD): δ 4.2 (1H,d,*J*=8Hz,H-1'), δ 3.9 (1H,q, CH₂), δ 3.87(1H,dd,H-6'), δ 3.76- 3.5 (4H,m), δ 3.6 (1H, m, H-5'), δ 3.25- 3.14(4H,m), δ 3.43 (1H,dd,H-4'), δ 1.92 (1H, s), δ 1.19 (3H,t, CH₃), δ 0.95 (1H, t, CH₂). **¹³C-NMR:** (100 MHz, MeOD), 14.29, 16.95, 17.54, 34.91, 58.88, 60.55, 63.04, 63.27, 64.84, 65.54, 67.51, 68.07, 69.93, 70.07, 71.00, 72.51, 73.53, 75.54, 75.79, 76.50, 77.11, 81.87, 82.50, 103.50,

Ethyl β-D-glucoside^(15, 16), ¹H-NMR (400 MHz,

MeOD): δ 4.3 (1H,d, $J=8$ Hz,H-1'), δ 3.9 (1H,q, CH₂), δ 3.86 (1H,dd,H-6'), δ 3.71 (1H,dd,H-3'), δ 3.6 (1H, m, H-5'), δ 3.55(1H,dd,H-2'), δ 3.41 (1H,dd,H-4'), δ 1.25(3H,t, CH₃). ¹³C-NMR (100 MHz, MeOD): 14.29, 61.18, 65.13, 70.15, 73.60, 76.35, 76.68, 102.51.

(3S,5R,6R,7E,9S) megastigmane-7-ene-3,5,6,9-tetrol 9-O-B-D-glucopyranoside⁽¹⁷⁾, ¹H-NMR (400 MHz, MeOD): δ 6.2(1H,d, $J=16$ Hz, H-7), δ 5.66(1H,d, $J=6.6$ Hz,H-8), δ 4.56(1H, $J=6$ Hz,H-9), δ 4.41(1H,d, $J=8$ Hz,H-1'), δ 4.07(1H,d, $J=16$ Hz,H-4), δ 3.87 (1H,d, $J=12$ Hz,H-6'b), δ 3.68 (1H,d, $J=12$ Hz,H-6'a), δ 1.14(3H,s,H-11), δ 1.26(3H,s,H-13), δ 1.47(1H,d, $J=12$ Hz,H-2 eq), δ 1.6- 1.9(m, H-4ax, eq), δ 0.93(3H,s,H-12). ¹³C-NMR: (100 MHz, MeOD), 20.95, 24.92, 25.58, 26.68, 39.34, 44.12, 45.01, 61.24, 63.7, 70.14, 73.45, 74.05, 76.41, 76.7, 77.87, 99.2, 131.72, 134.14.

Total phenolics content: Total phenolics content was determined using method described by Zhang et al. 2006⁽¹⁸⁾ to each of the 96 wells, 75 μ l of DDW was added, followed by 25 μ l of either sample or standard and 25 μ l of Folin–Ciocalteu reagent (diluted 1:1(v/v) with DDW). Then mixed and left for 6 min, 100 μ l of 75 g/L Na₂CO₃ was added to each well. The solutions were mixed again and the plates were covered and left in the dark for 90 min, absorbance was measured at 765 nm. Each standard and sample solution was analyzed in triplicate. Gallic acid was used as a standard at 0.78 - 200 μ g/ml to produce a calibration curve.

Total flavonoids content: Total flavonoids content was determined using method described by Herald et al. 2012⁽¹⁹⁾. Distilled water (100 μ l) was added to each of the 96 wells, followed by 10 μ l of 50 g/L NaNO₂ and 25 μ l of standard or sample solution. After 5 min, 15 μ l of 100 g/L AlCl₃ was added to the mixture; 6 min later, 50 μ l of 1 mol/L NaOH and 50 μ l of distilled water were added. The plate was shaken for 30 s in the plate reader prior to absorbance measurement at 510 nm. All samples and standards were measured against a methanol as blank. Rutin was used as a standard at 15 - 2000 μ g mL⁻¹ to generate a calibration curve.

Biological activity study:

Antioxidant assay: The free radical scavenging capacity of extracts was also studied using the ABTS radical cation decolorization assay⁽²⁰⁾. ABTS was dissolved in deionized water to 7 mM concentration. ABTS radical cation (ABTS^{•+}) was produced by reducing

ABTS solution with 2.45 mM potassium persulfate and allowing the mixture to stand in the dark at room temperature for 12-16h before use. For the study, the ABTS^{•+} solution was diluted in deionized water to an absorbance of 0.7 (± 0.02) at 734 nm. After the addition of 100 μ L of methanolic plant extract solution to 3 ml of ABTS^{•+} solution, the absorbance reading was taken at room temperature 10 min after initial mixing(A₁). All determinations were carried out in triplicate. Butylated hydroxyanisole was used as a standard at 15–250 μ g/ml to generate a calibration curve (average R² = 0.9999, fig.7). All samples and standards were measured against a methanol reagent blank.

Inhibition activity was calculated using the following formula:

$$\% \text{ inhibition} = (A_0 - A_1) / A_0 \times 100$$

Where A₀ is the absorbance of the control, A₁ is the absorbance of the standard/extracts.

Antimicrobial activity: Organisms used in this study were obtained from the antimicrobial activity unit of the Regional Center for Mycology and Biotechnology of Al-Azhar University and Microbiology Department of MUST and consisted of the fungi *Candida albicans* ATCC 10231, *C. glabrata* (RCMB 0049010), *Cryptococcus neoformans* (RCMB 0049001), *Aspergillus flavus* (RCMB 002002), *Aspergillus niger* (RCMB 002005) and *Aspergillus fumigatus* (RCMB 002008) and the bacteria *Staphylococcus aureus* ATCC 25923, *Serratia marcescens* (RCMB 029), *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *Bacillus subtilism* (RCMB 015), *Bacillus cereus* RCMB 027, *Klebsiella pneumoniae* (RCMB 0100223-5) and *Cryptococcus neoformans* (RCMB 0049001). Antimicrobial sensitivity was tested using the agar well diffusion technique according to⁽²¹⁾. The plant extract was dissolved in DMSO with concentration 200 mg/ml. Muller Hinton agar (MHA) plates were inoculated with bacterial suspension with a density adjusted to that of 0.5 McFarland standard under aseptic conditions and wells with diameter 6mm were filled with 50 μ l of the plant extract (dissolved in DMSO with concentration 200 mg/ml), positive and negative controls. The latter were applied using Gentamycin (4 μ g/ml), Ketoconazole (100 μ g/ml) and DMSO, respectively. When 70% ethanolic extract of (200mg/ml) is placed on agar, it will diffuse into the agar. The solubility of the chemical and its molecular size will determine the size of the area of

chemical infiltration around the well; if it susceptible to the chemical. This area of no growth around the well is known as a zone inhibition or clear zone. The zone diameter was then measured with slipping calipers.

Results

Phytochemical screening: Phytochemical screening of *R. madagascariensis* leaves total ethanolic extract revealed the presence of carbohydrates and/or glycosides, sterols and/or triterpenes, tannins, saponins and flavonoid aglycone/glycosides.

Identification of purified compounds: Structure elucidation of the purified compounds was based on their physicochemical and chromatographic properties, spectral analyses (UV, ESI-MS, ^1H NMR and DEPT-Q) and compared with authentic samples and literature. The isolated compound **1** was identified as **hexyl glucose**⁽¹⁴⁾, compound **2** as **ethyl β -D-glucoside**^(15,16) and compound **3** as **(3S,5R,6R,7E,9S) megastigmane-7-ene-3,5,6,9-tetrol 9-O- β -D-glucopyranoside**⁽¹⁷⁾ which these were isolated for the first time from *Ravenala madagascariensis* (Sonn.).

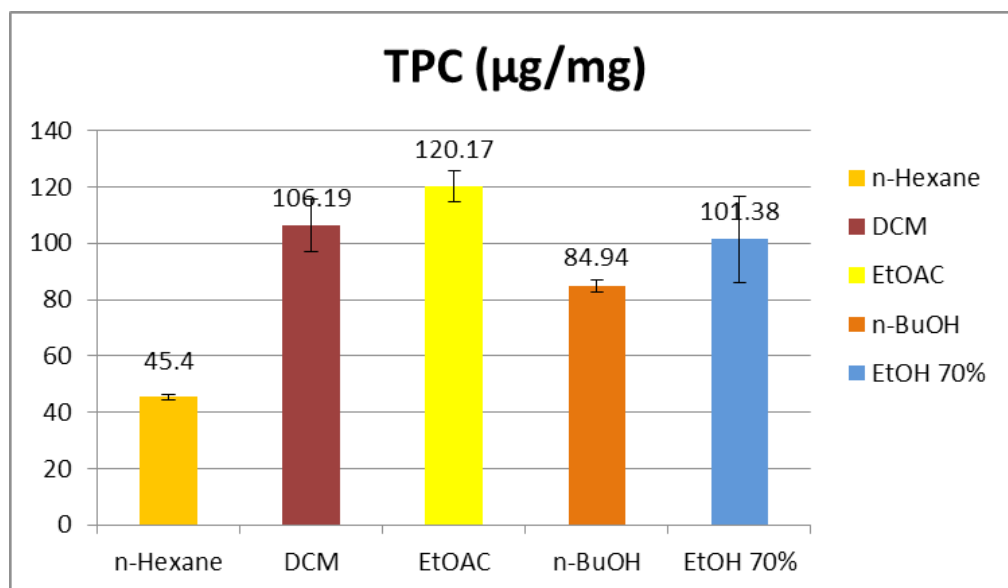


Figure 1: Total phenolic content (TPC) of different fractions of *R. madagascariensis* leaves.

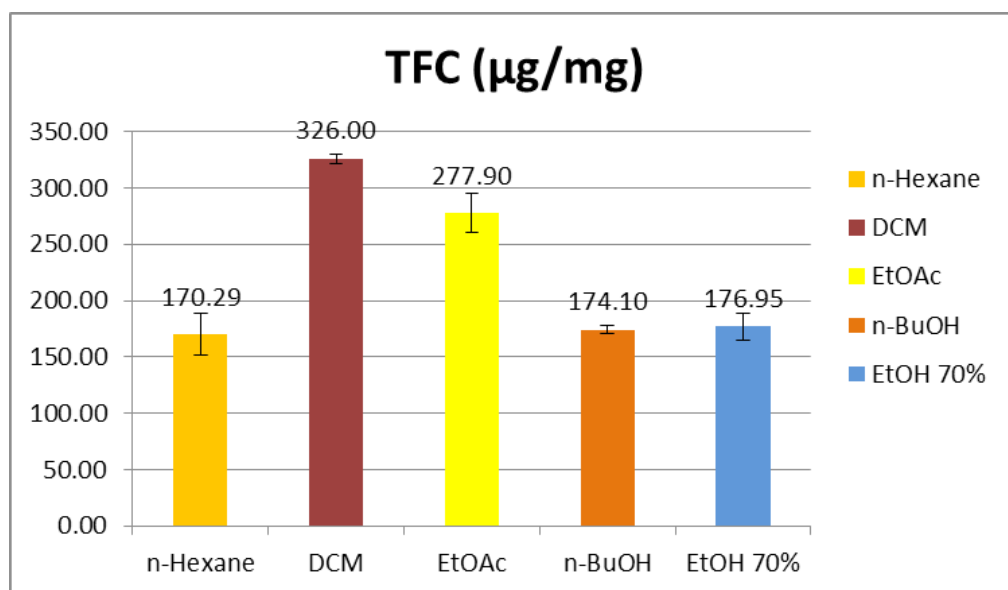


Figure 2: Total flavonoid content (TFC) of total ethanol 70% and successive fractions of *R. madagascariensis* leaves.

Antioxidant activity: ABTS is used for testing the radical scavenging activity of antioxidant compounds or plant extracts. The ABTS⁺, generated from oxidation of ABTS by potassium persulfate, is presented for determining the antioxidant activity of hydrogen

donating antioxidants and chain breaking antioxidants. The ABTS scavenging capacity of different fractions of *R. madagascariensis* leaves were expressed as inhibition capacity and the results are presented in figure 3.

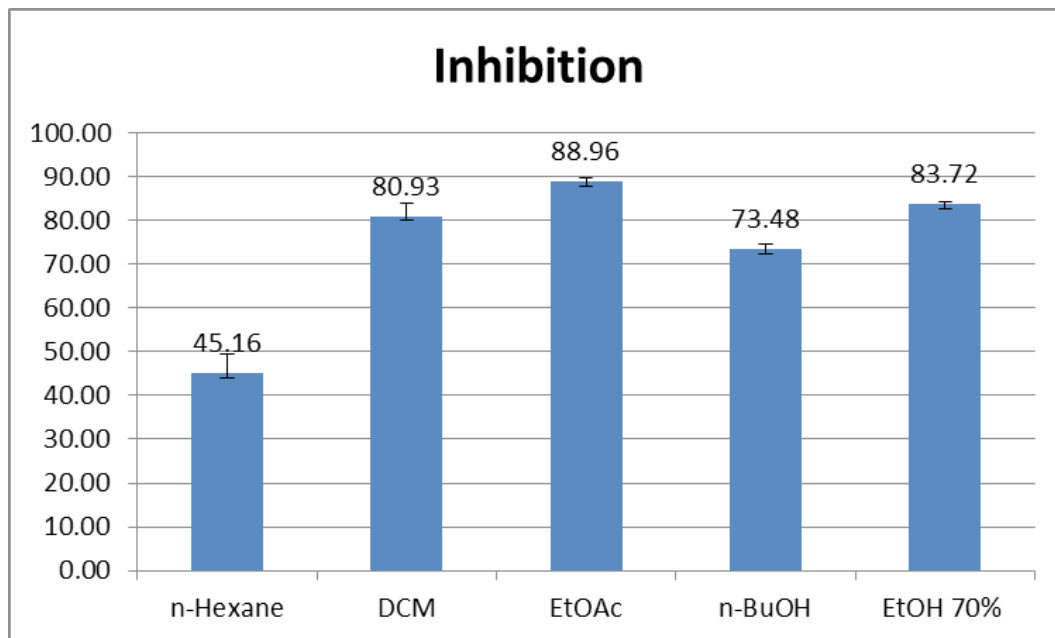


Figure 3: Inhibition activity of total ethanol 70% and successive fractions of *R. madagascariensis* leaves using ABTS assay.

Antimicrobial activity: The total ethanolic 70% extract showed selective antimicrobial activity against tested strains of the fungus of *Cryptococcus neoformans* (RCMB 0049001), the gram negative bacteria *Serratia*

marcenscens (RCMB 029) and the gram positive bacteria *Bacillus cereus* (RCMB 027) with zone of inhibition (13mm, 12mm, 15mm) respectively, the results are presented in Table 1.

Table 1: Antimicrobial effects of crude total ethanol 70% extract (200 mg/ml) *R. madagascariensis* leaves extract against different organisms

Test organism	Zones of inhibition (mm)		
	+ ve control	DMSO	Ethanol extract
Gram negative bacteria			
<i>Pseudomonas aeruginosa</i> ATCC 27853	44	-	-ve
<i>Escherichia coli</i> ATCC 25922	24	-	-ve
<i>Klebsiella pneumoniae</i>	35	-	-ve
<i>Serratia marcenscens</i> (RCMB 029)	18	-	12
Gram positive bacteria			
<i>Staphylococcus aureus</i> ATCC 25923	40	-	-ve
<i>Bacillus subtilis</i> RCMB 015	26	-	-ve
<i>Bacillus cereus</i> RCMB 027	25	-	15

Fungi			
Cryptococcus neoformans (RCMB 0049001)	25	-	13
Aspergillus fumigatus (RCMB 002008)	17	-	-ve
Aspergillus flavus (RCMB 002002)	16	-	-ve
Aspergillus niger (RCMB 002005)	15	-	-ve
Candida glabrata (RCMB 0049010)	19	-	-ve
Candida albicans ATCC 10231	23	-	-ve

Discussion

Based on scarce reports about the traveler's palm and according to the results of phytochemical screening which showed the presence of sterols, triterpenes, carbohydrates, glycosides, tannins and flavonoids compounds in total ethanol extract of *R. madagascariensis* encourage phytochemical and biological studies of the mentioned plant. These phytochemical classes encouraged us to evaluate the antioxidant activity⁽⁵⁾ of the crude total ethanol extract as well as *n*-hexane, CH₂Cl₂, EtOAc and *n*-BuOH successive fractions and antimicrobial activity of crude total ethanol. Due to results of antioxidant activity, the *n*-butanol fraction was subjected to different chromatographic method which led to isolate three phenolic compounds which identified as **Hexyl glucose, Ethyl β-D-glucoside and (3S,5R,6R,7E,9S) megastigmane-7-ene-3,5,6,9-tetrol 9-O-B-D-glucopyranoside**. Concerning the antimicrobial activity against different microorganisms, it was found that the total ethanol extract of *R. madagascariensis* has selective antimicrobial activity against the tested strains of *Cryptococcus neoformans* (RCMB 0049001), *Bacillus cereus* (RCMB 027) and *Serratia marcescens* (RCMB 029).

Conclusion

The ethyl acetate fraction of *R. madagascariensis* leaves showed significant antioxidant activity probably due to presence of the total phenolic contents. The total ethanol extract has selective antimicrobial activity against the tested strains of *Cryptococcus neoformans* (RCMB 0049001), *Bacillus cereus* (RCMB 027) and *Serratia marcescens* (RCMB 029).

Conflict of Interest Statement: The authors declare that there is no conflict of interest.

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Ethical Clearance: Not Applicable.

References

1. Liyanaarachchi GD, Samarasekera JKRR, Mahanama KRR, Hemalal KDP. Tyrosinase, elastase, hyaluronidase, inhibitory and antioxidant activity of Sri Lankan medicinal plants for novel cosmeceuticals. *Industrial crops and products*. 2018;111:597-605.
2. Aktumsek A, Zengin G, Guler GO, Cakmak YS, Duran A. Antioxidant potentials and anticholinesterase activities of methanolic and aqueous extracts of three endemic *Centaurea L.* species. *Food and Chemical Toxicology*. 2013;55:290-6.
3. Djeussi DE, Noumedem JA, Seukep JA, Fankam AG, Voukeng IK, Tankeo SB, et al. Antibacterial activities of selected edible plants extracts against multidrug-resistant Gram-negative bacteria. *BMC complementary and alternative medicine*. 2013;13(1):164.
4. Rakotoarivelo N, Razanatsima A, Rakotoarivony F, Rasoaviety L, Ramarosandratana AV, Jeannoda V, et al. Ethnobotanical and economic value of *Ravenala madagascariensis* Sonn. in Eastern Madagascar. *Journal of ethnobiology and ethnomedicine*. 2014;10(1):57.
5. Onifade A, Bello M, Fadipe D. Bioassay directed fractionation of antibacterial compounds from traveller's tree (*ravenala Madagascariensis sonnerat*) and its phytochemical constituents. *International Journal of Bioassays*. 2015;4(9):4299-304.
6. Cron GV, Pirone C, Bartlett M, Kress WJ, Specht C. Phylogenetic relationships and evolution in the Strelitzaceae (Zingiberales). *Systematic Botany*. 2012;37(3):606-19.
7. Ramiarantsoa H, Yao-Kouassi P, Kanko C, Assi K, Djakoure A, Tonzibo F. Chemical constituents of the antidiabetic plant *Ravenala madagascariensis*.

- International Journal of Pharmaceutical Sciences and Research. 2014;5(12):5503.
8. Reyad-ul-Ferdous M, Uddin N, Shahjahan DS, Hossen M, Arman MSI, Islam A. PRELIMINARY IN-VITRO POTENTIAL PHYTOCHEMICALS INVESTIGATION OF BARKS OF RAVENALA MADAGASCARIENSIS SONNERAT. 2014.
 9. Sharmin T, Chowdhury SR, Mian MY, Hoque M, Sumsujjaman M, Nahar FJWJoPS. Evaluation of antimicrobial activities of some Bangladeshi medicinal plants. 2014;2(2):170-5.
 10. Chowdhury S, Sharmin T, Hoque M, Sumsujjaman M, Das M, Nahar FJWJoPS, et al. Evaluation of thrombolytic and membrane stabilizing activities of four medicinal plants of Bangladesh. 2013;4(11):4223.
 11. Priyadarshini S, Vadivu R, Jayshree NJIJoPS. Hypolipidaemic and Renoprotective study on the Ethanolic & Aqueous extracts of leaves of Ravenala madagascariensis Sonn. on alloxan induced diabetic rats. 2010;2(1):44-50.
 12. Pandith JI. Phytochemical screening of certain plant species of Agra city. Journal of drug delivery and therapeutics. 2012;2(4).
 13. Pandey A, Tripathi S. Concept of standardization, extraction and pre phytochemical screening strategies for herbal drug. Journal of Pharmacognosy and Phytochemistry. 2014;2(5).
 14. Ojha S, Mishra S, Kapoor S, Chand S. Synthesis of hexyl α -glucoside and α -polyglucosides by a novel Microbacterium isolate. Applied microbiology and biotechnology. 2013;97(12):5293-301.
 15. Ogawa S, Asakura K, Osanai S. Thermotropic and glass transition behaviors of n-alkyl β -D-glucosides. RSC Advances. 2013;3(44):21439-46.
 16. Teague C, Holmes E, Maibaum E, Nicholson J, Tang H, Chan Q, et al. Ethyl glucoside in human urine following dietary exposure: detection by ¹H NMR spectroscopy as a result of metabonomic screening of humans. Analyst. 2004;129(3):259-64.
 17. Ho DV, Kodama T, Le HTB, Van Phan K, Do TT, Bui TH, et al. A new polyoxygenated cyclohexene and a new megastigmane glycoside from Uvaria grandiflora. Bioorganic & medicinal chemistry letters. 2015;25(16):3246-50.
 18. Zhang Q, Zhang J, Shen J, Silva A, Dennis DA, Barrow CJ. A simple 96-well microplate method for estimation of total polyphenol content in seaweeds. Journal of Applied Phycology. 2006;18(3-5):445-50.
 19. Herald TJ, Gadgil P, Tilley M. High-throughput micro plate assays for screening flavonoid content and DPPH-scavenging activity in sorghum bran and flour. Journal of the Science of Food and Agriculture. 2012;92(11):2326-31.
 20. Re R, Pellegrini N, Proteggente A, Pannala A, Yang M, Rice-Evans C. Antioxidant activity applying an improved ABTS radical cation decolorization assay. Free radical biology and medicine. 1999;26(9-10):1231-7.
 21. Jahangirian H, Haron MJ, Shah MH, Abdollahi Y, Rezayi M, Vafaei N. Well diffusion method for evaluation of antibacterial activity of copper phenyl fatty hydroxamate synthesized from canola and palm kernel oils. Digest J Nanomat Biostructures. 2013;8:1263-70.

New Approach of Hyaluronic Acid Bound Spermatozoa-ICSI in Iraqi Infertile Patients

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Abstract

Background: Ability of spermatozoa to binding to hyaluronan is related to sperm membrane maturity and fertilizing potential, thus it has been suggested that sperm selection using Hyaluronic acid (HA) could increase the implantation rate in Intracytoplasmic Sperm Injection(ICSI). Basically Physiological -ICSI (PICSI) is a scientific technique used in ICSI, is a specialized form and more filtered way of selecting the best competent sperm for fertilization process. Despite the fact that conventionally spermatozoa are selected for ICSI based on their morphology and motility.

Objective: To evaluate whether (PICSI) has the potential to improve the fertilization rate and embryo grading.

Patients, Materials and Methods: Fifty-three infertile couples subjected to an *in vitro* fertilization stimulation program; Thirty-five underwent (ICSI) cycle and eighteen underwent (PICSI) cycle, assessed the fertilization rate and embryo grading at cleavage stage then the results were statistically analyzed.

Results: In spite of the fertilization rate of PICSI group was better than ICSI group but statistically no significant difference was noticed between both of them. In regarding to embryo grading at cleavage stage, there was a significant increase($P<0.05$) in Grade 1 and Grade 2 for PICSI group as compared to ICSI group.

Conclusions: The percentage of fertilization for PICSI group is better than for ICSI group. In regarding to statistical analysis, there was no significant differences between two groups. Regarding to embryo quality at cleavage stage, the PICSI cycle significantly improves embryo quality(Grade 1 and Grade 2) at day 2 and day 3 of development as compared to the ICSI cycle.

Keywords: *Hyaluronic Acid Bound Sperm, ICSI, PICSI, infertile men.*

Introduction

Infertility is a complex disorder and a unique medical condition, it involves a couple, rather than a single individual with significant medical, psychosocial, and economic problems⁽¹⁾.

Male infertility is usually caused by either sperm production or its transport disorders⁽²⁾. Semen analysis has two major quantifiable attributes: the total number of spermatozoa which reflects sperm production by the testes and the patency of the post-testicular duct system and the total fluid volume formed by the various accessory glands which reflect the secretory activity of these glands⁽³⁾.

In Vitro Fertilization (IVF) is an assisted reproductive technology in which spermatozoa and oocytes are combined outside of the human body in a laboratory dish. The main steps in any IVF cycle are controlled ovarian hyperstimulation, retrieval of oocytes, fertilization, embryo culture and embryo transfer⁽⁴⁾.

The conventional IVF could not help the couples with severe male factor infertility including very low sperm count, motility impairment and abnormal sperm morphology as they leading to failure of fertilization⁽⁵⁾. The ICSI procedure means "entails the deposition of a single spermatozoon directly into the cytoplasm of the oocyte, thus bypassing the zona pellucida and the

oolemma⁷⁽⁶⁾. Up to 15% of all couples of reproductive age have been diagnosed with infertility and about one-third of them have male factor infertility as a contributing factor, ICSI has confirmed to be precious for couples with severely compromised semen parameters⁽⁷⁾.

Another proposed indication for the use of ICSI includes: unexplained infertility, poor quality oocyte, advanced maternal age, low oocyte yield, prior fertilization failure with conventional IVF, Pre implantation genetic diagnosis, fertilization after *in vitro* maturation, and fertilization of cryopreserved oocyte⁽⁸⁾.

Hyaluronic acid (HA) is the main component of the cumulus oophorus; it plays a role in the natural selection of mature spermatozoa during *in vivo* fertilization. Therefore, the sperm ability to bind to hyaluronic acid and subsequently to the zona pellucida can be used as the basis for *in vitro* sperm selection. Since HA is a physiological component of the cervix, cumulus cells and follicular fluid, it should pose no additional safety risks when used for sperm selection⁽⁹⁾. Huszar and colleagues discovered that sperm bound to hyaluronic acid *in vitro* have markers of cellular maturity, minimal DNA fragmentation, normal shape, and low frequency of chromosomal aneuploidies⁽¹⁰⁾.

In the past few years, both HA-mediated devices, the sperm HA- binding assessment in the Andrology laboratory, and the ICSI sperm selection device, the PICSI dish (an IVF Petri dish that carries an HA spot), has been increasingly accepted and used worldwide⁽¹¹⁾.

The PICSI dish may take only a few minutes. Further, the PICSI dish provides a spacious area for sperm selection. It's equipped with lines of orientation, and all spermatozoa are within the same level of microscopic focus range. Thus, the embryologist has a good opportunity to compare the available spermatozoa with respect to shape (morphology) and also HA binding, as well as the important specific response of the fully developed sperm to HA contact^(12,13). There are now several laboratories that have initiated HA mediated sperm selection. It's important that none of the groups practicing the HA sperm selection reported any adverse effects regarding fertilization or embryo development⁽¹⁴⁾.

Patients, Materials and Methods

A prospective study conducted in High Institute of Infertility Diagnosis and Assisted Reproductive Technologies/AL-Nahrain University. Fifty-three

infertile couples subjected to IVF stimulation program; Thirty-five infertile couples underwent (ICSI) cycle, and eighteen underwent (PICSI) cycle. Fifty-three infertile couples subjected to:

- Full history taking (age of women, type of infertility, duration & causes of male and female infertility, and number of previous IVF trials).
- Measurement of the body mass index (BMI).
- Baseline hormonal assay was performed at day 2 of the menstrual cycle include serum Follicle stimulating hormone (FSH), Luteinizing hormone (LH), Estradiol (E2), Prolactin and Thyroid stimulating hormone (TSH) for each woman.

The study included women that underwent to controlled ovarian stimulation (antagonist protocols) their age ranged between (20-40) years. The cases of infertile male with spermatozoa retrieval from testicular biopsy and frozen spermatozoa were excluded.

Oocytes retrieval was performed using a transvaginal probe 34-36 hours after the hCG injection just prior to the rupture of follicles. The procedure usually took 20-30 minutes. After that, the patients were given antibiotics, analgesics, and luteal phase support. All follicles within both ovaries are aspirated by ovum aspiration needle and follicular fluid given directly to the embryologist to identify the quality of the retrieved cumulus-oocytes complex⁽¹⁵⁾.

After recovery, the oocytes were washed free of the follicular fluid, the hyaluronidase concentration and exposure must be kept to a minimum, mechanical dissection of cumulus oophorus and corona radiata was done. After denudation, to remove traces of hyaluronidase, oocytes should be thoroughly washed. Grading of the oocytes into germinal vesicle, metaphase I (MI), and metaphase II (MII), also classified into normal or abnormal oocyte. Later on transferred into drops of IVF media overlaid by paraffin/mineral oil in an incubator at temperature 37°C with 5% CO₂, and at 95% humidity. Finally, those ova which have been extruded the first polar body (metaphase II) and morphologically intact were suitable for microinjection⁽¹⁶⁾. The oocytes inseminated for 4-6 hours after aspiration and the spermatozoa must be prepared during this time.⁽¹⁷⁾ After insemination, zygotes observed for 18-20 hours to check for the presence of 2 pronuclei. At day 1, the presence of 2 pronuclei considered as a good prognostic sign. After that, evaluation of embryos at day 2 and day

3. The embryos with (4 cells at day 2) or with (7-9 cells at day 3) and containing <10% of cytoplasmic fragments are considered as good quality embryos⁽¹⁸⁾. Embryo transfer generally done at day 2, or at day 3 or at day 5 post ICSI procedure depending on patient's age, embryo quality, and the number of embryos available⁽⁶⁾.

Luteal phase was supported since day of oocyte retrieval by vaginal progesterone (Cyclogest®400mg twice: or Crinone,® 8% progesterone gel) and continued daily. Serum β -hCG assay was done on day 14 after the embryo transfer⁽¹⁹⁾.

The Sperm Selection Device (PICSI) provides a means to select mature sperm based on their ability to bind to hyaluronan hydrogel. It's a polystyrene culture dish with three microdots of hyaluronan attached to the interior bottom. The device is sterile, free of endotoxin and non-toxic to embryos, the spermatozoa will be added to the pre-hydrated microdot in a volume equal to or greater than that used to pre-hydrate the dot (approximately 10 μ l). Then the tip of the micropipette containing the sperm will be touched to the edge of the hydrating drop at the dish under the oil and expel the sperm. Once bound, hyaluronan-bound sperm are easily identified, they exhibit no progressive migration despite vigorous tail beating. Sperm binding begin normally in 5 minutes or less. However, some microdots may require 30 minutes or more to reach full binding

capability. The captured sperm will be expelled into a Polyvinylpyrrolidone (PVP) drop to process them for ICSI, from the PVP droplet, select and load single, processed sperm for injection into the oocytes according to your standard injection protocol^(10,20).

Statistical analysis was done by using SPSS (statistical package for social sciences) version 20. For analysis, basic characteristics and hormones profile were analyzed using independent sample t-test. Chi square test was used to reveal the significant comparison among percentages of the fertilization rate, and embryo grading in this study.

Results

The current study illustrated that the percentage of infertile couples with primary infertility was (62.264%), while infertile couples with secondary infertility was (37.735%). All infertile couples who were enrolled in this study had different causes that led them to be infertile. The most common cases of males was oligoasthenoteratozoospermia and for females was polycystic ovaries syndrome. The statistical analysis in table (1) showed no significant differences for the female age, infertility duration, BMI and basal hormonal profile level at cycle day 2 between infertile couples underwent ICSI cycle and infertile couples underwent PICSI cycle.

Table (1): Basic characteristic and hormonal profile at cycle day 2 for both groups.

Parameter	ICSI group	PICSI group	P-value
Age (Year)	30.685 \pm 0.853	28.555 \pm 1.207	0.922
Duration of infertility (Year)	6.514 \pm 0.600	5.944 \pm 0.697	0.261
BMI (kg/m ²)	29.153 \pm 0.592	28.762 \pm 0.586	0.052
FSH (mIU/L)	6.278 \pm 0.449	6.647 \pm 0.720	0.552
LH (mIU/L)	7.139 \pm 0.985	6.901 \pm 1.391	0.984
Prolactin (mIU/L)	13.195 \pm 1.401	14.380 \pm 1.782	0.513
E ₂ (pg/ml)	45.136 \pm 1.755	43.477 \pm 2.621	0.997
TSH (mIU/L)	1.477 \pm 0.081	1.555 \pm 0.117	0.936

The fertilization rate for PICSI group higher than for ICSI group. In regarding to statistical analysis, there was no significant differences between both groups, p-value = 0.207.

Assessment of embryo quality at cleavage period, according to number and size of cells and the percentage of fragmentation. Therefore, the grading of

embryo divided into three grades (Grade 1, Grade 2 and Grade 3). The embryo with grade 1 represent the best embryo, while the worst embryo with grade 3. The statistical analysis showed significant increase in embryo grading (Grade 1 and Grade 2) for PICSI group, while no significant difference for Grade 3 for both groups, as shown in table (2).

Table 2: Comparison between ICSI group and PICSI group in main clinical embryological variables.

Chi square	P-value	PICSI group	ICSI group	Parameter	
1.596	0.207	78.378	63.385	Fertilization rate	
5.444	0.020	86.206	58.024	Grade 1	Day 2
13.889	0.000	10.344	35.802	Grade 2	
1.000	0.317	3.448	6.172	Grade 3	
5.321	0.021	82.758	55.555	Grade 1	Day 3
11.520	0.001	13.793	37.037	Grade 2	
1.600	0.206	3.448	7.407	Grade 3	

Discussion

In the current study there was no significant difference in basic characteristic and hormonal level at cycle day 2 for both groups to eliminate any variations that may affect the reproductive results.

Even though in this study the patients were treated with the same controlled ovarian stimulation regimen and ICSI was performed by the same embryologist, using the same instruments and media for gamete handling and culture. This study revealed that injection of HA-bound spermatozoa (HA-ICSI) determines a statistically significant improvement in embryo quality in day 2 and day 3 when performing HA- ICSI on a limited number of oocytes (between 1 and 3). It didn't observe a statistical significant difference in fertilization rate, in spite of the percentage of fertilization to selection of HA-bound spermatozoa group was higher than that for ICSI group .However,it's difficult to analyze the insignificant difference when HA-ICSI was performed on a limited number of oocytes and low number of patients which warrants further study to be carried out as a clinical trial.A statistically significant improvement in reproductive terms like fertilization rate, embryo quality and a reduction in the number of miscarriages were observed by WorriLOW *et al.* Performing PICSI ® (MidAtlantic Diagnostic) versus conventional ICSI, in a study of 240 patients⁽²¹⁾. Recently, Nasr-Esfahani *et al.* have published a study (performed on 50 couples) observing a higher fertilization rate when injecting oocytes with HA-selected spermatozoa⁽²²⁾. Against this, in two studies with a small number of patients involved [44 patients Van Den Berg *et al.*, and 18 patients Sanchez *et al.*], no differences in fertilization^(23,14).Use of hyaluronan-facilitated sperm selection did not exert any observed harmful effects to the recipient oocytes or resulting embryos. Consequently, the use of hyaluronan

binding sperm in ICSI may directly influence the genetic integrity of the paternal contribution to the conceptus, minimizing the potential risks inherent to ICSI ⁽²⁰⁾.

Conclusions

The percentage of fertilization for PICSI group is better than for ICSI group. In regarding to statistical analysis, there was no significant differences between two groups. Regarding to embryo quality at cleavage stage, the PICSI cycle significantly improves embryo quality(Grade 1 and Grade 2) at day 2 and day 3 of development as compared to the ICSI cycle.

Authors Contribution Statement: This research was done by Dr.Ezdehar N. Ali as a part of her Ph.D. thesis under the supervision of Assist. Professor Dr. Hayder A.L. Mossa (corresponding author).

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Ethical Clearance: The study was approved by Ethical Approval Committee.

Conflict of Interest: Conflict of Interest declared none.

Source of Funding: By the researchers themselves.

Application of ICSI by (PICSI) was used for the first time in High Institute for Infertility Diagnosis and ART's/Al-Nahrain University.

References:

1. Cousineau TM and Domar AD. Psychological impact of infertility. Best Pract Res Clin Obstet Gynaecol. 2007; 21(2):293-308
2. McLachlan R, and Cook R. Male infertility: a child of our own, 4th ed. Andrology Australia. 2004.

3. World Health Organization. WHO laboratory manual for the examination and processing of human semen. 5th edition. Geneva: WHO . 2010.
4. Perkins, KM. Boulet, SL. Kissin, DM. Jamieson, DJ. and the National ART Surveillance (NASS) Group, 'Risk of Ectopic Pregnancy Associated With Assisted Reproductive Technology in the United States, 2001–2011', *ObstetGynecol*, Jan 2015; 125(1): 70–8.
5. Devroey, Paul, and André Van Steirteghem. A review of ten years, experience of ICSI. *Human Reproduction Update*, 2004; 10(1):19–28.
- 6- Neri QV, Monahan D, Rosenwaks Z, Palermo GD, and Rosenwaks Z. ICSI: technical aspects. In :Gradner DK, Weissman A, Howles CM, References 92, Shoham Z, editors. *Textbook of Assisted Reproductive Technologies, Volume One: Laboratory Perspectives*, 4th ed. London: Informa Health care. 2012. Pp172-185.
7. Babayev SN., Park C W, and Bukulmez O. ICSI indications: how rigorous? *Seminars in reproductive medicine* 2014; 32(4): 283-290.
8. American Society for Reproductive Medicine (ASRM). A Practice Committee Report. ICSI for non-male factor infertility. *Ame Society Reprod Medic. FertilSteril* 2012; 98: 1395-1399.
9. David K, Ariel W, Colin M, and Zeev S.: *Textbook of Assisted Reproductive Techniques*; 5th edition vol. 1: *Laboratory Perspectives*, 2018: Pp119.
10. Huszar G, Ozenci CC, Cayli S,Zavaczki Z, HanschE, andVigue L. Hyaluronic acid binding by human sperm indicates cellular maturity, viability and unreacted acrosomal status. *Fertil Steril*,2003; 79(Suppl 3): 1616–24.
11. WorriLOW KC, Eid S, Woodhouse D,Witmyer J, Khoury C, and Liebermann J, . Prospective, multi-center, double-blind, randomized clinical trial evaluating the use of hyaluronan-bound sperm in ICSI: statistically significant improvement in clinical outcomes. Abstract, ASRM annual meeting. Florida: Orlando, 2011.
12. Aoki VW, and Carrell DT. Human protamines and the developing spermatid: their structure, function, expression and relationship with male infertility. *Asian J Androl* 2003; 5: 315–24.
13. Carrell DT, Emery BR, and Hammoud S,. Altered protamine expression and diminished spermatogenesis: what is the link? *Hum Reprod Update* 2007; 13: 313–27.
14. Sanchez M, Aran B, Blanco J, Vidal f, Veiga A, BarriPN . Preliminary clinical and FISH results on hyaluronic acid sperm selection to improve ICSI. *Hum Reprod* 2005; 20 Supp 1: i200.
15. Orvieto R. Triggering final follicular maturation-hCG, GnRH-agonist or both, when and to whom?. *J Ov Res* .2015 Aug 21; 8(1):60.
16. Varras M, Polonifi K, Mantzourani M, Stefanidis K, Papadopoulos Z, AkrivisC, andAntsaklis A. Expression of antiapoptosis gene survivin in luteinized ovarian granulosa cells of women undergoing IVF or ICSI and embryo transfer: clinical correlations. *Reproductive Biology and Endocrinology*. 2012 Sep 7; 10(1):74.
17. Popal W, and Nagy ZP. Laboratory processing and ICSI using epididymal and testicular spermatozoa: what can be done to improve outcomes?. *Clinics*. 2013;68: 125-30.
18. Marinakis, G. and Nikolaou, D. 'What is the role of assisted reproduction technology in the management of age-related infertility?',*Human Fertility*, Feb 2011;14(1):8-15.
19. Satterfield, MC. Dunlap, KA. Hayashi, K. Burghardt, RC. Spencer, TE. Bazer, FW. 'Tight and Adherens Junctions in the Ovine Uterus: Differential Regulation by Pregnancy and Progesterone', *Endocrinology*, 01 August 2007; 148 (8): 3922-31.
20. Yagci,A,W. Mark.J.Stronk and G.Huszar. Spermatozoa bound to solid state hyaluronic acid show chromatin structure with high DNA chain integrity :an acridine orange fluorescence study. *JAndrol*2010; 31(6):566-72.
21. WorriLOW KC, Huynh T, Bower JB, Anderson AR, Schillings W, Crain JL. PICSU VS ICSI: statistically significant improvement in clinical outcomes in 240 IVF patients. *FertilSteril* 2007; 88 Supp 1: s37.
22. Nasr-Esfahani MH, Razavi S, Vahdati AA, Fathi F, Tavalae M. Evaluation of sperm selection procedure based on hyaluronic acid binding ability on ICSI outcome. *J Assist Reprod Genet* 2008; 25: 197-203.
23. Van Den Bergh MJ, Fahy-Deshe M, Hohl MK. Pronuclear zygote score following ICSI of hyaluronan-bound spermatozoa: a prospective randomized study. *Reprod Biomed Online* 2009.

Depression and Meaning of Life of Middle-Aged Women: Mediating Effects of Self-Esteem and Social Network

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Abstract

Purpose: This study aims to verify the mediating effects of self-esteem and social network on the relation between depression and meaning of life of middle-aged women.

Method: The data was collected from total 119 middle-aged women in 40-64 years old. The data was analyzed using the descriptive statistics, Pearson's correlation coefficient and stepwise multiple regression by using the SPSS 22.0 Program.

Results: The meaning of life showed the significantly negative correlation with depression ($r = -.52, p < .001$) while it showed the positive correlations with self-esteem ($r = .74, p < .001$) and social network ($r = .56, p < .001$). In the relation between depression and meaning of life, the self-esteem and social network were the significant mediating variables.

Conclusion: This study could be used as the basic data for the development of integrated nursing intervention programs that could improve the quality of life of middle-aged women.

Keywords: *Middle-aged women, Depression, Meaning of life, Self-esteem, Social network.*

Introduction

As the most active period in lifetime, the middle age is the period to get ready for the upcoming new old age by bearing fruits of efforts so far and giving a new meaning to life.¹ However, in case of middle-aged women, they go through diverse emotional changes and physical symptoms as their ovarian function gets declined around the menopause.² Out of them, the depression of middle-aged women is an important health problem required for nursing intervention as it is related to the degree of life goal and achievement under the emotional confusion and wandering together with doubts about the meaning of life and the substance of themselves in the middle of their lives.¹

As an important variable having effects on the meaning of life of middle-aged women, the self-esteem is a variable having direct effects on the depression,³ and the depression has a correlation with the meaning of life of middle-aged women,¹ so that it is verified as a variable related to the meaning of life of middle-aged women. As an environmental variable, the social network has direct/indirect effects on individual's health by meeting the sociality which is a basic desire of human, providing information to individuals, and also motivating them to act for the enhancement of health.⁴ Thus, based on the preceding researches reporting the correlation between depression and meaning of life, the depression would have effects on the meaning of life of middle-aged women, and also the self-esteem and social network would work as mediating variables on the relation between those two variables. As a result, the quality of life after the middle age could be decided depending on how successfully the individuals adapt themselves to changes and loss in accordance with physical aging. Thus, it would be necessary to review the meaning of life by strengthening the establishment

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of social network, growing the self-regulating ability through the self-esteem enhancement training, and also enhancing the depression management ability.

Thus, this study aims to provide the basic data for the development of nursing intervention programs that could improve the quality of life of middle-aged women by verifying the mediating effects of self-esteem and social network on the relation between depression and meaning of life of middle-aged women.

Method

Subjects: This study selected the middle-aged women in 40-64 years old. Regarding the number of samples in this study, when setting up the medium-level effect size (.15), significance level (.05), and three predictor variables to secure the 95% statistical power for the correlation analysis and regression analysis by using the G*Power 3.12 Program, the number of minimum samples was calculated as 119. Thus, after distributing the questionnaires to 140 people, total 119 questionnaires were used for the final analysis.

Instruments

Depression: This study used the K-CESD-R (Korean version of Center for Epidemiologic Studies Depression Scale-Revised), verified for the validity and reliability by Lee et al.⁵ This tool is composed of 20 questions based on the 5-point scale (0-4point). The higher score means the higher degree of depression. Cronbach's $\alpha = .93$ in this study.

Self-esteem: This study used the self-esteem scale, developed by Rosenberg.⁶ This tool is composed of 10 questions based on the 4-point scale. The higher score means the higher degree of self-esteem. Cronbach's $\alpha = .83$ in this study.

Social Network: This study used the K-LSNS-R based on the LSNS-R (Social Network Scale-Revised) by Lubben et al.⁷ verified for the validity and reliability by Hong et al.⁴ This tool is composed of 12 questions based on the 6-point scale (0-5point). The higher score means the higher degree of social network. Cronbach's $\alpha = .92$ in this study.

Meaning of life: This study used the Korean version of meaning in life scale by Won, Doo-Ri et al.⁸ This tool is composed of total 10 questions based on the 7-point scale. The higher score means more subjective meanings in life. Cronbach's $\alpha = .96$ in this study.

Data collection: The data was collected from July 2018 to August 2018. The researcher collected data from middle-aged women visiting the bus terminal, sports and shopping. After explaining the purpose and objective of this study to the voluntary participants, they were asked to fill out the written consent form.

Ethical consideration: For the ethical consideration of subjects, this study submitted the research plan to the Public Institutional Review Board under the Ministry of Health and Welfare, and then received the deliberation exemption approval (P01-201806-21-017) before starting this study.

Data analysis: The general characteristics of subjects, and depression, self-esteem, social network, and meaning of life were determined by descriptive statistics using the SPSS/WIN 22.0 Program. The correlations between variables were analyzed through the Pearson's correlation coefficients. Also, the mediating effects of self-esteem and social network on the relation between depression and meaning of life were analyzed using the regression and Sobel test.

Results

General characteristics of subjects: The subjects in 40-49 years old were the most ($n=55$, 46.2%). In the degree of education, the graduation of college or up was the most ($n= 78$, 65.5%). Total 96 subjects (80.7%) had a spouse, and total 72 subjects (60.5%) had a religion. And total 67 subjects (56.3%) had an occupation. Regarding the economic status, total 95 subjects (79.8%) responded that they were in the middle status. In case of health status, total 61 subjects (51.3%) responded that they were in the normal status (Table 1).

Table 1. General characteristics of subjects (N=119)

Characteristics	Categories	n (%)
Age (Years)	40~49	55(46.2)
	50~59	54(45.4)
	60~64	10(8.4)
Education	≤High school	41(34.5)
	≥College	78(65.5)
Spouse	Yes	96(80.7)
	No	23(19.3)
Religion	Yes	72(60.5)
	No	47(39.5)
Occupation	Yes	67(56.3)
	No	52(43.7)

Characteristics	Categories	n (%)
Economicstatus	High	12(10.1)
	Middle	95(79.8)
	Low	12(10.1)
Healthstatus	Good	44(37.0)
	Normal	61(51.3)
	Bad	14(11.7)

The degree of depression, self-esteem, social network and meaning of life in subjects

The mean scores of depression and self-esteem of subjects were .63(±.69) and 2.94(±.43) respectively. The mean scores of social network and meaning of life of subjects were 2.43(±.81) and 4.65(±1.30) (Table 2).

Table 2. The degree of depression, self-esteem, social network and meaning of life

Variables	M±SD	Min	Max
Depression	.63±.69	0	3.90
Self-esteem	2.94±.43	1.90	4.00
Social network	2.43±.81	.33	4.25
Meaning of life	4.65±1.30	1.90	7.00

Correlations between depression, self-esteem, social network and meaning of life in subjects: The meaning of life had the significantly negative correlation with depression($r=-.52, p<.001$) while it had positive correlations with self-esteem($r=.74, p<.001$) and social network($r=.56, p<.001$). In other words, when the degree of depression was lower, and when the degrees of self-esteem and social network were higher, the degree of meaning of life was higher(Table 3).

Table 3. Correlations between depression, self-esteem, social network and meaning of life

Variables	Depression r(p)	Self-esteem r(p)	Social network r(p)
Depression	1		
Self-esteem	-.51 (<.001)	1	
Social network	-.38 (<.001)	.49 (<.001)	1
Meaning of life	-.52 (<.001)	.74 (<.001)	.56 (<.001)

The mediating effects of self-esteem and social network on the relation between depression and meaning of life in subjects: First, the mediating effects of self-esteem on the relation between depression

and meaning of life of middle-aged women are as follows(Table 4). In the first step, the depression as an independent variable had statistically significant effects on the self-esteem as a mediating variable($\beta=-.51, p<.001$), and the explanatory power of self-esteem was 26%. In the second step, the depression as an independent variable had significant effects on the meaning of life as a dependent variable($\beta=-.52, p<.001$), and the explanatory power of meaning of life was 27%. In the third step, in the results of conducting the regression analysis by taking the depression and self-esteem as predictor factors and the meaning of life as a dependent variable to understand the effects of self-esteem as a mediating variable on the meaning of life as a dependent variable, the depression($\beta=-.19, p=.007$) and self-esteem($\beta=.64, p<.001$) were the significant predictor factors on the meaning of life. In other words, when taking the self-esteem as a mediating variable in the third step, the depression was significant on the meaning of life. As the non-standardized regression coefficient was decreased from the absolute value .98 of the second step to the absolute value .36 of the third step, the self-esteem partially mediated.

Second, the mediating effects of social network on the relation between depression and meaning of life of middle-aged women are as follows(Table 4). In the first step, the depression as an independent variable had statistically significant effects on the mediating effects of social network($\beta=-.38, p<.001$), and the explanatory power of social network was 14%. In the second step, the depression as an independent variable had significant effects on the meaning of life as a dependent variable($\beta=-.52, p<.001$), and the explanatory power of meaning of life was 27%. In the third step, in the results of conducting the regression analysis by taking the depression and social network as predictor factors and the meaning of life as a dependent variable to understand the effects of social network as a mediating variable on the meaning of life as a dependent variable, the depression($\beta=-.36, p<.001$) and social network($\beta=.42, p<.001$) were the significant predictor factors on the meaning of life. In other words, when taking the social network as a mediating variable in the third step, the depression was significant on the meaning of life. As the non-standardized regression coefficient was decreased from the absolute value .98 of the second step to the absolute value .68 of the third step, the social network partially mediated.

In the results of Sobel test for the test of significance on the mediating effect size of the self-esteem and social network, the self-esteem and social network were the

significant mediating variable on the relation between depression and meaning of life ($Z=-5.26, p<.001, Z=-3.47, p<.001$).

Table 4. Mediating effects of Self-esteem and Social network on the Relation between Depression and Meaning of life

Step	Variables	B	β	t	p	R ²	Adj. R ²	F	p
Step 1	Depression → Self-esteem	-.322	-.512	-6.452	<.001	.262	.256	41.630	<.001
Step 2	Depression→Meaning of life	-.983	-.521	-6.609	<.001	.272	.266	43.685	<.001
Step 3	Depression, Self-esteem → Meaning of life					.576	.569	78.831	<.001
	1) Depression	-.363	-.192	-2.733	.007				
	2) Self-esteem	1.926	.642	9.125	<.001				
Sobel test : $Z=-5.26, p<.001$									
Step 1	Depression→Social network	-.442	-.377	-4.401	<.001	.142	.135	19.366	<.001
Step 2	Depression→Meaning of life	-.983	-.521	-6.609	<.001	.272	.266	43.685	<.001
Step 3	Depression,Social network→ Meaning of life					.426	.416	42.995	<.001
	1) Depression	-.682	-.362	-4.763	<.001				
	2) Social network	.681	.423	5.575	<.001				
Sobel test : $Z=-3.47, p<.001$									

Discussion

The cut-off score of this depression tool was 13, and the mean score of depression of subjects was .63(mean 12.7). Compared to the optimal cut-off score(16) of a foreign tool CESD-R, this tool shows the lower cut-off score. As the final score could be influenced by situations or method presented by the tool, and this result might reflect the sociocultural background of Korea, the developer emphasizes that there should be sufficient consideration of depression even when the score is relatively low.⁵ The mean score of self-esteem was 2.94. The self-esteem of female adults was lower, the prevalence of depression got higher. Thus, it was verified as a predictor factor of depression, which supports the results of this study.⁹ The mean score of social network was 2.43(mean 29.11), and in a research targeting the subjects in mean 57.58 year old, by the tool developer Hong et al,⁴ it was 30.53. Like this, the degree of social network shows a bit of differences and the differences in the degree cannot be compared, so that it would be necessary to have further researches. The mean score of meaning of life was 4.65 out of seven. A research targeting the middle-aged men and women by using the same tool, by Chang¹⁰ showed a bit higher score (4.81) than the result of this study. Considering the

results of a study by Chang & Sohn¹ reporting that the middle-aged men showed the higher score of meaning of life than the middle-aged women, this might be because this study targeted only middle-aged women.

In the correlations between depression, self-esteem, social network, and meaning of life, the meaning of life showed the significantly negative correlation with depression while it showed the positive correlations with self-esteem and social network. As the factors having effects on the meaning of life, the physical factors having direct effects on health and functions, personal factors like hardiness, environmental factors like social support, cognitive factors like self-esteem, and the emotional factors like depression and stress were mentioned,¹¹ which supports the results of this study. According to a research by Oh & Oh,¹² the low self-realization and interpersonal relationship have effects on the meaning of life in the middle age, and the social support works as a buffering agent of psychological symptoms such as stress or depression of middle-aged women,¹³ which supports the results of this study.

On the relation between depression and meaning of life, the self-esteem showed the partial mediating effects. In other words, even though the depression of

middle-aged women had direct effects on the meaning of life, the meaning of life could be positively influenced by self-esteem showing the mediating effects. According to a research by Choi,¹⁴ the most influential variable on the meaning of life is self-esteem, so that there should be further researches on the causality if the self-esteem would work as a mediating variable. On the relation between depression and meaning of life, the social network showed the partial mediating effects. In other words, even though the depression of middle-aged women had direct effects on the meaning of life, the meaning of life could be positively influenced by social network showing the mediating effects. According to a research targeting elderly women by Oh et al.¹⁵ the social network has significant effects on the depression, which supports the results of this study. However, there should be further researches targeting middle-aged women.

Conclusion

As a result, the quality of life after the middle age could be decided depending on how successfully individuals adapt themselves to changes and loss in accordance with physical aging. Thus, it would be necessary to review the meaning of life by strengthening the establishment of social network, growing the self-regulating ability through the self-esteem enhancement training, and also enhancing the depression management ability.

Ethical Clearance: Not required

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Conflict of Interest: Nil

References

1. Chang HK, Sohn JN. Factors related to meaning of life in middle adults. *Asia-pacific Journal of Multimedia Services Convergent with Art, Humanities, and Sociology*, 2017, 7(7), 609-21. <http://dx.doi.org/10.14257/ajmahs.2017.07.90>
2. Bosworth HB, Bastian LA, Kuchibhatla MN, Steffens DC, McBride CM, Skinner CS, et al. Depressive symptoms, menopausal status, and climacteric symptoms in women at midlife. *Psychosomatic Medicine*, 2001, 63(4), 603-8.
3. Cha BK. A path analysis of factors influencing health-related quality of life among male adults. *Journal of Korean Academy of Community Health Nursing*, 2016, 27(4), 399-409. <http://dx.doi.org/10.12799/jkachn.2016.27.4.399>
4. Hong M, Casado BL, Harrington D. Validation of Korean versions of the Lubben Social Network Scales in Korean Americans. *Clinical Gerontologist*, 2011, 34, 319-34. DOI: 10.1080/07317115.2011.572534
5. Lee S, Oh ST, Ryu SY, Jun YJ, Lee K, Lee E, et al. Validation of the Korean version of center for epidemiologic studies depression scale-revised (K-CESD-R). *Korean Journal of Psychosomatic Medicine*. 2016, 24(1), 83-93.
6. Rosenberg M. *Society and the adolescent self-image*. Princeton, NJ: Princeton University Press; 1965, 340.
7. Lubben J, Blozik E, Gillmann G, Iliffe S, von Renteln-Kruse W, Beck JC, Stuck AE. Performance of an abbreviated version of the Lubben Social Network Scale among three European community-dwelling older adult populations. *The Gerontologist*, 2006, 46(4), 503-13.
8. Won DR, Kim KH, Kwon SJ. Validation of the Korean version of meaning of life questionnaire. *The Korean Journal of Health Psychology*, 2005, 10(2), 211-25.
9. Cha BK. A path analysis of factors influencing eating problem among young female adults. *Journal of Nutrition and Health*, 2017, 50(6), 615-23. <https://doi.org/10.4163/jnh.2017.50.6.615>
10. Chang HK. Influencing factors on mid-life crisis. *Korean Journal of Adult Nursing*, 2018, 30(1), 98-105. <https://doi.org/10.7475/kjan.2018.30.1.98>
11. Steger MF, Mann JR, Michels P, Cooper TC. Meaning in life, anxiety, depression, and general health among smoking cessation patients. *Journal of Psychosomatic Research*, 2009, 67(4), 353-8. Doi:10.1016/j.jpsychores.2009.02.006
12. Oh ET, Oh HO. Relationship among mid-life crisis, health promotion behavior and life satisfaction. *The Korean Journal of Physical Education*, 2011, 50(6), 325-36.
13. Chung MS. Resilience, coping method, and quality of life in middle-aged women. *Journal of Korean Academy of Psychiatric and Mental Health Nursing*, 2011, 20(4), 345-54.

14. Choi MS. The relationship of self-esteem, mental health, perceived social support & social avoidance and distress according to purpose in life, *The Korean Journal of Health Psychology*, 2011,16(2),363-77.
15. Oh IG, Oh YS, Kim MI. Effect of social networks on the depression of elderly females in Korea: analysis of the intermediating effect of health promoting behavior, *Korean Journal of Family Welfare*, 2009, 3(14), 113-36.

Efforts in Improving Environmental Sanitation of Elementary School Students through Eco-education

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Abstract

In 2017, many schools were not yet equipped with good sanitation facilities. In Indonesia, 1.5 million children under five die of diarrhea every year. This community partnership program aims to increase students' knowledge about environmental sanitation and improve environmental sanitation behavior. The method used quantitative and qualitative method. Quantitative method is resultant from questionnaires data and qualitative method used to direct observation through Focus Group Discussion (FGD). The data of students' knowledge and behavior were analyzed using bivariate analysis. The results of this activity showed that at the pretest, the elementary school students' knowledge was 90.62%, which was in the good category, and the peer educator's knowledge was 82.14%, which was in the good category. At the posttest, the elementary school students' knowledge increased to 94.08%, which was in the good category, and the peer educator's knowledge increased to 90%, which was in the good category. The elementary school students' sanitation behavior was 67.60%, which can be categorized as good. Correlation test results showed no significant relationship between students' knowledge and behavior ($p > 0.05$). It can be concluded that there was an increase in students' and peer educators' knowledge about environmental sanitation after the implementation of community partnership program. Unfavorable sanitation behaviors were seen in the behaviors of littering, not washing hands before eating, and consuming unhealthy snack. Meanwhile, good sanitation behavior was seen in the behavior of bathing twice a day and defecating in the toilet/water closet.

Keywords: Sanitation, Elementary School, Cikeuting Udik.

Introduction

Health status of a person or a community in a society is the result of the interaction of various factors, i.e. internal and external factors¹. Internal factors include psychological and physical factors. External factors include factors of community culture, physical environment, social, education, politics, economics, and so on¹. Broadly speaking, health status is influenced by four factors, namely environment (45%), lifestyle/behavior (30%), health services (20%), and genetics/heredity (5%). Health status is a unity of various conditions, including physical, mental and social health¹. Therefore, each factor has a significant role in creating public health status. Environmental factor has major impacts on human health, one of which is waste management. Waste is considered as one of the urban problems. The existence of waste is considered as a

source of disease, it also damages the city's aesthetics. One of the easiest ways to deal with it is to dispose it in a place far from the settlement². The other environmental factor is sanitation facilities. One of three schools in Indonesia does not have access to water, 12.09% or 25,835 schools in Indonesia do not have water closets, 35.19% or 75,193 schools in Indonesia do not have hand washing facilities, and one of two schools in Indonesia does not have water closets that separate male students and female students³.

Based on the results of previous research, the water quality around Bantargebang, especially for microbiological parameters in the Ciketing Udik Urban Village in 2019, was below the quality standard⁴. The results of previous research also illustrated that the amount of waste that entered Bantargebang Integrated Waste Management Site for the period 2014-2015

fluctuated every month. The maximum amount was in December 2015, which was 214,972.08 tons/month, and the minimum amount was in June 2014, which was 151,770.58 ton/month⁵. The results of previous research also showed that the most medical expenses spent by the people in the three villages were for URTI, followed by diarrhea and malaria. The number fluctuated every month. The results showed that water sanitation in Sumur Batu area was classified as low, specifically the clean water and drinking water services. The results of observations and interviews showed that some residents and scavengers around the Waste Management Site did not have sanitation facilities that met the requirements⁶.

Method

The program was implemented at Elementary School of Dinamika Indonesia located in Bekasi Bantargebang Integrated Waste Management Site, Ciketing Udik Urban Village, Bantargebang Sub-District. The primary targets in this program were the students of Dinamika Indonesia Bantargebang and the secondary targets (peer educator) in this program were the staff in the school environment, including the headmaster, teachers and the educational community. The students and peer educators took a

pretest on knowledge about sanitation and questionnaire on elementary school students' behavior.

The pretest and posttest given to students and peer educators consisted of 10 questions. Students' and peer educators' knowledge were categorized based on the questionnaire. There were 3 categories of knowledge:

- a. Poor, if the correct answers were < 56%,
- b. Moderate, if the correct answers were 56%–75%,
- c. Good, if the correct answers were 76-100%.

The percentages were obtained by dividing the number of correct answers by the number of respondents then multiplied it by 100%. After calculating the percentage, the results can be categorized⁷. Environmental sanitation behavior categories were assessed using a hypothetical mean formula. The results of questionnaire on students' knowledge and behavior were then analyzed using bivariate analysis. The results were previously tested using normality test. Normality test results showed that the data were not normally distributed so the correlation test was conducted using Kendall's Tau-b test.

Results

Results of students' pretest are presented in Table 1.

Table 1. Results of Elementary School Students' Pretest

Number of Students	Total score per question										Total
	1	2	3	4	5	6	7	8	9	10	
96	93	90	94	95	94	93	44	80	94	93	870

Mean obtained from the questionnaire was 9.062.

Results of peer educators' pretest are presented in Table 2.

Table 2. Results of Peer Educators' Pretest

Number of Peer Educators	Total score per question										Total
	1	2	3	4	5	6	7	8	9	10	
14	11	14	12	14	13	12	13	13	12	1	115

Mean obtained from the questionnaire was 8.214.

Results of students' posttest after the familiarization to elementary school students are presented in Table 3.

Table 3. Results of Elementary School Students' Posttest

Number of Students	Total score per question										Total
	1	2	3	4	5	6	7	8	9	10	
71	69	71	69	70	71	70	56	55	68	69	668

Mean obtained from the questionnaire was 9.40.

Results of peer educators' posttest are presented in Table 4.

Table 4. Results of Peer Educators' Posttest

Number of Peer Educators	Total score per question										Total
	1	2	3	4	5	6	7	8	9	10	
13	12	13	13	13	13	13	13	12	13	2	117

Mean obtained from the questionnaire was 9.

Table 5. Frequency Distribution of Elementary School Students' Sanitation Behavior

Category	Total	Percentage
High	48	67.60%
Medium	23	32.40%
Total	71	100%

In the posttest results, it can be seen that the total correct answers was 870. It was divided by 96 and multiplied by 10 questions. The result was multiplied by 100%. The percentage obtained was 90.62%, which means that students' knowledge was in the good category. Categories of elementary school students' knowledge about sanitation are presented in Table 6.

Table 6. Categories of Elementary School Students' Knowledge

	Pretest Category	Posttest Category
Students	90.62% (Good)	94.08% (Good)
Peer educators	82.14% (Good)	90% (Good)

Relationship between students' knowledge and behavior variables was tested using Kendall's Tau-b test. Bivariate test results showed no significant relationship between student's knowledge and behavior ($p = 0.992$ or $p > 0.05$).

Discussion

Referring to Table 6 above, it can be seen that students' and peer educators' knowledge was in the good category even before the familiarization. The

implementation of familiarization to elementary school students and training of peer educators seemed to increase knowledge, as evidenced by an increase in the percentage of correct answers by elementary school students and peer educators. Bivariate analysis results showed no relationship between environmental sanitation knowledge and behavior. These results were not in line with the results of previous research, which found a positive correlation between environmental knowledge and behavior⁹. In addition, the results of previous research also indicated a correlation between students' knowledge and behavior¹⁰. Environmental education was proven to increase students' knowledge about the environment¹¹. Good student behavior can be formed through daily practice. It was in line with the results of previous research, which found that good practices in waste management must be applied in the school environment in order to change students' behavior¹².

Based on Table 5, elementary school students' sanitation behavior was quite good, but there were some behaviors that were not good enough. One of the bad behaviors was consuming unhealthy snack. Behavior of consuming street food had the highest percentage, 14.85% of students answered always and 56.34% of students answered often. It happened because there were no canteen facilities at Dinamika Indonesia. Therefore, students bought snacks on the roadside near the school. Some teachers had taken precautions so that students did not buy unhealthy snack by asking them to bring lunch box from home. Healthy eating behavior can be

improved by providing knowledge of the importance of healthy food to students and parents¹³. Hence, the need for policies regarding the promotion of healthy food in the school environment emerges¹⁴. In addition, schools must provide healthy canteens. Healthy canteens can support the availability of healthy food for students^{15, 16}.

Behavior of disposing waste properly was always done by 57.74% of students. The rest answered often, sometimes and never, which meant that 40% of students did not always dispose waste properly. It might be caused by the lack of waste containers provided by the school or the poor wastemanagement. Waste was not transported to the Waste Management Site regularly, causing waste containers full and waste scattered around containers because they can no longer accommodate the waste. This scene was witnessed by the researchers when they visited the school several times. Adequate disposal facilities can influence the habit of disposing waste properly¹⁷. In addition, it is necessary to provide environmental education, such as disposing waste properly as early as possible to elementary school students¹⁸.

Behavior of washing hands before eating was always done by 67.60% of students. The rest answered often, sometimes and never, which meant that approximately 33% of students did not always wash their hands before eating. It might be caused by the far distance to toilet facilities. Elementary school students whose classrooms were located on the 2nd floor must go down to the 1st floor to wash their hands in the lavatory. The lavatories were located only on the 1st floor. Moreover, Dinamika Indonesia had no sink. This was in line with the results of previous research, which stated that students' behavior of washing hand was influenced by hand washing facilities^{19, 20, 21}. In addition, it was necessary to conduct regular hand washing training to build students' good behavior of washing hand.²².

Behavior of defecating in the toilet/water closet and bathing twice a day were always done by > 80% of students. The result was supported by the previous research, which mentioned that most families living around Bantargebang Integrated Waste Management Site owned shared facilities for bathing and defecating⁴. The available facilities supported behavior of bathing twice a day and defecating in the toilet/water closet.

Conclusions

Elementary school students' and peer educators' knowledge increased after the implementation of

community partnership program, 2) elementary school students' and peer educators' knowledge about sanitation were in the good category, 3) Poor sanitation behaviors were seen in the behavior of littering, not washing hands before eating and consuming unhealthy snack, 4) good sanitation behaviors can be seen from the behavior of bathing twice a day and defecating in the toilet/water closet.

Recommendations that can be given as follows: 1) Dinamika Indonesia should be equipped with healthy canteen facilities, 2) Dinamika Indonesia should be equipped with toilets on each floor and sinks in front of classrooms for washing hands, 3) Dinamika Indonesia should increase the number of waste containers at students' gathering points.

Competing Interest: This research is part of the Community Partnership Program of the Ministry of Research, Technology and Higher Education of the Republic of Indonesia and the University of Indonesia, thus there is no competition in running this program.

Ethical Clearance: This program is approved by the Institutional Review Board (IRB) of the Faculty of Public Health and School of Environmental Science, University of Indonesia.

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References

1. Hapsari, D., Putri, S., Julianty, P. Effect of Healthy Environment and Healthy Life Behavior on Health Status. Center for Research and Development of Ecology and Health Status in Jakarta. Bulletin. Research Health. Supplement 2009; 40-49.
2. Maulana, Y.C., Rohmat, D., dan Ruhimat, M. Zoning of Bantargebang Integrated Waste Disposal (TPST). Journal Gea 2014; Vol 14 No 2

3. Ministry of Education and Culture. School Sanitation Profile. Jakarta: Center for Education and Culture Data and Statistics. 2017
4. Sukmana, H. Analysis of ground water quality and environmental sanitation, Social, Economic behavior on settlements of scavenger around integrated waste disposal site (TPST) Bantargebang Bekasi. [Thesis]. School of Environmental Sciences, University of Indonesia:2019
5. Sitio, R. Effect of the Amount of Waste Entering Bantargebang on the Health Costs of Ciketingudik and Sumurbatu Community. *Journal of Application Management, Economics and Business*2017; Vol. 2, No.1
6. Fauziah. The Relationship Between Individual Factors and Characteristics of Water Sanitation with the Incidence of Diarrhea in Toddlers Age 10-59 Months in Sumurbatu Village, Bantargebang District, Bekasi City in 2013. [Thesis]. Syarif Hidayatullah State Islamic University Jakarta: 2013
7. Siswanto, S. Level of Knowledge of Sayung Middle School 1 Students Against Keroncong Music. [Thesis]. Semarang State University: 2015
8. Creswell, J. Educational Research, Planning, Conducting, and Evaluating Quantitative And Qualitative Research. Boston: Pearson Education. 2012
9. Cimen, O and Yilmaz, M. Predictors of Behavior Factors of High School Predictors of Behavior Factors of High School Students Against Recycling. *International Electronic Journal of Environmental Education* 2016; Vol.6, Issue 1
10. Gusti, A. The Relationship of Knowledge, Attitudes, and Behavioral Intentions of Sustainable Waste Management on Primary School Students in City of Padang, Indonesia. *International Journal of Applied Environmental Sciences* 2016; Volume 11, Number 5
11. Hoang, T, T, H, P., and Kato, T. Measuring the effect of environmental education for sustainable development at elementary schools: A case study in Da Nang city, Vietnam. *Sustainable Environment Research* 2016; Vol 26
12. James, L. Facilitating Lasting Changes at an Elementary School. *International Electronic Journal of Elementary Education*2016; 8(3)
13. Giffari, M., Hatami, H., Rakhshanderou, S., and Heshmat, K. Effectiveness of Snack-centered Nutrition Education on Promoting Knowledge, Attitude, and Nutritional Behaviors in Elementary Students. *Int J Pediatr* 2017; Vol.5, N.12
14. Reeve, E., Thow, A, M., Bell, C., Engelhardt, K., Naliponguit, E, C, G., Go, J, J., and Sacks, G. Implementation lessons for school food policies and marketing restrictions in the Philippines: a qualitative policy analysis. *BioMed Central* 2018; Vol 14 No 8
15. Drummond, C and Sheppard, L. Examining primary and secondary school canteens and their place within the school system: a South Australian study. Oxford University Press 2011; Vol. 26 no. 4
16. Minguito, T, J., and Capunan, M, U. Canteen Operation and Management Assessment. *International Journal of Engineering Science and Computing* 2019; Volume 9 Issue No.2.
17. Kokoye, F, O., Onyali, L., Ezeugbor, C. Students' Waste Disposal: A Disciplinary Problem In Tertiary Institutions. *International Journal of Education and Research* 2015; Vol. 3 No. 10 October 2015
18. Licy, C,D., Vivek, R., Saritha, K., Anies, T,K., and Josphina, C,T. 2013. Awareness, Attitude and Practice of School Students towards Household Waste Management. *Journal of Environment* 2013; Vol. 02, Issue 06, pp. 147-150
19. Albashtawy, M. Assessment of hand-washing habits among school students aged 6–18 years in Jordan. *British Journal of School Nursing* 2017; Vol 12 No 1
20. Setyautami, T., Sermsri, S., and Chompikul, J. Proper hand washing practices among elementary school students in Selat sub-district, Indonesia. *Journal of Public Health and Development* 2012; Vol. 10 No. 2
21. Xuan, L, T, T., Rheinlander, Hoat, T, L, N., Dalsgaard, A., and Konradsen, F. Teaching handwashing with soap for schoolchildren in a multi-ethnic population in northern rural Vietnam. *Glob Health Action*. 2013
22. Cevizci, S., Uludag, A., Topaloglu, N., Babaoglu, U, T., Celik, M., and Bakar, C. Developing students' hand hygiene behaviors in a primary school from Turkey: A school-based health education study. *International Journal of Medical Science and Public Health* 2015; Vol 4, Issue 2

Determinants Associated with Regular Weighing of Under Five Children in Posyandu in Kelapa Gading Sub District, Jakarta

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Abstract

Background and Objectives: A Posyandu is an integrated health post as an extension unit of Puskesmas (community health center) providing several under-five child health programs, especially regular weighing every month, basic immunization and vitamin A supplementation and additional food provision. Monitoring of child growth in Posyanduis a very important activity in order to know early child growth faltering. Data of National Basic Health Research (RISKESDAS) 2010, proportion of regular weighing was only 49.4%.

Method: A cross-sectional study was conducted to interview 96 mothers of under-five children randomly selected from 7 neighborhood blocks in sub-district of Kelapa Gading, Jakarta. The multivariable analysis was done to analyze strength of association (using odds ratios) between some potential determinants and the regularity of mothers to weigh their children in Posyandu. Weighing 4 times or more within the past 6 months was considered to be regular.

Findings: The proportion of mothers weighing their children regularly in Posyandu in sub-district Kelapa Gading was 47.9%. The older the mothers, the lesser the probability to weigh regularly their children. Mothers who knew that Posyandu could provide Vitamin A and basic immunization freely for their children, were 2.7 times and 4.3 times respectively more likely to weigh their children regularly, as compared to mothers who did not know. Closer distance between mother's house and Posyandu gave the mothers higher probability to weigh their children regularly, as much as 18.5 times, as compared to farther distance. The likelihood of working mothers to weigh their children regularly, were 18.3 times, as compared to the likelihood of housewife mothers.

Conclusions: Mother's age, knowledge about the programs of Posyandu, distance between mothers' house and Posyandu, and mother's occupation status were important determinants of likelihood to weigh their children regularly in the Posyandu.

Keywords: *Posyandu, regularity of weighing, under-five children.*

Introduction

Weighing children under five years old regularly every month is one of the vital activities in monitoring

health and nutrition status. With regular monthly weighing, growth faltering can be identified early so that growth promotion can be done to prevent the occurrence of malnutrition^{1,2}. By monitoring intensively, if the child's weight does not rise or if a disease is found, recovery and prevention efforts could be made immediately in order to prevent malnourished. Quick and appropriate handling of malnourished children will reduce the risk of death so that mortality due to malnutrition can be suppressed, therefore, growth monitoring of children aged under five years is very important¹⁻⁴. Parents are recommended to weigh their children especially in the early weeks and months of life with health professional.

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If a child gains weight steadily this means that the child is growing satisfactorily. The World Health Organization (WHO) states that Growth Monitoring and Promotion (GMP) measures and graphs the child's weight and the result will be informed to the parent for advice, so that they can take action to improve child's growth in order to prevent malnutrition. Measurements begin at birth and must be done every month, accurately recorded on a growth chart and interpreted³. In Indonesia mostly growth monitoring activity is carried out in Posyandu (integrated service post)⁴. Posyandu is an Indonesian government program which is one of the Community-Based Health Efforts carried out by cadres who are part of the community with guidance from health workers in Puskesmas (Community health center). Posyandu has five main activities, consist of maternal and child health, family planning, immunization, nutrition improvement through weighing regularly and diarrhea therapy^{5,6}. The role of Posyandu in growth monitoring and promotion has decreased. Various obstacles faced by the Posyandu include insufficient health services and equipment in Posyandu, low skilled of Posyandu's cadres, lack of public awareness of mothers to weigh their children. Based on Riset Kesehatan Dasar/Riskesdas (National Basic Health Research) 2007: infants weighed regularly (4 times or more) was 45.4%, while those weighed 1-3 times and never weighed were, 29.1% and 25.5% respectively⁷. In Riskesdas 2010, the percentage of regular weighing increased slightly becoming 49.4%⁸ however the percentage of children aged 6-59 months who had never been weighed in the last six months was likely to increase from 25.5% (2007) to 34.3% (2013)⁹. According to the Minister of Health Regulation No. 43 of 2016 concerning Minimum Service Standards that in addition to administering vitamin A capsules twice a year and giving complete basic immunizations, every toddler must also receive weighing at least 8 times a year and measurement of length/height at least twice a year. Based on Riskesdas 2018, the percentage children who was weighed ≥ 8 per year was 54.6%¹⁰. This study objective was to determine the factors related to the regular weighing of children under five in Posyandu at sub district Kelapa Gading in North Jakarta

Method

A cross-sectional study was conducted in 2010 to interview 96 mothers of under-five children randomly selected from 7 neighborhood blocks in sub-district of Kelapa Gading, Jakarta. Mothers who became a sample were those who had KMS (Kartu Menujusehat/

Card towards health) and came to Posyandu in the last 3 months. The questionnaire used in the data collection was firstly tested in order to improve the questions so that it can be more understandable by the respondents and thereby can maintain the good validity of the data resulted from the interview. Ethical Clearance was obtained from YARSI University. Analysis of the data comprised univariate, bivariate and multivariate analysis. The Chi-Square test was used in bivariate analysis. Multivariate analysis using cox regression model was done to analyze the strength of association (using prevalence ratio) between several potential determinants and regular weighing in Posyandu. Weighing 4 times or more within the past 6 months was considered as regular weighing.

Result and Discussion

This study revealed that the proportion of mothers weighing their children regularly in Posyandu in sub district Kelapa Gading was 47.9%. This result was almost the same as in Riskesdas 2010, 49.4 percent children aged 6-59 months who were weighed routinely during the last six months (4 times or more)⁸. The frequency of weighing > 4 times slightly decreased in 2013 (44.6%)⁹. In Riskesdas 2018 regular weighing, which was stated as at least done 8 times a year, increased significantly 54.6%. This maybe because of the definition of regular weighing was changed from at least 4 for the last 6 months to minimum 8 times in one year¹⁰. In this study, there were 15.6% of children had only one time weighing in the last 3 months and there was no child had not been weighed. This result was better as compared to data in Riskesdas. Children aged 6-59 months who have never been weighed in the last six months increased from 23.8% in Riskesdas 2010 to 34.3% in Riskesdas 2013. However, there was no data in Riskesdas 2018⁸⁻¹⁰.

In bivariate analysis we found some potential factors related to regular weighing to Posyandu such as mother's age, mother's formal education, mother's working status, family income/socio-economic level, mother's knowledge, child's age, distance to Posyandu, and cadre's attitude (table 2). In Multivariate analysis using Cox Regression, we found that there were two determinants in regular weighing of children under five years in Posyandu, which were mother's knowledge and mother's working status (see table 2). Mothers who did not work were 2.1 times more likely to weigh regularly their children in Posyandu, as compared to working mothers (PR= 2.12; p-value=0.030). Mothers with

higher knowledge were 2.78 times more likely to weigh their children regularly as compared to mothers with lower knowledge (PR= 2.78; p-value=0.002).

Table 1. Potential Determinants associated to Regular Weighing

Determinant Factors	Regular Weighting				PR (Prevalence Ratio)	95% CI	p
	Regular		Irregular				
	n=46	%	n=50	%			
Mother's Age							
>30 years	27	75	9	25	2.37	1.56–3.59	0.000
≤ 30 years	19	31.7	41	68.3	1.0	.	
Mother's Formal Education							
Low	25	58.1	18	41.9	3.78	1.03–13.86	0.007
Medium	21	47.5	21	52.5	3.09	0.83–11.51	0.04
High	2	15.4	11	84.6	1.0		
Mother's Work Status							
Not Work	38	74.5	13	25.5	4.19	2.19–8.02	0.000
Work	8	17.8	37	82.2	1.0		
Socioeconomic level							
Low	29	61.7	18	38.3	1.78	1.14–2.78	0.008
High	17	34.7	32	65.3	1.0		
Mother's Knowledge							
High	30	73.2	11	26.8	2.52	1.60–3.95	0.000
Low	16	29.1	39	70.9	1.0		
Child's Age							
< 24 Months	39	57.4	29	42.6	2.29	1.17–4.50	0.004
≥ 24 Months	7	25	21	75	1.0		
Distance to Posyandu							
Close	43	61.4	27	38.6	5.32	1.81–15.68	0.000
Far	3	11.5	23	88.5			
Father's Attitude							
Support	20	60.6	13	39.4	1,47	.98–2.20	0.072
Not Support	26	41.3	37	58.7			
Cadres Attitude							
Support	38	63.3	22	36.7	2.85	1.50–5.41	0.000
Not Support	8	22.2	28	77.8			

Table 2. Determinants associated to regular weighing

Determinant	B	P value	PR	95% C.I.PR	
				Lower	Upper
Mother's Knowledge	.752	.030	2.121	1.074	4.189
Mother's Work Status	1.023	.002	2.780	1.462	5.286

In Indonesia, Posyandu is a very important place of weighing children under five so that its existence is needed both by the community and by health workers.

Posyandu is a form of community participation in health development, but the role of Posyandu in growth monitoring and promotion has decreased in scope.

Various obstacles faced by the Posyandu included insufficient equipment, low skilled of Posyandu cadre, lack of public awareness to weigh their children and health services in Posyandu were not yet optimal². The community activeness in monitoring growth of their children in the Posyandu continued to decline^{3,11}. One of the reasons that mothers did not take their children to weigh regularly was that they felt that weighing children in Posyandu was not important (20.8%). This perception was especially from working mothers which might affect the decrease of the weighing of the children under five in Posyandu. One factor driving this was the mother's ignorance of the benefits of weighing her child at the Posyandu, leading to reluctance to bring their children to Posyandu. Other reasons comprised Posyandu was not regularly scheduled (29.2%), the mothers were working (31.3%) and children were weighed in other health services (18.8%)¹². In Riskesdas 2018 it was stated that the reasons for children not to be weighed: children were already old (≥ 1 years) 14.1%, children had immunization (10.8%), children did not want to be weighed (8.1%), lazy (15.1%), forget/did not know the schedule (12.8%), there was no place for weighing (2.8%), the place was far (6.8%), busy/hassle (28.3%), body scale was not available (1.3%)¹⁰.

There was such a tendency that the higher age child group, the lower the scope of routine weighing (≥ 4 times during the last six months). Conversely the higher the age of the child the higher the percentage of children who had never been weighed. This study revealed that younger age (< 24 months) tend to be weighed 2.3 times as compared to older age (PR=2.3; see table 1). The same pattern was also found in Riskesdas 2018¹⁰.

A very significant relationship between the level of maternal knowledge with the frequency of weighing children under five in Posyandu (PR=2.121). This result was similar to what Ariyani et al. found in their research in Posyandu Desa Pilangrejo¹⁶. The same result was also related to mother working status. Ariyani et al. found a significant relationship between mother's work and the frequency of weighing children under five in Posyandu, Pilangrejo Village, Wonosalam District, Demak Regency. Mother who did not work were more frequently weigh their children in Posyanduas compared to mothers who worked¹³. These results were very compatible with the theory from Green about health behavior which states that a person's behavior is motivated by 3 factors, one of which is a predisposing factor that contains knowledge¹⁴. Mother's knowledge

is very important for mothers in order to get optimum results in growth monitoring program.

In Ethiopia most of mother did not know immediately about growth monitoring unless the topic was raised simultaneously with issue of immunization. Therefore, their awareness of growth monitoring was low as compared to attention to immunization. Most mothers mentioned that a regular growth monitoring program was mainly provided for children below two years of age³.

Based on research by Kusumawati et al. there was a significant relationship between the attitudes and behavior of cadres to the frequency of weighing toddlers¹⁵. However according to Trintrin et al 2003, knowledge of cadres in interpreting the growth curve in the growth chart was very low; it was only nine percent of cadres that were able to interpret the growth curve correctly. There was 98% of cadres did not know that the weight change in monthly weighing should be told to mother in nutrition counseling¹⁶.

Conclusions and Recommendation

Mother's knowledge about the programs and mother's work status were very important determinants of weighing children regularly in Posyandu.

Recommendation:

1. Increase awareness of mothers through cadres to more actively and regularly weigh their children, in order to decrease nutritional problem of under five children.
2. Strengthening CIE (communication, information and education) program in Puskesmas to increase mother's knowledge about the importance of monitoring the child growth through regular weighing to prevent growth faltering.
3. Health workers should provide information to the mothers through counselling in which mother can communicate and interact actively, so that mothers can take action to promote child growth. This is the way also to make them aware of the benefits of weighing at the Posyandu.

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References

1. Hall D M B. 2000. Growth monitoring. *Arch Dis Child* 2000;82:10–15
2. The Ministry of Health of the Republic of Indonesia 2019, *Indonesia Health Profile 2018* pp 163-64
3. Bilal SM, Moser A, Blanco R, Spigt M, Dinant GJ. Practices and Challenges of Growth Monitoring and Promotion in Ethiopia: A Qualitative Study. *Journal Health Population Nutrition* 2014; 32 (3);441-451
4. Sandjaja. Setyowati T, Sudikno. Coverage of monthly weighing among under five years old children in Indonesia. *PGM* 2005,28(2): 56
5. Ministry of Health RI 2012. *Ayo ke Posyandu setiap Bulan*. Pusat Promosi Kesehatan.
6. Ministry of Health RI. 2006. *Buku Kader Posyandu Dalam Usaha Perbaikan Gizi Keluarga*. Jakarta. Departemen Kesehatan RI.
7. Ministry of Health RI. *Laporan Hasil Riset Kesehatan Dasar Indonesia–Tahun 2007* Jakarta: Ministry of Health, the Republic of Indonesia; 2007.
8. Ministry of Health RI. *Laporan Hasil Riset Kesehatan Dasar Indonesia–Tahun 2010*. Jakarta: Ministry of Health, the Republic of Indonesia; 2010.
9. Ministry of Health RI. *Laporan Hasil Riset Kesehatan Dasar Indonesia–Tahun 2013*. Jakarta: Ministry of Health, the Republic of Indonesia; 2013.
10. Ministry of Health RI. *Laporan Hasil Riset Kesehatan Dasar Indonesia–Tahun 2018*. Jakarta: Ministry of Health, the Republic of Indonesia; 2018.
11. Djaiman, H. 2009. Pengembangan Media Praktis Tentang Pertumbuhan Balitadengan Sasaran Ibu Balita Pengunjung Pelayanan Kesehatan. <http://www.gizi.litbang.depkes.go.id/>
12. Soedirman 2009. Pedoman Pemantauan Wilayah Setempat Kegiatan (PWS KIA). *Jurnal Keperawatan Volume 7, No. 3, November* 171 Depkes, RI. Jakarta.
13. Ariyani R D, Susanti R, Mardiyarningsih E 2012. Faktor yang berhubungan dengan frekuensi penimbangan balita di Posyandu *Jurnal Keperawatan Soedirman (The Soedirman Journal of Nursing), Volume 7, No.3, November* 2012
14. Notoatmodjo, Soekidjo, 2007. *Promosi Kesehatan dan Ilmu Perilaku*. Jakarta: Rineka Cipta
15. Kusumawati E., Ernawati, Rohmatika D. Relationship of cadre attitudes and behavior according to mothers who have toddlers to the frequency of weighing toddlers in Posyandu Teras Boyolali district.
16. Trintrin T Mudjiyanto; Tjetjep S Hidayat Hermina; Erna Luciasari; Nunl Afriansyah dan Noviati Fuada, Faktor faktor positif untuk meningkatkan potensi kader posyandu dalam upaya mencapai keluarga sadarglzl (kadarzi) *PGM* 2003,26(2): 27-34.

Molecular Sequencing Study of *Salmonella* spp Which Isolated from Cattle Meat and Human Stool

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Abstract:

Aim of our study is investigation of the genetic relationships between *Salmonella* spp isolates which taken from human stool isolates and *Salmonella* spp isolates which taken from cattle meat. The total number of study isolates is one hundred (50 cattlebeef and 50human stools. Bacterial isolation and bacterial identification are used for testing the samples for culturing and examined by biochemical tests then detected by using 16S rRNA gene in PCR that designed by NCBI and make DNA sequencing for two positive isolates. Our results revealed that percentage of *Salmonellaspp* was 8/50(16%) which isolated from cattle beef and was 10/50(20%) which isolated from human stool. The PCR was demonstrated highly specific and sensitive. DNA sequencing of part of 16S rRNA was show highly similarity with NCBI-Blast data and the phylogenetic study was reveal genetic homology at (0.5 genetic change) between animals and human isolates and then the gene sequence deposited into NCBI-Genbank accession numbers accession numbers (MN523665.1) and (MG388337.1). In conclusion, our study is done for first-time in Iraq of the genetic correlating between *Salmonellaspp* which isolated from cattle meat and human stool. So, it is important to know the cattle meat is significant source for spreading infection between human and animals.

Keywords: Sequencing, *Salmonellaspp*, Cattle, Human stool.

Introduction

Salmonella is negative gram bacteria causing of contamination of food products, which is a way of transmitting pathogens to humans^[1&2] this pathogen It can hide in the digestive tract of healthy animals and the environment^[3].

The significant loss of economic production in the food and animal industries is associated with moderate and severe salmonella disease and mortality in field animals^[4], *Salmonella* bacteria cause various syndromes of diseases and host specificities based on its antigenic effects, intestinal *Salmonella* is considered the leading cause of food diseases in animals and humans worldwide^[5-7].

Serotypes of salmonella are divided to (3) groups (bacteremia, enteritis and typhoid fever)^[8].

Materials and Method

Samples Collections: (100) samples divided into (50) fresh beef meat, provided from slaughterhouse and

butchers in different sites of Al- Qadissiya province and fifty stools of Human samples. All the samples were keeping in cold box then sent to microbiology Laboratory. In Vet Med. College for swabbing then submitted to culturing and biochemical test for culture and identifying of *Salmonella* spp.

Salmonella spp isolation and identification:

The samples were inoculated in nutrient *salmonella* differentiated from other enterobacteriaceae bacteria. The single pure colony was cultured *Salmonella*-Shigella agar and XLD agar to identification *Salmonella* from another lactose fermenter enterobacteriaceae in figure (1) (2).





Figure (1) and (2): salmonella colony on SS agar and XLD agar.

Genomic DNA Extraction: Genomic DNA of *Salmonellaspp* isolates was extracted by using a kit called (mini genomic DNA. China. Geneaid Company). 1ml of new bacterial growth (for overnight) in the nutrientbroth was put in the microtubes (1.5 ml). These tubes were centrifuged for one minute at 10 thousand rpm. The DNA extracted from bacterial cells based on company instruction. For determining purification and concentration, Nanodrop spectrophotometeris used for this purpose then the product kept in freezer (-20)°C.

PCR: It was doneby using a designedprimer at (880)bp of (16s rRNA) gene in all (F) primer (TG ATC GTT TAC GGC GTG GAC),and(R) primer (A ATA CCA AGT CTC AAG AGT G) were provided by (Korea, Bioneer co.). Preparation of PCR master mix is done by using a kit called (Korea, Bioneer Company, AccuPower® PCR PreMix). Compositions of the premixtube are:

1. Polymerase enzyme
2. dNTPs
3. KCl
4. Tris-HCl
5. MgCl2
6. Stabilizer
7. Stain

Preparation of PCR master mix was done depend on kit directions in total volume (20) µl by mixing with DNA (5) µl and F primer (1.5) µl and R primer (1.5) µl, then adding PCR premix tube bywater for (20) µl then shaking by vortex (Korea Bioneer). All stage of the reaction is done into thermocycler (Germany Eppendorf) as:

1. The first stage five minute at (95)°C.
2. The second stage (denaturation stage) at 95°C for (30) cycles for (30) second.
3. The third stage (annealing stage)thirty seconds in (60)°C
4. The fourth stage (extension stage) thirty seconds in (72)°C
5. The fifth stage (final extension stage) ten minute in (72)°C.

The products were prepared in electrophoresis on agarose gel (1.5)%, and then Ethidium bromideis used for dyeing then putting under (UV)light apparatus for visualized.

DNA Sequencing: It was done for confirmative detection,and Phylogenetic relationship of *Salmonellaspp* depended on (16s rRNA)gene by analysis of phylogenetic tree (MEGA 6) program. (880) bp PCR product was placed in agarose gel by using extraction kit called (EZ EZ-10 Spin Column DNA Gel, made in Canada Biobasic company). The PCR product which contains(16s rRNA) gene was sent to Korea in Bioneer Com. for doing DNA sequencing.

The Results: One hundred of study samples(50) are cattle meat and (50) human stool are cultured of clinical samples and examine by Conventional PCR. Only 8/50 (16%) of cattle beef and 10/50 (20%) samples of human stool which appeared positive for *salmonella spp* at (880) bp PCR product of (16srRNA) gene on agaroseelectrophoresis as a table (1) and Figure (3).

Table (1): Number and percentage of study samples

Sample	Total N.	Positive	Positive Percentage	Negative	Negative Percentage
Cattle Meat	50	8	16%	42	84%
Human Stool	50	10	20%	40	80%
Total	100	18	18%	82	82%

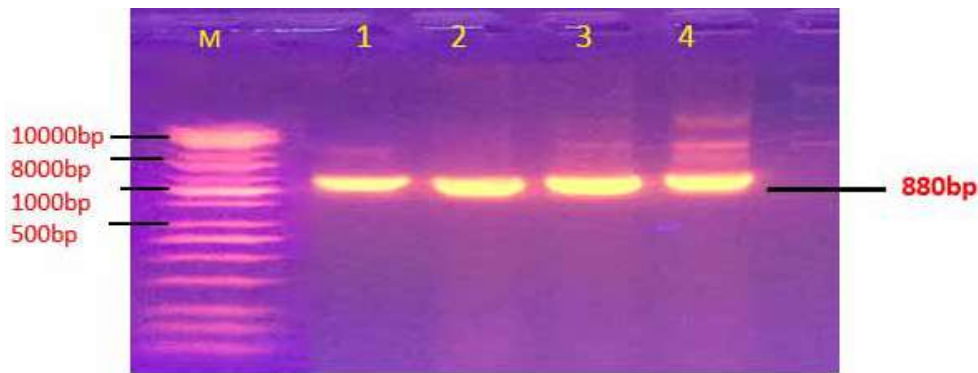


Figure (3):band on Agarose gel by using electrophoresis device represent partial 16S rRNA gene of salmonella sp.

Sequence analysis was done to determine the results of PCR. These sequences form the conserved region of 16s rRNA of the *Salmonella* spp provided accession numbers (MG388337.1) from beef cattle at NCBI. Analysis of DNA sequencing of (16s rRNA) gene by many sequence alignment (BLAST-NCBI) reveals detection of the results of phylogenetic analysis in most

of the Iraqi isolates that grouped mainly with the same branch *salmonella* spp enterica serovar *Typhimurium*. South Korea, only one clone in this study clustered in the same branch of Jordanian in clade A. while bat corona virus, SARSV and neoromicacorna virus were out group clustered in the separated branch as Fig(4).

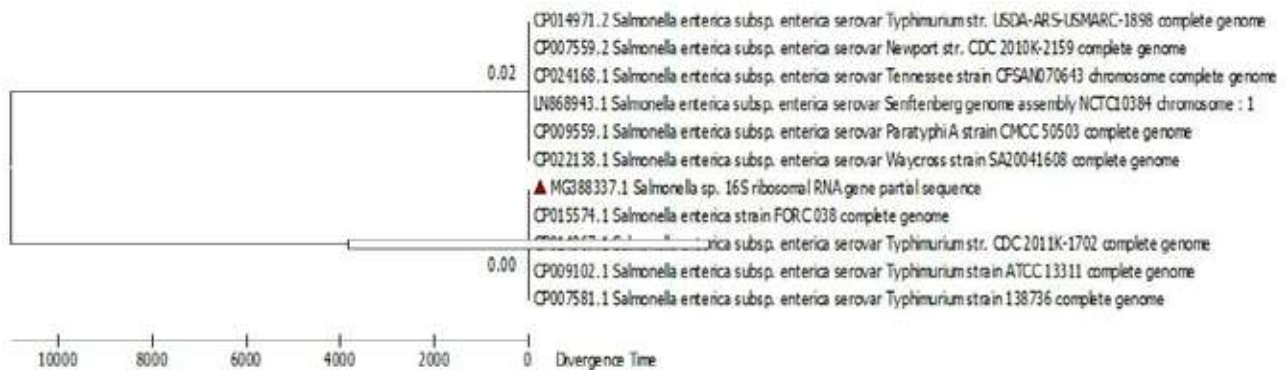


Figure (4): Phylogenetic tree of my isolates with references world salmonella sp and their accession no.

Discussion

According to our results, percentage of *salmonella* spp that isolated from cattle meat samples by using polymerase chain reaction was (16)%, that close to results of [9] and [10] were (17.5)% and (20)% respectively in beef meat by using PCR. While [11] and [12] are recorded (55)% and (100)% respectively in meat beef by using PCR and that was more than rates of results.

Some the studies founded low rates of *salmonella* spp by using PCR in meat beef such as [13-15] wherever they founded (6.7)%, (6.5)% and (4.35)% respectively.

The prevalence of *salmonella* spp is varied due to several causes such as rate of contamination, hygienic management, general cleaning, sterilization techniques in meat factories and butcher shops, also depends on temperature degree of meats store. All these; causes lead to different rates of contamination and spreading the pathogen [16].

Depending on our results, percentage of *salmonella* spp that isolated from a human stool by using polymerase chain reaction was (20)%, wherever (10) found prevalence of *salmonella* spp in children stool was

(10.7)% by using PCR, and that considered less than our results.

While [17] recorded a higher percentage than our rates, it was (95)% of *Salmonella* spp by using PCR which isolated from faeces of children.

Prevalence of infection of *salmonella* spp depended on several factors such as degree contamination water and food by bacteria, immune status of the host, season (because environment temperature degree has significant role), host type and age, vaccination and sterilization techniques which applied [18 & 19].

Our report studied sequencing of two samples (one sample from human stool and one sample from cattle feces), and confirm the accession number of 16S ribosomal RNA gene of *salmonella* spp in NCBI-Genbank website, wherever our study founded that great match of sequencing of nucleotides of 16S ribosomal RNA gene of *salmonella* spp with sequence confirmed in NCBI-Genbank company, This explains the concomitant epidemic of disease in the animal and humans simultaneously, The same isolates cause disease in both animals and humans.

Many studied, and reports provided same of our results which included great similarity between salmonella isolates samples and data of NCBI between human and animals in many genes such as [20-22].

Finally, *Salmonella* spp isolates which isolated from animals is essential to source of spreading the pathogen to human.

Conflict of Interest: Nil

Source of Funding: Self

Ethical Clearance: Not required

References

- Millemann, Y., S. Gaubert, D. Remy, and C. Colmin. Evaluation of IS200-PCR and comparison with other molecular markers to trace *Salmonella* enterica subsp. enterica serotype Typhimurium bovine isolates from farm to meat. *J. Clin. Microbiol.* 38:2204–2209
- Roels, T. H., P. A. Frazak, J. J. Kazmierczak, W. R. Mackenzie, M. E. Proctor, T. A. Kurzynski, and J. P. Davis. Incomplete sanitation of a meat grinder and ingestion of raw ground beef: contributing factors to a large outbreak of *Salmonella* typhimurium infection. *Epidemiol. Infect.* 1997; P.119:127–134.
- Bell, C. Approach to the control of enterohaemorrhagic *Escherichia coli* (EHEC). *Int. J. Food Microbiol.* 2002;(78:197–216).
- Malkawi HI, Gharaibeh R (2004). Rapid and simultaneous identification of two *Salmonella* enterica serotypes Enteritidis and Typhimurium from chicken and meat product by multiplex PCR. *Biotechnol.*, 3(1): 44-48
- Ranjbar R, Giammanco GM, Aleo A, Plano MR, Naghoni A, Owlia P, Mammìna C. (2010). Characterization of the first extended-spectrum beta lactamase-producing non-typhoidal *Salmonella* stains isolated in Tehran, Iran. *Foodborne Pathog. Dis.*, 7(1): 91-95.
- Lim YH, Hirose K, Izumiya H, Arakawa, Shi HT, Terajima J, Itoh K, Tamura K, Kim S, Watanabe H (2003). Multiplex Polymerase chain Reaction Assay for selective of *Salmonella* enterica serovar Typhimurium. *Jpn. J. Infect. Dis.*, 56: 151-155.
- Agron GP, Walker RL, Kind H, Sawyer SJ, Hayes DC, Wollard J, Andersen GL (Identification by subtractive hybridization of sequences specific for *Salmonella* serovar Enteritidis. *Appl. Environ. Microbiol.*, 2001. 67(11): 4984-4991.
- Renato L. Santosa, Shuping Zhanga, Renée M. Tsolisa, Robert A. Kingsleyb, L. Garry Adamsa, Andreas J. Bäumlerb. Animal models of *Salmonella* infections: enteritis versus typhoid fever. *Microbes and Infection*, 2001; 3, 1335–1344
- Tze Y. Thung, Son Radu, Nor A. Mahyudin, Yaya Rukayadi, Zunita Zakaria, Nurzafrizah Mazlan, Boon H. Tan, Epeng Lee, Soo L. Yeoh, Yih Z. Chin, Chia W. Tan, Chee H. Kuan, Dayang F. Basri and Che W. J. Wan Mohamed Radzi. Prevalence, Virulence Genes and Antimicrobial Resistance Profiles of *Salmonella* Serovars from Retail Beef in Selangor, Malaysia. *Front. Microbiol.*, 2018; p.11.
- Raafat Hassanein, Sohaila Fathi Hassan Ali, Ashraf Mohamed Abd El-Malek, Moemen, A. Mohamed and Khalid Ibrahim Elsayh. Detection and identification of *Salmonella* species in minced beef and chicken meats by using Multiplex PCR in Assiut city. *Veterinary World*, 2011; Vol.4 (1):5-11.
- Gallegos-Robles MA, Morales-Loredo A,

- Alvarez-Ojeda G, Osuna-García JA, Martínez IO, Morales-Ramos LH, Fratamico P. PCR detection and microbiological isolation of Salmonella spp. from fresh beef and cantaloupes. *J Food Sci.*2009; 74(1):M37-40.
12. Elsayed MSA, Abdeen E, Akiela MA, Farouk T, Zahran R. Real-time and conventional PCR for characterization of Salmonella sp. from imported meat to Egypt. *Adv. Anim. Vet. Sci.*2014; 2 (4): 199–203.
 13. Daniele Bier, Jalusa D. Kich, Sabrina C. Duarte, Márcio R. Silva, Luiza M. Valsoni, Carlos A.N. Ramos, Dália P. Rodrigues and Flábio R. Araújo. Survey of Salmonella spp. in beef meat for export at slaughterhouses in Brazil. *Pesq. Vet. Bras.* 2018;vol.38 no.11 Rio de Janeiro.
 14. Fratamico PM. Comparison of culture, polymerase chain reaction (PCR), TaqMan Salmonella, and Transia Card Salmonella assays for detection of Salmonella spp. in naturally-contaminated ground chicken, ground turkey, and ground beef. *Mol Cell Probes.* 2003;17(5):215-21.
 15. Behzad Nikbakht and Ali MohamadiSani (2016). Identification of salmonella spsFrom contaminated meat samples by multiplex pcr-based assay, *Journal of Experimental Biology and Agricultural Sciences* <http://www.jebas.org>.2000; No. 2320–8694
 16. Aida Jadidi, Seyed Davood Hosseni, Alireza Homayounimehr, Adel Hamidi, Sepideh Ghani and Behnam Rafiee. Simple and rapid detection of Salmonella sp. from cattle feces using polymerase chain reaction (PCR) in Iran.*African Journal of Microbiology Research.*2012; Vol. 6(24) pp. 5210-5214, 28.
 17. Cheng-hsunchiu and jonathan t. ou Rapid identification of salmonella serovars in feces by specific detection of virulence genes, inva and spvc, by an enrichment broth culture-multiplex pcr combination assay.*journal of clinical microbiology.*1996; p. 2619–2622 Vol. 34, No. 10
 18. Qadoumi Samar¹, Dura Susan A.M.², Darwish Maysa¹, Ahmad M. Nahed² & El-Banna, Nasser. PCR detection of Salmonella spp. in Fresh Vegetables and Feed. *International Journal of Biology.* 2019; Vol. 11, No. 3; ISSN 1916-9671 E-ISSN 1916-968X Published by Canadian Center of Science and Education.
 19. B. Malorny and J. Hoorfar. Toward Standardization of Diagnostic PCR Testing of Fecal Samples: Lessons from the Detection of Salmonellae in Pigs. *J ClinMicrobiol.*2005;43(7): 3033–3037.
 20. SuchawanPornasukarom, Arnoud H M van Vliet, and Siddhartha Thakur. Whole genome sequencing analysis of multiple Salmonella serovars provides insights into phylogenetic relatedness, antimicrobial resistance, and virulence markers across humans, food animals and agriculture environmental sources. *BMC genomics.* 2018; 6;19 (1):801.
 21. Laura Ford, Danielle Ingle, Kathryn Glass, Mark Veitch, Deborah A. Williamson, Michelle Harlock, Joy Gregory, Russell Stafford, Nigel French, Samuel Bloomfield, Zoe Grange, Mary Lou Conway, and Martyn D. KirkComments to Author. Whole-Genome Sequencing of Salmonella Mississippi and Typhimurium Definitive Type 160, Australia and New Zealand. 2019;Volume 25, Number 9.
 22. George M. Ibrahim and Pau M. Morin Salmonella Serotyping Using Whole Genome Sequencing. *Front.* 2018; Microbiol., 13 | <https://doi.org/10.3389/fmicb.2018.02993>

What is New about Magnetic Resonance Imaging of Multiple Sclerosis?

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Abstract

Background: Multiple sclerosis (MS) is a demyelinating disease of the central nervous system. Magnetic resonance imaging (MRI) has an important role in early diagnosis of MS.

Patients and Method: Thirty patients with clinically diagnosed to have MS according to McDonald criteria were included and referred to department of radio-diagnosis, Faculty of Medicine, Minia University. Imaging was performed on a 1.5T Philips MR system using double inversion recovery (DIR), fluid attenuated inversion recovery (FLAIR), T2-weighted, T1-weighted and susceptibility-weighted imaging (SWI) sequences with the parameters including field of view (FOV), matrix, slice thickness and voxel size. They were done after the approval of ethical committee of our institution. Data analysis was performed using the SPSS version 20 and p-value as well as comparative study were gained.

Results: The detection rate of white matter lesions in T2 was (88%); while for grey matter lesions was (10%). In FLAIR sequence, we found that; the detection rate of white matter lesions was (96%); while for grey matter lesions was (25%). As regarding DIR sequence, the detection rate of white matter lesions was (90%); while for grey matter lesions was (95%). Comparative study between serial MRI sequences (T2, FLAIR and DIR) revealed; significant increase in detected number of grey matter lesions; in DIR-MRI sequence ($p < 0.0001$). In SWI, a central vein sign was detected in 96 lesions (66 in periventricular lesions and 30 in subcortical lesions).

Conclusion: From this study we concluded that new imaging modalities of MRI as regarding DIR and SWI are a valuable MRI sequences in imaging of multiple sclerosis; thus, we recommend adding DIR and SWI sequences in routine MR protocols for MS patients.

Keywords: MRI, multiple sclerosis, Double inversion recovery (DIR), SWI, T2, FLAIR.

Introduction

Multiple sclerosis (MS) is chronic autoimmune, inflammatory demyelinating disease of the central

nervous system (CNS). It is recognized as the most common cause of progressive neurologic disability in young adults worldwide with higher rates in females compared to males.⁽¹⁾ It poses a major personal and socioeconomic burden as the average age of disease onset is 30 years which is a time that is decisive for work and family planning.⁽²⁾ The advances in non-conventional magnetic resonance imaging (MRI) techniques show a more global MS pathology and it is believed that MS may not be truly characterized by “multiple” areas of sclerosis but rather a “diffuse” representation of sclerosis. The acknowledgment of grey matter (GM)

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involvement in the disease has led to the incorporation of juxtacortical lesions in the recent diagnostic criteria for MS as well as increased interest in the role of normal appearing grey matter (NAGM) damage in determining cognition and disability. ⁽³⁾ Detection of cortical lesions by conventional MRI techniques is difficult. So it is important to detect different types of cortical lesions using new imaging technique as double inversion recovery (DIR) sequence which is used to image the gray matter by nulling the signal from white matter and cerebrospinal fluid (CSF). ⁽⁴⁾ Double inversion recovery (DIR) imaging provided higher image contrast ratios between lesions and normal-appearing gray matter (NAGM) in all anatomic locations compared with fluid attenuated inversion recovery (FLAIR) and T2WI imaging (fig1). Moreover, DIR imaging provided better delineation of the white matter lesions with higher contrast between the lesions and normal-appearing white matter. ⁽⁵⁾

On other hand, susceptibility-weighted imaging (SWI) is another new imaging modality used to assess damage of the brain by iron in multiple sclerosis which might be related to oxidative stress with release of free radicals that has been specifically seen in the vessel walls of veins giving the perivascular relationship with MS (perivenular lesions) with the characteristic central vein sign. ⁽⁶⁾ Susceptibility-weighted imaging (SWI) has the potential to recognize the presence of iron in MS lesions based on the advantage of the T2*-shortening effect of deoxyhemoglobin in venous blood. ^(7 & 8)

Aim of the work: The aim of this study is to assess the efficacy of variable magnetic resonance imaging techniques in assessment of multiple sclerosis as regarding degree of severity by highlighting the role of DIR in imaging the gray matter lesions and presence of central vein sign using SWI.

Patients and Method

Study design and population: In a prospective study 30 patients with clinically diagnosed to have MS according to McDonald criteria were included diagnosed in neuropsychiatry department and they were referred to department of radio-diagnosis, Faculty of Medicine, Minia University. The study was done between December 2018 to September 2019. They underwent MRI imaging after meeting the inclusion criteria. All patients signed a written informed consent before MRI examination.

Inclusion and exclusion criteria: All patients included in this study were diagnosed with MS (clinical and laboratory), age of the patient varying between 18 years and 50 years and expanded disability status scale (EDSS) scoring system varying from 1-7. However, general contraindications to MRI as the presence of any paramagnetic substances such as pacemakers, metallic clips or claustrophobic patients were excluded from the study. Also patients with age above 50 years old or less than 18 years and patients with concomitant neurological disease in conjunction with MS were excluded.

Method

MRI technique: MR imaging was performed using 1.5 Tesla MR Scanner (Ingenia, Philips Healthcare, Netherlands). All patients were imaged in the supine position using standard quadrature head coil. The MRI examination was conducted on the brain including conventional MRI sequences; axial T2 weighted images utilizing the following parameters: repetition time (TR) of 4800 msec/echo time (TE) of 110 msec, slice thickness of 5 mm, number of signal averages (NSA)=3, matrix 512x 512, gap 1–2 mm, flip angle=90 ° and field of view (FOV)= 230mm. Axial and sagittal FLAIR images utilizing the following parameters: repetition time (TR) of 6000 msec/echo time (TE) of 140 msec, slice thickness of 5 mm, (NSA) 3, matrix 512x 512, gap 1–2 mm, flip angle=90 ° and FOV = 230mm. Axial DIR images utilizing the following parameters: repetition time (TR) of 96 msec/echo time (TE) of 25 msec, slice thickness of 3 mm, matrix 512x 512, gap 1–2 mm and FOV = 230mm. Axial SWI images utilizing the following parameters: repetition time (TR) of 43 msec/echo time (TE) of 25 msec, slice thickness of 3 mm, matrix 300x300, gap 1–2 mm, flip angle=20 ° and FOV = 230mm.

Data processing and image interpretation: The images were transformed to Philips 881030 IntelliSpace IX/LX Workstation. Each MR sequence findings were evaluated as following:

Image interpretation: Conventional and advanced MRI sequences were evaluated for: the total number of the lesions in T2, FLAIR, DIR and SWI. Lesion location (White matter: including peri-ventricular and subcortical regions- Grey matter: including basal ganglia and cortical regions - infratentorial: including brainstem and cerebellar regions) in T2, FLAIR and DIR. Number of cortical lesion in FLAIR, T2 and DIR.

Number of lesions in white matter (deep white matter and subcortical regions) in T2, FLAIR and DIR. Number of lesions with central vein sign in SWI. Each lesion appears in FLAIR in periventricular and subcortical regions were correlated with its similar on SWI and it was assessed if a central vein present or not.

Statistical analysis: Statistical analysis was performed using the SPSS software for Windows v. 20 (SPSS Inc., Chicago, IL). Tests of significance (Repeated measures ANOVA, Cochran’s Q tests, Kappa statistics and ROC Curve analysis). P-values less than 0.05 (5%) was considered to be statistically significant. Mean, standard deviation (\pm SD) and range for parametric numerical data, while median and inter-quartile range (IQR) for non-parametric numerical data. Frequency and percentage of non-numerical data.

Results

Our study included 30 female patients with multiple sclerosis according to McDonald criteria. We found that; the mean age of all patients was (36.24) years and as regarding gender of the patients (84%) of patients were females and (16%) were males. (65%) of patients had visual disorder, (57%) had tingling and numbness; (40%) had muscle weakness and (9%) of patients had hemiparesis. We found that detection rate of white

matter lesions in FLAIR sequence was (100%); and of grey matter lesions was (36.6%). In DIR sequence, the detection rate of white matter lesions was (96.6%) while for grey matter lesions was (100%). In T2, it was (90%) for white matter lesions and (20%) for grey matter lesions. Comparative studies between T2, FLAIR and DIR sequences revealed significant increase in sensitivity and specificity of detection of grey matter lesions in DIR sequence with highly significant statistical difference ($p < 0.001$) as in (table I). However, no significant difference in detection of white matter lesions could be detected between three pulse sequences ($p > 0.05$) as in (table II). Double inversion recovery (DIR) was significantly superior to FLAIR sequence in detection of infratentorial lesions ($P < 0.001$). As regarding detection of overall MS lesions in whole brain, DIR sequence showed significant increase in sensitivity and specificity of detection of the total lesions over T2 and FLAIR sequences ($P = 0.004$). In SWI, a central vein was detected in 96 lesions (66 in periventricular lesions and 30 in subcortical lesions). In FLAIR, a central vein was detected in 55 lesions (40 in periventricular lesions and 15 in subcortical lesions). Comparative studies between FLAIR and SWI sequences revealed significant increase in sensitivity and specificity of detection of periventricular lesions with central vein sign in SWI sequence with highly significant statistical difference ($p < 0.0001$).

Table I: detection of grey matter lesions in each pulse sequence using Roc-curve analysis:

Variable	AUC	P value	SE
Grey matter lesions in FLAIR	0.720	0.0001	0.047
Grey matter lesions in DIR	0.987	<0.0001	0
Grey matter lesions in T2	0.497	0.015	0.032

SE= Standard Error, AUC= Area under curve, ROC =Receiver operating characteristic.

Table II: Comparison between 30 MS patients in multiple MRI sequences as regarding detection of white matter and grey matter lesions:

Variable	T2-MRI sequence	FLAIR-MRI sequence	DIR-MRI sequence	Cochran’s Q test
				P value
Detection rate of grey matter lesions	6(20%) ^^	11(36.66%) ^^	29 (96.6%) ^^	= 0.097 #
Detection rate of white matter lesions	27 (90%) ^^	30 (100%) ^^	29 (96.6%) ^^	= 0.097 #

^^% per total of 29 patients, # Cochran’s Q test.

Discussion

Multiple sclerosis is chronic inflammatory autoimmune disease. MRI has been part of the International Panel criteria for the diagnosis of MS since 2001 and its use has become increasingly vital as reflected in the last changes by the committee guidelines. It plays major role in elucidating the mechanisms underlying disease progression and in monitoring the accumulation of abnormal features underpinning disability. Multiple sclerosis has heterogeneous clinical and imaging manifestations which differ between patients and change within individual patients over time. So these caveats should be borne in mind as conventional MRI cannot explain the wide heterogeneity of the clinical outcomes of the disease so recent researches emphasizes the importance of non conventional MRI to allow visualization of its various pathophysiological mechanisms. The acknowledgment of grey matter (GM) involvement in the disease has led to the incorporation of juxtacortical lesions in the recent diagnostic criteria for MS as well as increased interest in the role of normal appearing grey matter (NAGM) damage in determining cognition and disability. From this point of view, it is important to detect cortical and deep grey matter lesions using DIR which used to selectively image the gray matter by nulling the signal from white matter and cerebrospinal fluid. Detection of perivenular lesions in the brain (the “central vein sign”) is also important as it improves the pathological specificity of MS diagnosis.⁽⁹⁾ Our study aims to assess grey matter lesions in patients known to have multiple sclerosis using DIR, FLAIR and T2 as well as detect central vein sign using SWI which increase diagnostic accuracy of MS. This study included 30 patients were diagnosed to have MS according to MacDonald’s criteria and their age varying between 25 to 40 y. Most of our patients were females (84%) and the most affecting symptoms were visual disorders and numbness.

In the current study DIR was the most important sequence in detection of grey matter lesions (cortical or deep grey matter lesions). Double inversion recovery (DIR) allows visualization of juxta-cortical (which just abuts the cortex) and intracortical lesions.⁽¹⁰⁾ An assessment of cortical lesions (CL) contributes to the identification of patients with CIS who are at risk of evolution to definite MS. ^(11,12) We are in agreement with several authors as De Graaf et. al. and Simon et. al studies who reported that the DIR showed more intra-cortical lesions compared to FLAIR and T2WI sequences (fig 2).

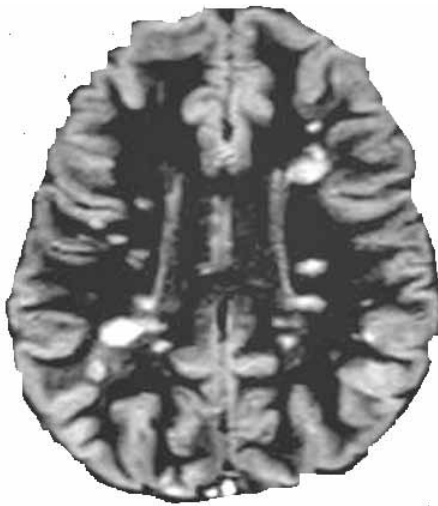


Figure 1: Axial DIR shows cortical lesions (intracortical and juxtacortical) as well as white mater lesions (subcortical and periventricular).



Figure 2: Axial DIR shows cortical lesions (intracortical and juxtacortical lesions).

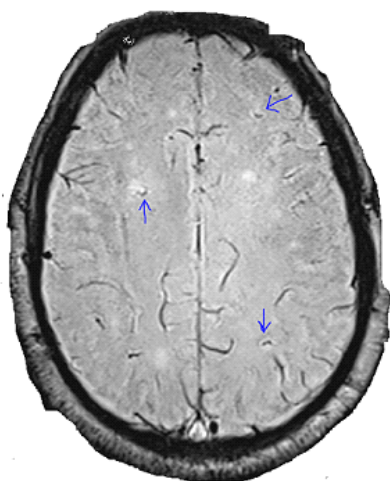


Figure 3: Axial SWI: shows central vein signal within the lesions.

We agree with M.P. Wattjes et. al. study who stated that total number of the lesions were higher in DIR sequence than FLAIR and T2 sequences. In addition, we agree with him that DIR has higher sensitivity for the infratentorial region compared with the FLAIR sequence.

Central vein assessment, provided by susceptibility-based MRI, significantly improves the diagnostic accuracy and specificity of MS diagnosis as it can differentiate MS from vasculopathies involving CNS which are difficult to diagnose accurately as they have clinical and radiological presentations very similar to MS. As concerning radiological findings of central vein sign in SWI, we agree with Lane JJ et al, who stated that there is significant increase in sensitivity and specificity of detection of periventricular lesions with central vein sign in SWI sequence over FLAIR sequence (fig3).

Conclusion

Finally, in our study we were in agreement with the findings reported by the other studies regarding the great value of DIR sequence in detecting grey matter lesions particularly cortical lesions over other sequences (T2WI and the FLAIR sequences) and its value to detect more MS lesions than other sequences. In this issue we also detect that central vein sign in SWI increase diagnostic accuracy of MS. Future implementation of automated imaging post-processing techniques (i.e., central vein sign detection) should allow direct translation of the central vein sign into the everyday clinical practice.

Ethical Clearance: Taken from ethical committee in El-Minia university hospital.

Source of Funding: Self funding.

Conflict of Interest: Nil.

References

1. Alonso A1, Hernan MA. Temporal trends in the incidence of multiple sclerosis: a systematic review. *Neurology*. 2008 Jul 8; 71(2):129-35.
2. Kaufman DW1, Reshef S2, Golub HL3, Peucker M4, Corwin MJ5, Knappertz V7, Goodin DS6, Pleimes D2, Cutter G8. Survival in commercially insured multiple sclerosis patients and comparator subjects in the US. *Mult Scler Relat Disord*. 2014 May; 3(3):364-71.
3. McDonald WI, Compston A, Edan G, Goodkin D, Hartung HP, Lublin FD, McFarland HF, Paty DW, Polman CH, Reingold SC, Sandberg-Wollheim M, Sibley W, Thompson A, van den Noort S, Weinshenker BY, Wolinsky JS. recommended diagnostic criteria for multiple sclerosis: guidelines from the International panel on the diagnosis of multiple sclerosis. *Ann Neurol*. 2001 Jul; 50(1):121-7.
4. Madelin G1, Oesingmann N, Inglese M. Double Inversion Recovery MRI with fat suppression at 7 tesla: initial experience. *J Neuroimaging*. 2010 Jan;20(1):87-92.
5. Ahmed F Youssef, Ahmed E.M Shaalan, Shima A El-Sabbagh. Department of Radiology, Benha University, Benha, Egypt Diagnosis of gray matter lesions in multiple sclerosis using variant sequences of magnetic resonance imaging (T2, fluid-attenuated inversion recovery, and double inversion recovery) 2018;35 (3): 386-393.
6. Sati P, Oh J, Constable RT, Evangelou N5, Guttman CR6, Henry RG7, Klawiter EC8, Mainero C9, Massacesi L10, McFarland H1, Nelson F11, Ontaneda D12, Rauscher A13, Rooney WD14, Samaraweera AP5, Shinohara RT15, Sobel RA16, Solomon AJ17, Treaba CA9, Wuerfel J18, Zivadinov R19, Sicotte NL20, Pelletier D21, Reich DS1; NAIMS Cooperative. The central vein sign and its clinical evaluation for the diagnosis of multiple sclerosis: a consensus statement from the North American Imaging in Multiple Sclerosis Cooperative. *Nat Rev Neurol* 2016;12:714-722.
7. Haacke EM, Mittal S, Wu Z, Neelavalli J, Cheng YC Susceptibility-weighted imaging: technical aspects and clinical applications, part 1. *AJNR Am J Neuroradiol* 2009;30:19–30.
8. Tallantyre EC1, Dixon JE, Donaldson I, Owens T, Morgan PS, Morris PG, Evangelou N. Ultra-high-field imaging distinguishes MS lesions from asymptomatic white matter lesions. *Neurology* 2011;76:534–539.
9. Vuolo L, Sati P, Massacesi L, Reich DS. Efficiency of FLAIR* at 1.5T, 3T, and 7T for detecting perivenular lesions in multiple sclerosis (MS). [abstract P479]. Presented at the 31st Congress of the European Committee for Treatment and Research in Multiple Sclerosis (2015).
10. Calabrese M, De Stefano N. Cortical lesion counts

- by double inversion recovery should be part of the MRI monitoring process for all MS patients: Yes. *Mult Scler J.* 2014;20:537–8.
11. Calabrese M, Filippi M, Gallo P. Cortical lesions in multiple sclerosis. *Nat Rev Neurol.* 2010;6(8):438-444.
 12. Filippi M, Rocca MA, Calabrese M, Sormani MP, Rinaldi F, Perini P, Comi G, Gallo P. Intracortical lesions: relevance for new MRI diagnostic criteria for multiple sclerosis. *Neurology.* 2010;75(22):1988-1994.

Parenting Style on School Age Children that Addicted to Mobile Phone (A Phenomenology Study)

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Abstract

Nowadays, the development of technology is progressing in various sectors, one of which is felt by society is the development in the communication sector through the availability of advanced communication tools, known as mobile phones. Nowadays, mobile phones are used more as a companion or friend living at all ages, both children and adults. Currently, parents provide mobile phones to children to facilitate communication and as a tool for education, but without any special supervision of parent causes the child addiction that disrupts the development of children. This study purposed to explore the experience of parents in caring for children who addicted to mobile phone. The method used is a qualitative research design with interpretive phenomenological approach. Data collection techniques obtained through in-depth interviews with semi-structured interview guide to explore the understanding and experience of participants. The number of participants in this study there were 6 women with inclusion criteria: mothers with school-age children (6-12 years) who are addicted to mobile phones that have been diagnosed by a psychiatrist/psychologist, living together and getting therapy more than >1 month. Selection participants conducted by researchers using purposive sampling technique that involves participants in accordance with the criteria. Based on the results of data analysis in this study, it was found the following themes: making the rules of the use of mobile phones, full time assisting children and compact implement rules for using mobile phones. Children have freedom in using mobile phones cause the child to fall on the condition of dependency or addiction that makes a child can not be separated from mobile phones so that parents set rules that must be followed when children use mobile phones. In addition, assistance is one way parents in assisting children who are already addicted. Parents also must be compact in implementing the rules and shall be the prime example for children in using of mobile phones. Need for setting rules from parents to children in terms of the use of mobile phones to prevent mobile phone addiction. Thus, parents need to provide special assistance to children in order to prevent adverse effects of mobile phones and continues to regard development of the child.

Keywords: Parenting style, school age children, mobile phone addiction

Introduction

Parents give mobile phones to children as a tool for communication and education. At school, in an atmosphere of learning always involves the Internet to find resources in the completion of task. School-age children still have an emotional response and self-control that are still unstable, given the opportunity to use mobile phones without the assistance and supervision would make the child wrong in using it. Children will use it as they please without any understanding of the negative impact on development. Parents also provide

entertainment applications such as games which are very interesting cause children will spend more time playing games than studying or doing other activities. Children who experience addiction to mobile phones is a child who is unable to control the desire to play the game and affect emotions, behavior and social relationships of children⁽¹⁾. Based on the results of the asian parent insights survey revealed that 98% of children are mobile phone users and used it to access games⁽²⁾. Data of Riskesda 2013 recorded approximately 9.5% to 14.2% of preschool children in the area of Yogyakarta has emotional social issues that negatively impact the development and

school readiness⁽³⁾. In the Regional Mental Hospital of Dr. RM. Soedjarwadi Klaten recorded from the month of June 2017 until July 2018, there were 7 cases of children who are addicted to mobile phones.

Parents realize that the impact of the freedom given to children in the use of mobile phones caused problems, either physical, psychological or mental influence children development. Parents make rules for using mobile phones is to provide guidance, oversight and limitation of time such as a day children are only allowed to play for an hour with features that correspond to the child's age. Supervision in accessing the services in the mobile phone becomes the responsibility of parents. Parents should have a variety of ideas and knowledge in order to prevent children in the use of excessive gadget, one of which is to train a consistent discipline for children and parents themselves in the use of any related gadgets that can and can not be accessed⁽⁴⁾. Parents should put the phone away from the reach of children or not laid carelessly allowing the child to use it without parental consent⁽⁵⁾

The family is responsible for shaping the personality, affection, attention, harmony and health are the parents. To create a good environment in the family needed good parenting, according to⁽⁶⁾there are three parenting style in family, namely: a) Authoritarian, Authoritarian is a type of family environment restrictive and do not allow freedom at all, all the rules of the parents should be followed, without thinking about the willingness and ability of the children; this resulted in the inability of children in developing potential and ability. b) Democratic. Democratic environment is an environment in families that provide flexibility for children to develop all the potential of the child by not rule out the family rules and norms that have been established by parents c) Permissive or free. Free is kind of parenting style that giving occasion to children in acting and behaving without rule and norm that should be obeyed by children, thus children are easy to trap into negative things⁽⁶⁾. Parenting is important for the psychological health of children and parenting is a pattern of interaction between parents and children that include parental attitudes and behavior in children, how to apply the rules, values, norms, concern and affection for the children.

Purposes: This study purposes to explore the experiences of parents in caring for children who addicted to mobile phones.

Material and Method

This qualitative study using interpretive phenomenological approach to parents with children who are addicted to mobile phones. Participants of six people who were selected through purposive sampling with the following inclusion criteria: 1) women who have school-age children (6-12 years old) with addiction mobile phone that has been diagnosed by a psychiatrist/psychologist. 2) the biological mother who lives with children who are addicted to mobile phones. 3) The school-age children with addiction mobile phone is getting therapy more than >1 month. Data were obtained through in-depth interviews using a semi-structured interview guidelines, all the data recorded by utilizing a recording applications found on mobile phones. Data were analyzed using Interpretative Phenomenological Analysis (IPA).

Results

The results of this study illustrate the meaning of each utterance participants related to changes in parenting of mothers to children with mobile phone addiction. The themes described on these results, among others, make rules for use of mobile phones, full time assisting children and compact implement rules for using mobile phones.

Theme 1: Making the rules for the using of mobile phones.

Parents used to provide freedom that means there are no rule of the parents in the use of mobile phones, children access the mobile phone freely without supervision of a parent but now parents together establish rules for using mobile phones. Here are excerpts of participants according the statement above:

“... Using mobile phone and they used it every day whenever “ (smiling) (P4)

“... My son used to used mobile phone all day. (pointing towards her son) “(P3)

The rule of mobile phone usage here is everything that has been set up and assigned parents to be implemented by the child. Participants submit the matter through the following quote:

“Should be monitored, they should reduce to use their mobile phone... I limit the time in using the mobile phone, five minutes. (P1)

“There are limits to use it... after learning I give them allowance to operate mobile phone only thirty minutes” (P3)

Theme 2: Full time accompany children in the use of mobile phones

Parents need to accompany children in the use of mobile phones. Mentoring is carrying out when children use mobile phones to learn and play. Here’s an excerpt of participants:

“... We accompany them ... when they playing mobile phone” (P3)

“... I always monitor them while operating mobile phone, even during learning” (P6)

“Yes it is not to be authoritarian or be like this but it needs to provide guidance during they operating mobile phone” (P4)

Theme 3: Compact implementing rules for using mobile phones

Parents must agree in implementing rules that have been established in the use of mobile phones. Here’s an excerpt from the statement following participants:

“...the vision and mission of parents ... exemplifies of children not to use the phone ... there are the same rules, should be applied to parents both father and mother to be compact in educating children, especially in using mobile phone” (P1)

Discussion

Rule is a provision agreed to by more than one person with tying goal. Similarly, in the enforcement of rules on children’s use of mobile phones. The incidence of mobile phone addiction in children exists because parents failed in supervising the use of mobile phones. Learning from this experience, the parents finally create a statute or rules that apply to all members of the family to minimize the incidence of addiction to mobile phones⁽⁷⁾. The use of devices (mobile phones) in children is very necessary role of parents to supervise. The child will grow and develop in accordance with the environment where the child is, in this case the parents who provide education about the pros and cons of using mobile phones. Children will use it well when parents provide proper education on its use. In contrast, children will incorrectly use the phone if the parents do not either

provide education in its use, there is no specified rules such as time limits and always provide guidance by not removing the child to play alone⁽⁸⁾

Mentoring is an act accompanied. Children who have experienced addiction desperately need help from others to be able to restore it in this case the parents who play an important role in its success. Participants said that all would be conduct to make her recover and currently do give a lot of time with children, especially when children use mobile phones.

The role of parents should always be done should not replace by providing a mobile phone as a friend of children playing. How that should be carried out by parents is to control every site where your kids on the phone, fill spare time with the child to discuss or question and answer session on the experience every day. With discussion or tell stories with children will make your child comfortable and confident to express all the creative ideas he has in mind⁽⁹⁾

Parents also need to understand the principles of parenting in the age of technology. The principle that should be known by parents are when children need it, their observations and communications while using, determine the punishment if the child broke a promise, give understanding to the children on the rules created and explain what sites should be seen and not to be opened⁽¹⁰⁾. Parents who give consent for children to use mobile phones, subject to the mentoring and supervision of parents. Monitoring carried out by asking what is seen or opened in the mobile phone child. Attitudes of children who are given permission to use the phone more open is to tell and show about what they see. In mentoring parents already make clear rules that previously disepakatin such as school achievement should not be decreased and the use of mobile phones in the time of no-school hours and no more than one hour. While the nature of the child’s psychological as more open communication between parents and children continuously interwoven, creating closeness and harmony⁽¹¹⁾

Parenting also affect to children using mobile phones freely. Permissive parenting with free or bear children who are addicted to mobile phones. Parents who are adopting a child has a permissive will shape attitudes can not control yourself, do not obey and do not like to get involved with the activities of the surrounding environment. By nurturing that gives freedom will have a negative impact on children, namely children tend to

be less independent, less confident, selfish and socially immature. While applying authoritarian parenting children become cantankerous, happier alone, had no creativity, introverted, not very talkative and when dealing with parents always tried to be obedient, but if they are behind parents of children to be rebellious⁽¹²⁾

With the freedom that children using mobile phones cause the child to fall on the condition of dependency that makes a child can not be separated from the phone, thus the parents set commands that should be followed when children use mobile phones. The same thing was delivered by the participants that there are the same rules that should be applied by parents, both father and mother are compact in terms of educating for children to use mobile phones. In addition, participants also say parents should still not be allowed to change in forbid children to use mobile phones and not at random to put down the mobile phone, thus child is not easy to use without parental consent.

The willingness and the need for direct involvement by parents are fathers and mothers in anticipation for any child in the use of mobile phones. The means used by parents are making the same goals and rules to do with the child. Parents are responsible to provide guidance and oversight and ensure children use mobile phones to disclose information that related with the learning and in accordance with the age of the child⁽¹³⁾. Parenting behavior will greatly affect a child's behavior. In his research, parents are required to fulfill the established rules for children to follow or imitate what is done by the parents as the scheduled time not to watch or activate the mobile during study hours⁽¹⁴⁾. Parents are required to be the prime example for the their child in using a mobile phone and prudent in applying discipline in children.

Conclusion

This study purposed to explore the experiences of parents in parenting the children who addicted to mobile phone answered on the first theme; make rules for the use of mobile phones, second; full time to assist children in the use of mobile phones, three; implement rules for using mobile phones compactly.

Conflict of Interest: There is no conflict of interest in this study.

Source of Funding: Sources of funding in this study were derived from personal funds research.

Ethical Clearance: This research has gained airworthiness ethics committee of ethics of the Medical Faculty of Brawijaya University with number 346/EC/KEPK - S2/12/2018.

References

1. Mustafa, DA F, editors. Efforts to Overcome Children's Addiction to Gawai (Gadgets) Through the Interactive Communication Model of Parents and Children Based on the Al- Quran. Paper Presented at the Proceeding Ancoms UIN Sunan Ampel Surabaya; 2017.
2. Wonsun, Shin, Benjamin L. Parental Mediation Of Children's Digital Technology Use In Singapore. *Journal Of Children and Media*. 2017;11 No 1:1-19.
3. RISKESDAS. Community Research and Development Agency. Basic Health Research Report (RISKESDAS) 2013. Jakarta: 2013.
4. Warisyah Y, editor The Importance of Parental Dialogical Assistance in Using Gadgets in Early Childhood. Proceedings of the National Seminar on Education "Learning Innovations for Advancing Education"; 2015; FKIP University of Muhammadiyah Ponorogo.
5. Smahel D WM, Cernikova M. . The impact of digital media on health: children's perspectives. *journal Public Health*. 2015;60:131-137.
6. Saputra H TO. Influence of the Family Environment on Psychosocial Development in Preschool children *Journal of Nursing Practice* 1(1):1-8;1:1-8. 2017.
7. Rakhmawati, Istina. The Role of Families in Child Care. *Islamic Counseling Guidance*. 2018;Vol 6 No 1.
8. Radliya, Rabbi AN, Tria ZR. Influence of Social Development Emotional Gawai Against Childhood. *ECD Agapedia Journal*, Vol1 No1. 2017.
9. Chusna, Puji A. Gadget Media Influence On Children Character Development. *The Dynamics Research: Religious Social Communication Media*. 2017;vol.17 No.2.
10. Palupi, Yulia, editors. Digital Parenting as a vehicle for therapy to balance the digital world with the real world for children. Paper Presented at the seminar Nasional Universitas PGRI Yogyakarta; 2015.
11. Rohmiyati Y. Media Literacy at the Semarang Digital Native. *Journal Undip (ANUVA)*; Vol2 No2 2018.

12. Widiastuti N, ES. D. Parenting as an Effort to Grow the Attitude of Responsibility in Children in Using Communication Technology. *Journal Ilmiah UPT P2M STKIP Siliwangi*. 2015;Vol.2 No.2.
13. Pangastuti, Rachael. The phenomenon Gadgets And Social Development For Early Childhood. *Indonesian Journal of Islamic Early Childhood Education* Vol2 No 2. 2017.
14. Kylie HD, T.Hinkley, Campbell, J.Karen. Childrens Physical Activity And Screen Time: Qualitative Comparison Of Views Of Parents Of Infants And Preschool Children. *International Journal of Behavioral Nutrition and Physical Activity*. 2012.

Flowcytometric Determination of T-lymphocyte Expression of CD4⁺ and CD8⁺ Cells in Systemic Lupus Erythematosus

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Abstract

The Purpose: Flow cytometric analysis to quantify the T-lymphocyte expression of CD4⁺ and CD8⁺ cells.

Patients and Method: This study was conducted along the period from March 2018 to March 2019 on patients diagnosed as having systemic lupus erythematosus. The patients were selected from those who attended Rheumatology and Nephrology outpatient clinics, Minia University Hospital, Egypt.

Group I: It consists of 40 apparently healthy women to serve as a control group.

Group II: It comprised 40 SLE women.

Results: The area under ROC curve of lymphocyte expression of CD4⁺ and CD8⁺ were 0.815 (95% CI= 0.712-0.893, p<0.001), at a cutoff value of < 32% and 0.675 (95% CI= 0.561-0.776, p=0.004) at a cutoff value of < 18.8, respectively. CD4 lymphocyte expression exhibited sensitivity, specificity, PPV, NPV, and accuracy of 77.5%, 87.5%, 86.1%, 79.5% and 82.5%, respectively, whereas those of CD8 were 32.5%, 100%, 100%, 59.7% and 66.2%, respectively.

Conclusion: We provided more scientific insights into the flow cytometric analysis to quantify the T-lymphocyte expression of CD4⁺ and CD8⁺ cells.

Keywords: SLE; CD4; CD8.

Introduction

SLE is a systemic autoimmune condition characterised by a wide spectrum of clinical manifestations, partly related to the disease itself, but also linked to its comorbidities and drugs adverse reactions. Following the previous annual reviews, we focused on new insights in SLE clinical features, pathogenic pathways, biomarkers of specific organ involvement and therapeutic strategies. Finally concentrated on SLE aspects that could significantly influence patients' quality of life and that need to be investigated in detail through the development and validation of diseasespecific patient-reported outcomes.⁽¹⁾

Rate of SLE varies between countries from 20-70/100,000⁽²⁾. Women are affected about 9 times more than men⁽³⁾, begins between the ages of 15 and 45⁽⁴⁾

SLE is an autoimmune disorder caused by a complex combination of genetic, epigenetic and environmental factors that lead to altered gene expression and function of several molecules which lead to abnormal T cell responses⁽⁴⁾.

Aim of the work: In this study we aimed to provide more scientific insights into the flow cytometric analysis to quantify the T-lymphocyte expression of CD4⁺ and CD8⁺ cells.

Patients and Method

This study was conducted along the period from March 2018 to March 2019 on patients diagnosed as having systemic lupus erythematosus who were compared with a group of apparently healthy volunteers. The patients were selected from those who attended

Rheumatology and Nephrology outpatient clinics, Minia University Hospital, Egypt.

Therefore, the current study included two groups:

Group I: It consists of 40 apparently healthy women to serve as a control group. Their ages ranged from (18-35) years with mean + SD of (26.8 + 5.4) years.

Group II: It comprised 40 SLE women. Their ages ranged from (16-37) years with mean + SD of (24.7 + 5.3) years.

The diagnosis of SLE was done according to Systemic Lupus Erythematosus International Collaborating Clinics (CLICC) 2018 and SLE sheet and systemic lupus erythematosus diseases activity index Selene modification (SLEDAI Score)

Exclusion criteria: We excluded patients with rheumatic disease other than SLE, SLE patients who had prior treatment with monoclonal antibodies or other biological drugs, malignant tumours and ongoing infections.

All patients and controls were subjected to careful History taking, Clinical Examination, routine investigations including *complete blood count (CBC)*, Erythrocyte sedimentation rate (*ESR*); *Liver function tests*, *Renal function tests*, *Urine analysis*, *24 hour urine proteins*, *Rheumatoid factor (RF)*, *C-reactive protein (CRP)*

Patients with systemic lupus erythematosus diagnosed by Anti-nuclear antibody (ANA), Anti double strand DNA, Complement 3 (C3) and Complement 4 (C4).

All patients and controls were subjected to special investigations including Flow cytometry

Flow cytometric analysis for identification and enumeration of cluster differentiation (CD) 4 and CD8 T-lymphocytes was done by Flow cytometry, BD FACS canto™ USA.

A. Staging procedure of flow cytometry:

1. Whole blood was collected in evacuated tubes containing EDTA.

2. For each sample, two tubes were prepared labeled 1 & 2 (control and test).
3. 100 µl of blood sample was added to the tubes.
4. 10 µl of anti CD4 FLTC conjugated was added (only two the test tube) and vortex.
5. 10 µl of anti CD8 PE conjugated was added (only two the test tube) and vortex.
6. Cells were incubated for 15-20 minutes at room temperature in the dark.
7. Cells were washed by PBS twice to remove any unbound antibodies.
8. Followed by red cell lysis using 2 ml lysing solution then incubated for 10 min at room temperature in the dark.
9. Cells were centrifuged for 5 minutes, supernatant was discarded and 2 ml of PBS were added.
10. Wash by PBS was repeated twice then the cells were resuspended in 400µl of PBS for final flow cytometric analysis.

Statistical Analysis: Analysis was carried out using a (PD-FACS FLOW Argon Laser U.S.A.) Flow cytometry at 515 nm.

Comparisons between two categorical variables were made with Mann Whitney test for non-parametric quantitative data (expressed as median) between the two groups

*: Significant level at P value < 0.05

All statistical analyses were performed using IBMSPSS Statistics version 17 (SPSS for Windows, Chicago, IL).

Results

Concerning the percentage of CD4 lymphocytes expression it was statistically significantly lower in SLE patients than controls (30.5 (27.3-32) vs. 35.9 (33.6-38.3)%, p<0.001). Similar trend was observed for CD8 lymphocytes expression (22.1 (16.1-25.1)% for SLE patients vs. 25.4 (21.3-29)% for controls, p=0.007).

Table 1: Results of flow cytometric analysis in the study groups

Variable		Control	Cases	P value
		N=40	N=40	
Lymphocytes CD4 expression (%)	Median	35.9	30.5	<0.001*
	IQR	(33.6-38.3)	(27.3-32)	
Lymphocytes CD8 expression (%)	Median	25.4	22.1	0.007*
	IQR	(21.3-29)	(16.1-25.1)	

Apart from a significant correlation between CD4 and CD8 lymphocyte expression ($r=0.847$, $p<0.001$), no significant correlation could be detected between either CD4, CD8 and any of the studied parameters.

Table 2 : Correlation between CD4 lymphocyte expression and different studied parameters in systemic lupus erythematosus patients

Variable	CD4 lymphocyte expression (%)	
	r	P value
Age (Years)	0.088	0.591
Duration of disease (years)	0.112	0.491
White blood cells ($\times 10^3/\mu\text{l}$)	-0.020	0.904
Red blood cells ($\times 10^3/\mu\text{l}$)	-0.187	0.249
Hemoglobin (gm/dl)	-0.171	0.292
Platelets ($\times 10^3/\mu\text{l}$)	-0.020	0.901
Absolute Lymphocytes count ($\times 10^3/\mu\text{l}$)	-0.175	0.280
Alanine aminotransferase (U/L)	0.140	0.389
Aspartate transaminase (U/L)	0.070	0.669
Total Bilirubin(mg/dl)	0.114	0.485
Direct Bilirubin(mg/dl)	-0.256	0.110
Albumin (g/dl)	-0.133	0.415
Urea(mg/dl)	0.143	0.377
Creatinine(mg/dl)	-0.104	0.523
First hour erythrocyte sedimentation rate (mm/h)	-0.231	0.151
Second hour erythrocyte sedimentation rate (mm/h)	-0.268	0.095
Rheumatoid factor (-ve/+ve)	-0.289	0.071
C-reactive protein (-ve/+ve)	-0.171	0.290
Proteinuria/24hour (mg)	0.065	0.688

Table 2 shows no significant correlation between CD4 and other parameters

Table 3 : Correlation between CD8 lymphocyte expression and different studied parameters in systemic lupus erythematosus patients

Variable	CD8 lymphocyte expression (%)	
	r	P value
Age (years)	0.051	0.752
Duration of disease(years)	0.075	0.647
White blood cells ($\times 10^3/\mu\text{l}$)	-0.123	0.449
Red blood cells ($\times 10^3/\mu\text{l}$)	-0.298	0.062
Hemoglobin (gm/dl)	-0.161	0.320
Platelets ($\times 10^3/\mu\text{l}$)	-0.221	0.171
Absolute Lymphocytes count ($\times 10^3/\mu\text{l}$)	0.060	0.715

Variable	CD8 lymphocyte expression (%)	
	r	P value
Alanine aminotransferase (U/L)	0.034	0.837
Aspartate transaminase (U/L)	-0.022	0.892
Total Bilirubin(mg/dl)	0.105	0.520
Direct Bilirubin(mg/dl)	-0.122	0.452
Albumin (g/dl)	-0.150	0.356
Urea(mg/dl)	0	0.999
Creatinine(mg/dl)	-0.161	0.321
First hour erythrocyte sedimentation rate (mm/h)	-0.244	0.129
Second hour erythrocyte sedimentation rate (mm/h)	-0.367	0.020
Rheumatoid factor (-ve/+ve)	-0.330	0.037
C-reactive protein (-ve/+ve)	-0.237	0.141
Proteinuria/24hour (mg)	0.053	0.746

Table 3 shows no significant correlation between CD8 and other parameters

Table 4: Results of proteinuria in the studied groups

Variable		Control	Cases	P value
		N=40	N=40	
Proteinuria/24 h (mg)	Median IQR	30 (0-50)	800 (50-1000)	<0.001*

SLE patients had a statistically significantly higher values of proteinuria/24 hour(800 (50-1000) vs. 30 (0-50) mg, p <0.001)

Discussion

SLE is recognized as chronic, often severe autoimmune disease with largely unknown etiology⁽⁴⁾.

In this study we found significantly lower levels of CD4⁺ lymphocyte expression in patients with SLE compared to healthy volunteers (p<0.001). Similar trend was observed for CD8⁺ lymphocyte expression (p=0.007)

Although there was no significant correlation between% of lymphocyte expression of either CD4⁺ or CD8⁺ with any of the studied parameter, we noticed a significant positive correlation between CD4⁺ and CD8⁺ (p<0.001). We found that the area under ROC curve of lymphocyte expression of CD4⁺ and CD8⁺ were 0.815 (95% CI= 0.712-0.893, p<0.001), at a cutoff value of < 32% and 0.675 (95% CI= 0.561-0.776, p=0.004) at a cutoff value of < 18.8, respectively. CD4 lymphocyte expression exhibited sensitivity, specificity, PPV, NPV, and accuracy of 77.5%, 87.5%, 86.1%, 79.5% and 82.5%, respectively, whereas those of CD8 were 32.5%, 100%, 100%, 59.7% and 66.2%, respectively.

In our study, proteinuria/24 hours was reported in our SLE patients as evident by statistically significantly higher levels of proteinuria/24 hours in lupus patients compared with healthy controls

These results go hand with hand with those **Zahran et al.**,⁽⁵⁾ who studied the effects of royal jelly (RJ) supplementation on regulatory T cells in 20 SLE children received 2 g of freshly prepared RJ daily, for 12 weeks and resulted in children with SLE, before treatment there was an observed imbalance between CD4⁺ and CD8⁺ lymphocytes; this may be explained by the immune dysregulation in cases of SLE. Their results showed that patients with SLE (both before and after RJ treatment). The frequency of CD4⁺ T lymphocytes was significantly increased after RJ treatment versus baseline value. This was not true for CD8⁺ T lymphocytes as it did not show any significant changes with RJ treatment or any difference between the SLE children and normal control group.

Our results are in accordance with what was found by **Zhang et al.**⁽⁶⁾ who examined the levels and

function of peripheral blood immunoregulatory T-cell subpopulations in SLE. They found normal percentages of CD8+ T cells in peripheral blood in all SLE patients. Interestingly, about CD4+, they found about half of the SLE patients had markedly depressed CD4+ cell levels and in turn significantly lower CD4+/CD8+ cell ratio, whereas the remaining half of the patients had normal levels of CD4+ cells (normal CD4+/CD8+ cell ratio)⁽⁵⁾.

Ethical Statement: The material has not been published anywhere. Authors of the manuscript have no financial ties to disclose and have met the ethical adherence.

Disclosure of Interest: The authors declare that they have no competing interests.

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Conflict of Interest: None

Financial: None

References

1. Di Battista M, Marcucci E, Elefante E, Tripoli A, Governato G, Zucchi D, Tani C, Alunno A. One year in review 2018: systemic lupus erythematosus. *ClinExpRheumatol*. 2018 Sep-Oct;36(5):763-777.
2. Danchenko N, Satia JA, Anthony MS: Epidemiology of systemic lupus erythematosus : a comparison of worldwide disease burden. *Lupus* 2006; 15(5), 308–318.
3. Tsokos GC. Mechanisms of disease: systemic lupus erythematosus. *The New England Journal of Medicine*. 2011;365(22):2110–2121.
4. Zahran, A. M., Elsayh, K. I., Saad, K., Elloseily, E. M., Osman, N. S., Alblihed, M. A., ... & Mahmoud, M. H. (. Effects of royal jelly supplementation on regulatory T cells in children with SLE. *Food & nutrition research*, 2016; 60(1), 32963]
5. Zhang B, Zhang X, Tang FL, Zhu LP, Liu Y, Chen W, et al. Clinical significance of increased CD4CD25Foxp3T cells in patients with new-onset systemic lupus erythematosus. *Ann Rheum Dis* 2008; 67: 103740.

Effect of Black Seed (*Nigella Sativa*) Extract on Release of Some Minerals from Human Enamel: An in Vitro Study

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Abstract

Background: Black seed of *Nigella sativa* has been used for centuries to promote health due to its anti-microbial, anti-oxidant and anti-inflammatory effects. This study was conducted to evaluate the ability of black seed water extract to reduce the release of potassium and zinc ions from enamel after acidic attack.

Materials and Method: Twenty five maxillary human premolars were prepared and divided into five groups. The test solutions were included, black seed water extract in three concentrations (3%, 5% and 7%), sodium fluoride (0.05%) as control positive and de-ionized water as control negative. The teeth in each group were immersed separately in 40 ml of the test solution for two minutes, once daily and for twenty days. The teeth then prepared for subsequent etching and analysis by atomic flame spectrometer to measure the concentration of the released potassium and zinc ions.

Result: The highest mean value of dissolved potassium ion was found in de-ionized water group followed by 3% water extract of black seed while the lowest one was recorded in 7% black seed water extract. The statistical difference between the five groups was highly significant ($p < 0.01$) by using ANOVA test. The highest mean value of dissolved zinc ion was found in de-ionized water group followed by 0.05% sodium fluoride and 3% black seed extract while the lowest one was recorded in 7% water extract of black seed. The statistical difference between the five groups was also highly significant ($p < 0.01$).

Conclusion: Water extract of black seed has the ability to reduce the dissolution of potassium and zinc ions from the tooth and might increase tooth resistance against acid attack.

Keywords: *Nigella Sativa*, potassium ion, zinc ion.

Introduction

There is a worldwide increasing interest on the use of herbs or plants in the treatment of various diseases especially in developing countries. Black seed of *Nigella sativa* is an annual flowering plant that widely used in nutrition and medicine. This seed is rich in phenolic compounds, essential fatty acids, proteins and bioactive compounds⁽¹⁾. Previous studies had searched for its anti-oxidant, anti-cancer, anti-inflammatory and anti-microbial activities of this miracle seed^(2,3,4).

Enamel is the hardest tissue in the human body. Dental enamel is 95% mineral, 4% water and 1% organic matter by weight percentage. The minerals are composed mainly from calcium and phosphate in addition to the

presence of small quantities of other elements⁽⁵⁾. Zinc is essential trace element. It accumulates in the surface structures of teeth and occurs in low concentrations in subsurface material. Zinc can reduce enamel demineralization and increase enamel resistance to acid dissolution⁽⁶⁾. Regarding potassium ion, enamel content of this ion is very low in comparison with calcium and phosphorus contents⁽⁷⁾. However, little data are available about the relation between tooth resistant to acid attack and potassium content. A possible relationship between enamel minerals content and caries susceptibility has been advised⁽⁸⁾. No previous study was conducted for the effect of water extract of *Nigella sativa* on the release of zinc and potassium ions from human enamel, so this study was conducted.

Materials and Method

Extracted maxillary first premolar teeth from patients aged 10-13 years old were selected from orthodontic department (college of dentistry, university of Baghdad). The total number of teeth was 25. The teeth were cleaned by using conventional hand piece and rubber cup with non-fluoridated pumice and deionized water. After cleaning, the teeth were stored in 0.1% thymol solution at 4° C until use to minimize microbial growth. This step also was done to prevent the dryness and brittleness of teeth. The water extract of black seed was prepared by the modified method of Ibraheem et al⁽⁹⁾. The teeth were divided into five equal groups; each group consisted of five teeth. The test solutions were included, water extract of black seed in three concentrations (3%, 5% and 7%), sodium fluoride (0.05%) as control positive and de-ionized water as control negative. The teeth in each group were immersed separately for two minutes, once daily, for twenty days in 40 ml of the test solution. After each immersion, the specimens were washed in de-ionized water for 5 minutes and then stored in de-ionized water with thymol (0.1%) at room temperature till the next immersion.

After the treatment period (20 days), a rounded area (3 mm in diameter) were prepared on buccal surface of each tooth by applying adhesive disc and avoiding hypoplastic areas or microscopic cracks. The rest of enamel for each tooth was covered by a sticky wax, leaving only the rounded area (window) exposed for subsequent etching. The windows were etched for ten seconds in separated polyethylene tubes. Each tube is containing five ml of 2NHCL⁽¹⁰⁾. The concentrations of released potassium and zinc ions were determined calorimetrically by using flame atomic absorption spectrometer.

Statistical analysis: The data was processed using SPSS version 20 statistical software. Means and

standard deviation were calculated for each group. One way ANOVA and Dunnett T3 (post hoc test) were used to evaluate the significance of difference between the five groups. Probability values less than 0.05 were considered statistically significant (P<0.05). Values less than 0.01 were considered highly significant (P<0.01).

Results

Concentration of potassium ion release (mean, standard deviation and statistical analysis of ANOVA are illustrated in Table 1. The highest mean value of dissolved potassium ions was found in de-ionized water group followed by 3% water extract of black seed while the lowest mean was recorded in 7% concentration of black seed. The statistical difference between the five groups was highly significant (p<0.01). Table 2 is showing the mean differences of dissolved potassium ions concentrations between each two agents. No statistical significant differences were found between the de-ionized water and black seed extract in concentrations: 3%, 5% and 0.05% of sodium fluoride. No significant difference was found between 5% black seed extract and 0.05% sodium fluoride.

Concentration of zinc ion release (mean, standard deviation and statistical analysis of ANOVA are illustrated in Table 3. The highest mean value of dissolved zinc ion was found in de-ionized water group followed by 0.05% sodium fluoride and black seed extract 3%, while the lowest mean was recorded in water extract of black seed 7%. The statistical difference between the five groups was highly significant (p<0.01). Table 4 is showing statistical mean differences of dissolved zinc ions concentrations between each two agents. No statistical significant difference was found between the black seed extract in 5% and 7%. No significant difference was found between 3% black seed extract and 0.05% sodium fluoride.

Table 1: The released potassium ion concentrations among the selected agents

Selected Agents	No	Mean ± SD	F value	P value
Water black seed extract 3%	5	0.910±0.07	19.44	0.00**
Water black seed extract 5%	5	0.660±0.07		
Water black seed extract 7%	5	0.484±0.06		
Sodium Fluoride 0.05%	5	0.730±0.05		
Deionized water	5	1.634±0.48		

** Highly significant (p<0.01), df (Between Groups=4, Within Groups=20, Total=24)

Table 2: Post hoc test between each two agents (potassium ion concentrations)

Agent 1	Agent 2	Mean Difference	Significant
Water black seedextract 3%	Water black seed extract 5%	0.250**	0.005
	Water black seed extract 7%	0.426**	0.000
	Sodium Fluoride 0.05%	0.180*	0.022
	Deionized water	-0.724	0.159
Water blackseed extract5%	Water black seed extract 7%	0.176*	0.027
	Sodium Fluoride 0.05	-0.070	0.573
	Deionized water	-0.974	0.063
Water blackseed extract 7%	Sodium Fluoride 0.05	-0.246**	0.002
	Deionized water	-1.150*	0.035
Sodium Fluoride0.05%	Deionized water	-0.904	0.081

*The mean difference is significant at the 0.05 level., ** The mean difference is highly significant at the 0.01 level.

Table 3: The released zinc ion concentrations among the selected agents

Selected Agents	No	Mean ± SD	F value	P value
Water black seed extract 3%	5	4.6260±0.30	168.547	0.00**
Water black seed extract 5%	5	3.3240±0.28		
Water black seed extract 7%	5	2.7760±0.29		
Sodium Fluoride 0.05%	5	4.7260±0.45		
Deionized water	5	8.6140±0.54		

** Highly Significant (p<0.01), df (Between Groups=4, Within Groups=20, Total=24)

Table 4: Post HOC test between each two agents (zinc ion concentrations)

Agent 1	Agent 2	Mean Difference	Significant
Water black seedextract 3%	Water black seed extract 5%	1.302**	0.001
	Water black seed extract 7%	1.850**	0.000
	Sodium Fluoride 0.05	-0.100	1.000
	Deionized water	-3.988**	0.000
Water blackseed extract 5%	Water black seed extract 7%	0.548	0.129
	Sodium Fluoride 0.05	-1.402**	0.006
	Deionized water	-5.290**	0.000
Water blackseed extract 7%	Sodium Fluoride 0.05%	-1.950**	0.001
	Deionized water	-5.838**	0.000
Sodium Fluoride 0.05%	Deionized water	-3.888**	0.000

*The mean difference is significant at the 0.05 level., ** The mean difference is highly significant at the 0.01 level.

Discussion

In dentistry, the extract of black seed was tested in many studies to verify its oral effects due to the interested organic and inorganic constituents. The black seed showed its antimicrobial action against *Streptococcus mutans*, *Streptococcus mitis* and other types of bacteria isolated from the oral cavity^(11,12). In addition to that,

Nigella Sativa extract had an obvious effect on the healing process of oral ulcer⁽¹³⁾. In previous Iraqi study, water extract of black seed was able to decrease the dissolution of inorganic phosphorous ions from teeth⁽¹⁴⁾. In the current study, the water extract of black seed was tested in three concentrations to approve its ability to decrease the dissolution of zinc and potassium ions

from the tooth surface and thus increase the hardness of the tooth and the resistant to acid attack. Sodium fluoride was used as control positive due to its effect in inhibiting demineralization and enhancing remineralization of tooth surface. It is able to react with the outer enamel surface resulting in the formation of calcium fluoride⁽¹⁵⁾.

The study showed that the release of potassium ions was the least for the 7% extract and the highest release was recorded in deionized water group. The effect of sodium fluoride 0.05% in reducing the release of potassium ion was better than that reported for 3% extract.

The study also reported that the release of zinc ions was the least for the 7% extract and the highest release was recorded in deionized water group. The effect of 3% extract was almost equal to the effect of sodium fluoride 0.05% in reducing the release of zinc ions. This may indicate that the application of black seed water extract can decrease the demineralizing effect of the acid used. It was also obvious from this study that, if the concentration of the extract increases, there mineralizing effect of the water extract will increase. These results approve the findings of other studies regarding the effect of black seed water extract to improve the hardness of the tooth^(14,16). This effect could be attributed to the chemical composition of black seed and its mineral contents (calcium, phosphorous, potassium, sodium, zinc and iron) which was reported by previous studies^(17,18). However, the finding of this study is needed to be confirmed by further investigations and larger sample size before the application of this extract in the above mentioned concentration as mouth wash in preventive dentistry.

Conclusion

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Water extract of black seed or *Nigella Sativa* has the ability to reduce the dissolution of potassium and zinc ions from the tooth. This effect might increase tooth hardness and its resistance to acid attack.

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References

1. Dinakaran S, Sridhar S, Eganathan P: Chemical composition and antioxidant activities of black seed oil (*Nigella sativa* L.). *Int J Pharm Sci Res* 2016; 7(11): 4473-4479.
2. Burits M, Bucar F. Antioxidant activity of *Nigella sativa* essential oil. *Phytotherapy Research* 2000; 14(5):323–328.
3. Randhawa MA, Alghamdi MS. Anticancer activity of *Nigella sativa* (Black Seed) -a review. *AJCM* 2011; 39(6):1075–1091.
4. Abd-Awn BH, Al-Dhaher ZA, Al-Dafaai RR. The effect of black seed oil extracts on mutans streptococci in comparison to chlorhexidine gluconate (in vitro). *J Bagh Coll Dentistry* 2012; 24(4):126-131.
5. Baldassarri M, Margolis HC, Beniash E. Compositional determinants of mechanical properties of enamel. *J Dent Res* 2008; 87:645–649.
6. Brudevold F, Steadman LT, Spinelli MA, Amdur BH, Grøn P. A study of zinc in human teeth. *Archives of Oral Biology* 1963; 8(2): 135-144.
7. Kunin AA, Evdokimova AY, Moiseeva NS. Age-related differences of tooth enamel morphochemistry in health and dental caries. *EPMA J* 2015; 6:3.
8. Gutiérrez-Salazar MP, Reyes-Gasga J. Enamel hardness and caries susceptibility in human teeth. *Rev Latin Am Met Mat* 2001; 21(2): 36-40.
9. Ibraheem NK, Ahmed JH, Hassan MK. The effect of fixed oil and water extracts of *Nigella sativa* on sickle cells: an in vitro study.
10. Barbakow F, Sener B, Snr Lab Tech, Lutz F. Dissolution of phosphorus from human enamel pretreated in vitro using SnF₂ stabilized with amine fluoride 297. *Clin Prev Dent* 1987; 9(5): 3-6.
11. Mohammed NA. Effect of *Nigella Sativa* L. extracts against *Streptococcus mutans* and *Streptococcus mitis* in Vitro. *J Bagh College Dentistry* 2012, 24(3):154-7.
12. Nader MI, Al-Thwaini AN, Abdul-Hassan IA, Ali WA. Effect of *Nigella Sativa* (Black Seed), *Salvadora Persica* (Siwak) and Aluminum Potassium Sulphate (Alum) Aqueous Extracts On Isolated Bacteria From Teeth Root Canal. *Iraqi J Biotech* 2010; 9(1): 99-104.

13. Al-Douri AS, Al-KazazSGhA. The Effect of Nigella Sativa Oil (Black Seed) on the Healing of Chemically Induced Oral Ulcer in Rabbit (Experimental Study). *Al-Rafidain Dent J* 2010; 10(1):151-157.
14. Hoobi NM, Rzoqi M G. Dissolution of Inorganic Phosphorous Ion from Teeth Treated with Different Concentrations of Aqueous Extract of Nigella Sativa (Black Seed) in Comparison with Sodium Fluoride: An in Vitro Study. *IJSR* 2017;6(2): 1962-1965.
15. Brar GS, Arora AS, Khinda VI, Kallar S, Arora K. Topographic assessment of human enamel surface treated with different topical sodium fluoride agents: Scanning electron microscope consideration. *Indian J Dent Res* 2017;28:617-22.
16. Hussein B. Effect of Nigella Sativa (Habbatul Baraka) Water Extract on Micro-hardness of Initial Carious Lesion of Permanent Teeth Enamel Compared to Sodium Fluoride (An in Vitro Study). *IJSR* 2018; 7(1):215-220.
17. Al-Naqeep GN, Ismail MM, Al-Zubairi AS, Esa NM, 2009. Nutrients Composition and Minerals Content of Three Different Samples of Nigella sativa L. Cultivated in Yemen. *Asian Journal of Biological Sciences* 2009; 2: 43-48.
18. Jasim NA, Abid FM. Determination of mineral composition of Iraqi Nigella Sativa L. seed by Atomic absorption spectrophotometer. *Iraq Nat J Chem* 2011; 42:178-84.

Effect of Zinc, Vitamin A-Based School Snack and Nutritional Status on Diarrheal Morbidity among Children Aged 5-7 Years in Tuban: A Crosssectional Study

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Abstract

In many developing countries, about 25% of children deaths were due to diarrheal disease. Diarrheal infection and malnutrition have always been intricately related. Micronutrient deficiencies have increased susceptibility to infection, and infection caused food intake disorder, nutrient malabsorption, and intermediary metabolism. Among children ages 5-7 years, school snacks provide almost 40% of the daily intake. This study aimed to determine the effect of zinc and vitamin A containing on school snacks and nutritional status on episodes of diarrheal among children 5-7 years in Tuban. This was an analytical observational study with crosssectional design. This study was conducted in Tuban from March until May 2018. From 521 kindergarten in Tuban district, 11 kindergarten were randomly selected, and 113 children aged 5-7 years were sampled. The data were collected by 3x24 hours food recall, and a set of questionnaire. The data was analyzed used Spearman test with a significance value of $p < 0.05$. This study found that there were no effect between zinc ($p=0.336$) and vitamin A ($p=0.492$) contained on school snacks with episodes of diarrhea, but there was significantly effect of nutritional status on episodes of diarrhea ($p=0.013$). This study conclude that zinc and vitamin A contained on school snacks has no effects on episodes of diarrhea, but nutritional status was significantly related with episodes of diarrhea.

Keywords: *Diarrhea, school snacks, zinc, vitamin A, nutritional status.*

Introduction

Diarrhea is defined as a change in stool consistency and increased frequency of defecation. It caused by various bacterial, virus, and parasitic organism contaminant. Nearly 90% of diarrheal disease is attributed to inadequate sanitation such as contaminated food, lack of safe drinking water, lack of sanitation and hygiene, as well as poorer overall health. Diarrheal disease is a major public health problem globally, and particularly in low- and middle-income countries. Diarrhea among children under 5 years of age causes

considerable morbidity and contributes to child mortality for about 525 million children every years around the worldwide.¹ The mortality of diarrheal disease were more abundant than the mortality of AIDS, malaria, and measles disease.² In Indonesia, diarrhea is an endemic disease which is still become a potential disease of extraordinary events that often occurs with a fairly high Case Fatality Rate (CFR) and it is still become a problem that government need to be solved. In 2017, it is seen that the CFR of extraordinary incidences of diarrhea which often accompanied by children death is still quite high (1,97%), thus nationally the government program did not reach the target yet.³

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Based on the East Java health profil data, the service coverage target for diarrheal patient who come to the health facilities in 2011 and 2012 was 69%, 72,43% respectively from the estimated number of diarrheal sufferers. It still far away under the national target

which 100%. Tuban district is one of the district which did not reach the national target of service coverage for diarrhea patient. In East Java, there were only 7 districts/city which reach the national target (100%) such as Bondowoso district, Situbondo district, Mojokerto district, Sampang district, Kediri city, Pasuruan city and Mojokerto city.

Based on Riskesdas (2013), the prevalence of diarrhea among children ages of 5-14 years was 7.2%, and Tuban district health facilities only covered of 12.8% services of children affected by diarrhea.⁴

In the group age of 5-7 years, the children commonly study at kindergarten schools. In this group of ages, snacking provide almost 40% of the daily intake. Listiyorini et al.⁵ found that incidence of diarrhea closely associated with food hygiene which bought from schools canteen or roadside snack. It is also closely related with nutritional status, due to related to food intake disorder, nutrient malabsorption, and intermediary metabolism. Based on previous study conducted by Clifton et al.⁶ the increasing of episodes of diarrhea among the children, significantly caused deficiency of zinc and vitamin A. Fedriansyah⁷ concluded that zinc and vitamin A status on the body related with episodes of diarrhea. Deficiency of Vitamin A closely related to diarrheal infection, and supplementation of vitamin A 60 mg RE can decreased the morbidity of diarrheal infection case.⁸ Vitamin A can repair the damaged of intestinal epithel due to acute infections. Vitamin A has an important role on cell proliferation and cell differentiation which increasing immune system respond through increase the production of B-lymphocytes. So that, the deficiency of Vitamin A caused decreasing of immune system respond which depend on lymphocytes as cellular immune.⁹ Besides vitamin A, zinc also plays main role on peripheral tissue and needed in oxidative process of vitamin A become retinal oxidase. Deficiency of zinc can causes disruption of vitamin A metabolism, and several immune system metabolism such as the maturation of limfosit T and interleukin-2 production. Zinc is the precursor of tymulin hormone which plays an important role on immune system and the activity of tymulin hormone are closely related with zinc concentration on serum. So the deficiency of zinc will impact on vitamin A concentration cause a disruption on immune system such as, differentiation of lymphocyte T and lymphocyte B, apoptosis inhibition, and malfunction of maintain the integrity and function of mucosal surfaces.⁷

Based on the background above, the researcher is interested to conducting study about the effect of zinc and vitamin A containing in school snacks and nutritional status on diarrheal morbidity among children 5-7 years of age, in Tuban.

Material and Method

This study was carried out in Tuban Regency, East of Java, Indonesia. This study was conducted from March until May 2018. This study was an analytical quantitative observational with crosssectional design. Subjects were sampled by simple random sampling techniques. From 521 Kindergarten schools in Tuban Regency, 11 kindergarten schools were selected among 11 village in sub-district of Tuban.

The inclusion criteria in this study such as (1) age of children 5-7 years in kindergarten residing in Tuban City; (2) Their parent agreed to participate in this study proven by informed consent, while the exclusion criteria in this study; (1) The children were absent when the study conducted; (2) consumed worm medicine during 6 month ago.

Primary data was obtained directly from the subjects of the study, which are the interviews from the mothers or caretaker of the subjects guided by a validated questionnaire. Primary data consisted of: characteristics of subjects, data of snack intake from recall of 3x24 hours, data of episodes of diarrhea occurrences and nutritional status data from anthropometric measurements (height and weight).

Secondary data was data from the Health Profile Data and the Education Profil to find out the number of kindergarten students in Tuban Regency and the highest prevalence of diarrheal infection.

IBM SPSS statistics v.23 software was used for statistical analyses. The characteristics of subjects described with descriptive analyses, and the bivariate analyses using Spearman test with a significance value of $p < 0.05$.

Findings: This study involved a total of 113 subjects from 11 kindergarten in several sub-district in Tuban Regency. There was no subjects whom dropped out from this study. Age of subjects, zinc containing on snacks, vitamin A containing on snacks, and nutritional status were assessed by the current study. The majority (60%) subjects were 6 years of age. About 40.7% of the

subjects had a severe deficiency of zinc from snacks intake and approximately 62.8% of subjects had a severe deficiency of vitamin A from snacks intake. The majority (50.4%) nutritional status of the subjects were normal while 18.6% subjects were underweight and 14.2% were obesity. The episodes of diarrhea of subjects showed that majority of subjects (65.5%) had never diarrhea, but 19.5% subjects had twice episodes of diarrhea within a month (Table 1).

Table 1. Frequency distribution based on the Characteristic of subject

Characteristics	N= 113		
	n	%	Mean
Age of Years			
5 years	26	23	5.9 years
6 years	68	60	
7 years	19	16.8	
Zink Intake*			
Excessive	44	38.9	2.91 g/day
Enough	16	14.2	
Mild deficit	5	4.4	
Moderate deficit	2	1.8	
Severe deficit	46	40.7	
Vitamin A intake*			
Excessive	21	18.6	3.84 g/day
Normal	11	9.7	
Mild deficit	4	3.5	
Moderate deficit	6	5.3	
Severe deficit	71	62.8	

Characteristics	N= 113		
	n	%	Mean
Nutritional Status**			
Underweight	21	18.6	
Normal	57	50.4	
Overweight	19	16.8	
Obesity	16	14.2	
Episodes of diarrhea***			
Never	74	65.5	
1 times diarrhea	17	15.0	
2 times diarrhea	22	19.5	

Notes: *: categorized by provision of Health Ministry (1996) with criteria >120%: excessive, 90-119%: normal; 80-89%: mild deficit; 70-79%: moderate deficit; <70%: severe deficit, **: categorized by Supariasa (2017) with criteria <-3 until -2 SD; normal: -2 until +2 SD; overweight > +2 SD; obesity: > 3 SD, ***: categorized by Listyorini (2012)

The results showed the subjects who suffered severe deficit of vitamin A, 14 of them had twice episodes of diarrhea within recently month, while the subjects who suffered severe deficit of zinc, 11 of them had twice episodes of diarrhea. The subject who had underweight nutritional status, 10 of them had twice episodes of diarrhea (Table 2).

Table 2. Correlation between zinc and vitamin A containing school snacks, nutritional status with episodes of diarrhea

Variables	Episodes of Diarrhea			Total
	Absent of Diarrhea	Once	Twice	
Vitamin A intake				
Excessive	16	1	4	21
Normal	7	2	2	11
Mild deficit	3	0	1	4
Moderate deficit	3	2	1	6
Severe deficit	45	12	14	71
Zink Intake				
Excessive	31	6	7	44
Normal	10	2	4	16
Mild deficit	4	1	0	5
Moderate deficit	1	1	0	2
Severe deficit	28	7	11	46

Variables	Episodes of Diarrhea			Total
	Absent of Diarrhea	Once	Twice	
Nutritional Status				
Underweight	9	2	10	21
Normal	39	11	7	57
Overweight	13	3	3	19
Obesity	13	1	2	16

Notes: *: categorized by provision of Health Ministry (1996) with criteria >120%: excessive, 90-119%: normal; 80-89%: mild deficit; 70-79%: moderate deficit; <70%: severe deficit, **: categorized by Supriasa (2017) with criteria <-3 until -2 SD; normal: -2 until +2 SD; overweight > +2 SD; obesity: > 3 SD, ***: categorized by Listyorini (2012)

The results showed that there were correlation between vitamin A intake with zinc intake ($p=0.000$), and nutritional status ($p=0.002$), but there were no correlation between vitamin A intake with episodes of diarrhea ($p=0.492$). Similarly, the zinc intake also correlated with vitamin A intake ($p=0.000$),

and nutritional status ($p=0.007$), but there were no correlation between vitamin A intake with episodes of diarrhea ($p=0.336$). While nutritional status correlated with vitamin A intake ($p=0.002$), zinc intake ($p=0.007$), and episodes of diarrhea ($p=0.013$) (Table 3).

Table 3. Analyze of zinc and vitamin A containing school snacks, nutritional status with episodes of diarrhea

Variabel	Vitamin A intake	Zink intake	Nutritional Status	Episodes of diarrhea
Vitamin A intake		0.000*	0.002*	0.492
Zink intake	0.000*		0.007*	0.336
Nutritional Status	0.002*	0.007*		0.013*
Episodes of diarrhea	0.492	0.336	0.013*	

Notes: Spearman's rho test; $\alpha = 0,05$, *: statistically significant

Discussion

The results of this study showed that the incidence rate of diarrheal morbidity among children age 5-7 years was quietly high (34.5%). This prevalence higher than prevalence of diarrhea in India which only 12.43%¹⁰ and higher than prevalence of diarrhea in Italia which only 26.1%¹¹.

The younger children are most vulnerable with the incidence of either acute or chronic diarrhea due to weakened immune system.¹²

This study showed that nutritional status closely associated with the episodes of diarrhea. Childhood malnutrition was associated with dehydrating diarrhea. The association between malnutrition and the diarrheal morbidity was bidirectional and has been reported for the past decades.¹³ Malnutrition after diarrheal illness caused anorexia, reduced absorptive function, and mucosal

damage as well as nutrient exhaustion associated with episodes of diarrhea. Diarrheal illness affects the weight reducing as well as height gains.¹⁴ On the other side, malnutrition leads to reduced the children performance, inadequate physical growth and development, decreased of immune system function which increased the opportunity to be infected and worsen the frequency, duration, and severity of diarrheal episodes.¹⁵ Food-based intervention and nutritional dietary improvement among severe-malnourished children should be done rather than only treating the diarrheal infection.¹⁶

In this study, zinc containing on schools snacks did not related with the episodes of diarrhea among children 5-7 years in Tuban. This finding, did not supported by mostly previous study which concluded that zinc plays an positives effect of zinc intake during acure diarrhea.¹⁷⁻¹⁸ Even WHO recommends zinc supplementation for children in developing countries who have acute or

persistent diarrhea at a dose of 20 mg in infants daily for 10-14 days. It is more necessary for malnourished children as they already have a zinc deficient, which predisposes them to diarrhea and worsens it.¹⁹

Zinc's mechanism of action for the treatment of diarrhea is not fully understood, but it might be zinc is crucial for many cell function, such as protein synthesis, and cell growth and differentiation.¹⁷ Zinc also plays a role for regulation of intestinal fluid, mucosal integrity and modulation of expression of genes encoding important zinc-dependent enzymes like cytokines, which play important roles in immune system and in modulation of oxidative stress.¹⁸

In this study, vitamin A containing on school snack also did not showed significantly associated with the episodes of diarrhea. This finding, opposite with previous review that conclude and indicating that vitamin A supplementation is associated with large and important reduction in morbidity and mortality of diarrhea in low and middle income countries.²⁰ Vitamin A deficiency may caused by maternal undernutrition, poor dietary quality, and losses during infection such as diarrhea, while the other side it is increases vulnerability to a range of illnesses such as diarrhea. Vitamin A deficiency can leading causes of mortality when infection compounded by coexisting malnutrition.²¹ Vitamin A refers to a subclass of retinoic acids long understood to help regulate immune function and reduce morbidity and mortality of infectious disease such as diarrhea. Vitamin A mainly required for normal function of the visual system, maintenance of cell function for growth, epithelial integrity, production of red blood cells, immunity, and reproduction.²²

The difference results of this study might be caused this study just analyzed zinc and vitamin A intake from school snack which approximately only 20-40% of total daily intake.

Conclusion

There were no effect of zinc and vitamin A containing on school snacks on the episodes of diarrhea. There was a significantly effect of nutritional status on the episodes of diarrhea. A well nourished children will decreased the vulnerability of illnesses such as diarrhea. Limitation of this study was bias memorize because the parents or caretakers have to reminded what the children ate for 3 days past.

Ethical Clearance: Ethical Clearance of this study was taken from Ethical Committee of Medical Faculty Sebelas Maret University, Indonesia.

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Conflict of Interest: There is no conflict of interest in this study.

References

1. WHO. Diarrhoeal disease. 2017. <https://www.who.int/news-room/fact-sheets/detail/diarrhoeal-disease>.
2. CDC. Diarrhea: Common Illness, Global Killer. 2015. <https://www.cdc.gov/healthywater/pdf/global/programs/globaldiarrhea508c.pdf>
3. Health Ministry of Republic Indonesia. Indonesian Health Profile years of 2017. 2017. <http://www.depkes.go.id/resources/download/pusdatin/profil-kesehatan-indonesia/Profil-Kesehatan-Indonesia-tahun-2017.pdf>
4. Health Department of East Java. Monthly reports of diarrheal services coverage. Health Department of Tuban Districts. 2017.
5. Listiyorini, W. Association of Hand-washing habits among pre-school children with Incidence of diarrhea on Pajang Community Health Center, Surakarta. Universitas Muhammadiyah Surakarta, Surakarta. 2012. <http://eprints.ums.ac.id/>
6. Clifton E, Lougee D, Murno J. Diarrhea and Dehydration. *American Academy of Pediatrics*. 2016; 6: 10-18.
7. Fedriyanshah. Association between zinc and vitamin A level on prevalence of upper airway infection and diarrhea. *Sari Pediatri*. 2010; 12(4): 6-12.
8. Azrimaidaiza. Vitamin A, immunity, and it correlation with infectious disease. *Journal of Public Health*. 2007.
9. Septa M. Effect of vitamin A supplementation on duration of diarrhea among the children aged 14-51 month in Sukarami Community Health Center, Palembang. 2015. <https://media.neliti.com/media/publications/181681-ID-pengaruh-suplementasi-vitamin-a-terhadap.pdf>
10. Ali F, Singh OP, Dutta A, Haq ZU, Ghatak A, Ashtankar T. Assessing critical gaps in

- implementation of WHO and UNICEF'S 7-point diarrhea control and prevention strategy in Uttar Pradesh, India. *Annals of tropical medicine and public health*. 2017; 10(3) 571-579.
11. Bitew BD, Woldu W, Gizaw Z. Childhood diarrheal morbidity and sanitation predictors in a nomadic community. *Italian Journal of Pediatrics*. 2017; 43: 91-100.
 12. Mokomane M, Kasvosve I, Goldfarb DM. The global problem of childhood diarrhoeal diseases: emerging strategies in prevention and management. *Therapeutic advanced in infectious disease*. 2018; 5(1): 29-43
 13. Roy SK, Buis M, Weersma R, Khatun W, Chowdhury S, Begum A, Sarker D, Thakur SK, Khanam M. Risk factors of mortality in severely-malnourished children hospitalized with diarrhoea. *Journal of Health Population Nutrition*. 2011; 29 :229–235.
 14. Kazandjian S, Dupierrix E, Gaash E, Love IY, Zivotofsky AZ, De Agostini M, Chokron S. Egocentric reference in bidirectional readers as measured by the straight-ahead pointing task. *Brain Respiration*. 2009; 1247 :133–141.
 15. Brown KH. Diarrhea and Malnutrition. *Journal of Nutrition*. 2003; 22: 3166-3774.
 16. Dewey KG, Mayers DR. Early Child Growth: How Do Nutrition and Infection Interact?. *Maternal and Child Nutrition*. 2011; 7(3)
 17. Kulkarni H, Mamtani M, Patel A. Roles of zinc in the pathophysiology of acute diarrhea. *Curr Infect Dis Rep*. 2012; 14(1): 24–32
 18. Berni CR, Buccigrossi V, Passariello A. Mechanisms of action of zinc in acute diarrhea. *Current Opinion of Gastroenterol*. 2011; 27(1): 8-12.
 19. World Health Organization. The treatment of diarrhoea: a manual for physicians and other senior health workers. WHO : Geneva. 2005.
 20. Imdad A, Yakoob MY, Sudfeld C, Haider BA, Black RE, Bhutta ZA. Impact of vitamin A supplementation on infant and childhood mortality. *BMC Public Health*. 2011; 11: 20-30.
 21. Black RE, Cousens S, Johnson HL, Lawn JE, Rudan I, Bassani DG, et al. Global, regional, and national causes of child mortality in 2008: a systematic analysis. *Lancet*. 2010; 375: 1969-1987.
 22. Semba RD, de-Pee S, Sun K, Bloem MW, Raju VK. The role of expanded coverage of the national vitamin A program in preventing morbidity and mortality among preschool children in India. *Journal of Nutrition*. 2009; 140: 208-212.

Neurological And Non Neurological Role of Brain-Derived Neurotrophic Factor (BDNF) in Developing Jaw

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Abstract

Background: Brain-derived neurotrophic factor (BDNF), recognized to be involved in differentiation and proliferation of specialized cell such as endothelial cell and osteoblast cell.

Aim of the Study: The study was designed to identify the effect of exogenous BDNF on development of jaw and on neural marker expression.

Materials and Method: Twenty pregnant rats, ten injected (I.M) with normal saline, other ten injected (I.M) with 0.1 ml of BDNF that received three doses at intervals (0, 7, 14 day of gestation period). Embryos at 16th and 18th intra-uterine life were used for histological and immunohistochemical evaluation for the development of prenatal jaw .

Results: Illustrate an enhancement of bone development during proceeding embryonic periods for both study groups .Moreover, the experimental group shows a high significant difference in the mean of bone cell count at the period 18th day in comparison to 16th day IUL, and in comparison to control at 18th day IUL. Results show positive expression of neuronal marker by proliferating nerve cells in control and experimental groups with significant difference.

Conclusion: The study suggest that BDNF contributes to promoting the differentiation of bone cells and enhancement of bone formation by increasing expression of neuron marker.

Keywords: Brain derived neurotrophic factor, bone, embryogenesis, osteogenic cell, bone stem cell, rat development.

Introduction

Neurotrophins and their receptors are important molecules that have a role in the development and maintenance of nervous organs and have been recognized to be involved in regulating of organogenesis of skeletal tissues^[1,2]. Studies have shown that neurotrophins are widely expressed in skeletal tissues, and shared in chondrogenesis, osteoblastogenesis,

and osteoclastogenesis.^[3,4] They illustrated to be involved in regulating skeletal tissue formation and in healing events^[5]. Moreover, BDNF stimulates and controls growth of new neurons from neural stem cells (neurogenesis) ^[6,7], and BDNF protein and mRNA have been identified in most neural areas of developing tissues.^[8,9]

This study used Brain-derived neurotrophic factor (BDNF) to investigate its potential roles on expression of neural marker in developing bone of prenatal rat jaw.

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Material and Method

Twenty pregnant Wistar rats, aged (11–12-week-old) with weight (220–270 g) were used and maintained in the animal department of (National Center of Drug

Control and research/Iraq) under control conditions of temperature, drinking and food consumption and all experimental procedures were carried out in accordance with the ethical principles of animal experimentation .The animals divided randomly into 2groups, each consisting of 10 animals.

Group I, control group received 0.1ml(I.M injection) of distilled water.

Group II, experimental group received 0.1 ml BDNF (I.M injection).Both groups received 3doses at gestation interval periods (0,7,14 day).

Five rats from each group were sacrificed at 16th and 18thday of gestation date respectively and their embryos were obtained.

Materials

- A lyophilised BDNF protein 10 µg (ab9794)/ Abcamwas reconstitute in water to a concentration of 0.01 mg/ml and used for experimental group.
- Anti-Neu N antibody [1B7] - Neuronal Marker (ab104224) ABCAM

Method

Histological Examination: Embryo jawwas resected, fixed by 10% buffered formalin, dehydrated, and embedded in paraffin, 5µm section was stained with Hematoxylin and Eosin (H & E). The histological examination was done under light microscope by examining four microscopical fields for each slide and counting the number of the bone mesenchymal stem

cells (BMSCs), osteocytes, osteoblast. Mean readings were calculated and used in statistical analysis .

Immunohistochemistry on tissue sections: The Neuronal Marker (ab104224) ABCAM was used. Preparation and characterization of these monoclonal antibody has been described and verified according to the manufacture data sheets.

Positive peroxidase staining produces brown color on light microscopy,the percentages of positively stained cells were counted at 5 representative fields (40X).

Immunohistochemical scoring: Quantification method of Immuno-reactivity was estimated for positive cell that expressed neuronal Marker .It was assessed by identifying and scoring 100 cells in five fields (X40) along examined area of different sections,the scoring is:

(Score 0, none; score 1, <10%; score 2, 10-50%; score 3, 51-80%; score 4, >80%).^[10]

Radiological examination: All the embryo’s head were radiographed by Plain X-ray with standard dental radiographic film.Voltage(kV)=60, Current(mA)=70, Exposure(s)=0.08 statistic analysis

The data were analyzed using one-way ANOVA test with multiple comparisons by (LSD Method).

Findings:

1. **Histological and immunohistochemical results:** Control group at 16th IUL shows new apposition of thin trabeculae surrounding by proliferating bone stem cells,at 18th day histologic section shows bone trabeculae with osteoblast on it’s surface.

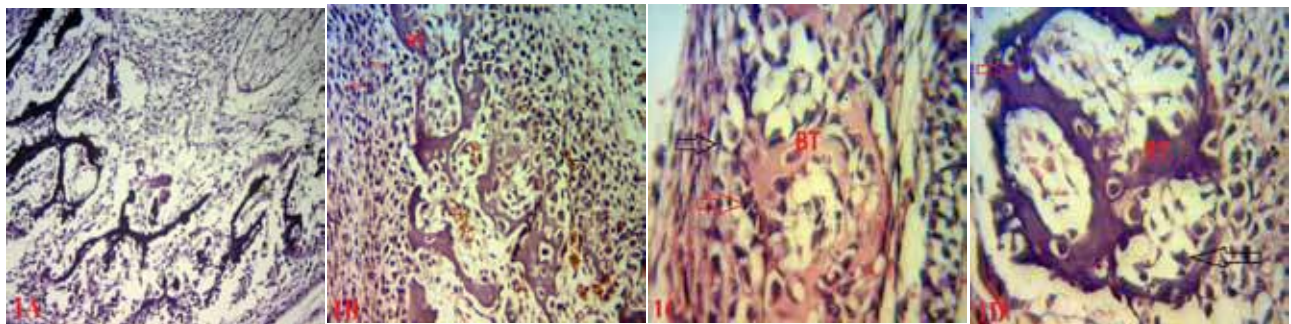


Figure (1): Embryonic bone at 16th & 18th IUL 1A: Control at 16th IUL H & E x10 1B: Embryonic bone (control) at 18th IUL shows Bone trabeculae (BT),bone mesenchymal stem cell.(arrows). H & Ex20 1C: Exp. At 16th IUL, shows bone trabeculae (BT); osteoblast (red arrow) Mesenchymal cell (black arrow). H & Ex40 1D: Embryonic bone (exper.) at 18th IUL, bone trabeculae (BT); osteocyte (red arrow) osteoblast (black arrow) H & Ex40

Experimental group at 16th IUL shows bone trabecule with osteoblast, proliferating bone stem cell was detected around the trabeculae. At 18th day of gestation period illustrates well, thick organized trabeculae surrounding by osteoblast and osteocyte cell trapped inside the trabeculae. Figure (1).

Immunohistochemical expression of neuronal marker for embryonic bone (control & exp.) at 16th & 18th IUL shows positive DAB stain by proliferating neural cells in developing jaw, score 1 for control and score 2 for experimental figure (2).

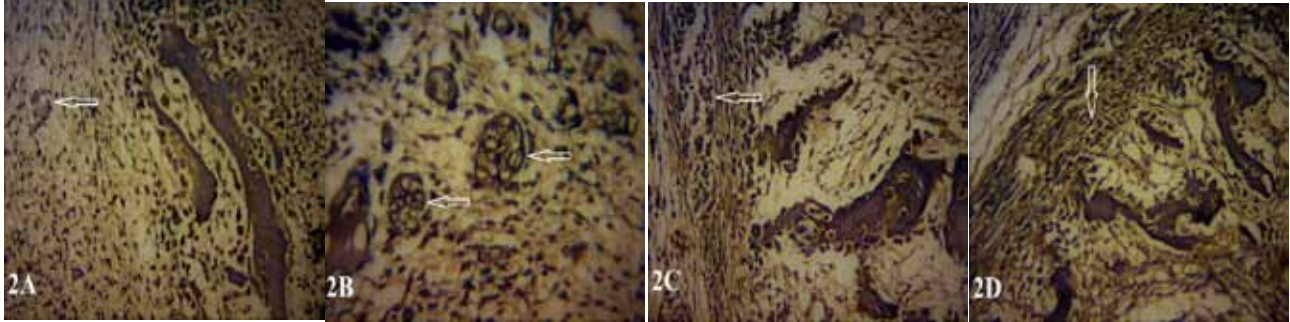
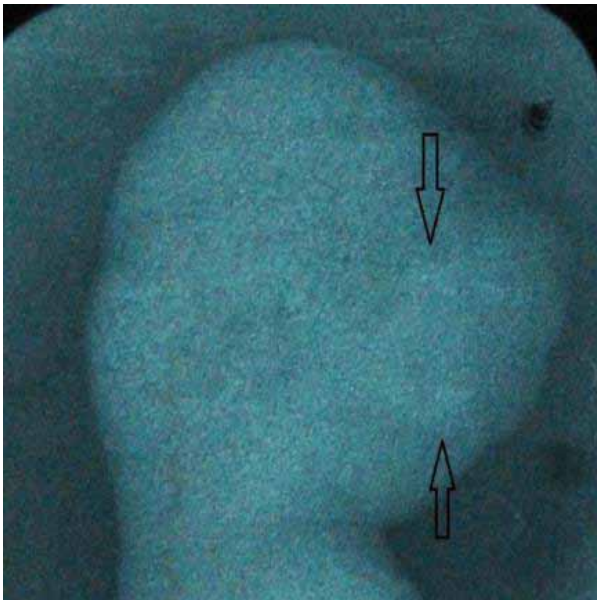


Figure (2): Immunohistochemical expression of neuronal marker for embryonic bone (control & exp.) at 16th & 18th IUL, 2A: Control at 16th IUL shows positive expression of neural cells (arrow).DAB stain x10, 2B:Control at 18th IUL shows positive expression of neural cells (arrows).DAB stainx20, 2C: Exp. at 16th IUL, shows positive expression of neural cells (arrow).DAB stainx20, 2D: Exp. at 18th IUL, shows positive expression of neural cells (arrow).DAB stainx10

2. **Radiological Results:** Radiographic evaluation for the study groups of embryos at 18th IUL illustrated that control group shows faint streaky radio-opacity in upper and lower jaws, while experimental group shows more organized, linear radio-opacity in upper and lower jaws. Figures(3,4)



Figure(3): Stippled, streakyopaque radio-density represented upper and lower jaw (arrows) For control group at 18th IUL.

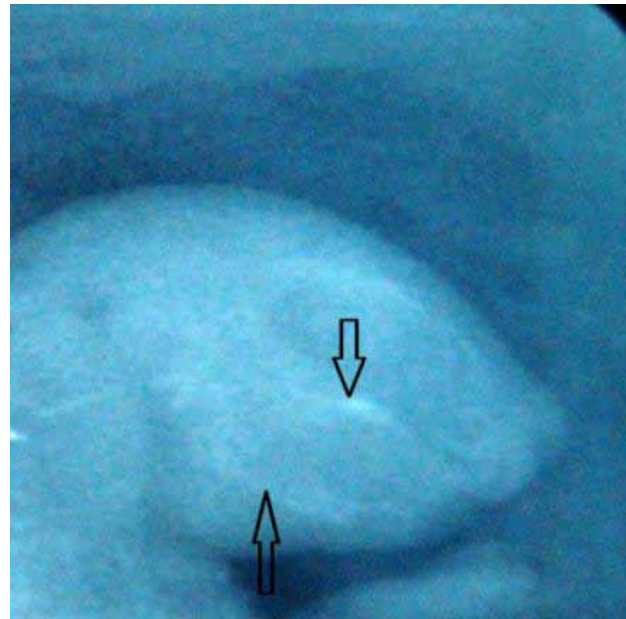


Figure (4): Linear opaque radio-density represented upper and lower jaw(arrows) for Experimental group at 18th IUL

3. **Statistic analysis:** Table (1) illustrates mean of bone cell (osteoblast and osteocyte) with bone mesenchymal stem cells for control and experimental groups at the 16th and 18th gestation periods. Multiple comparisons by (LSD Method)

of bone cells and BMSC count shows a high significant value for the experimental group at the period 18th day in comparisum to 16th day IUL, and in comparisum to control at 18th day IUL .

Table (2) illustrates mean of neuron cells that expressed positive neuron marker .The results show a

high record in the mean of positive cells in experimental for both periods in comparisum to control with a high significant value. On other hand, the mean record for experimental group show to be high at period 16th in comparisum to 18th period that reversed the result in control.

Table (1): Statistic analysis with multiple comparisons by (LSD Method) among all pairs of different (S.O.V.) effect’s Parameters in compact form, for the bone cells count Parameter in studied trials

Groups/Bone cells /periods	Sample No.	Mean	Std. Dev.	Std. Error	95% C. I. for Mean		Min.	Max.
					L.bound	Up.bound		
Control - Osteoblast - 16 th IUL	10	8.97	1.03	0.42	6.58	10.75	6	11
Control - Osteoblast 18 th IUL	10	14.00	1.10	0.45	11.79	15.15	12	16
Control - Osteocyte -16 th IUL	10	4.67	1.88	1.58	3.59	5.74	3	6
Control - Osteocyte - 18 th IUL	10	8.87	2.07	0.84	6.50	10.83	7	12
Control - BMSCs 16 th IUL	10	28	0.63	0.26	27.1	29.6	26	29
Control - BMSCst - 18 th IUL	10	22	0.55	0.22	21.3	23.3	18	24
Exp-Osteoblast - 16 th IUL	10	10.70	1.64	0.67	9.78	11.22	9	12
Exp-Osteoblast -18 th IUL	10	26.88	0.75	0.31	24.04	27.62	24	28
Exp-Osteocyte - 16 th IUL	10	8.00	0.89	0.37	7.06	9.94	6	10
Exp-Osteocyte - 18 th IUL	10	12.89	1.83	0.75	10.91	13.76	10	14
Exp.-BMSCs-16 th IUL	10	24	0.52	0.21	22	25.4	20	26
Exp.- BMSCs - 18 th IUL	10	20.5	0.75	0.31	19.6	21.7	19	22
Groups	periods	Mean Difference		Sig.(*)	C.S.			
Control/Exp.	16 th IUL	0.14		0.655	NS			
Control/Exp.	18 th IUL	0.67		0.007	HS(*)			
control	16 th /18 ^h IUL	0.16		0.522	NS			
Exp.	16 th /18 th IUL	0.71		0.0001	HS(*)			

(*)HS: Highly Sig. at P< 0.01; Non Sig. at P> 0.0

Table (2): Multiple comparisons by (LSD Method) among all pairs of different (S.O.V.) effect’s of Density Parameter in compact form for positive expression of neuron marker

Groups	Periods	Mean of +ve cell	Mean Difference	Sig.(*)	C.S.
Control/Exp.	16 th IUL	7.33/12.44	0.16	0.000	HS(**)
Control/Exp.	18 th IUL	9.34/8.67	0.43	0.011	S(*)
Control	16 th /18 ^h IUL	7.33/9.34	0.22	0.000	HS(**)
Exp.	16 th /18 th IUL	12.44/8.67	0.41	0.000	HS(**)

(**) HS: Highly Sig. at P< 0.01; S: (*)Sig. at P< 0.05

Discussion

The study focused on jaw development of rat model to confirm how concurrent use of brain-derived neurotrophic factor can affect formation and aggravation of bone.

Recent studies have found that neurotrophins and Trk receptors are expressed in mouse osteoblastic cell lines^[11,12].

In our animal model, it appeared that using of exogenous BDNF play a role in development of the

jaw as appeared in histological, immunohistochemical investigations and radiologic examination.

The results can be explained as followings:

First: BDNF is a key molecule which controls neuronal differentiation and survival, synaptic formation and plasticity, as well as activity-dependent changes in synaptic structure and function [13].

Second: BDNF promotes the differentiation of bone cells, as the present results show that the mean of bone cell (osteoblast and osteocyte) with bone mesenchymal stem cells for experimental group were higher in comparison to control [14,15].

Third: Enhancement of bone formation, by the action of the increment of expression of neuronal marker that affected on mesenchymal stem cell and formative bone cell [16,17].

In experimental group, we observed that new bone trabeculae formation starts at 16th day proceeding the control group with a coincidence of an increment for expression in neuron marker and at 18th day of gestation period a well, thick organized trabeculae surrounding by osteoblast and osteocyte was detected histologically and the result was confirmed radiologically as the radiographic film showed a linear opaque radio-dense demarcated the jaw.

Conclusion

Brain-derived neurotrophic factor (BDNF) has neurological and non-neurological effects on bone formation and may act as osteoinductive agent by increasing expression of neuronal marker with increment of the number of bone progenitor cells and bone forming cells.

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Conflict of Interest: Nil

Source of Funding: By ours

Ethical Clearance: All work of this study had done according to the National Council's guide for the care of laboratory animals.

References

1. Mikami Y, Suzuki S, Ishii Y, Watanabe N, Takahashi T, Isokawa K, Honda MJ. The p75 neurotrophin receptor regulates MC3T3-E1 osteoblastic differentiation. *Differentiation*. 2012 Dec;84(5):392-9.
2. Skaper SD. Neurotrophic Factors: An Overview. *Method Mol Biol*. 2018;1727:1-17.
3. Mogi M, Kondo A, Kinpara K, Togari A. Anti-apoptotic action of nerve growth factor in mouse osteoblastic cell line. *Life Sci*. 2000;67(10):1197-206.
4. Skaper SD. The biology of neurotrophins, signalling pathways, and functional peptide mimetics of neurotrophins and their receptors. *CNS Neurol Disord Drug Targets*. 2008 Feb;7(1):46-62.
5. Hankenson KD, Gagne K2, Shaughnessy M2. Extracellular signaling molecules to promote fracture healing and bone regeneration. *Adv Drug Deliv Rev*. 2015; 1(94):3-12.
6. Sun CY, Chu ZB, She XM, Zhang L, Chen L, Ai LS, Hu Y. Brain-derived neurotrophic factor is a potential osteoclast stimulating factor in multiple myeloma. *Int J Cancer*. 2012 Feb 15;130(4):827-36.
7. Liu Y, Zhang X, Dai Y, Shu C, Qu P, Liu YX, Yang L, Li TY. Effects of bone marrow mesenchymal stem cells on learning and memory functional recovery in neonatal rats with hypoxic-ischemic brain damage. *Zhonghua Er Ke Za Zhi*. 2008 Sep;46(9):648-53.
8. Krimm RF. Factors that regulate embryonic gustatory development. *BMC Neurosci*. 2007 Sep 18;8 Suppl 3:S4.
9. Kaplan DR, Miller FD. Developing with BDNF: a moving experience. *Neuron*. 2007; 55:1-2.
10. Suzuki S, Dobashi Y, Hatakeyama Y, Tajiri R, Fujimura T, Heldin CH, Ooi A. Clinicopathological significance of platelet-derived growth factor (PDGF)-B and vascular endothelial growth factor-A expression, PDGF receptor-β phosphorylation, and microvessel density in gastric cancer. *BMC Cancer*. 2010 Nov 30; 10:659.
11. Su YW, Chung R, Ruan CS, Chim SM, Kuek V, Dwivedi PP, Hassanshahi M, Chen KM, Xie Y, Chen L, Foster BK, Rosen V, Zhou XF, Xu J, Xian CJ. Neurotrophin-3 induces BMP-2 and VEGF

- Activities and Promotes the Bony Repair of Injured Growth Plate Cartilage and Bone in Rats. *J Bone Miner Res.* 2016 Jun;31(6):1258-74
12. Su YW, Chim SM, Zhou L, Hassanshahi M, Chung R, Fan C, Song Y, Foster BK, Prestidge CA, Peymanfar Y, et al. Osteoblast derived-neurotrophin-3 induces cartilage removal proteases and osteoclast-mediated function at injured growth plate in rats. *Bone.* 2018;116:232-247.
 13. Park H, Poo MM. Neurotrophin regulation of neural circuit development and function. *Nat Rev Neurosci.* 2013;14:7-23.
 14. Lee SK1, Kim YS, Oh HS, Yang KH, Kim EC, Chi JG. Prenatal development of the human mandible. *Anat Rec.* 2001 Jul 1;263(3):314-25.
 15. Su YW, Zhou XF, Foster BK, Grills BL, Xu J, Xian CJ. Roles of neurotrophins in skeletal tissue formation and healing. *J Cell Physiol.* 2018;233(3):2133-2145.
 16. Kurihara H, Shinohara H, Yoshino H, Takeda K, Shiba H. Neurotrophins in cultured cells from periodontal tissues. *J Periodontol.* 2003 Jan; 74(1):76-84.
 17. Chung R, Xian CJ. Recent research on the growth plate: Mechanisms for growth plate injury repair and potential cell-based therapies for regeneration. *Mol Endocrinol.* 2014; 53(1):T45-61.

Efficacy of *Catharanthus Roseus* Extract against Dengue Virus Type 2 Infection *In Vitro*

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Abstract

Catharanthus roseus, known as Madagascar periwinkle is an herbal and traditional plant used for treatment of various diseases. A study was carried out to test the cytotoxicity and antiviral effects of methanol extract from the leaves of *C. roseus*. The leaves of *C. roseus* were extracted using methanol to produce crude methanol extract. *In vitro* cytotoxicity test was performed to determine the concentration value of the extract causing 50% cell death (CC₅₀) using MTT assay. The antiviral activity has been confirmed by conducting foci forming unit reduction assay (FFURA) which involved post-treatment, pre-treatment and virucidal tests. Cytotoxicity test was performed on Vero cells indicates the CC₅₀ value for *C. roseus* extract towards Vero cells was 0.13 mg/mL. The 50% Effective Concentration, EC₅₀ of *C. roseus* extract was 0.025 mg/mL. Selectivity index of *C. roseus* extract against DENV-2 was 5.2. Three treatments were used in the antiviral test; 1) post-treatment, 2) pre-treatment, and 3) virucidal. The results revealed that the post-treatment was more effective in inhibiting viral replication compared to pre-treatment and virucidal. The results of this research showed that *C. roseus* extract has good potential for prospective nature-based antiviral drug.

Keywords: *Catharanthus roseus*, Antiviral Activity, Dengue Virus Type 2, MTT, FFURA.

Introduction

In this study, we investigate the cytotoxicity and antiviral properties of *C. roseus* to explore its potential as anti-DENV-2 agent. *Catharanthus roseus* (L.) G. Don (Apocynaceae) a perennial herb plant is widely used as an ornamental species in many tropical countries. It is more commonly known as Madagascar periwinkle. In Malaysia its known as *Kemuningcina*. This plant produces a combination of pink, purple and white flowers. These flowers are often grown for their attractive appearance and to decorate shady areas¹. Methanol extracts of *C. roseus* has been reported to exhibit significant anti-cancer activity against different cell types *in vitro*². Crude extracts of *C. roseus* showed antibacterial activity against Gram-positive and Gram-negative bacteria³. In addition, *C. roseus* extract also showed antifungal properties against *A. fumigatus*, *C. albicans*, *A. niger* and *F. moniliforme*⁴.

Dengue virus (DENV) is a positive-sense, single-stranded RNA virus with a genome size of at least 10.7

kb. It is a member of the Family Flaviviridae, genus Flavivirus. There are four different DENV serotypes (DENV-1, DENV-2, DENV-3, and DENV-4) which are primarily transmitted between humans by the mosquito vector *Aedes aegypti* and *Aedes albopictus*^{5,6}. Dengue virus can cause asymptomatic infection to mild dengue fever or severe dengue hemorrhagic fever and dengue shock syndrome⁷. All DENV serotypes are widespread geographically throughout the tropics. The incidence of dengue has grown dramatically around the world in recent decades⁸. Recovery from infection by one serotype provides lifelong immunity against that particular serotype. However, cross-immunity to the other serotypes after recovery is only partial and temporary. Secondary infection by other serotypes increase the risk of developing severe dengue⁹.

Materials and Method

Plant Material and Extraction: Leaves of *C. roseus* were washed under running tap water and finally rinsed with distilled water then air dried for 48h,

homogenized into a fine powder and stored in air-tight plastic containers. Dried leaves were finely ground and then extracted in a soxhlet extractor using methanol solvent. After that, the extract was evaporated to dryness using a rotavap. Lastly, freeze dry technique was performed to lyophilize the extract.

Cell and virus: Vero cell from American Type Culture Collection (ATCC) CCL-81 was used for both cytotoxicity and antiviral test. Dulbecco's Modified Eagle's Medium (DMEM) supplemented with 5% fetal bovine serum (FBS) was used for Vero cell maintenance throughout the experiment. C6/36 cells maintained in L-15 medium supplemented with 5% FBS were used for virus propagation. Dengue virus type-2 (DENV-2) used in this study is a prototype of the New Guinea C strain, a kind gift from the Faculty of Biosciences and Medical Engineering, Universiti Teknologi Malaysia. Briefly, the virus was propagated in C6/36 cells, harvested and the virus titer was determined by focus forming assay using Vero cells¹⁰.

Cytotoxicity Test: Cytotoxicity of *C. roseus* extract against Vero cells was determined using the MTT assay¹¹. Briefly, a confluent monolayer of Vero cells in 96-well cell culture microplate were treated with increasing concentrations of *C. roseus* extract triplicates with starting concentration of 10 mg/mL. After 48 h of incubation, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) was added into each well and was further incubated for 3 h. After removing excess MTT, 100 μ L of dimethylsulfoxide (DMSO) was added. The absorbance values of the wells were measured at 570 nm using a 96-well plate reader. Dose-response curve was plotted using Graph Pad Prism 5 and the half maximal cytotoxic concentration (CC₅₀) of *C. roseus* extract was determined from the plot.

Foci forming unit reduction assay (FFURA): FFURA was done to screen for anti-DENV-2 activity of *C. roseus* extract with different concentrations. Infected Vero cells which were treated with *C. roseus* extract was incubated for 4 days post infection in growth medium supplemented with 2% FBS and 1.5% carboxymethyl cellulose. The number of DENV-2 foci was counted using a stereomicroscope and the virus titer was expressed as Foci Forming-Unit (FFU). Antiviral activities of the compounds were determined by calculating the percentage of foci reduction (%RF) compared against the controls using the following formula:

$$\text{RF}(\%) = (C-T) \times 100/C$$

where, C is the mean of the number of foci from triplicates treatment without extract added and T is the mean of the number of foci from triplicates of each treatment measures with the extract¹².

Antiviral Activity: Antiviral assays composed of post-treatment, pre-treatment and virucidal assays.

Pre-treatment: In order to determine the prophylactic effects of *C. roseus* extract against DENV-2 replication, different concentrations of *C. roseus* were added to the confluent Vero cells (2.0×10^5 cell/well) in 12-wells microplate after 5 h of virus infection. The treatment medium was removed and the treated cells were washed twice with PBS. The cells were then infected with 200 FFU of DENV-2 and incubated at 37°C for 4 days, 5% CO₂. After 4 days of infection, antiviral activity was determined by the reduction in foci number as previously described.

Post-treatment assay: Vero cells (2.0×10^5 cell/well) grown into 12 well plate were infected with 200 FFU of DENV-2. Cells were incubated for 1.5 h to allow virus adsorption. After adsorption period, cells were washed twice with PBS to remove any residual unbound viruses. This was followed by the addition of different concentrations of *C. roseus* extract. The cells were then infected with 200 FFU of DENV-2 and incubated at 37°C for 4 days in the presence of 5% CO₂. After 4 days of infection, antiviral activity was determined by the reduction in foci number as previously described.

Virucidal assay: A viral suspension containing 200 FFU of DENV-2 incubated with equal volume of the different concentrations of *C. roseus* extract for 1.5 h at 37°C. After incubation, all tubes were diluted and titrated. Then, Vero cells were infected with the diluted treated viral suspension. Cells were washed twice with PBS after 1.5 h adsorption at 37°C and cells were overlaid by 1.5% CMC containing DMEM supplemented with 2% FBS. After 4 days of incubation, direct virucidal activity of *C. roseus* extract was determined by foci reduction as previously described.

Statistical Analysis: Values were expressed as means \pm standard errors of the mean. Significance difference, determined as $p < 0.05$, was calculated using Student's t-test (Microsoft Excel).

Results and Discussion

To determine the nontoxic dose, Vero cells were exposed to twofold serially diluted *C. roseus*

methanolextract at concentrations ranging from 1 to 0.03 mg/mL. In this assay, the CC_{50} value of *C. roseus* extract was determined at 0.13 mg/mL. Figure 1 shows the percentage of cell viability versus concentration of *C. roseus* extract. Thus, maximum concentration that was used in the subsequent antiviral studies was fixed at 0.078 mg/mL.

Figure 2 shows the result obtained from antiviral assays using *C. roseus* extract. In post-treatment assay, more than 60% foci reduction was observed in *C. roseus* extract at the highest concentration (0.078 mg/mL). The lowest concentration (0.005 mg/mL) of *C. roseus* extract still exhibited mild reduction which was more than 30%. The antiviral activity of *C. roseus* extract was observed to be concentration dependent as the percentage of foci reduction is reduced with reducing *C. roseus* extract concentration. For pre-treatment assay, *C. roseus* extract showed weak activity which was less than 2% foci reduction at highest concentration (0.078 mg/mL). In virucidal assays, exposure of DENV-2 to the *C. roseus* extract at highest concentration (0.078 mg/mL) reduced more than 30% of foci reduction. This result confirms the mild virucidal activity observed in *C. roseus* extract.

The EC_{50} value of the SPD tested against the DENV-2 was 0.025 EC_{50} (mg/mL), as shown in figure 3. The effectiveness of the *C. roseus* as an anti-DENV-2 expressed as selectivity index (SI). *Catharanthus roseus* possessed a moderate anti-DENV-2 activity with SI value of 5.2. Any antimicrobial agent that has SI values higher than 10 ($SI > 10$) ensures the potential to be developed as an agent of antiviral drug. Meanwhile, SI value less than 1 are considered to be weak antiviral agent. SI value above 1 have moderate activity as antiviral agent¹³.

Catharanthus roseus is an important medicinal plant distributed all over the world. The interest in this plant are due to the reports that more than 130 alkaloids and several of them exhibit potent pharmacological properties can be found in *C. roseus*¹⁴. Based on phytochemical analyses, *C. roseus* has been proven to be rich in secondary metabolites such as alkaloids, flavonoids, phenols, tannins, saponin, terpenoids, quinines and cardiac glycosides^{15,16}. *Catharanthus roseus* have been reported by many researchers to be rich in alkaloid^{17,18,19}. Alkaloid from *C. roseus* inhibited simplex herpes virus (type I) and showed an antiparasitic effect against *Trypanosoma*²⁰. Flavonoids groups have been reported by several researchers to exhibit a wide range of biological activities such as antimicrobial,

antioxidant, anti-analgesic, anti-inflammatory, anti-cancer and anti-allergic²¹. There have been reports on flavonoids from plant inhibited dengue virus type -2 (DENV-2) in Vero cell via Foci Forming Unit Reduction Assay (FFURA)²². Flavonoids from *C. roseus* were found to cause maximum antimicrobial activity towards Gram positive and Gram negative bacteria²³. Thus, the richness of alkaloid and flavonoid in *C. roseus* may contribute to anti-DENV-2 properties.

Conclusion

This study demonstrates the variable effects of *C. roseus* extract on DENV-2 replication in Vero cells. Extract had mild antiviral activities and low prophylactic function. In order to elucidate the mechanisms of inhibition, further studies are required to determine the underlying mechanisms that contribute to its antiviral activity.

Ethical Clearance: Nil

Source of Funding: University

Conflict of Interest: Nil

References

1. Padua de LS, Bunyapraphatsara N, emmens RHMJ. Plant resources of Southeast Asia. Prosea Found. Bogor Indonesia, 1999, 12: 411-412.
2. Ueda JY, Tezuka Y, Banskota AH, Le Tran Q, Tran QK, Harimaya Y, Saiki I, Kadota S. Antiproliferative activity of Vietnamese medicinal plants. Biological and Pharmaceutical Bulletin, 2002, 25: 753-760.
3. Goyal P, Khanna A, Chauhan A, Chauhan G, Kaushik. 2008. In vitro evaluation of crude extracts of *Catharanthus roseus* for potential antibacterial activity. International Journal of Green Pharmacy, 2008, 176-181.
4. Kumari K, Gupta S. Antifungal properties of leaf extract of *Catharanthus roseus* L (g.) Don. American Journal of Phytomedicine and Clinical Therapeutics, 2013, 1(9): 698-705.
5. Mukhopadhyay S, Kuhn RJ, Rossmann MG. A structural perspective of the flavivirus life cycle. Nature Reviews Microbiology, 2005, 3(1): 13-22.
6. Rossmann M, Kuhn R, Zhang W, Pletnev S, Corver J, Lenches E, Jones C, Mukhopadhyay S, Chipman P, Strauss E, Baker T, Strauss J. Structure of dengue

- virus: implications for flavivirus organization, maturation, and fusion. *Acta Crystallographica Section A Foundations of Crystallography*, 2002, 58(s1): c6-c6.
7. Kalayanarooj S. Clinical Manifestations and Management of Dengue/DHF/DSS. *Tropical Medicine and Health*, 39(4SUPPLEMENT), 2011, S83-S87.
 8. Rodriguez-Roche R, Gould EA. Understanding the Dengue Viruses and Progress towards Their Control. *BioMed Research International*, 2013, 1-20.
 9. Reich NG, Shrestha S, King AA, Rohani P, Lessler J, Kalayanarooj S, Yoon I, Gibbons RV, Burke DS, Cummings DAT. Interactions between serotypes of dengue highlight epidemiological impact of cross-immunity. *Journal of The Royal Society Interface*, 10(86), 20130414–20130414.
 10. Abd Wahab NZ, Ibrahim N, Kamarudin MKA, Lananan F, Juahir H, Ghazali A, Ireana Yusra AF. Cytotoxicity and antiviral activity of *Annona muricata* aqueous leaves extract against dengue virus type 2. *Journal of Fundamental and Applied Sciences*, 2018. 10(1S): 580-589.
 11. Mosmann T. Rapid colorimetric assay for cellular growth and survival: Application to proliferation and cytotoxicity assays. *Journal of Immunological Method*, 1983, 65: 55-63.
 12. Laille M, Gerald F, Debitus C. In vitro antiviral activity on dengue virus of marine natural products. *Cellular and Molecular Life Sciences*, 1998, 54, 167–70.
 13. Chattopadhyay D, Chawla- Sarkar M, Chatterjee T, Dey RS, Bag P, Chakraborti S, Khan MTH. Recent advancements for the evaluation of Antiviral activities of natural products. *New Biotechnology*, 2009, 25(5): 347-365.
 14. Hisiger S, Jolicoeur M. Analysis of *Catharanthus roseus* alkaloids by HPLC. *Phytochemistry Reviews*, 2007, 6(2-3), 207–234.
 15. Mir MA, Kumar A, Goel A. Phytochemical Analysis and Antioxidant Properties of the Various Extracts of *Catharanthus roseus*. *Journal of Chemical and Pharmaceutical Research*, 2018, 10(10): 22-31.
 16. Kabesh K, Senthilkumar P, Ragunathan R, Raj Kumar R. Phytochemical Analysis of *Catharanthus roseus* Plant Extract and its Antimicrobial Activity. *International Journal of Pure & Applied Bioscience*, 2015, 3 (2): 162-172.
 17. Othman L, Sleiman A, Abdel-Massih RM. Antimicrobial Activity of Polyphenols and Alkaloids in Middle Eastern Plants. *Frontiers in Microbiology*, 2019, 10:911.
 18. Patil PJ, Ghosh JS. Antimicrobial Activity of *Catharanthus roseus* - A Detailed Study. *British Journal of Pharmacology and Toxicology*, 2010, 1(1): 40-44, 2010.
 19. Sathiya S, Karthikeyan B, Jaleel AB, Azooz MM, Iqbal M. Antibioqram of *Catharanthus roseus* Extracts. *Global Journal of Molecular Sciences*, 2008, 3 (1): 01-07.
 20. Ozcelik B, Kartal M, Orhan I. Cytotoxicity, antiviral and antimicrobial activities of alkaloids, flavonoids, and phenolics acids. *Pharmaceutical Biology*, 2011, 49:396-402.
 21. Igbinsosa OO, Igbinsosa QC, Aiyegoro OA. Antimicrobial activity and phytochemical screening of stem bark extracts from *Jatropha curcas* (Linn). *African Journal of Pharmacy and Pharmacology*, 2009, 3: 58-62.
 22. Zandi K, Teoh BT, Sam SS, Wong, PF, Mustafa M, AbuBakar S. Antiviral activity of four types of bioflavonoid against dengue virus type-2. *Virology Journal*, 2011, 8(1), 560.
 23. Rani J, Kapoor M, Kaur R. In-vitro anti-bacterial activity and phytochemical screening of crude extracts of *Catharanthus roseus* L. (G.) Don. *Agricultural Science Digest*, 2017, 37(2): 106-111.

Psychometric Evaluation of a Feedback Conception Scale: Building Positive Feedback Practises of Charge Nurses in Public Hospitals

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Abstract

Charge nurses who have a good level of understanding on feedback conceptions will be able to practise feedback effectively towards their staffs. The purpose of this pilot study was to provide the evidence of psychometric evaluation of 'Teachers' Conceptions of Feedback (TCof) scale of charge nurses using the Rasch Measurement Model. There are 9 constructs with 37 items altogether. One hundred and sixty-three (N=163) charge nurses from three states had completed the questionnaire. The content validity was checked by three experts in the field of measurement and medical health. The findings revealed that most items fit the model as their MNSQ values are between 0.60 and 1.40 except for four items. PMC value for all items are more than 0.20 except for three items. Two items showed a negative value of PMC. Most items are in a same direction so the item discrimination is good. Item reliability and item separation is 0.87 and 7.29 respectively, while person reliability and person separation is 0.81 and 2.81 respectively. The reliability value for item and person is high and acceptable. The separation index for item and person are also acceptable. In total, five items were deleted. The statistical analysis provides strong evidence to support the validity and reliability of the scale. The findings show that sample selection is appropriate. Hence, this instrument could be adapted or adopted by other researchers in the Malaysian health care system context.

Keywords: charge nurse, feedback conceptions, validity, Rasch Measurement Model.

Introduction

Feedback is one of the most influences on someone's achievement. Feedback, by definition is any information given to someone by teachers, peers, parents, books, self or experience in providing knowledge, skills and attitude¹⁰. What type of information are we talking about? It could be an alternative strategy, a clarification of ideas or the correctness of a response. Feedback can be accepted, modified or rejected¹¹. And, feedback which is gained from learners could make teaching become more effective as it can be used to adjust teaching approaches¹⁹. On the other hand, feedback is incapable

in reinforcing someone or initiating further action of someone. Feedback might threaten someone if the information given is not familiar or obtrusive to them. Before we go into detail, let us look at the 'conception' of feedback. One's conceptions are the beliefs, attitudes and intentions that someone has⁴. So, in this study, conception of feedback refers to the charge nurses' beliefs, attitudes and intentions towards feedback. These feedback conceptions could influence their feedback practises towards their nursing staffs while they are on duty as¹ stated that one's conceptions contribute a lot to one's behaviour. In general, the aim of feedback is to improve achievement. Feedback is also conducted to develop confidence of learners to do peer-assessment or self-assessment, to ensure that learners are actively engaged in their own learning and to promote learning⁶. It should not be something personal or confidential but it has to be based on real evidence. To gain this, a feedback has to be constructive. ²has listed few characteristics of a constructive feedback which are the goal and standard

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of the feedback has to be clear, exact and not vague, the information given to learners must be in a descriptive form. Next, a good feedback must be action-oriented and also solution-oriented. In addition, it has to be strictly confidential as to maintain trust between the assessor and the one being assessed. The least effective way is to give grade to the staff under them²¹. By giving only grades, the students are not able to determine what they are supposed to do to improve towards their goals. The best ways to give feedback is to provide an information on the correct answers plus some explanation and specific activities for improvement.

Problem Statement: Every day, charge nurses will face various kinds of challenges when dealing with staff nurses such as specific assignments requested by staff nurses or the challenges in increasing staff satisfaction¹⁷. And, one of the five main principles listed by The American Nurses Association is to assess staff skills. When assessing staff skills, not only the clinical skills that the charge nurses have to consider, but it is more than that. The whole scope of practices have to be considered such as the staff nurses characteristics, competencies, years of experience, culture and emotional intelligence and so on. When assessing, feedback will come into play as feedback could serve as a medium to enhance thinking skills⁸ of staff nurses. An effective feedback might give opportunities for staff nurses to change their skills which they have previously misinterpreted or to change their motivational beliefs and self esteem²³. In addition, interviews have been conducted with few of charge nurses in public hospitals and they agree that they do not really understand the concept of feedback elements like peer and self-feedback, timeliness of feedback and things that they are supposed to focus at when giving feedback to staffs. Lack of understanding in feedback conceptions might be the reason why they are sometimes confused when it comes to assessing their staffs formatively. Hence, the researchers decided to gain data using this exclusive set of questionnaire from New Zealand researchers which has been tested in few countries⁵. Since this instrument was to be used in the Malaysian health care context, this instrument has to go under pilot study to check for validity and reliability of the instrument as only valid and reliable instrument can be used for real study.

Method

This study is using a quantitative approach which involves 163 charge nurses randomly selected from three

states. The instrument used is 'Teacher Conceptions of Feedback (TCoF) inventory adapted from⁹. It consists of 9 constructs altogether with 37 items. They are Conception-Irrelevance (Students Ignore)—4 items, Conception-Improvement (Student Use)—4 items, Conception-Accountability (Expected)—3 items, Conception-Encouragement + Self Type (Praise)—6 items, Task Type—3 items, Process Type—4 items, Self-Regulation Type—5 items, Peer & Self Assessment—3 items and Timeliness—5 items). An example of item from the second construct is 'Staff uses feedback given to improve his/her work', item from the fourth construct is 'Peers are the best source in giving feedback'. The scales were measured using a 6-point Likert scale ranging from strongly disagree to strongly agree. Using Rasch, the data was analysed to determine the validity and reliability of the TCoF. Initially, the data was not fit at all. When using data from 163 person, the value for raw variance explained by measures is -440.0% and the value for unexplained variance in 1st contrast is 69.4% which does not agree with what suggested by¹³. 58 data were deleted and it left with 105 data only and the data was analysed again. The report of the findings was discussed below.

Findings: The analysis was conducted to test item fit, item polarity, unidimensionality and local independence, items and respondents' reliability and separation index.

Item Fit: The item fit statistics (infit and outfit MNSQ) is the degree of equality between the response pattern and the expected model for each item for all respondents³. The misfit item due to the high value of MNSQ or Z-value could affect the unidimensionality of subscales (Linacre, 2007). According to Smith et al. (2006), MNSQ is more stable than Z-std value. According to¹⁴, item with high value of MNSQ is a threat to validity compared to low value of MNSQ. For this study, the acceptable range of values for the infit and outfit MNSQ measures are in the range of 0.6 to 1.4¹⁴. The range for Z-std is $-2 < Zstd < +2$. All items which stay within this range is a productive items. If the items are not within this range, it is suggested to eliminate the items. The Rasch model prepare a fit statistics which could help researchers to come out with important decisions about the data¹⁸. Table 1 shows most MNSQ infit and outfit values are less than 1.0 which means that there is a lack of variation from the model. All of the items laid between 0.6 to 1.4 except for four items (item A2, A4, E18 and I37). Most items have a good overall

fit and they are retained. Four items are deleted. Looking at the Z-std value, the same thing is concluded. All the four items deleted are not in the range of -2 to +2 so it is better to delete those items.

Table 1: Item measure (INFIT, OUTFIT) MNSQ and Point Measure Correlation

Entry Number	Measure	Standard Error	INFIT MNSQ ZSTD		OUTFIT MNSQ ZSTD		PTMEA CORR	Item
1	1.05	.13	1.28	2.1	1.29	2.2	.27	A1
2	1.66	.12	1.82	5.1	1.88	5.1	.09	A2
3	2.53	.17	1.37	2.2	1.34	2.1	-.08	A3
4	2.18	.17	1.77	4.2	1.70	3.6	-.03	A4
18	-0.04	.13	1.66	3.6	1.58	3.7	.41	E18
35	1.35	.13	1.40	3.4	1.40	3.5	.31	I35
37	0.16	.13	1.88	5.2	1.88	5.7	.29	I37

Item Polarity: Item polarity is an indicator showing that the items moving in one direction as intended by constructed constructs. Point Measure Correlation (PMC) is a statistical item showing the correlation results between one points and scores for all candidates. Item polarity analysis using PMC is an early detection method for construct validity. The positive value shows that the item is in the same direction with the construct. However, if the value is negative, it shows that something has to be done by the researcher as it indicates that the item or the respondent contradict with the variables¹². However, the acceptable value is 0.2 or more. In this study, the PMC value of all items are more than 0.2 except for the three items which are item A2 (PMC=0.09) A3 (PMC=-0.08) and item A4(PMC=-0.03). All the three items are deleted. So, most items have a good discrimination value.

Unidimensionality and Local Independence: This two measures are important as they are interconnected with each other¹⁰. Unidimensionality refers to a condition where items are measuring in one dimension²¹.

Furthermore, unidimensionality and local independence allow us to detect whether an item is showing a different dimension or not, the item is understood or not and whether the response shows the respondents’ special skills. Principal Component Analysis is used to detect unidimensionality and local independence. A good unidimensionality is when the raw variance explained by measures is more than 40%² or more than 60%¹⁶. The unexplained variance in the 1st contrast must be less than 15%² or less than 5%¹⁶.² states that for raw variance explained by measures, values higher than 40% is a strong dimension, higher than 30% is a moderately strong dimension and if it is more than 20%, it is a moderate dimension. The raw variance explained by measures show a value of 52.0% (higher than 40.0%) and the unexplained variance in 1st contrast is 5.2% (less than 15%) (Table 2). So, it is clear that items are not confusing with a strong dimension measures. When unidimensionality assumptions are fulfilled, then the local independence characteristics would be fulfilled automatically¹⁶.

Table 2. Standard residual variance (in Eigenvalue units)

		Empirical		Modeled
Total raw variance in observations	70.6	100.0%		100.0%
Raw variance explained by measures	32.1	52.0%		51.4%
Raw variance explained by persons	6.1	10.3%		10.0%
Raw variance explained by items	26.0	36.8%		36.7%
Raw unexplained variance (total)	38.0	52.0%	100.0%	52.2%
Unexplained variance in 1 st contrast	3.5	5.2%	11.1%	
Unexplained variance in 2 nd contrast	3.2	5.2%	9.4%	

Reliability and Separation: Reliability of an instrument is precision. Item reliability indicates whether items are interacting well with one another showing the same attributes²¹. On the other hand, person reliability shows reproducibility as expected if the samples are measuring the same construct in a set of items²². This is the same as the Cronbach Alpha value. Next is the item and person separation index. Item separation index shows the separation of item difficulty level whereas person separation index shows the separation or the difference of individual following different capability. For both measures, as long as it is more than 2.0, the measures are good. The summary of statistics of person and item are shown in Table 3. For summary of 37 measured item, item reliability is 0.87. For summary

of 102 measured person, person reliability is 0.81. This shows that the reliability values are high and acceptable¹⁵.¹⁴also stresses that for an instrument to be reliable, the reliability value has to be more than 0.80. Furthermore, it shows that person factor is stable and consistent when measured. The instrument separation should at least be more than 1.0 and a value less than that shows that there might be an overlapping items or less person variability in the trait. In this study, item separation index was 7.29 which indicated the existance of 7 to 8 item strata while person separation index was 2.81 which indicated the existance of 3 people strata. However, as stated by¹³, for both measures, as long as it is more than 2.0, then the measures are good.

Table 3. Summary of person and item measure

Summary of Person Measurement					
		INFIT		OUTFIT	
	Measurement	MSQ	ZSTD	MSQ	ZSTD
Mean	0.33	1.00	-0.1	1.00	-0.1
SD	0.67	0.37	1.9	0.39	1.2
Separation	2.81				
Person Reliability	0.81				
Summary of Item Measurement					
Mean	0.00	0.99	-0.2	1.00	-0.1
SD	1.05	0.36	2.5	0.29	2.7
Separation	7.29				
Item Reliability	0.87				

Discussion and Conclusion

This study aims to validate an instrument in assessing feedback conceptions amongst charge nurses in public hospitals in Malaysia using Rasch Model. The findings suggested that most items fit the model as their MNSQ values are between 0.6 to 1.4 except for four items, items A2, A4, E18 and I37 which have MNSQ infit and outfit more than 1.5. Three items do not agree with the item polarity accepted range. Two items show a negative value and the other one item has a value of less than 0.2. So, all the three items are deleted. Unidimensionality is not really an issue as it shows a good unidimensionality when the raw variance explained by measures is 52.0% which is more than 40.0%. This indicates that all the nine constructs are quite different from one another. This instrument with 37 items which represents 9 constructs shows good and

acceptable indices of item and person reliability. This shows that items are consistent. After going through data analysis, finally five items were deleted. The overall item quality was good. The instrument is capable in assessing charge nurses’ conceptions of feedback in the Malaysian health care system context. However, a more detailed analysis is needed, if possible. Maybe an Item Response Theory could be used for further investigation. In conclusion, for any instrument to be used in real study, it has to go through pilot testing to check for its validity and reliability. The development of this instrument in a different context cannot be assumed that it could fit with any other samples.

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References

1. Ajzen, I., & Fishbein, M. The influence of attitudes on behavior. In D. Albarracín, B.T. Johnson, & M.P. Zanna (Eds), *The Handbook of Attitudes*, pp. 173-222, Mahwah, New Jersey: Lawrence Erlbaum Associates, 2005.
2. Black, P. Formative Assessment: Promises or problems? Available at: <http://www.mantleoftheexpert.com/studying/articles/Paul%20Black2007.pdf/>, 2007.
3. Bond, T. G., & Fox, C. M. *Applying the Rasch Model: Fundamental Measurement in the Human Sciences* (3rd ed.). Mahwah, NJ: L. Erlbaum, 2015.
4. Brown, G. T. L. *Conceptions of assessment: Understanding what assessment means to teachers and students*. New York: Nova Science Publishers, 2008.
5. Brown, G. T. L., Harris, L. R., & Harnett, J. Teacher beliefs about feedback within an Assessment for Learning environment: Endorsement of improved learning over student well-being. *Teaching and Teacher Education*, doi: 10.1016/j.tate.2012.05.003, 2012.
6. Cheryl A. J. *Assessment for learning* Available at: <https://dera.ioe.ac.uk/7800/1/AssessmentforLearning.pdf>, 2005.
7. Forkmann, T., Boecker, M., Norra, C., Eberle, N., Kircher, T., Schauerte, P., Mischke, K., Westhofen, M., Gauggel, S. & Wirtz, M., Development of an item bank for the assessment of depression in persons with mental illnesses and physical diseases using Rasch Analysis, *Journal of Rehabilitation Psychology*. 2009, 54, pp. 186–197.
8. Hargreaves, E. *Assessment for learning? Thinking outside the (black) box*, *Cambridge Journal of Education*, 2005, 35(2), pp. 1-23.
9. Harris, L. R., & Brown, G. T. *Teachers' Conceptions of Feedback inventory*. Unpublished test. Auckland, NZ: University of Auckland, Measuring Teachers' Assessment Practices (MTAP) Project, 2008.
10. Hattie, J. & Timperly, H. *The Power of Feedback*, *Review of Educational Research*, 2007, 77(1), pp. 81-112.
11. Kulhavy, R.W. *Feedback in written instruction*. *Review of Educational Research*, 1977, 47 (1), pp. 211-32.
12. Linacre, J. M. *Optimizing rating scale effectiveness*. In., E. V., Smith, Jr, & R. M. Smith. (Eds.). *Introduction to Rasch model*. Maple Grove, Minnesota: JAM press, pp. 258-278, 2004.
13. Linacre, J. M. *Test validity, and Rasch measurement: Construct, content Rasch measurement transactions*, 2005.
14. Linacre, J. M. *A user's guide to WINDTEPS Rasch-model computer programs*. Chicago, Illinois: MESA Press, 2007.
15. Pallant J. *SPSS Survival Manual: A Step By Step Guide to data analysis using SPSS*. Allen & Unwin, Sabon by Bookhouse, Sydney, 2007.
16. Reckase M. D. *Multidimensional item response theory*. New York, NY: Springer, 2009.
17. Siebert, S. & Chiusano, J. *Understanding the charge nurses' role in staffing* <https://www.americannursetoday.com/wp-content/uploads/2015/09/Special-Report-Workforce-Understanding.pdf>, 2015.
18. Smith E. *Detecting and evaluating the impact of multidimensionality using item fit statistics and principal component analysis of residuals*. *Journal of Applied Measurement*, 2002, 3(2), pp. 205-231.
19. Wiggins, G. *Educative assessment : Designing assessments to inform and improve student performance*. San Francisco, CA: Jossey-Bass, 1998.
20. Wiliam, D. *What is assessment for learning?* *Studies in educational evaluation*, 2011, 37, pp. 3-14.
21. Wright, B. D. & Stone, M. H. *Best Test Design: Rasch Measurement*. Chicago, IL: Mesa Press, 1979.
22. Wright, B. D., and Masters, G. N. *Rating scale analysis*. Chicago: MESA Press, 1982.
23. Young, S. and Giebelhaus, C. *Formative Assessment and Its Uses for Improving Student Achievement*. *Education Data Management Solutions, STI*. Available at: www.cbohm.com/news/STI/STI_White_Paper.pdf, 2005.

Cytotoxic Activity and Selectivity Index of *Solanum Torvum* Fruit on T47D Breast Cancer Cells

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Abstract

Solanum torvum has antioksidan. This study aimed to analyse cytotoxic activity and selectivity index of *Solanum torvum* on T47D breast cancer cells invitro. Identification of *Solanum torvum* fruit chemical compounds with LCMS containing Clorogenic acid, 4-O-caffeoylquinic acid, 3-O-caffeoylquinic acid, 3-O-feruloylquinic acid, 5-O-feruloylquinic acid, 3-O-feruloylquinic acid, 3,4 - O dicaffeoylquinic acid, 3,5-dicaffeoylquinic acid, 3-O-feruloylquinic acid, 5-O-feruloylquinic acid, putative dicaffeoylquinic lactone. Cytotoxic assays showed that the *Solanum torvum* Without Fermentation were IC₅₀ (IGT) 1111.62 µg/mL, IC₅₀ (MGT) 1889.20 µg/mL, IC₅₀ (EGT) 1171.90 µg/mL, IC₅₀ (FEGT) 305.98 µg/mL. Cytotoxic assays showed that the treatment of fermentation was IC₅₀ (IBT) 1760.36 µg/mL, IC₅₀ (MBT) 1631.06 µg/mL, IC₅₀ (EBT) of 1111.58 µg/mL, IC₅₀ (FEBT) 39.17 µg/mL, IC₅₀ (FHBT) 85.58 µg/mL. Index of selectivity (IS) *Solanum torvum* (without fermentation) were IS (IGT) 5.23, IS (MGT) 0.61, IS (EGT) 1.06, IS (FEGT) 1.45. Index of selectivity of *Solanum torvum* (fermentation treatment) were IS (IBT) 2.41, IS (MBT) 0.78, IS (EBT) 0.18, IS (FEBT) 4.64, IS (FHBT) 1.67. The best results are treatment of ethyl acetate fraction of *Solanum torvum* (FEBT) has IC₅₀ was 39.17 µg/mL and Index selectivity was 4.64, declared safe/not toxic to normal cells, thus potentially developed as T47D breast anticancer cells.

Keywords: Cytotoxic, T47D Breast Cells, Selectivity Index, *Solanum torvum*.

Introduction

Solanum torvum in Indonesia in fertile soils has antioksidan. *Solanum torvum* contains steroids, terpenoids, saponins, tannins, alkaloids, fatty acids, 3-o-acetyl-stigmasta-5, 25-diene-2, 3-diol, methyl stearate, 21, 25-dimethylmelianodiol⁽¹⁾. *Solanum torvum* extraction on seeds and fruit peel has compounds of flavonoids, sterols and saponins⁽²⁾. *Solanum torvum* has alkaloids, flavonoids, saponins, tannins, glycosides⁽³⁾. *Solanum torvum* has constituent chemicals such as neochlorogenin 6-O-β-D-quinovo-pyranoside, neochlorogenin 6-O-β-D-xylopyranosyl- (1 → 3) -β-D-quinovopyranoside, 6-O-α-L -rhamnopyranosyl- (1 → 3) -β-D-quinovopyranoside, solagenin 6-O-β-D-quinovopyranoside, solagenin 6-O-α-L-rhamnopyranosyl (1 → 3) -β-D-quinovopyranoside, .isoque-rctin, routine, kaempferol and quercetin⁽⁴⁾. The wild eggplant fruit (*Solanum torvum*) in Indonesia was relatively used by the population because it has not been cultivated. *Solanum torvum* containing sesquiterpen

functions immunosuppressive⁽⁵⁾. Clorogenic acid serves to prevent and treat anti-inflammatory diseases⁽⁶⁾. Chlorogenic acid is a polyphenol compound proven to stimulate anti-inflammatory, antibacterial and antioxidant activities as agents for clinical treatment of hepatic I/R injuries⁽⁷⁾. Carcinogenesis is the process of the occurrence of multi-stage cancer that undergoes genetic changes and progressive transformation of normal cells into malignant cells⁽⁸⁾. The biggest cancer causes of death in the world are breast, cervix, colon, lung and stomach cancer⁽⁹⁾. The most common causes of death for women are cervical cancer and breast cancer. T47D breast cancer cells used in this study have unlimited replication ability, high homogeneity and was easily replaced with frozen stock in the event of contamination⁽¹⁰⁾. This was supported by research that states that the methyl caffeoyl compound in *Solanum torvum* fruit functions as an anti-cancer⁽¹¹⁾. The study aimed to analyze antioxidant compounds found in *Solanum torvum* fruit extracted with various solvents

to function as cytotoxic and selectivity index for T47D breast cancer cells.

Materials and Method

Solanum torvum: *Solanum torvum* was obtained from Sumber Manjing village Malang. Fruit wild eggplant was sorted, washed, drained. In the next stage processing into dry powder using 2 types of treatment. Treatment 1 was the fruit that has been cleaned in a small chunk and then vacuum dryer temperature 50⁰ C for 14 hours. The two treatments were fermented, namely 5 days curing, 6.18 hours fermentation time, 50⁰ C drying temperature and 14 hours drying time, thus there stored on main raw material.

Chemical materials: Materials include, water, aquabides, methanol pa, ethanol pa, n hexane pa, ethyl acetate (p.a.), DMSO, alcohol, T47D cells and vero cells, RPMI, M199 media, FBS, PS, trypsin-EDTA, SDS in 0.01 N HCL, MTT, and PBS, Rnase, ethanol, 2 N hydrochloric acid, lead (II) acetate 0.4 M, isopropanol, chloroform, Molish, 2 N hydrochloric acid, iron (III) chloride reagent, Liebermann-Burchard, n-hexan, DPPH 0.1 mM, methanol, Folin-Ciocalteai, Gallic Acid, AICl₃, Quercetin, Sodium Nitrite, Diethyl ether, Na₂CO₃. Chemicals obtained from the parasitology laboratory of the UGM medical faculty jogjakarta.

Analyzing Solanum Torvum using LCMS: UHPLC The brand of ACCELLA type 1250 made by Thermo Scientific which consists of vacuum degassers. Solvents A = 0.1% wet format in water and B = formic acid in Acetonitrile. A mobile phase gradient with a speed of 300 µl/minute with the following settings: 0.0-0.6.00 minutes 5% B, 0.6 - 3.0. is 2 µL at 160⁰C. The column is controlled at 30⁰C, and the autosampler compartment is set to 16⁰C. Use LCMS/MS Triple minutes 75% B, 3.0 - 3.5 minutes 75% B, 4.0- 5.5 minutes 5%. The injection volume in the TSQ Quantum Access Max spectromethemic acid LC from Thermo Finnigan with an ESI ionization source is controlled by TSQ Tune software which is operated in negative mode. The ionization conditions of ESI are as follows: 3.0 kV spray voltage; evaporation temperature of 250⁰C; capillary temperature of 300⁰C; nitrogen as sheath gas pressure 40 psi, and 10 psi pressure aux gas with argon gas (12)

Preparation of breast cancer cells T47D (13)

Ethanol extraction: Samples weighed 10 grams plus

80% ethanol as much as 100 ml then placed on elenmeyer diprasi for 24 hours while being shaken. The results of the extract were filtered put in an impermeable container, the sample was again macerated with 80% ethanol solvent which was repeated until 3 times. The results of the ethanol extract put together are concentrated with a rotary evaporator vacuum temperature of 40⁰C until concentrated, then stored in bottles that are impermeable to drying with nitrogen gas until the solvent evaporates, stored in a safe place.

Methanol extraction: 10 grams of the test sample were extracted with 100 ml of methanol concentration of 95% with 24-hour maceration. The extract was filtered with Whatman no 1 filter paper. Then evaporator until thick and with nitrogen gas until dry, stored in a safe place.

Water extraction: 10 grams of the test sample were each extracted with 100 ml of hot water in an infusion pan for 15 minutes. The extract was filtered with Whatman filter paper No. 1. The dirotarievapore extract until thick and the results stored in a bottle then dried with freeze drying, stored in a safe place.

Hexane fractionation: Ethanol extract of *Solanum torvum* fruit powder was inserted in a separating funnel, added hexane and water each 50 ml (1: 1) shaken so that 2 layers were formed. The hexane layer is collected, the water layer is extracted again with hexane up to 3 times. The results are applied with a vacuum rotary evaporator until thick and dried with nitrogen gas so that stored in a safe place.

Ethyl acetate fractionation: Ethanol extract of the test sample was put in a separating funnel added with ethyl acetate and 50 ml (1: 1) of water each shaken to form 2 layers. Ethyl acetate layer is accommodated, the water layer is extracted again with ethyl acetate up to 3 times. The results are applied with a vacuum evaporator until thick and dried with nitrogen gas, thus stored in a safe place.

Citotoxic analysis via MTT: Citotoxic analysis in T47D breast cells with 9 samples treatment *Solanum torvum* were 31,25 ppm, 62,5 ppm, 125 ppm, 250 ppm, 1000 ppm with ELISA reader (Benchmark Bio Rad), wavelength 595⁽¹³⁾.

Index selectivity analysis: The principle works the same as cytotoxic analysis but the complete media uses M199. The test sample concentrations were 1000ppm,

500ppm, 250ppm, 125 ppm, 6.25 ppm, 31.125 ppm. The results of Selectivity Index formula was (13).

$$\text{Selectivity index} = \text{IC}_{50} \text{ Cells Vero} / \text{IC}_{50} \text{ Cells T47D}$$

Result

Identification of chromatographic chemical compounds with LCMS: The results of the identification of chemical compounds in the Solanum torvum fruit (without fermentation treatment) can be seen in Figure 2 and Table 1.

Table 1: Chemical components of Solanum torvum

No	TR	(M- H)- (m/z)	MS ² (m/z)	Compounds
1	3,72	353	191,127	chlorogenic acid
2	4,46	353	173,179	4-O- caffeoylquinic
3	3,9	353	191,179	3-O- caffeoylquinic
4	5,00	367	193,191	3-O-feruloylquinic acid
5	5,54	367	191	5-O-feruloylquinic acid
6	5,03	367	193	3,4-O-dicaffeoylquinic acid
7	7,01	515	353	3,4-O-dicaffeoylquinic acid
8	7,19	515	353	3,5-O-dicaffeoylquinic acid
9	7,37	529	367	3-O-feruloylquinic acid
10	7,54	529	367	5-O-feruloylquinic acid
11	7,87	497	335	putative dicaffeoylquinic lactone

In Table 3, it shows the identification of chemical compounds using the LCMS (With Fermentation treatment)

Table 2. Chemical components of fruit Solanum torvum

No	TR	(M- H)- (m/z)	MS ² (m/z)	Compounds
1	3,69	353	191	Clorogenic acid
2	4,46	353	179	4-O- caffeoylquinic acid
3	3,9	353	179	3-O-caffeoylquinic acid
4	5,03	367	191	3-O-feruloylquinic acid
5	5,54	367	191	5-O-feruloyquinic acid
6	4,67	367	193	3-O-feruloylquinic acid
7	7,01	515	353	3,4,O- dicaffeoylquinic acid
8	7,34	515	353	3,5-O-dicaffeoylquinic acid
9	7,31	529	367	3- O- feruloylquinic acid
10	2,8	529	367	5-O- feruloylquinic acid
11	7,34	497	355	putative dicaffeoylquinic lactone

Cytotoxic Analysis Results of Solanum torvum: In the cytotoxic test samples on T47D breast cancer cells in Table 4.

Table 3. Cytotoxic Test Data on T47D breast cancer cells

Sample testing	IC 50 (µg/mL)
1. Infusion of Solanum torvum fruit powder (without fermentation) IGT	1111,62
2. Methanol extract of Solanum torvum fruit (without fermentation) MGT	1889,20
3. Ethanol extract of Solanum torvum fruit (without fermentation) EGT	1171,90
4. Ethyl acetate fraction of Solanum torvum fruit (without fermentation) FEGT	305,98
5. Solanum torvum fruit infusion (fermentation treatment)IBT	1760,36
6. Methanol Extract of Solanum torvum Fruit (Fermentation Treatment) MBT	1631,06
7. Ethanol Extract of Solanum torvum Fruit (Fermentation Treatment) EBT	1111,58
8. Ethyl Acetate Fraction of Solanum torvum Fruit (Fermentation Treatment) FEBT	39,17
9. Solanum torvum Fruit Hexane Fraction (Fermentation Treatment) FHBT	85,58
10. Doxorubicin (Cancer Drug)	36,76

Solanum torvum Selectivity Index Results

The results of a good and non-toxic objectivity test for normal cells were infusion of Solanum torvum without fermentation treatment with index selectivity of 5.23 and ethyl acetate fraction of Solanum torvum fermentation treatment having a selectivity index of 4.64, can be seen in Table 5.

Table 4. Index test data on the selectivity

Sample testing	Selectivity Index	Remarks
1. Infusion of Solanum torvum (without fermentation) IGT	5,23	Selective
2. Methanol extract of Solanum torvum (without fermentation) MGT	0,61	Non-Selective
3. Ethanol extract of Solanum torvum fruit (without fermentation) EGT	1,06	Non-Selective
4. Ethyl acetate fraction of Solanum torvum fruit (without fermentation) FEGT	1,45	Non-Selective
5. Infusion Solanum torvum fruit (fermentation treatment) IBT	2,41	Non-Selective
6. Methanol Extract of Solanum torvum Fruit (Fermentation Treatment) MBT	0,78	Non-Selective
7. Ethanol Extract of Solanum torvum Fruit (Fermentation Treatment) EGT	0,18	Non-Selective
8. Ethyl Acetate Fraction of Solanum torvum Fruit (Fermentation Treatment) FEBT	4,64	Selective
9. Solanum torvum Fruit Hexane Fraction (Fermentation Treatment) FHBT	1,67	Non-Selective

Discussion

Identification of *Solanum torvum* fruit chemical compounds with LCMS containing Chlorogenic acid, 4-O-caffeoylquinic acid, 3-O-caffeoylquinic acid, 3-O-feruloylquinic acid, 5-O-feruloylquinic acid, 3-O-feruloylquinic acid, 3,4 - O dicaffeoylquinic acid, 3,5-dicaffeoylquinic acid, 3-O-feruloylquinic acid, 5-O-feruloylquinic acid, putative dicaffeoylquinic lactone. This was supported by opinions⁽¹⁴⁾The results of phytochemical analysis of *Solanum torvum* fruit extraction with organic solvents contained alkaloids, indole alkaloids, saponins glycosides, flavonoids, phenols, sterols, proteins, carbohydrates, alkaloid lepac, vitamin A, Vitamin C, Vitamin E, polyphenols. The results of research that have a good selectivity index are samples IGT and FEBT (Table 5).The selectivity index value greater than 3 indicates that extract is selective and

not toxic, and vice versa if the selectivity index is less than 3, meaning that the extract used is not selective and has a toxicity to normal cells⁽¹⁵⁾. Antioxidants in small concentrations can prevent or slow down the rate of free radical oxidation or lipid oxidation. These antioxidant compounds can function as free radical scavengers, forming complexes with metal elements as antioxidants and functioning as reducing compounds⁽¹⁶⁾. Antioxidants were useful in preventing tumors and cancer, premature aging⁽¹⁷⁾. The best cytotoxic activity in this research was ethyl acetate fraction of *Solanum torvum* fruit (Fermentation Treatment) IC₅₀ value of 39,17 µg/mL. Doxorubicin as a positive control has an IC₅₀ value of 36.76 µg/mL⁽¹⁸⁾. A very effective anticancer agent for breast cancer metastasis was doxorubicin⁽¹⁹⁾. The criteria for compounds that have antiproliferative potential are IC₅₀ ≤ 100 µg/ml⁽²⁰⁾. The research Chromatographic

analysis of *Solanum torvum* containing Clorogenic acid and derivative. That clorogenic acid functions to prevent and treat anti-inflammatory diseases ⁽²¹⁾A new clorogenic oxide called oxovanadium complex has the potential for antioxidant agents and anti cancer (human breast cancer) ⁽²²⁾.

Conclusion

The results of Chromatographic analysis containing Clorogenic acid, and derivative. So the best research results as cytotoxic activity of *Solanum torvum* ethyl acetate fraction having IC₅₀ which was 39.17 µg/mL and index selectivity of 4.64 which means it was not toxic to normal cells, thus potentially developed as T47D breast anticancer

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Conflict of Interest Statement: Herevy we declare that the entire authors of this manuscript have no conflict of interest.

Ethical Clearance: This study was approved by the Department of Food Technology Brawijaya University. According to the research ethics, this research has no ethical violation and the process of collecting data was in accordance with experimental ethics.

References

1. Karmakar K, Islam MA, Chhanda SA, Tuhin TI, Muslim T, Rahman MA. Secondary Metabolites from the Fruits of *Solanum torvum* SW. Journal of Pharmacognosy and Phytochemistry. 2015 May 1;4(1).
2. Rammohan M, Reddy CS. Anti-inflammatory activity of seed and fruit wall extract of *Solanum torvum*. J Hygeia JD Med. 2010;2(2):54-8.
3. Chah KF, Muko KN, Oboegbulem SI. Antimicrobial activity of methanolic extract of *Solanum torvum* fruit. Fitoterapia. 2000 Apr 1;71(2):187-9.
4. Yuan-Lu Y., Guang LJ., and Yi K., *Chemical constituents from Solanum torvum*. 2011.. Chinese Journal of Natural Medicines-9 (1) : 0030- 0032.
5. Yuan PL, Wang XP, Jin BL, Yang YF, Chen KX, Jia Q, Li YM. Sesquiterpenes with immunosuppressive effect from the stems of *Solanum torvum*. Phytochemistry letters. 2016 Sep 1;17:126-30.
6. Hwang SJ, Kim YW, Park Y, Lee HJ, Kim KW. Anti-inflammatory effects of chlorogenic acid in lipopolysaccharide-stimulated RAW 264.7 cells. Inflammation Research. 2014 Jan 1;63(1):81-90.
7. Yun N, Kang JW, Lee SM. Protective effects of chlorogenic acid against ischemia/reperfusion injury in rat liver: molecular evidence of its antioxidant and anti-inflammatory properties. The Journal of nutritional biochemistry. 2012 Oct 1;23(10):1249-55.
8. Tsao AS, Kim ES, Hong WK. Chemoprevention of cancer. CA: A Cancer Journal for Clinicians. 2004 May;54(3):150-80.
9. Yaacob NS, Hamzah N, Kamal NN, Abidin SA, Lai CS, Navaratnam V, Norazmi MN. Anticancer activity of a sub-fraction of dichloromethane extract of *Strobilanthes crispus* on human breast and prostate cancer cells in vitro. BMC complementary and alternative medicine. 2010 Dec;10(1):42.
10. Burdall SE, Hanby AM, Lansdown MR, Speirs V. Breast cancer cell lines: friend or foe?. Breast cancer research. 2003 Apr;5(2):89.
11. Balachandran C, Emi N, Arun Y, Yamamoto Y, Ahilan B, Sangeetha B, Duraipandiyan V, Inaguma Y, Okamoto A, Ignacimuthu S, Al-Dhabi NA. In vitro anticancer activity of methyl caffeate isolated from *Solanum torvum* Swartz. fruit. Chemicobiological interactions. 2015 Dec 5;242:81-90.
12. Ortega N, Romero MP, Macià A, Reguant J, Angles N, Morelló JR, Motilva MJ. Comparative study of UPLC–MS/MS and HPLC–MS/MS to determine procyanidins and alkaloids in cocoa samples. Journal of Food Composition and Analysis. 2010 May 1;23(3):298-305.
13. Fitriasari A, Dewi D, Ikawati M, Meiyanto E. Prosedur Tetap Uji Sitotoksik Metode MTT. Cancer Cemoorevention Reaserch Center Fakultas Farmasi UGM, Yogyakarta. 2009.
14. Jaiswal BS. *Solanum torvum*: a review of its traditional uses, phytochemistry and pharmacology. International Journal of Pharma and Bio Sciences. 2012 Oct;3(4):104-11.
15. Weerapreeyakul N, Nonpunya A, Barusrux S, Thitimetharoch T, Sripanidkulchai B. Evaluation of the anticancer potential of six herbs against a hepatoma cell line. Chinese medicine. 2012 Dec;7(1):15.

16. Droge W. Free radicals in the physiological control of cell function. *Physiological reviews*. 2002 Jan 1;82(1):47-95.
17. Tamat SR, Wikanta T, Maulina LS. Aktivitas antioksidan dan toksisitas senyawa bioaktif dari ekstrak rumput laut hijau *Ulva reticulata* Forsskal. *METODE*. 2003 Jun.
18. Fista, E.Y. Uji Aktifitas Sitotoksik Senyawa 7-O-Propil 3, 4- Dimetoksik isoflavon Hasil Sintesis Pada Kultur Sel Kanker Payudara MCF -7, FK UGM, 2014, Yogyakarta.
19. Chuang, P.Y., Huang, C. and Huang, H.C., 2013. The use of a combination of tamoxifen and doxorubicin synergistically to induce cell cycle arrest in BT483 cells by down-regulating CDK1, CDK2 and cyclin D expression. *Journal of Pharmaceutical Technology and Drug Research*, 2(1), p.12.
20. Kamuhabwa A, Nshimo C, de Witte P. Cytotoxicity of some medicinal plant extracts used in Tanzanian traditional medicine. *Journal of ethnopharmacology*. 2000 May 1;70(2):143-9.
21. Hwang SJ, Kim YW, Park Y, Lee HJ, Kim KW. Anti-inflammatory effects of chlorogenic acid in lipopolysaccharide-stimulated RAW 264.7 cells. *Inflammation Research*. 2014 Jan 1;63(1):81-90.
22. Naso LG, Valcarcel M, Roura-Ferrer M, Kortazar D, Salado C, Lezama L, Rojo T, González-Baró AC, Williams PA, Ferrer EG. Promising antioxidant and anticancer (human breast cancer) oxidovanadium (IV) complex of chlorogenic acid. Synthesis, characterization and spectroscopic examination on the transport mechanism with bovine serum albumin. *Journal of inorganic biochemistry*. 2014 Jun 1;135:86-99.

The Relationship between Father Involvement with Growth and Social-Emotional Development in Preschool Children

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Abstract

Background: Growth and social-emotional development in preschool children must have cared for parents. Although evidence exists of the association between them, especially mothers' involvement, only a few studies have examined fathers' involvement in parenting.

Method: This research uses Cross sectional study design. It has 106 pairs of fathers and preschool age children selected using consecutive sampling technique. Those fathers complete the questionnaire on father's involvement in parenting and questionnaire on Age Stages Questionnaire Social Emotional (ASQ-SE) based on their child's age. Furthermore, the Z-score is calculated based on the child's Body Weight/Body Height index to assess their growth. The data are analyzed using chi-square test at significance level of $p < 0.05$.

Result: Father's involvement in parenting is relatively good at 51.9%. In terms of child growth based on the calculation of Z-score from Body Weight/Body Height index, 77.4% of the children are found to have normal growth. Most of the children have the risk of experiencing socio-emotional issues at 58.5%. In terms of the association between father's involvement in parenting and preschool children's growth, a value of $p > 0.05$ is obtained, and in terms of the association between father's involvement in parenting and socio-emotional development of preschool children, a value of $p < 0.05$ is obtained.

Conclusion: This research finds that father's involvement in parenting is not associated with preschool age children's growth, yet it has a significant association with preschool age children's socio-emotional development.

Keywords: *Father involvement, parenting, growth, social-emotional, Preschool.*

Introduction

The initial stage of a child's growth and development determines the conditions in the next stages. Preschool is the period when the father's involvement with their children is at peak than when children are still in their infancy or at elementary school.¹ In Indonesia, according to the result of nutritional status monitoring in 2018, it is reported that infants in Indonesia experience growth

issues, i.e. being highly thin and thin at 10.2% and obese at 8%.² In addition to growth, child development issues are as extremely important for child welfare as social development which plays a role in child's health.³

Father's involvement in positive aspects of their child's life will promote positive achievement as well in children at their preschool years.⁴ These positive achievements include positive social behavior, nutritional status improvement,⁵ and low obesity occurrence.⁶

Pleck identifies some components of father's involvement which consist of positive engagement activities, warmth and responsiveness, control along, indirect care, and process responsibility.⁷ In developing countries, the role of a father in their child's health has not received adequate attention. The role that a father

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plays in child's growth and development has not been a frequent topic for research. Some studies emphasize that mothers play an important role in their children's lives and fathers are treated fairly shallowly by merely emphasizing their economic status on child's health.^{8,9}

Therefore, a further study is needed to see the association between father's involvement in parenting and preschool age children's growth and social-emotional development.

Method

Research Design: This research was conducted in the area of Puskesmas Nglipar I, Gunung Kidul Regency on April-May 2019. It used cross sectional study design and its population was all pairs of father and preschool age child in the area of Puskesmas Nglipar I, Gunung Kidul Regency. This research had obtained a clearance from the ethical committee of Medicine, Public Health and Nursing Faculty at Gadjah Mada University under number KE/FK/0380/EC/2019.

Sampling: Pairs of father and preschool age child (3-6 years old) living within the area of Puskesmas Nglipar I and willing to sign the informed consent. The father should be literate (capable of reading and writing). The exclusion criteria in this research were children who had developmental disorders, such as mental retardation, autism, or cerebral palsy and fathers with physical disability and mental emotional disorder. To assess the mental emotional disorder, a screening was done using Self-Reporting Questionnaire-20 (SRQ-20)

Instrument:

1. Questionnaire of father's involvement in parenting of preschool children. This questionnaire was prepared by the researcher for the purpose of this research, consisting of 28 statements using Likert scale. From the result of validity test, the construct was declared valid, i.e. r statistic $>$ r table (0.361). From the reliability test result, the value of cronbach's alpha was found to be $0.732 > 0.60$. The father's involvement in parenting was divided into 2 categories, namely good (total score ≥ 72) and poor (total score < 72).
2. Age and Stage Questionnaire Social Emotional (ASQ:SE): The research used ASQ:SE, particularly questionnaire of 36, 48, and 60 years of age. This questionnaire had been tested for its validity and reliability in Indonesia in Indonesian language by

Ariyani (2017). From the validity test, the value of r statistic was (0.241-0.694), which was greater than r table. The reliability test value with cronbach's alpha was $0.743 > 0.60$.

3. The instruments used to measure the child's growth status were microtoice as the body height measuring instrument and digital scale as the body weight measuring instrument. The value of Z-score of body weight per body height based on age was calculated using WHO Anthro software.

Procedure: Those fathers who qualified the inclusion and exclusion criteria were given an explanation on the research procedure and asked for their consent by signing an informed consent. The father completed demographic questionnaire, questionnaire on father's involvement in parenting, and the child's growth and development questionnaire according to the child's age as calculated in months by the researcher. The correctly completed questionnaires were then submitted. The child's body height and body weight measurements were done by coming to the schools or posyandu (integrated service post) of the children whose fathers had agreed to be involved in the research.

Statistic: The statistical test used was correlation test, i.e. chi-square test with the level of confidence used being 95%.

Result

106 pairs of fathers and children of 3-5 years old served as the research respondents. Most of them were male (63 or 59.4%). Most of these fathers had higher education (54 or 53.8%). They mostly had formal occupations (64 or 60.4%) and most of their mothers were unemployed at 73.6%. Most of these families had low monthly income at 55.7% or below the City Minimum Wage of Gunung Kidul Regency.

From the completed questionnaire on father's involvement in parenting, it was found that 55 (51.9%) fathers had a good involvement and 51 had a poor involvement, meaning that 48.1% were less involved in parenting. The correlation between father's characteristics and their involvement in parenting could be seen in Table 1.

The result of data analysis showed that father's education variable with a p value of 0.002, mother's education with a p value of 0.001, mother's occupation with a p value of 0.018, and family income with a p

value of 0.017, had significant correlations with father's involvement in parenting.

Table 1: Father's involvement in care based on the characteristics of the respondents

Variabel	Father Involvement				p-value
	Well		Less		
	n	%	n	%	
Father Education					
High education	8	100	0	0,0	0,002
Middle education	25	54,3	21	45,7	
Low education	22	42,3	30	57,7	
Mother Education					
High education	10	83,3	2	16,7	0,001
Middle education	24	66,7	12	33,3	
Low education	21	36,2	37	63,8	
Father Occupation					
Government employees	3	100	0	0,0	0,066
Private employees	8	47,1	9	52,9	
Laborer	19	43,2	25	56,8	
Entrepreneur	19	67,9	9	32,1	
The farmer	6	42,9	8	57,1	
Does not work	0	0,0	0	0,0	
Mother Occupation					
Government employees	3	100	0	0,0	0,018
Private employees	2	40,0	3	60,0	
Laborer	6	54,5	5	45,5	
Entrepreneur	9	90,0	1	10,0	
The farmer	4	30,8	9	69,2	
Does not work	31	48,4	33	51,6	
Family Income					
≥1.571.500	42	89,4	5	10,6	0,017
<1.571.500	40	67,8	19	32,2	

Table 2: Growth of Preschoolers based on Respondent Characteristics

Variable	Growth				p-value
	Normal		Abnormal		
	n	%	n	%	
Father Education					
High education	8	100	0	0	0,198
Middle education	33	71,7	13	28,3	
Low education	41	78,8	11	21,2	
Mother Education					
High education	10	83,3	2	16,7	0,409
Middle education	30	83,3	6	16,7	
Low education	42	72,4	16	27,6	
Father Occupation					
Government employees	3	100	0	0,0	0,766
Private employees	13	75,5	4	23,5	
Laborer	34	77,3	10	22,7	
Entrepreneur	22	78,6	6	21,4	
The farmer	10	71,4	4	28,6	
Does not work	0	0,0	0	0,0	

Variable	Growth				p-value
	Normal		Abnormal		
	n	%	n	%	
Mother Occupation					0,086
Government employees	3	100	0	0,0	
Private employees	3	60,0	2	40,0	
Laborer	11	100	0	0,0	
Entrepreneur	8	80,0	2	20,0	
The farmer	8	61,5	5	38,5	
Does not work	49	76,6	15	23,4	
Family Income					0,016
≥1.571.500	42	89,4	5	10,6	
<1.571.500	40	67,8	19	32,2	

Table 3: Emotional Social Development of Preschool Children based on Respondent Characteristics

Variable	Sociat-Emotional Development				p-value
	Not at risk		Risk		
	n	%	n	%	
Father Education					0,127
High education	6	75,0	2	25,0	
Middle education	17	37,0	29	63,0	
Low education	21	40,4	31	58,5	
Mother Education					0,019
High education	7	58,3	5	41,7	
Middle education	20	55,6	16	44,4	
Low education	17	29,3	41	70,7	
Father Occupation					0,177
Government employees	2	66,7	1	33,3	
Private employees	6	35,3	11	64,7	
Laborer	21	47,7	23	52,3	
Entrepreneur	13	46,4	15	53,6	
The farmer	2	14,3	12	85,7	
Does not work	0	0,0	0	0,0	
Mother Occupation					0,034
Government employees	3	100	0	0,0	
Private employees	3	60	2	40,0	
Laborer	2	18,2	9	81,8	
Entrepreneur	6	60,0	4	40,0	
The farmer	3	23,1	10	76,9	
Does not work	27	42,2	37	57,8	
Family Income					0,113
≥1.571.500	24	51,1	23	48,9	
<1.571.500	20	33,9	39	66,1	

The physical growth of preschool age children was measured based on anthropometric method with body weight per body height index. The body weight was measured using a digital scale and the body height was measured using microtoice. From the 106 children measured, 1 child was found highly thin, 14 children

were thin, and 9 children were fat. Furthermore, for the purpose of bivariate analysis, those children with growths other than normal one (highly thin, thin, and fat) combined to be an abnormal growth category, hence in the bivariate analysis, the growth variable was divided into 2 categories, i.e. normal and abnormal.

The correlation between father’s characteristics and child’s growth could be seen in table 2. The data analysis result indicated that the family income variable with a p value of 0.016 had a significant correlation with the child’s growth.

Table 4. Relationship of Father’s Involvement in Parenting with Growth

Variable		Growth				p-value
		Normal		Abnormal		
		n	%	n	%	
Father Involvement	Well	47	85,5	8	14,5	0,063
	Less	35	68,8	16	31,4	

Table 3 showed the analysis result where the mother education variable with a p value of 0.019 and mother’s occupation variable with a p value of 0.034 were found

to have a significant correlation with the child’s socio-emotional development.

The bivariate analysis result of father’s involvement in parenting with preschool age children’s growth using Chi-square test could be seen table 4.47 children raised by fathers who were well involved in parenting and 35 children raised by fathers who were poorly involved in parenting were found to have a normal growth. In terms of the children experiencing abnormal growth which was an accumulation of highly thin, thin, and fat ones, 16 of them were raised by those fathers who were poorly involved in parenting and 8 of them were raised by those fathers who were involved well in parenting. From the statistical test result, a significance value of 0.063 (p value> 0.05) was obtained, meaning that there was no correlation between father’s involvement in parenting and preschool age children’s growth.

Table 5: Relationship of Father’s Involvement in Parenting with Social-Emotional Development

Variable		Social-Emotional Development				p-value	Odd Ratio	95% CI
		Not at risk		Risk				
		n	%	n	%			
Father Involvement	Well	33	60,0	22	40,0	0,000	5,455	2,313-12,865
	Less	11	21,6	40	78,4			

Table 5 showed the result of statistical test where a significance value of 0.000 (p-value< 0.05) was obtained, meaning that there was a correlation between father’s involvement in parenting and the socio-emotional development in preschool age children.

The value of odd ratio was found to be 5.455, meaning that those children raised by fathers with poor involvement in parenting had 5.455 times risks of having socio-emotional issues than those children raised by fathers with a good involvement in parenting. The confidence interval values range from 2.313 to 12.865, meaning children raised by father’s poor involvement had at least 2.313 times and a maximum of 12.865 greater risks of having socio-emotional issues.

Discussion

Most fathers had a good involvement in parenting. Nevertheless, the difference in number of fathers with good and poor involvements was shown not too substantial, i.e. 51.9% had a good involvement and

48.9% had a poor involvement. It was found that father’s involvement in parenting had no correlation with child’s growth as seen from the body weight per body height status based on the child’s age (p value> 0.05).

Child’s growth served as a direct impact of the intake of food in a long run and the child’s health. The better the quality and quantity of food that the children consumed and their health, the better they will grow. In addition to food intake and disease, parents’ presence also played a certain role in the child’s growth.

Parenting became an indirect factor in child’s growth. The parenting process was not just done by the mother, rather the father also needed to take part. However, the mother played an important role in providing and serving nutritious foods in the family, thus it had an influence on child’s growth.¹⁰ Thus, when the father was less involved in parenting, yet the mother could meet this direct factor, then it would allow the child to have a good growth.

This research also found that most children had the risk of encountering socio-emotional development issues at 58.5%. The analysis in this research showed that father's involvement in parenting had a correlation with socio-emotional development in preschool age children (pvalue = 0.000).

The father played an important role in their child's socio-emotional development and behavior.^{11,12} When the father was actively involved in parenting, their children were less likely to have behavioral problems.¹³ An improvement to the quantity and quality level of father's involvement gave a positive influence on the child's social and emotional development.¹⁴ Parenting during preschool period significantly influenced the child's social and emotional competence.¹⁵

Research limitation: This research used cross sectional method. The research result would be better if it used a longitudinal study method to see the father's involvement in parenting from time to time and its influence on the child's growth and social-emotional development.

Conclusion

From the discussion above, it could be concluded that there was no correlation between father's involvement in parenting and preschool children's growth, yet it had a significant correlation with preschool children's socio-emotional development.

Conflict of Interest: None

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References

- Lamb ME. The role of the father in child development fifth edition. New York: John Willey & Sons Inc. 2010.
- Ministry of Health of the Republic of Indonesia. Basic Health Research 2018. Jakarta: Health Research and Development Agency. 2018.
- Duncan GJ, Ziol-Guest KM, Kalil A. Early-childhood poverty and adult attainment, behavior, and health. *Child development*. 2010 Jan;81(1):306-25.
- Gorvine BJ. Head start fathers' involvement with their children. *Journal of Family Issues*. 2010 Jan;31(1):90-112.
- Wells MB. Literature review shows that fathers are still not receiving the support they want and need from Swedish child health professionals. *Acta Paediatrica*. 2016 Sep;105(9):1014-23.
- Wong MS, Jones-Smith JC, Colantuoni E, Thorpe Jr RJ, Bleich SN, Chan KS. The Longitudinal Association Between Early Childhood Obesity and Fathers' Involvement in Caregiving and Decision-Making. *Obesity*. 2017 Oct;25(10):1754-61.
- Pleck J. Paternal involvement: revised conceptualization and theoretical linkages with child outcomes' (pp. 58-93). 2010) *The role of father in child development*. New York: John Willey. 2010.
- Owoaje E, Onifade O, Desmennu A. Family and socioeconomic risk factors for undernutrition among children aged 6 to 23 Months in Ibadan, Nigeria. *The Pan African medical journal*. 2014;17.
- Tessema M, Belachew T, Ersino G. Feeding patterns and stunting during early childhood in rural communities of Sidama, South Ethiopia. *Pan African Medical Journal*. 2013;14(1).
- Lejarraga H, Berardi C, Ortale S, Cotreras MM, Sanjurjo A, Lejarraga C, Martínez MC, Rodriguez L. Growth, development, social integration and parenting practices on children living with their mothers in prison. *Archivos argentinos de pediatria*. 2011 Dec;109(6):485-91.
- Cabrera NJ, Tamis-LeMonda CS, editors. *Handbook of father involvement: Multidisciplinary perspectives*. Routledge; 2013 May 7.
- Panter-Brick C, Burgess A, Eggerman M, McAllister F, Pruett K, Leckman JF. Practitioner review: engaging fathers—recommendations for a game change in parenting interventions based on a systematic review of the global evidence. *Journal of Child Psychology and Psychiatry*. 2014 Nov;55(11):1187-212.
- Ramchandani PG, Domoney J, Sethna V, Psychogiou L, Vlachos H, Murray L. Do early father–infant interactions predict the onset of externalising behaviours in young children? Findings from a longitudinal cohort study. *Journal of Child Psychology and Psychiatry*. 2013 Jan;54(1):56-64.

14. Volker J, Gibson C. Paternal involvement: A review of the factors influencing father involvement and outcomes. *TCNJ Journal of Student Scholarship*. 2014 Apr;15:1-8.
15. Russell BS, Lee JO, Spieker S, Oxford ML. Parenting and preschool self-regulation as predictors of social emotional competence in 1st grade. *Journal of Research in Childhood Education*. 2016 Apr 2;30(2):153-69.

Factors Associated with Hypertension among Adults in West Java, Indonesia

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Abstract

Background: Hypertension is influenced by various factors including genetic, environmental and lifestyle factors.

Objectives: We aimed to identify factors associated with hypertension among adults in West Java, Indonesia.

Material and Method: The study design was a cross-sectional approach using secondary data from the 'Cohort Study of Non-Communicable Diseases (NCD)' conducted in Kebon Kalapa Village, Bogor City, Indonesia in 2017. This descriptive study used a structured questionnaire to collect primary data distributed to respondents after obtaining their consent. Nutritional status and blood pressure data were collected from participants. A 24-h dietary recall was conducted to collect nutrient intake data. Data were analysed using IBM SPSS software version 24.0.

Results: The prevalence of hypertension in this study was 34.2% and 23.9% of respondents were hypertensive. Bivariate analysis revealed that age 45–59 years, female gender, history of hypertension, overweight, and obesity were associated with hypertension status (P values = 0.0005, respectively, and odds ratios = 2.59, 2.37, 40.06, 7.60 and 10.04, respectively).

Conclusions: Factors associated with hypertension among adults in West Java, Indonesia included older age, female gender, history of hypertension, and nutritional status.

Keywords: *hypertension, factors, adults, cross-sectional.*

Introduction

Hypertension is a disorder of blood pressure (BP) regulation due to increased cardiac output or total peripheral vascular resistance.¹ Late diagnosis of hypertension can lead to various other diseases, such as heart disease, stroke and kidney failure.²

The prevalence of hypertension in Indonesia based on the Indonesian Basic Health Research 2018

was 34.1%. Based on these data, among the 34.1% of people who experienced hypertension, only 1 in 4 were diagnosed and only 54.4% took regular medication for hypertension.³

Many studies have identified the main risk factors for developing hypertension to be male gender,⁴⁻⁵ older age,^{4,6,7} overweight,^{4,8,6} obesity,^{4,8,6,9} retirement, smoking habit,^{4,10} illiteracy,^{4,10,7} upper socioeconomic status, alcohol consumption, marriage,^{4,5} smoking habit,^{4,9} lack of physical activity,⁹ and diabetes.^{7,9}

The major risk factors for hypertension and the extent of their contribution remain unclear. Overcoming hypertension is challenging, given the high prevalence and lack of awareness of its long-term clinical impact. Furthermore, hypertension increases the risk of future health impact if it is not detected and treated early.

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Studies have shown that targeting factors associated with hypertension is one of the best preventives that can be considered when determining intervention strategies for hypertension. Therefore, the present study aimed to identify factors associated with hypertension among adults in West Java, Indonesia.

Materials and Method

The study design was a cross-sectional approach using secondary data from the 'Cohort Study of Non-Communicable Diseases (NCD)' conducted in Kebon Kalapa Village, Bogor City in 2017. The population included permanent residents aged 25–59 years which was registered in the cohort study 2017. The study sample was selected by total sampling, and included individuals with and without hypertension.

There were 1186 initial respondents in total. We excluded respondents with heart disease, stroke and pregnant ($n = 118$), age ≥ 60 years ($n = 49$), users of hormonal contraception (pills, injections, implants) ($n = 132$) and outliers based on nutrient intake ($n = 160$). A final total of 727 respondents were included in the study.

The dependent variable was hypertension status. The independent variables were age, gender, smoking habits, family history of stroke, physical activity, history of hypertension, medication compliance, nutritional status, and nutrient intake.

Systolic and diastolic blood pressure (SBP and DBP) were measured using a digital tensimeter. Hypertension status was determined based on an average SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg¹¹ and/or taking anti-hypertensive drugs.¹² Body height was measured using a height measuring device with 0.1-cm accuracy, while

body weight was measured using a digital weighing device with an accuracy of 0.1 kg. Nutritional status was categorised based on body mass index (BMI) as follows: underweight (<18.4 kg/m²), normal (18.5–25.0 kg/m²), overweight (25.1–27.0 kg/m²) and obese (≥ 27 kg/m²).¹³

Characteristics of study participants were collected using a questionnaire developed specifically for NCD cohort studies. Age was divided into two groups: 25–44 and 45–59 years.

Food consumption data was collecting using 24-h dietary recall. Nutrient intake was calculated based on the Indonesian recommended dietary allowance in the normal population, while intake in the hypertensive population was calculated based on the Dietary Approaches to Stop Hypertension (DASH) recommendations.¹⁴ Nutrient intake was grouped as low ($<90\%$), moderate (90%–119%) and excessive ($\geq 120\%$).

Data were analysed using IBM SPSS software version 24.0 including univariate and bivariate analysis. Bivariate analysis was used to determine the relationship between each independent variable and dependent variable using the chi-square and Fisher exact test. Risk was calculated using odds ratios (ORs). A simple logistic regression test was used to calculate *P*-value and OR for independent variables with more than two categories.

Results

The average age, SBP, and DBP in the hypertensive group was higher than that in the normal population. Fat and sodium intake was higher in the normal population compared with that of the hypertensive group. The distribution of numerical variables of the participants is presented in Table 1.

Table 1: Distribution of numerical variables of study participants

Variable	Normal population		Hypertensive population		Total	
	N	Mean \pm SD (min–max)	N	Mean \pm SD (min–max)	N	Mean \pm SD (min–max)
Age (Years)	553	45.97 \pm 7.83 (30–59)	174	50.82 \pm 6.30 (31–59)	727	47.13 \pm 7.77 (30–59)
SBP (mmHg)	459	120.77 \pm 13.89 (87.50–167.00)	150	148.11 \pm 19.75 (103.50–207.00)	609	127.50 \pm 19.49 (87.50–207.00)
DBP (mmHg)	459	79.15 \pm 9.48 (55.50–109.50)	150	94.77 \pm 11.94 (69.70–141.30)	609	82.99 \pm 12.17 (55.50–141.30)
Weight (kg)	459	59.76 \pm 11.61 (32.80–100.30)	150	64.59 \pm 12.83 (36.50–97.20)	609	60.95 \pm 12.09 (32.80–100.30)

Variable	Normal population		Hypertensive population		Total	
	N	Mean ± SD (min–max)	N	Mean ± SD (min–max)	N	Mean ± SD (min–max)
Height (m)	459	1.56 ± 0.08 (1.33–1.81)	150	1.52 ± 0.06 (1.38–1.69)	609	1.55 ± 0.08 (1.33–1.81)
BMI	459	24.76 ± 4.74 (14.51–39.54)	150	27.94 ± 5.15 (17.03–42.33)	609	25.54 ± 5.03 (14.51–42.33)
Nutrient intake:						
Energy (kcal/day)	458	2034.85 ± 619.26 (719.88–3571.42)	150	1652.42 ± 478.89 (748.29–2729.62)	608	1940.50 ± 610.12 (719.88–3571.42)
Protein (g/day)	458	63.22 ± 21.16 (16.25–119.14)	150	52.95 ± 16.84 (16.18–101.33)	608	60.69 ± 20.65 (16.18–119.14)
Carbohydrate (g/day)	458	274.66 ± 91.71 (87.83–508.33)	150	228.68 ± 73.35 (75.54–429.34)	608	263.32 ± 89.70 (75.54–508.33)
Fat (g/day)	458	77.55 ± 31.81 (8.14–161.34)	150	58.77 ± 21.82 (16.78–107.41)	608	72.91 ± 30.73 (8.14–161.34)
Sodium (mg/day)	458	2374.47 ± 1195.38 (221.98–5495.63)	150	1839.63 ± 839.56 (205.57–4092.47)	608	2242.52 ± 1151.11 (205.57–5495.63)

The prevalence of hypertension in the present study was 34.2%, and 23.9% of respondents were hypertensive. Excessive fat and sodium intake was observed in 247 (40.6%) and 371 (60.1%) participants, respectively. Bivariate analysis revealed that age 45–59 years, female gender, history of hypertension and nutritional status were found to be associated with hypertension status.

Respondents aged 45–59 years showed a 2.59-fold higher risk of hypertension compared with those aged 25–44 years. Females showed a 2.37-fold higher risk than males, and respondents with a history of hypertension showed a 40.06-fold higher risk. Nutritional status

was a risk factor for developing hypertension, and was 7.60-fold higher for overweight and 10.04-fold higher for obese individuals compared with those with normal nutritional status.

While excessive fat and sodium intake showed a 0.46 and 0.53-fold lower risk, respectively, compared with low fat and sodium intake.

The results of the bivariate analysis between characteristics of participants with and without hypertension status are presented in Table 2.

Table 2. Relationship between the characteristics of study participants according to hypertension status.

Variables	Hypertension Status				Total		OR	P-value
	No		Yes		N	%		
	N	%	N	%				
Age (Years)								
25–44	167	78.8	45	21.2	212	100.0	1	Ref
45–59	234	58.9	163	41.1	397	100.0	2.59	0.0005*
Gender								
Male	182	77.1	54	22.9	236	100.0	1	Ref
Female	219	58.7	154	41.3	373	100.0	2.37	0.0005*
Smoking habit								
No	21	24.4	65	75.6	86	100.0	1	Ref
Yes	188	66.9	93	33.1	281	100.0	0.16	0.0005*

Variables	Hypertension Status				Total		OR	P-value
	No		Yes		N	%		
	N	%	N	%				
Family history of stroke								
No	363	66.4	184	33.6	547	100.0	1	Ref
Yes	38	61.3	24	38.7	62	100.0	1.25	0.511
Physical activity:								
High								
Yes	32	76.2	10	23.8	42	100.0	1	Ref
No	366	64.9	198	35.1	564	100.0	1.73	0.187
Moderate								
Yes	381	64.9	206	35.1	587	100.0	1	Ref
No	17	89.5	2	10.5	19	100.0	0.25	0.048*
Low								
Yes	214	64.5	118	35.5	332	100.0	1	Ref
No	184	67.2	90	32.8	274	100.0	0.89	0.542
History of hypertension								
No	384	83.7	75	16.3	459	100.0	1	Ref
Yes	17	11.3	133	88.7	150	100.0	40.06	0.0005*
Medication compliance								
Yes	0	0.0	77	100.0	77	100.0	1	Ref
No	2	13.3	13	86.7	15	100.0	0.000	0.997
Nutritional status								
Underweight	39	45.3	47	54.7	86	100.0	12.69	0.0005*
Normal	200	91.3	19	8.7	219	100.0	1	Ref
Overweight	54	58.1	39	41.9	93	100.0	7.60	0.0005*
Obese	108	51.2	103	48.8	211	100.0	10.04	0.0005*
Nutrient Intake:								
Energy								
Low	204	59.8	137	40.2	341	100.0	1	Ref
Moderate	133	72.3	51	27.7	184	100.0	0.57	0.005*
Excessive	63	75.9	20	24.1	83	100.0	0.47	0.007*
Protein								
Low	150	49.2	155	50.8	305	100.0	1	Ref
Moderate	126	80.3	31	19.7	157	100.0	0.24	0.0005*
Excessive	124	84.9	22	15.1	146	100.0	0.17	0.0005*
Carbohydrate								
Low	259	64.3	144	35.7	403	100.0	1	Ref
Moderate	103	66.9	51	33.1	154	100.0	0.89	0.563
Excessive	38	74.5	13	25.5	51	100.0	0.62	0.150
Fat								
Low	116	56.9	88	43.1	204	100.0	1	Ref
Moderate	101	64.3	56	35.7	157	100.0	0.73	0.151
Excessive	183	74.1	64	25.9	247	100.0	0.46	0.0005*
Sodium								
Low	82	56.6	63	43.4	145	100.0	1	Ref
Moderate	55	59.8	37	40.2	92	100.0	0.88	0.624
Excessive	263	70.9	108	29.1	371	100.0	0.53	0.002*

*P< 0.05

Discussion

The results of the present study revealed that hypertension was influenced by age. High incidence of hypertension was associated with increasing age, caused by changes in the structure of large blood vessel, such as narrowing of the lumen and stiffening of blood vessel walls, as a result of increased SBP.¹⁵ Another factor related to hypertension was female gender. This finding is consistent with the findings of some studies.^{16,17} In this study, most respondents in the age 45–59 years and hypertensive groups were females. In women, incidence of hypertension increases after menopause. Before age 50, women show a lower prevalence of hypertension compared with men, but after age 55, women show a greater age-related increase in proximal aortic stiffness, leading to a higher incidence of systolic hypertension. Women have two other features that tend to reduce DBP and widen pulse pressure. First, short stature causes a faster return of pulse waves to increase peak systolic pressure, and second, a faster heartbeat produces a shorter diastolic period.¹⁵ However, other studies found that hypertension is more common in men.⁴⁻¹⁰

Hypertensive respondents tend to experience high BP more frequently due to inelastic blood vessels. Other factors may also play a role, such as lifestyle, medication compliance and nutritional status. Although medication adherence helps to control BP, this still requires a healthy lifestyle.¹⁸ In the present study, medication compliance data was not sufficient to explain this finding.

Overweight and obese respondents had a higher risk of hypertension than those with normal nutritional status. An association between excessive activation of the sympathetic nervous system and the renin–angiotensin–aldosterone system (RAAS) was shown in obese people, increasing the risk of high BP.¹⁹ High RAAS has been shown to increase sodium reabsorption which carries water so that the body tends to be hypervolemic, which ultimately increases cardiac output and BP.²⁰

In the present study, excessive fat and sodium intake showed less risk compared with low fat and sodium intake. This could be due to hypertension being affected by many risk factors. Alternatively, respondents with low fat and sodium intake may have had a history of hypertension. People with hypertension tend to decrease their sodium and fat intake to prevent disease complications. This diet pattern would affect the outcome of the relationship between fat and sodium intake with

hypertension status. This relationship may be affected by weight status or presence of metabolic disorder.²¹ In the present study, most respondents with low fat and sodium intake were overweight and obese.

There is conflicting evidence about the effect of dietary fat intake on BP. Some studies have shown a positive correlation between dietary cholesterol intake and BP, while others found no significant correlation.²¹ In another study, the relationship between dietary cholesterol and SBP was slightly stronger in the non-hypertensive group. Possible mechanisms include dietary cholesterol related to endothelial dysfunction and reduced nitric oxide bioavailability, which may lead to functional arterial stiffening leading to high BP.²²

Conclusion

In the present study, the prevalence of hypertension was 34.2%, and 23.9% of respondents were hypertensive. Older age, female, history of hypertension and nutritional status were associated with hypertension status.

Our findings may help to determine suitable interventions to overcome and prevent the incidence of hypertension and also to find further strategies to prevent uncontrolled hypertension complications. Further studies are required to alleviate hypertension from year to year based on factors that influence the incidence of hypertension.

Conflict of Interest Statement: There are no conflicts of interest.

Ethical Clearance: This research had received ethical approval from The Research and Community Engagement Ethical Committee Faculty of Public Health Universitas Indonesia Ket-550//UN2.F10/PPM.00.02/2019.

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References

1. Runge, MS; Patterson, C; Stouffer G. *Netter's Cardiology*. 2nd ed. O'Grady E, editor. Philadelphia: Saunders Elsevier, Inc; 2010. 397 p.
2. A global brief on hypertension | A global brief on Hypertension [Internet]. 2013 [cited 2019 Oct 16]. Available from: www.who.int
3. Ministry of Health Republik Indonesia. *Laporan Nasional Riset Kesehatan Dasar 2018*. 2018;582.
4. Singh S, Shankar R, Singh GP. Prevalence and Associated Risk Factors of Hypertension: A Cross-Sectional Study in Urban Varanasi. *Int J Hypertens*. 2017;2017.
5. Khader Y, Batiha A, Jaddou H, Rawashdeh SI, El-Khateeb M, Hyassat D, et al. Hypertension in Jordan: Prevalence, Awareness, Control, and Its Associated Factors. *Int J Hypertens*. 2019;2019.
6. Naidu BM, Yusoff MFM, Abdullah S, Musa KI, Yaacob NM, Mohamad MS, et al. Factors associated with the severity of hypertension among Malaysian adults. *PLoS One*. 2019;14(1):1–16.
7. Bushara S, Noor S, Ibraheem AA, Elmadhoun W, Ahmed M. Prevalence of and risk factors for hypertension among urban communities of North Sudan: Detecting a silent killer. *J Fam Med Prim Care*. 2016;5(3):605.
8. Liu X, Xiang Z, Shi X, Schenck H, Yi X, Ni R, et al. The Risk Factors of High Blood Pressure among Young Adults in the Tujia-Nationality Settlement of China. *Biomed Res Int*. 2017;2017.
9. Pilakkadavath Z, Shaffi M. Modifiable risk factors of hypertension: A hospital-based case-control study from Kerala, India. *J Fam Med Prim Care*. 2016;5(1):114.
10. Liew SJ, Lee JT, Tan CS, Huat C, Koh G. Sociodemographic factors in relation to hypertension prevalence, awareness, treatment and control in a multi-ethnic Asian population: a cross-sectional study. 2019;1–10.
11. Williams B, Mancia G, Spiering W, Rosei EA, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Vol. 36, *Journal of Hypertension*. Lippincott Williams and Wilkins; 2018. p. 1956–2041.
12. Crim MT, Yoon SS, Ortiz E, Wall HK, Schober S, Gillespie C, et al. National surveillance definitions for hypertension prevalence and control among adults. *Circ Cardiovasc Qual Outcomes*. 2012 May;5(3):343–51.
13. Ministry of Health Republik Indonesia. *Pedoman Praktis Memantau Status Gizi Orang Dewasa*. 2011.
14. US Department of Health and Human Services. *Your Guide to Lowering Your Blood Pressure with DASH*. DASH Eating Plan. 2006.
15. Kaplan NM, Victor RG, Flynn JT. *Kaplan's Clinical hypertension*. Eleventh. Philadelphia: Wolter Kluwers; 2015.
16. Shirani S, Gharipour M, Khosravi A, Kelishadi R, Habibi HR, Abdalvand A, et al. Gender differences in the prevalence of hypertension in a representative sample of iranian population: The Isfahan healthy heart program. *Acta Biomed*. 2011;82(3):223–9.
17. Abd Elaziz KM, Dewedar SA, Sabbour S, El Gafaary MM, Marzouk DM, Fotouh AA, et al. Screening for hypertension among adults: Community outreach in Cairo, Egypt. *J Public Heal (United Kingdom)*. 2015;37(4):701–6.
18. Kimani S, Mirie W, Chege M, Okube OT, Muniu S. Association of lifestyle modification and pharmacological adherence on blood pressure control among patients with hypertension at Kenyatta National Hospital, Kenya: A cross-sectional study. *BMJ Open*. 2019;9(1).
19. Amira C., Sokunbi DO., Sokunbi A. The prevalence of obesity and its relationship with hypertension in an urban community: Data from world kidney day screening programme. *Int J Med Biomed Res*. 2012;1(2):104–10.
20. Kotsis V, Stabouli S, Papakatsika S, Rizos Z, Parati G. Mechanisms of obesity-induced hypertension. Vol. 33, *Hypertension Research*. 2010. p. 386–93.
21. Sabour H, Norouzi-Javidan A, Soltani Z, Mousavifar SA, Latifi S, Emami-Razavi SH, et al. The correlation between dietary fat intake and blood pressure among people with spinal cord injury. *Iran J Neurol [Internet]*. 2016 Jul 6 [cited 2019 Oct 12];15(3):121–7. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/27648172>
22. Sakurai M, Stamler J, Miura K, Brown IJ, Nakagawa H, Elliott P, et al. Relationship of dietary cholesterol to blood pressure: The INTERMAP study. *J Hypertens*. 2011;29(2):222–8.

Symptoms and Activities of Daily Living in Patients with Chemotherapy-induced Peripheral Neuropathy

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Abstract

Objective: To compare symptoms and impairment in activities of daily living (ADL) between faller and non-faller patients with chemotherapy-induced peripheral neuropathy (CIPN).

Method: Participants were 247 cancer inpatients of the hematology-oncology department at the university hospital in Korea.

Results: Among participants investigated, 11.7% had fall experiences due to CIPN symptoms. The faller group showed higher rates of metastasis, radiotherapy, and items in ADL impairment than the non-faller group. The faller group also experienced higher degree of sleep disturbance, depression, and peripheral neuropathy symptoms.

Conclusion: This study provides directional relationship between negative effects on ADL and falls in patients with CIPN. It suggests that more attention is needed to develop fall prevention programs for patients with CIPN who has history of metastasis or radiotherapy to improve their ADL capability.

Keywords: Falls, Peripheral neuropathy, Activities of daily living, impairment, cancer.

Introduction

Patients with cancer who undergo chemotherapy experience various adverse effects such as loss of sensation in extremities, weakness, nausea, vomiting, pain, loss of appetite, and fatigue during and after treatment due to widespread cell destruction induced by chemotherapy¹. Treatment with cisplatin, paclitaxel, and vincristine chemotherapy agents may cause chemotherapy-induced peripheral neuropathy (CIPN)

that can have serious consequences such as immune dysfunction and discontinuation of treatment due to side effects related to neurologic toxicity²⁻⁴. However, medical teams tend to pay more attention to chemotherapy-induced bone-marrow suppression or other major organ damage than to symptoms of peripheral neuropathy⁵.

Symptoms of peripheral neuropathy manifest assensory, motor, and autonomic neuronal damages, with sensory symptoms such as numbness in hands or feet (a burning or stabbing sensation) and anesthesia (a loss of sensation) being the most prominent. When motor nerves are involved, corresponding muscles can be weakened or atrophy sometimes. It is difficult to peripheral neuropathy without a neurologic examination because it may be overshadowed by the presence of other symptoms such as fatigue, depression, and cachexia⁶. Symptoms associated with damage to the autonomic nervous system include constipation, orthostatic hypotension, and urinary incontinence⁷⁻⁹. The degree of paresthesia or hyperalgesia experienced by patients is increased with increasing treatment duration, cumulative doses, and

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the frequency of chemotherapy. In addition, diminished muscle strength in patients can lead to difficulties in performing ADLs and decreased quality of life^{4,8,10}.

Previous studies have reported that patients with CIPN show decreases in walking speed and changes in walking pattern^{11,12}. The decrease in mobility can affect the independence of patients and impair their sense of balance on postural sway, thus increasing their risk of falling¹³. Patients with cancer frequently experience falls while undergoing high-dose chemotherapy¹⁴. These falls occur more frequently in patients who have severe neuropathic symptoms. They are directly associated with the degree of impairment in sense of balance and the number of chemotherapy sessions in patients¹¹. Gewandter et al.¹⁵ reported that 11.9% of cancer survivors who experienced CIPN symptoms answered that they had fallen within the last three months. They concluded that the presence of motor neuropathy could increase the risk of falls. Death rate was also increased in cancer patients who experienced injuries caused by falling during treatment¹⁶. To promote the safety and security of patients who receive chemotherapy, it is important to confirm the development of peripheral neuropathy, verify the severity of symptoms, and define factors associated with falls in these patients. Previous studies investigating falls in patients with CIPN had mainly discussed their functional disorders^{13,14,17}, injuries¹⁸, factors associated with walking¹², and quality of life^[8]. Few studies have investigated the directional relationship between impairment of ADL and falls in patients with CIPN including its severity.

Materials and Method

Study Design: Descriptive correlational research design was used to investigate the severity of CIPN and define the relationship between its negative effect on ADL and falls in patients with CIPN.

Setting and samples: Participants included convenient samples of 247 patients with cancer who were inpatients in the Department of Hematology-Oncology at the University Hospital located in Seoul, South Korea. Selection criteria were: aged 18 years or more, with a history of undergoing platinum or taxane-based chemotherapy, ability to walk, and experienced symptoms of numbness or tingling in hands or feet after undergoing chemotherapy. Patients were excluded if they had mental and cognitive disorders or nervous

and musculoskeletal system disabilities such as cerebral infarction, osteoporosis, or multiple sclerosis.

Measurements: Sociodemographic characteristics such as age, gender, education, marital status, occupation, economic status, and body mass index were evaluated for all patients included in this study. Disease-related characteristics including types, stages, chemotherapeutic agents and cycles, presence or absence of metastases, history of radiotherapy, and any adverse event were graded according to the National Cancer Institute-Common Toxicity Criteria (NCI-CTC, version 2)¹⁹. Stages of peripheral neuropathy were measured by the NCI-CTC before distribution of questionnaires for self-administered surveys.

Patients were categorized into the faller group who answered “yes” to the following question: “Have you ever fallen or slipped because of numbness or tingling in hands or feet after chemotherapy within 3 months?”. Those who answered “no” were classified into the “non-faller group.”

Symptoms of peripheral neuropathy were measured according to neurotoxicity symptom areas from the Functional Assessment of Cancer Therapy/Gynecology Oncology Group/Neurotoxicity (FACT-GOG/NTX)²⁰. This scale had 11 questions. Each question was answered on a 5-point scale (0-4), with higher score indicating more severe peripheral neuropathy symptoms. The Cronbach alpha coefficient of the instrument reliability in the present study was .91. The presence or absence of impairment of ADLs was assessed using the modified version of the Patient Neurotoxicity Questionnaire (PNQ)²³. These 11 questions were applied to patients of this study. Each question was answered “not disturbed” or “disturbed” to measure the level of ADL. Data were collected from August 2015 to March 2016.

Data analysis: All data were analyzed using SAS for Windows (ver. 9.2). Fall occurrence rates, sociodemographic characteristics, disease-related characteristics were reported with descriptive statistics. Differences in all variables of peripheral neuropathy symptoms and level of ADL impairment between the faller and non-faller groups were verified with the following tests: t-test, χ^2 -test, Fisher’s exact test, and Wilcoxon rank sum test.

Results

Sociodemographic characteristics between the

faller and non-faller groups: Among 247 participants, 29 (11.7%) had experienced falls due to the presence of symptoms of CIPN. The mean age of all patients was 56.7 years, showing no significant difference between the faller and non-faller groups. Three (10.3%) participants in the faller group had occupations, which was less than the number in the non-faller group in which 68(31.2%) participants had occupations ($p=.020$).

Disease-related characteristics between the faller and non-faller groups: Twenty-two (78.6%) participants in the faller group and 127 (58.8%) participants) in the non-faller group($p = .044$) had metastasis. Seven (24.1%) patients in the faller group and 23(10.6%) in the non-faller group ($p=.035$) received radiotherapy.

Peripheral neuropathy symptoms between the faller and non-faller groups: Patients in the faller group scored 15.10 of 44 for experiencing symptoms of peripheral neuropathy. This score was higher than the

score of 10.00 for patients in non-faller group($p=.002$). Regarding the sensory domain, numbness or tingling in hands ($p=.027$), numbness or tingling in feet ($p=.001$), discomfort in hands ($p=.050$),and discomfort in feet ($p=.005$) were more severe in the faller group than those in the non-faller group. In the dysfunction domain, difficulties in buttoning clothing ($p<.001$) and feeling the shape of small objects were more severe in the faller group than those in the non-faller group ($p=.002$) (Table 1).

Impairment of ADLs between the faller and non-faller groups: The rate of participants with impairment of ADLs in the faller group was higher than that in the non-faller group for all daily activities. The faller group demonstrated the highest rates of impairment in ADLs for climbing stairs and walking ($p<.001$)[at 72.4% (21 participants) and 69.0% (20 participants), respectively], followed by impairment for working ($p=.002$), buttoning clothes ($p<.001$), using chopsticks ($p<.001$), and writing ($p=.004$).

Table 1: Comparisons of Peripheral Neuropathy Symptoms Between Faller and Non-faller Groups. (N=247)

Characteristics	Faller (n=29,%=11.7)	Non-faller (n=218,%=88.3)	z	p
	M±SD	M±SD		
Sensory				
Numbness or tingling in hands	2.00±1.28	1.45±1.34	2.22	.027
Numbness or tingling in feet	2.41±1.30	1.51±1.47	3.27	.001
Discomfort in hands	1.38±1.42	0.94±1.30	1.97	.050
Discomfort in feet	1.62±1.32	1.04±1.40	2.83	.005
Hearing				
Trouble hearing	0.62±1.05	0.37±0.84	1.57	.118
Ringing or buzzing in ears	0.41±0.68	0.49±0.93	0.02	.985
Motor				
Joint pain or muscle cramps	1.34±1.63	0.81±1.16	1.36	.176
Weak all over	2.10±1.42	1.62±1.32	1.76	.080
Trouble walking	1.72±1.25	1.15±1.28	2.38	.018*
Dysfunction				
Difficulty buttoning clothing	1.10±1.29	0.45±0.97	3.88	<.001
Difficulty in feeling the shape of small objects	0.38±0.78	0.07±0.36	3.09	.002
Total	15.10±8.10	10.00±8.20	3.15	.002

M=Mean; SD=Standard deviation.

Discussion

In this study, 11.7% of patients fell or slipped due to the presence of symptoms of CIPN. This rate well

matched with that of a previous study showing that 11.9% of patients with CIPN had survived falls¹⁵. The rate of patients who were employed was lower in the

faller group than that in the non-faller group. This might be because patients in the faller group did not have adequate recovery of health to permit them to return to work. As returning to work is an important socioeconomic aspect influencing quality of life in patients with cancer, future studies are needed to investigate correlations among the severity of CIPN, episodes of falling, and loss of employment.

Patients in the faller group experienced more severe symptoms of peripheral neuropathy than those in the non-faller group. Numbness or tingling in hands and feet can cause difficulty in grasping, lifting, or driving. Impaired sensation in the lower extremities can make it difficult to maintain balance and a steady walking pace, thereby increasing susceptibility to injuries related to falling¹². Patients with CIPN experience numbness or tingling in the hands and feet the most. Severe symptoms can decrease their quality of life²². Therefore, periodically evaluating and managing symptoms of CIPN are necessary.

This study showed that more patients in the faller group had difficulties with buttoning clothing or feeling the shape of small objects. In a previous study, foot-touch perception in patients with CIPN was negatively correlated with difficulties in buttoning clothing²².

Patients in the faller group were found to experience greater impairment of ADLs than those in the non-faller group. Similarly, Gewandter et al.¹⁵ have reported that survivors with CIPN show difficulties in shopping or doing moderate housework and that levels of sensory or motor-associated symptoms are more severe in the faller group. Patients with impairment in ADLs become dependent on others and exhibit increased risk of falling¹³. The risk of falling was decreased in a group of high-risk patients, including patients with peripheral neuropathy, when they received training to enhance their muscle strength and their capability to maintain balance¹⁴.

In this study, many patients had difficulties in walking and ascending stairs. In patients with peripheral neuropathy, the speed of walking was decreased so much that it took twice time to walk compared to normal adults. Postural sway is also increased in these patients, which widens their stride and increases the risk of falling because of gait instability even during slow walking^{12,13}. Thus, patients with CIPN need to be trained to use more muscle strength in the lower limbs while walking or ascending stairs to avoid fall.

This study has limitation to define a relationship between the cause of fall and CIPN level. In addition, we could not count the number of falls in patients. However, this study was meaningful in that patients with CIPN were divided into faller and non-faller groups and their symptoms and interference with ADLs were investigated. This could provide basic data for the development of interventions to prevent falls in such patients. To provide proper nursing to patients with CIPN, it is very important to prevent falls. Medical team's attention change and new program are required to prevent falls.

Conclusion

Our results suggest that history of metastases or undergoing radiotherapy, severity of sleep disturbance, and depression in patients must be considered when developing programs to prevent falls in patients with CIPN. Furthermore, training to enhance endurance, strength, and sensorimotor skill must be emphasized while taking the severity of numbness or tingling sensation in hands and feet, the degree of impairment in activities (namely, walking, ascending stairs, working, and buttoning clothing) into consideration.

Conflict of Interest: The author reports no conflicts of interest in this work.

Source of Funding: Nil

Ethical Clearance: Institutional Ethics Committee clearance was obtained. Informed consent has been taken from the study participants.

References

1. De Castria TB, da Silva EMK, Gois AFT, Riera R. Cisplatin versus carboplatin in combination with third generation drugs for advanced non-small cell lung cancer. *The Cochrane Database of Systematic Reviews*. 2013;16(8):CD009256.
2. Argyriou AA, Kyritsis AP, Makatsoris T, Kalofonos HP. Chemotherapy-induced peripheral neuropathy in adults: a comprehensive update of the literature. *Cancer Management and Research*. 2014;6:135-47.
3. Jaggi AS, Singh N. Mechanisms in cancer-chemotherapeutic drugs-induced peripheral neuropathy. *Toxicology*. 2012;291:1-9.
4. Kim JH, Lee KM, Jeon MJ, Seol ME, Lee SH, Park JM. Symptom and interference of activities of daily living of chemotherapy-induced peripheral

- neuropathy in patients receiving taxanes and platinum. *Asian Oncol Nurs*. 2013;13(3):145-51.
5. Shimozuma K, Ohashi Y, Takeuchi A, Aranishi T, Morita S, Kuroi K, et al. Feasibility and validity of the patient neurotoxicity questionnaire during taxane chemotherapy in a phase III randomized trial in patients with breast cancer: N-SAS BC 02. *Supportive Care Cancer*. 2009;17(12):1483-91.
 6. Frigeni B, Piatti M, Lanzani F, Alberti P, Villa P, Zanna C, et al. Chemotherapy-induced peripheral neuro-toxicity can be misdiagnosed by the National Cancer Institute Common Toxicity scale. *J Peripher Nerv Syst*. 2011;16:228–36.
 7. Ellen ML, Susan LB, Jeffrey C. The total neuropathy score: a tool for measuring chemotherapy-induced peripheral neuropathy. *Oncol Nurs Forum*. 2006;35:96-102.
 8. Kwak MK, Kim EJ, Lee ER, Kwon IG, Hwang MS. Characteristics and quality of life in patients with chemotherapy-Induced peripheral neuropathy. *J Korean Oncol Nurs*. 2010;10(2):231-9.
 9. Tzatha E, DeAngelis LM. Chemotherapy-induced peripheral neuropathy. *Oncology*. 2016;30(3):240-4.
 10. Hile ES, Fitzgerald FK, Studenski SA. Persistent mobility disability after neurotoxic chemotherapy. *Physical Therapy*. 2010;90(11):1649-1659.
 11. Tofthagen C. Patient perceptions associated with chemotherapy-induced peripheral neuropathy. *Clin J Oncol Nurs*. 2010;14(3):E22-8.
 12. Wuehr M, Schniepp R, Schlick C, Huth S, Pradhan C, Dieterich M, et al. Sensory loss and walking speed related factors for gait alterations in patients with peripheral neuropathy. *Gait Posture*. 2014;39:852-8.
 13. Niederer D, Schmidt K, Vogt L, Egen J, Klingler J, Hubscher M, et al. Functional capacity and fear of falling in cancer patients undergoing chemotherapy. *Gait Posture*. 2014;39:865–9.
 14. Tofthagen C, Overcashm J, Kip K. Falls in persons with chemotherapy-induced peripheral neuropathy. *Supportive Care Cancer*. 2012;20:583-9.
 15. Gewandter JS, Fan L, Magnuson A, Mustian K, Peppone L, Hecker C, et al. Falls and functional impairments in cancer survivors with chemotherapy-induced neuropathy (CIPN): a university of Rochester CCOP study. *Supportive Care Cancer*. 2013;21:2059-66.
 16. Toomey A, Friedman L. Mortality in cancer patients after a fall-related injury: the impact of cancer spread and type. *Injury*. 2014;45(11):1710-6.
 17. Kim JH, Choi KS, Kim TW, Hong YS. Quality of life in colorectal cancer patients with chemotherapy-induced peripheral neuropathy. *J Korean Oncol Nurs*. 2011;11(3):254-62.
 18. Ward PR, Wong MD, Moore R, Naeim A. Fall-related injuries in elderly cancer patients treated with neurotoxic chemotherapy: A retrospective cohort study. *J Geriatr Oncol*. 2014;5(1):57-64.
 19. Postma TJ, Heimans JJ. Grading of chemotherapy-induced peripheral neuropathy. *Annals of Oncology*. 2000;11(5):509-13.
 20. Calhoun EA, Welshman EE, Chang CH, Lurain JR, Fishman DA, Hunt TL, et al. Psychometric evaluation of the functional assessment of cancer therapy/gynecologic oncology group-neurotoxicity (FACT/GOG-Ntx) questionnaire for patients receiving systemic chemotherapy. *Int J Gynecol Cancer*. 2003;13(6):741-8.
 22. Yoo YS, Cho OH. Relationship between quality of life and nurse-led bedside symptom evaluations in patients with chemotherapy-induced peripheral neuropathy. *Asian Nurs Res*. 2014;8(1):36-41.
 23. Hausheer FH, Schilsky RL, Bain S, Berghorn EJ, Lieberman F. Diagnosis, management, and evaluation of chemotherapy induced peripheral neuropathy. *Semin Oncol*. 2006;33:15–49.

Biliary Atresia Outcome in Egypt a Descriptive Study

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Abstract

Biliary atresia is a rare disease that affects children and neonates, nowadays the current management of BA is portoenterostomy with or without liver transplantation, in this study we described the outcome of BA in single center.

We included 48 patients in this study with type 3 BA and measured the incidence of clearance of jaundice and cholangitis the incidence of clearance of jaundice was 43% and cholangitis was 20% also the mean age was 74.6 ± 21.8 days which is quite high.

We concluded that early diagnosis and centralization is the key point for getting best outcome for patients of BA

Keywords: Biliary Atresia, Portoenterostomy, Jaundice clearance, cholangitis.

Introduction

BA is an obstructive cholangiopathy, an inflammatory process that affects both intra and extra hepatic bile ducts causing obliteration of the bile ducts ends up to cirrhosis and liver cell failure if left untreated⁽¹⁾.

Although it is an uncommon disease occurring in 1/10000- 1/15000 live births worldwide it is rare but with obvious geographical variation as in Europe and North American for example it has an incidence of 1 in 15–,20,000 live births and by contrast can be sensationalistic births in Taiwan and presumably mainland China. It is not a homogenous, uniform disease and within the umbrella term are several variants which have separate and distinct causes and different outcomes. These make comparison of treatment options difficult but not impossible⁽²⁾.

The etiology of BA is unknown but thought to be multifactorial, currently there are 3 main types of BA; cystic type of BA, isolated BA and syndromic BA which is thought to be congenital in nature⁽³⁾.

The first porto enterostomy was done by Prof Moro Kasai 1953 by chance while he was dissecting in the porta hepatis and noted bleeding then he put the duodenum for hemostasis then the patient's stool got coloured since then many modifications have been done to this operation and became the first line of treatment of BA with or without liver transplantation⁽⁴⁾.

There are many factors that affect the outcome of Kasai procedure, the most important factor is patient's age at time of operation, the second is the type of BA the best in prognosis is cystic type of BA while the worst is the syndromic BA, attacks of cholangitis also affect the outcome also adjuvant therapy may play a role in improving the outcome⁽³⁾.

The prognosis of BA has dramatically changed in the last decades: before the Kasai operation most BA patients died, while nowadays with the sequential treatment with Kasai operation, with or without liver transplantation, BA patient survival is close to 90%. Early diagnosis is very important since the chances of success of the Kasai procedure decrease with time⁽⁵⁾.

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In Egypt and due to limitation of liver transplant inpatient with BA below one year of age we have to do our best to increase the success rate of the portoenterostomy inpatient with BA including both clearance of jaundice and the percentage of native liver survival

Patients and Method

48 patients were included in this trial we included all cases of BA type 3 after investigations were done including Lab investigations which showed direct hyperbilirubinemia, elevated GGt and Alkaline phosphatase, ultrasound showed absent or non contractile gall bladder, liver biopsy showed marked inflammation and bile duct proliferation .

All cases were operated and managed at Cairo University Children Hospital (CUPSH) and after referral to the surgical department the case is admitted 48 hours before surgery and preoperative labs were done, blood crossmatching and preoperative antibiotics were given .

On the OR patients were anesthetized supine with endotracheal intubation and sonar guided CVL.

The infant was positioned supine to ensure a non obstructed view for cholangiography, which was not routinely required. surgical exploration commenced through an extend edkocher's incision centered to the right. This incision could be extended across the midline if biliary reconstruction was required . the left upper quadrant was examined to determine splenic anatomy.

Liver consistency was noted and the porta hepatis is inspected. Cholangiography has a distinct role in this patients. If the gallbladder had a lumen, diluted contrast material (diatrizoate Hypaque) was injected to determine the continuity of the biliary tree between the liver and duodenum. Complete extra hepatic duct patency was confirmed when contrast appears distally in the duodenum and proximally in the liver radicles. The size of the ducts is assessed by cholangiography to determine whether biliary hypoplasia or obstruction to bile flow from inspissation was present. If the contrast material moved only distally into the duodenum and not into the liver, gently occluding the distal common bile duct while reinjecting the gallbladder to encourage proximal ductal filling, although this maneuver rarely succeeded. If extra hepatic biliary patency is demonstrated, regardless of whether the ducts were of normal caliber or diminutive, a liver biopsy is performed and the incision closed.

If ductal patency was not confirmed, portal dissection and biliary reconstruction was performed (the Kasai procedure).

According to delivery of the liver some surgeons preferred to deliver the both lobes of the liver from the abdominal cavity after dividing both triangular ligaments, some preferred to deliver the left lobe only and minority prefer not to deliver either lobes and doing the portoenterostomy in situ.



Figure 1: liver delivery before dissection

The fibrous common duct was ligated distally with non absorbable suture and transected. Gentle traction applied to the remnant facilitates dissection toward the porta, where a cone of fibrous tissue anterior to the bifurcating portal vein is encountered.

When there was discontinuity of the biliary tree, exploration of the tissue overlying the portal vein bifurcation will almost invariably reveal the fibrous cone. Placing a suture in this fibrous tissue will facilitate establishing the plane above the portal vein.

Once dissection was complete, fine stay sutures were placed at the lateral margins of the fibrous cone. While maintaining moderate tension, the fibrous cone was sharply transected,

The resected biliary structures with attached gallbladder remnant are sent for pathologist to measure

the size of the biliary ductules for later prognostic evaluation.

Recently we standardized our technique by making wide portal plate extending from Rexfossato the gallbladderfossa (innominatefossa) for allowing maximum drainage of bile through the porto-enterostomy.

The porto-enterostomy was done retrocolic through an incision in the transverse mesocolon just to the right of the middle colic artery.

The prto-enterostomy was done end to side by making an incision of the anti-mesentric border of the roux limb 1-2 cm of its distal end to avoid blind pouch and then the anastomosis is done using parachuting technique for the posterior wall which allows better vision.

After completing the porto-enterostomy the roux limb was sutured to the glisson's capsule and transverse mesocolon to decrease the tension on anastomosis.

Drain was usually inserted and removed on the 5th day postoperative.

Regional anaesthesia (TAP block) is injected at the lateral border of rectus sheath to decrease postoperative pain, the dose was calculated through the anaesthesia team.

Abdomen was closed in 2 layers and Subcuticular closure for the skin was done.

Postoperative management: Patient was kept on the ICU on nasal oxygen if needed with proper analgesia, Iv fluids and postoperative CBC was done routinely to detect any need for blood transfusion.

Gradual feeding was introduced once intestinal motility was regained

Patient was followed up through CBC with differential and CRP to detect early sepsis and upgrade antibiotic line accordingly.

Discharge: Patients were discharged when they reached their full feeding with no fever and no laboratory signs of sepsis.

Outpatient follow up: After discharge Patients were followed up regularly at the hepatology clinic for followup,

At day 12 postoperative, 1,3 and 6 months postoperative.

General medical examination was done, jaundice is detected recording of any complication such as cholangitis, etc.,

The following data were recorded:
Hepatosplenomegaly Presence of jaundice, Colour of stool Fever and cholangitis

Results

Concerning our patients the range of age was **(30-118)** with a mean age was **74.6±21.8**. 25 were males (52%) while 23 were females (48%)

In our study 25 cases were male (52.1%) and 23 cases were female (47.9%)

In our study 21 cases (43.8%) were jaundice free with in the first 6 months postoperative.

27 cases (**56.3%**) were still jaundiced at 6 months postoperative. 35 cases (72.9%) has coloured stool while only in 13 cases (27.1%) clay coloured stool have persisted.

The median preoperative bilirubin was 9.8 mg/dl while the median bilirubin after 6 months were 5.1 mg/dl.

Discussion

Although our study seems to be intermediate in number of cases and this limits the presence of statistical significance of the data but this happened however this happened due to relatively short duration of the study which was only 2 years, Davenport made his trial over 11 years and the START trial was done over 6 years.⁽¹⁾

Concerning age in our study the mean age was 74.6±21.8 (30-118), 14 cases were less than 60 days (29.2%), 23 cases were 60-90 days (47.9%) and 11 cases were 90-120 days (22.9%).

By comparing the mean age with the mean age of the similar studies that discuss the use of steroids the mean age of this study is the oldest age, in the study of Tyraskis and Davenport 2016 the mean age was reaching 46 days (12-70) days⁽¹⁾. while In the START trial done by Bezerra 2014 the mean age was 69 days⁽⁶⁾, also at the study of Escobar 2006 the mean age was 43 days⁽⁷⁾,

theme an age of the study of Petersen 2008 was 62 days⁽⁸⁾. Chung 2008 also has a mean age of 70 days⁽⁹⁾.

From the previous data we can conclude that the youngest age was at Davenport study (45 days(12-70))and we think that this could be achieved by the centralization system that the NHS provide to allow early detection and management of those cases and due increased awareness of this disease among pediatrician⁽¹⁾.

On the other hand in EGYPT and due to lack of awareness of this disease among pediatrician and due to lack of ability of differentiation between BA and physiological jaundice there is a delay in the management of these cases, In our study we excluded the cases aged above 120 days due to controversy about benefit of porto-enterostomy for those patients and if we didn't exclude those cases the mean age would be much higher .

Conclusion

For achieving best outcome for patients of BA two main factors should be present the first is early diagnosis and management of biliary atresia either by screening or increasing awareness of this disease between pediatricians the second factor is centralization which should increase surgical success.

Ethical Clearance: from ethical committee Cairo university 2015 ethical committee approval number I-111015.

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Conflicts of Interests: Nil.

References

1. Tyraskis A, Davenport M. Steroids after the Kasai procedure for biliary atresia: the effect of age at Kasai portoenterostomy. *Pediatric surgery international*. 2016 Mar 1;32(3):193-200.
2. Lillegard JB, Miller AC, Flake AW. Biliary Atresia. In *Fundamentals of Pediatric Surgery 2017* (pp. 629-636). Springer, Cham.
3. Petersen C, Davenport M. Aetiology of biliary atresia: what is actually known?. *Orphanet journal of rare diseases*. 2013 Dec 1;8(1):128.
4. Hirzel AC, Madrazo B, Rojas CP. Two rare cases of hepatocellular carcinoma after Kasai procedure for biliary atresia: a recommendation for close follow-up. *Case reports in pathology*. 2015;2015.
5. Nizery L, Chardot C, Sissaoui S, Capito C, Henrion-Caude A, Debray D, Girard M. Biliary atresia: clinical advances and perspectives. *Clinics and research in hepatology and gastroenterology*. 2016 Jun 1;40(3):281-7.
6. Bezerra JA, Spino C, Magee JC, Shneider BL, Rosenthal P, Wang KS, Erlichman J, Haber B, Hertel PM, Karpen SJ, Kerkar N. Use of corticosteroids after hepatopertoenterostomy for bile drainage in infants with biliary atresia: the START randomized clinical trial. *Jama*. 2014 May 7;311(17):1750-9.
7. Escobar MA, Jay CL, Brooks RM, West KW, Rescorla FJ, Molleston JP, Grosfeld JL. Effect of corticosteroid therapy on outcomes in biliary atresia after Kasai portoenterostomy. *Journal of pediatric surgery*. 2006 Jan 1;41(1):99-103.
8. Petersen C, Harder D, Melter M, Becker T, Wasielewski RV, Leonhardt J, Ure BM. Postoperative high-dose steroids do not improve mid-term survival with native liver in biliary atresia. *The American journal of gastroenterology*. 2008 Mar;103(3):712.
9. Chung HY, Kak Yuen Wong K, Cheun Leung Lan L, et al. Evaluation of a standardized protocol in the use of steroids after Kasai operation. *Pediatr Surg Int*. 2008;24(9):100

Registration Accuracy between Maxillary and Mandibular Teeth for Fixed Restoration Construction

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Abstract

Objectives: This study was carried out to evaluate the dimensional accuracy of conventional bite registration material and CAD/CAM bite registration material in patients with a single missing tooth.

Method: Twenty patients with one missing tooth (who needed a fixed partial denture) were selected and included in the present study. A full veneered preparation was done. The patient bit on bite registration material in centric and eccentric movement. A wire “3 cm in length “was bonded with composite on adjacent teeth to the preparation. The length of wire impression on bite registration material was measured and after 24 hours to evaluate the possible effect with time factor.

Results: The effect of duration on the dimensional accuracy of bite registration materials at horizontal centric and eccentric occlusion was statistically significant between immediate and later who recorded higher values with both types of bite registration materials tested. Also a statistical significant differences between the two types of occlusion irrespective to the duration, type of restorations and types bite registration materials, as eccentric occlusion recorded higher values.

Conclusions: Futar D and Futar scan bite registration materials provided accurate records with no differences between them. Dimensional accuracy was influenced by time factor of the recording materials.

Keywords: Registration accuracy, conventional bite registration material, CAD/CAM, centric, eccentric, immediate, late.

Introduction

The Bite Registration is an interocclusal record which defined as an accurate and precise recording of maxillo-mandibular relationship¹. The importance of bite registration in recording the maxillo-mandibular relationship is to transfer the relationship to the articulator so laboratory procedure on the casts will correspond to the patient's mouth². There are various methods of recording maxillomandibular relationships graphic, functional, cephalometric and direct interocclusal recordings³. Direct interocclusal records are most commonly used to record maxillomandibular relationships because of their simplicity. The arches are brought into a relationship with or without tooth contact, and a space is created between the teeth. The recording material, which is initially soft, fills the spaces between

teeth, hardens, and records the specific relationship of the arches. The hardened material is then transferred onto casts to be mounted on an articulator⁴. Therefore, an ideal registration material and technique combination would allow the placement of an indirectly fabricated prosthesis intraorally with minimal occlusal adjustment¹. The ultimate accuracy in relating maxillary and mandibular dental casts is dependent on the accuracy and dimensional stability of the material used to record the interjaw relationships⁵. Futar D and Futar D Fast have different setting times; and both materials have different final hardness from Futar Scan. The latter can be scanned using an optical scanner as required for CAD /CAM system because of its matte surface which makes it suitable for collecting three-dimensional data⁶. An ideal interocclusal recording material should be able to represent the maxillomandibular relationships

accurately and should also be dimensionally stable over some days of storage ⁷. The purpose of this study was to evaluate the dimensional accuracy of conventional bite registration material and CAD/CAM bite registration material in patients with Single missing tooth.

Materials and Method

Ethical regulation: Full detailed explanation of the procedures to be done will be offered to the patient and will be asked to sign an informed consent before commencing the treatment. This study was made to evaluate the accuracy of different bite registration materials used for recording the interocclusal relation.

I. Materials:

1. Vinyl polysiloxane bite registration cream “Futar D Fast” (Conventional bite registration material)
2. Vinyl polysiloxane bite registration cream (scannable) “Futar Scan” (CAD/CAM bite registration material)

II. Method:

1. **Preparation of teeth:** Twenty patients with one missing tooth (who needed a fixed partial denture) were selected and included in the present study.

Crown preparation to the tooth in the fully dentate patient will be done using depth cutter stone on the occlusal surface to provide 2mm occlusal clearance to allow placement of 2mm thickness of registration material.

The other patients with one missing tooth, a full veneered preparation to the two abutments will be done.

The patient will bite on bite registration material in centric and eccentric movement.

2. Preparaing a wire as a guide to calculate dimensional changes:

A wire “3 cm in length “, which will be measured by stereo microscope and then will be bonded with composite on adjacent teeth to the preparation in a horizontal position to be recorded on the bite registration material and after setting of bite registration material (according to the manufacturer instructions). The length of wire impression on bite registration material was measured and after 24 hours to evaluate if there was effect with time factor ⁽⁵⁾.

3. Method of measurement:

Using stereomicroscope (light stereomicroscope BX60, Olympus, Japan).

4. Statistical analysis:

Statistical analysis was performed by Microsoft Office (Excel) and Statistical Package for Social Science (SPSS) version 20.

Data were presented as mean and standard deviation (SD) values.

The significant level was set at $P \leq 0.05$.

Anova for repeated measurement was used to assess effect of time and material over accuracy of bite registration material

Univariate anova was used to assess effect of material over accuracy of bite registration material

Results

Table (1): Effect of duration on the dimensional accuracy of bite registration materials at horizontal centric occlusion

Types of Restoration	Duration (immediate)		Duration (later)	
	Types bite registration materials			
	Futar D Fast (Mean ± SD)	Futar Scan (Mean ± SD)	Futar D Fast (Mean ± SD)	Futar Scan (Mean ± SD)
Three Units (one missing tooth)	2.9234 ^a (± 0.4321)	2.5160 ^a (± 0.5231)	2.6283 ^b (± 0.5792)	2.6946 ^b (± 0.4732)

Same letter denotes no significant difference: The effect of duration on the dimensional accuracy of bite registration materials at horizontal centric occlusion is represented in table 1. Results showed statistical

significant differences between immediate and later who recorded higher values with both types of bite registration materials tested.

Table (2): Effect of duration on the dimensional accuracy of bite registration materials at horizontal eccentric occlusion

Types of Restoration	Duration (immediate)		Duration (later)	
	Types bite registration materials			
	Futar D Fast (Mean ± SD)	Futar Scan (Mean ± SD)	Futar D Fast (Mean ± SD)	Futar Scan (Mean ± SD)
Three Units	2.9341 (± 0.2109)	2.5262 (± 0.5214)	2.7182 (± 0.5321)	2.8078 (± 0.2895)

Same letter denotes no significant difference: The effect of duration on the dimensional accuracy of bite registration materials at horizontal centric occlusion is represented in table 2. Results showed statistical significant differences between immediate and later who recorded higher values with both types of bite registration materials tested.

Table (3): Comparison between the two types of occlusion irrespective to the duration, type of restorations and types bite registration materials regarding horizontal occlusion

Centric occlusion	Eccentric occlusion
2.7435 ^a	2.5922 ^b

Same letter denotes no significant difference: Comparison between the two types of occlusion irrespective to the duration, type of restorations and types bite registration materials is represented in table 3. Results showed a statistical significant differences between the two types of occlusion irrespective to the duration, type of restorations and types bite registration materials, as eccentric occlusion recorded higher values.



Figure 1: A wire bonded on tooth with composite



Figure 2: Wire impression on futarscan bite registration material

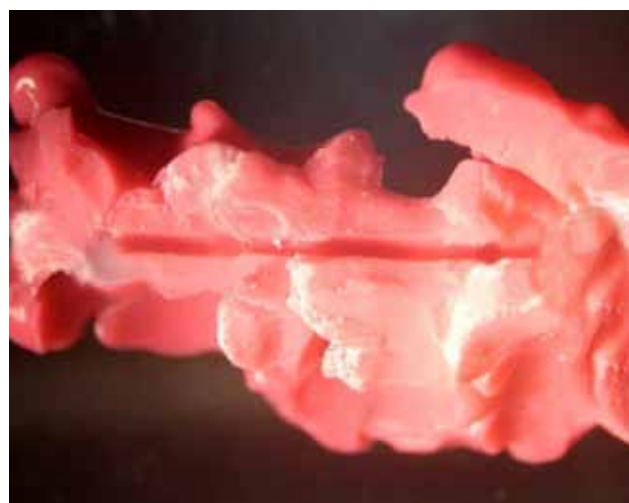


Figure 3: Wire impression on futar d fast bite registration material

Discussion

An interocclusal record is a precise recording of maxilla mandibular position⁸. An accurate transfer of the interocclusal relationship to the articulator is essential for the fabrication of prosthesis. The accurate articulation of working casts results in less time spent adjusting

occlusion. This has a direct effect on the quality of the restoration and the operational cost of treatment⁹. The precise assessment of a patient's maxilla-mandibular relations is a key aspect of diagnosis and complex restorative therapy in oral rehabilitation¹⁰. However, this assessment is insufficient without mounting the maxillary and mandibular casts in accordance with the recorded jaw relation on the articulator¹¹. The interocclusal record is a registration of the positional relationship of the opposing teeth or arches and has become the most popular method of transferring maxillomandibular relations from the mouth to the articulator¹². The Bite Registration is an interocclusal record which defined as an accurate and precise recording of maxillo-mandibular relationship¹³. The importance of bite registration in recording the maxillo-mandibular relationship is to transfer the relationship to the articulator so laboratory procedure on the casts will correspond to the patient's mouth¹⁴. There are various method of recording maxillomandibular relationships graphic, functional, cephalometric and direct interocclusal recordings. The recording materials whenever possible were automatically mixed with gun so as to give a proper, consistent and homogenous mix free of void. This study was carried out to evaluate the dimensional accuracy of conventional bite registration material and CAD/CAM bite registration material in patients with a single missing tooth. In the present study; two materials were chosen for recording interocclusal registration (Futar D Fast and Futar scan). Twenty patients with one missing tooth (who needed a fixed partial denture) were selected and included in the present study. A full veneered preparation was done. The patient bit on bite registration material in centric and eccentric movement. A wire "3 cm in length" was bonded with composite on adjacent teeth to the preparation. The length of wire impression on bite registration material was measured and after 24 hours to evaluate the possible effect with time factor. Injection technique for recording interocclusal relationship was used as it is the most popular technique used in dental work and produces a homogenous consistent mix which is free of voids¹⁵. All the specimens were stored in sealed dry polyethylene bags at room temperature (28 + 2) as dimensional changes of elastomers can be reduced by storage in a sealed dry containers at room temperature as moisture caused considerable expansion of elastomeric impression materials¹⁶. In the present study; there was no statistical significant difference between the two tested types of bite registration materials for 2 types of restorations at horizontal centric or eccentric occlusions

either immediate or late among the included cases. Also there was no statistical significant differences between the two tested types bite registration materials irrespective to the duration, type of restorations and type of occlusion. On the other hand; regarding the effect of duration on the dimensional accuracy of bite registration materials at horizontal centric and eccentric occlusions, there was statistical significant differences between immediate and later who recorded higher values with both types of bite registration materials tested. A statistical significant differences was found also between the two types of occlusion irrespective to the duration, type of restorations and types bite registration materials, as eccentric occlusion recorded higher values. It was also found that; no significant effect on dimensional accuracy of recording. These were in agreement with *Wieckiewicz et al*¹⁷ who compared the dimensional stability of interocclusal registration materials between dentate and partially dentate and concluded that; there was no statistically difference significant between them and concluded that increasing volume of the material did not affect closure yet, closure would be dependent on the viscosity of the material. Regarding the effect of **time of storage** on dimensional accuracy of the recording materials, it was found that time of storage had a significant effect on the dimensional accuracy of both recording materials. This finding was in accordance with *Anup et al*¹⁸ who studied the effect of time of storage on dimensional accuracy of elastomeric materials and concluded that the dimensional stability decreased with increase in time and was influenced by both material and time factor. It was also conducted that, for VPS recording materials, there were no statistically significant differences in dimensional changes immediately and after one week. This result was with agreement with the experimental findings of *Persson et al*¹⁹ who studied the physical properties of interocclusal recording media and concluded that addition silicone materials showed little dimensional change in a horizontal plane. *Ghazal and Kern*²⁰ who studied the detail reproduction and dimensional stability of elastomeric impression materials and explained that; the setting reaction of polymer-based materials started as soon as the base and catalyst pastes come into contact with each other. This continuous process of polymerization and cross-linking resulted in molecular densification and shrinkage. As for VPS this polymerization reaction continued resulting in negative change in dimension after 24h. **For the materials effect** on dimensional accuracy, it was found that there was no statistically significant differences

between both materials. These results was in agreement with Michalakos *et al*²¹ who compared the dimensional stability of different interocclusal materials and concluded that no significant difference between them.

Conclusions

Futar D and Futar scan bite registration materials provided accurate records with no differences between them. Dimensional accuracy was influenced by time factor of the recording materials.

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Ethical Clearance: It was approved by the ethics committee of Minya university.

References

1. Kapur K and Yurkstas A. An evaluation of centric relation records obtained by various techniques. *J Prosthet Dent* 2013; 7:770-86.
2. Sonune S, Dange S and Khalikar A. An accurate interocclusal record by creating vertical stop. *J Prosthodont* 2015; 5(3):119-21.
3. YurkstasA, KapurK. Factors influencing centric relation records in edentulous mouths. *J Prosthet Dent* 2005; 93: 305- 10.
4. Shikha N, Himanshu S and Pankaj G. Inter-occlusal record materials used in Prosthodontic Rehabilitations. *Int J Enh Res Med & dent care*. 2014; 1(9):8-12.
5. Krahenbuhl J,Irelan J, and Bansal N.Accuracy and precision of occlusal contacts of stereo lithographic castsmounted by digital interocclusal registrations. *The Journal of Prosthetic Dentistry* 2016; 116 (2): 231–6.
6. Ghazal M, Albashaireh G, and Kern M. The ability of different materials to reproduce accurate records of interocclusal relationships in the vertical dimension. *Journal of Oral Rehabilitation* 2008; 11: 816–20.
7. HellmannN, Etz E, Giannakopoulos N and Rammelsberg P. Accuracy of transfer of bite recording to simulated prosthetic reconstructions. *Clinical Oral Investigations* 2013; 17 (1): 259–67.
8. NagrathM, Lahori H, Kumar V, and Gupta D. A comparative study to evaluate the compression resistance of different interocclusal recording materials: an in vitro study. *The Journal of Indian Prosthodontic Society* 2014; 14: 76–85.
9. YuzbasiogluE, Kurt H, Turunc R and Bilir H. Comparison of digital and Conventional impression techniques: evaluation of patients' perception, treatment comfort, Effectiveness and clinical outcomes. *BMC Oral Health* 2014; 14:1-10.
10. Kim S, Kim J, Han J and Yeo S. Accuracy of dies captured by an intraoral digital impression system using parallel confocal imaging. *Int J Prosthodont* 2013; 26(2):161–3.
11. Christensen G. Impressions are changing: deciding on conventional, digital or digital plus in-office milling. *JADA* 2009; 140:1301–4.
12. Sweeney S, Smith D and Messersmith M. Comparison of 5 types of interocclusal recording materials on the accuracy of articulation of digital models. *Am J Orthod Dentofacial Orthop*. 2015;148 (2):245-52.
13. Ghazal M, Hedderich J and Kern M. An In Vitro Study of Condylar displacement Caused by Interocclusal Records: Influence of Recording material,Storage Time, and Recording Technique. *Journal of Prosthodontics* 2016; 15: 1–7.
14. Nagrath P, Lahori M, Kumar V, and Gupta V. A comparative study to evaluate the compression resistance of different interocclusal recording materials: an in vitro study. *The Journal of Indian Prosthodontic Society* 2014; 14: 76–85.
15. Megremis S, Tiba A, and Vogt A. An evaluation of eight elastomeric occlusal registration materials. *The Journal of the American Dental Association* 2017; 114: 1358–60.
16. Tejo S, Kumar A, Kattimani V and ChaitanyaK. A comparative evaluation of dimensional stability of three types of interocclusal recording materials- an in-vitro multi-centre study. *Head and Face Medicine* 2012; 8: 1–9.
17. Wieckiewicz P, Grychowska N,Zietek M, and Wlodzimierz W. Evaluation of the Elastic Properties of Thirteen Silicone Interocclusal Recording Materials” *BioMed Research International* 2016; 13: 123-5.
18. AnupG, Ahila S, and Vasantha M. Evaluation of dimensional stability, accuracy and surface hardness of interocclusal recording materials at various time intervals: an in vitro study,” *The Journal of Indian Prosthodontic Society* 2017; 11: 26–31.

19. Persson A, Od'en A, Andersson N, and Sandborgh G. Digitization of simulated clinical dental impressions: virtual three-dimensional analysis of exactness. *Dental Materials* 2018; 25: 929–36.
20. Ghazal M and Kern M. Mounting casts on an articulator using interocclusal records,” *Journal of Prosthetic Dentistry* 2017; 100: 408–11.
21. Michalakis K, Pissiotis A, Anastasiadou V, and Kapari D. An experimental study on particular physical properties of several interocclusal recording media. *Journal of Prosthodontics* 2014; 4: 233–4.

The Relationship Consumption Patterns of Pokea Clams (*Batissa violacea* var. *Celebensis*, von Martens, 1897) and Lipids with Total Cholesterol Levels and Triglycerides in Patients with Hypertension

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Abstract

Introduction: The purpose of this study was to determine the relationship between pokea clams and lipid consumption patterns with total cholesterol and triglyceride levels in hypertensive patients in the Sampara District.

Method: This study uses an analytic observational with a case control design the population of this research is the people who consume pokea clams. Sample of this research amount 60 people, divided into 30 cases and 30 control. The sampling technique uses purposive-sampling method. Data taken by using a questionnaire consumption pattern of pokea clams, questionnaire of Semi Quantitative Food Frequency Questionnaire (FFQ-SQ) and the blood pressure were taken by using a mercury sphygmomanometer. Data analysis use the calculation of Odds Ratio.

Results: Statically, p values and OR value that is obtained from the consumption pattern of pokea clams (*Batissa violacea* var. *celebensis* von Marten, 1897) (p value = 0,342; OR = 1,750; CI 95% = 0,548-5,586), pattern of lipid consumption (p value = 1,000; OR = 1,027; CI 95% = 0,247-4,273) to total cholesterol level in Sampara district region. Statistically, p value and OR value from all respondents with the pokea consumption pattern (von Marten, 1897. *Batissa violacea* var. *celebensis*) by control and cases group (p value = 2,05; OR = 2,31; CI 95% = 0,72-7,4). The statistical result of lipid consumption pattern between the control and cases group (p value = 0,47; OR = 0,44; CI 95% = 1,00-1,97) agains triglyceride levels in the Sampara District.

Conclusion: There is no relationship between consumption pattern of pokea clams and pattern of lipid consumption with total cholesterol and triglyceride levels in hypertension patient in Sampara district region.

Keywords: *Pokea Clamp, Lipid, Total Cholesterol, Triglyceride, Hypertension.*

Introduction

Hypertension or high blood pressure is a condition of increasing blood pressure above normal which

can increase the amount of morbidity and death⁽¹⁾. Hypertension is an increase in systolic blood pressure of more than or equal to 140 mmHg and diastolic pressure of more than or equal to 90 mmHg⁽²⁾.

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Based on the results of the measurement of the prevalence of hypertension in Indonesia in 2013 at the age of ≥ 18 years the results were obtained with a percentage of 25.8%. The highest prevalence of hypertension is in Bangka Belitung Province (30.9%) and the lowest is

in Papua (16.8%). The prevalence of hypertension in Indonesia obtained through a questionnaire diagnosed by health workers is 9.4%, which was diagnosed by health workers or is taking medicine at 9.5%, this means that there are 0.1% who take their own medication. Respondents with normal blood pressure but taking hypertension medication were 0.7%⁽³⁾.

During visits to service units such as the Puskesmas and its network, it was found that the population aged > 18 years was 82,425 (8%) and those who experienced an increase in blood pressure or hypertension were 31,817 (38.60%) people. Judging from the gender of the respondents, the incidence of hypertension was more common in men (50.32%) than in women (34.67%)⁽⁴⁾. Based on the top 10 most diseases in the Sampara Health Center, hypertension was in 4th position in 2017⁽⁵⁾, where of 3,061 people, there were 312 people (10.2%) suffering from hypertension⁽⁵⁾.

Factors that influence the incidence of hypertension are divided into two major groups, namely unmodifiable factors such as gender, age, genetics and modifiable factors such as diet, exercise habits and others⁽⁶⁾. Hypertension can be associated with abnormalities of total cholesterol lipids. Dyslipidemia can increase the risk of hypertension⁽⁷⁾. Various factors can increase the risk of hypertension, including age, sex, genetic, obesity, stress, physical activity, smoking, consumption alcohol and nutrient intake. One of the factors that can be controlled is the intake of nutrients, such as intake of protein, saturated fat, sodium, potassium, calcium, magnesium and fiber. National and local hypertension control policies and strategies have been implemented that include 3 components, namely surveillance and monitoring, prevention and reduction of risk factors, early detection, timely and continuous treatment. One of the factors that play an important role in controlling hypertension is dietary factors, especially low-fat food diets. Fat intake can be described in the profile of dyslipidemia which includes total cholesterol, LDL, HDL, and triglycerides.

In the human body, cholesterol derived from daily food is classified as exogenic cholesterol and cholesterol resulting from synthesis in the body as endogenic cholesterol⁽⁸⁾. According to Soleha⁽⁹⁾, high level of cholesterol or hypercholesterolemia can be a trigger for hypertension due to blockages in peripheral blood vessels that can reduce blood supply to the heart.

Dyslipidemia results in hypertension through the mechanism of endothelium dysfunction which can increase the production of the release and activation of nitric oxide in blood vessels resulting in changes in the structure of enlarged arteries that follow the process of atherosclerosis. According to the theory, triglycerides play an important role in the pathophysiological mechanism of increasing blood pressure.

One of the factors that influence cholesterol levels in the body is the individual's consumption patterns. The consumption pattern is the composition of food which includes the type and amount of foodstuffs on average per person per day, which is generally consumed by people in a certain period of time. The type of clams that is considered to have a high cholesterol content is the type of *Batissa violacea* (Pokeaclams) which is considered to be a cause of various cardiovascular diseases⁽¹⁰⁾. Pokea clams is bivalves that live in several rivers in Southeast Sulawesi that is unique compared to similar species from other regions⁽¹¹⁾.

For the Sampara community, clams are the main nutritional intake and often consumed. Clams is one of the main sources of animal protein with good protein content and high biological value. Clams protein is categorized as complete protein due to its high essential amino acid levels. In addition, clams also contains fat and water soluble vitamins as well as a major source of minerals that the body needs⁽¹⁰⁾.

Material and Method

This research uses observational analytic method with case control design. The study was located in Andepali Village, Andadowi Village, Pohara Village, Polua Village, Totombe Village, and Konggamea Village in the coastal area of the Pohara River, Sampara District, Konawe District, from March to July 2019. Using a purposive sampling method, a total sample size was determined. The 60 samples divided into 30 cases and 30 controls. Primary data were obtained from interviews about the consumption patterns of meat consumption of pokea clams, and lipids using the Semi-Quantitative Food Frequency Questionnaire (FFQ-SQ), and blood pressure examination with mercury sphygmomanometers while sampling blood is carried out by clinical laboratory personnel. Secondary data was obtained from service profile data at Puskesmas Sampara.

Findings:

Table 1. Analysis of the Relationship between Consumption Patterns of Pokea clams Meat with Total Cholesterol Levels in Sampara District

Consumption Pattern of Pokea Clams	Total Cholesterol level						p value	OR	95% CI	
	Abnormal		Normal		Amount				LL	UL
	n	%	n	%	N	%				
Sufficient	6	10	11	18,3	17	28,3	0,342	1,750	0,548	5,586
Less	21	35	22	36,7	43	71,7				
Total	27	45	33	55	60	100				

Table 2. Analysis of the Relationship between Lipid Consumption Patterns with Total Cholesterol Levels in Sampara District

Consumption Pattern of Lipid	Total Cholesterol level						p value	OR	95% CI	
	Abnormal		Normal		Amount				LL	UL
	n	%	n	%	n	%				
Risk	4	6,7	5	8,3	9	15	1,000	1,027	0,247	4,273
Not Risk	23	38,3	28	46,7	51	85				
Total	27	45	33	55	60	100				

Table 3. Relationship Consumption Patterns of PokeaClams with Triglyceride Level in the Community of Pohara, Konawe Regency.

Consumption Pattern of Pokea Clams	Triglyceride Level						p value	OR	95% CI	
	Abnormal		Normal		Amount				LL	UL
	n	%	n	%	n	%				
Sufficient	12	20	5	8,3	17	28,3	0,79	0,57	0,17	1,93
Less	25	41,7	18	30	43	71,7				
Total	37	61,7	23	38,3	60	100				

Table 4. Relationship Lipid Consumption Patterns with Triglyceride Levels in the Community of Pohara, Konawe Regency.

Lipid Consumption pattern	Triglyceride Level						p value	OR	95% CI	
	Abnormal		Normal		Amount				LL	UL
	n	%	n	%	n	%				
Risk	6	10	3	5	9	15	1,00	0,77	0,17	3,45
Non risk	31	51,7	20	33,3	51	85				
Total	37	61,7	23	38,3	60	100				

Discussion

Pokea clams (*Batissa violaceav* var. *Celebensis* von Martens, 1897) is a type of bivalvia of the *Corbiculidae* family that has a dark brown to blackish-purple shell and has a slightly flattened and rounded shape⁽¹⁰⁾. This type of clams has become one of the sources of community livelihoods around the Pohara River, Konawe Regency, and Southeast Sulawesi. These clams are usually sold in

the form of fresh whole, fresh peeled, and satay. Pokea clams are usually consumed in the form of stew by the local community⁽¹⁰⁾.

The study is in line with research conducted by Yeni et al⁽¹⁰⁾ regarding the effect of boiling on the content of fatty acids and cholesterol in pokea clams. The results in his research showed the fatty acid content of Pokea clams after boiling was relatively stable. Fresh and boiled

clam meat is identified as having fatty acids consisting of Saturated Fatty Acid or SFA, Mono Unsaturated Fatty Acid or MUFA and Poly Unsaturated Fatty Acid or PUFA. The highest total fatty acid content in fresh and boiled clam meat is SFA type of fatty acid which is dominated by palmitic acid.

In contrast to Sudayasa et al⁽¹²⁾ conducted research on the relationship of pokea clams consumption toward blood pressure in Pohara coastal communities. Based on the interview results, most of respondents consumed pokea clams meat by frying. In this study, most of respondents consumed pokea clam meat by boiling.

Apart from the consumption patterns of Pokea clams, factors that can affect total cholesterol levels are physical activity and obesity. Physical activity can be in the form of exercise and daily routine activities can reduce the risk of cardiovascular disease by maintaining the stability of the heart's pumping system and balancing blood cholesterol levels⁽¹⁰⁾. The more physical activity is carried out, the more ATP needs and will cause a lack of total cholesterol formation and Low Density Lipoprotein (LDL) cholesterol and an increase in High Density Lipoprotein (HDL) cholesterol⁽¹⁰⁾.

The results of bivariate analysis OR = 1.027, can be interpreted that respondents who consumed lipids were at 1,027 times greater risk of an increase in total cholesterol levels compared to respondents who did not consume lipids. Based on the respondents' characteristics, it is found that the comparison of respondents with normal total cholesterol levels with respondents with abnormal total cholesterol levels is 1: 1, which indicates that lipids affect the total cholesterol level in the body.

Based on the results of interviews with respondents using the FFQ-SQ questionnaire that was converted into the Nutrisurvey application (2007), the highest lipid consumption value was 142.2 g (risky or > 67 grams/day) and the lowest lipid consumption value was 4, 3 gr (no risk or ≤ 67 gram/day). The types of food that most influence the total value of lipid consumption are palm oil and chicken eggs.

Frequent consumption of high-fat foods is a major cause of increased total cholesterol in the blood. The high cholesterol level in the blood is a serious problem because it is one of the risk factors for various non-communicable diseases such as heart disease, stroke and diabetes mellitus⁽⁴⁾.

The results of this study are in line with research conducted by Yoentafara and Martini⁽⁴⁾ regarding the effect of diet on total cholesterol levels. The results of his study showed the value of $p = 0.285$ ($p > 0.05$), which showed no relationship between high-fat diets with total cholesterol levels. This research is inversely proportional to the results of a study conducted by Septianggi et al⁽¹³⁾, where the value of $p = 0.026$ ($p < 0.05$), which shows that there is a positive relationship between fat intake and total cholesterol levels in outpatient of coronary heart disease in the Tugurejo General Hospital Semarang in 2013.

The results of the study by Gayet-Boyer et al⁽¹⁴⁾ found no linear relationship between consumption of fat with HDL, LDL and total cholesterol levels. This is different from research conducted by Prabowo et al⁽¹⁵⁾ where the results of p value = 0,000 ($p < 0.05$) means that there is a significant relationship between diet and cholesterol levels both positive correlations the higher correlation of foods based on fatty diets, the higher the cholesterol level.

The meaninglessness in the results of the statistical test of this study might be because people in the Sampara area have a risk-free lipid consumption pattern or within safe limits in accordance with standard which states that lipid consumption is risky if the levels are > 67 grams/day and not at risk if the levels are ≤ 67 gram/day. Based on the results of interviews conducted during the study, most of respondents have reduced the consumption of foods with high fat content because it is related to their blood pressure.

Communities in Sampara Subdistrict, especially those who live around the Pohara River, often consume pokea clams (*Batissa violacea celebensis* von Marten, 1897). This clam is endemic because it is only found in the Pohara River, Konawe Regency, Southeast Sulawesi, about 25 km towards the estuary at a depth of 1-9 meters. Pokea clams have become an important commodity for the communities around the Pohara River, because they can be sold in the form of fresh, fresh peeled and satay so that they have the potential to become one of the regional primary products⁽¹⁰⁾.

Based on the results of bivariate analysis, there was no relationship between the pattern of consumption of Pokea clams on triglyceride levels in patients with hypertension in the District of Sampara. Based on the results of interviews, people more often process pokea

clam meat by boiling 2-3 times before consumption and then fried or sauteed. The use of cooking oil can add fatty acids in processed Pokea clams meat consumed by the communities.

Free fatty acids in coconut oil are saturated fatty acids that will be the ingredients of the formation of triglycerides and cholesterol in the blood. If consumption is carried out continuously for a long period of time it can cause blood fat levels to increase, resulting in the accumulation of a layer of fat in the blood vessels that makes blockages in blood vessels and causes blood pressure to increase⁽¹⁶⁾.

This is not in line with research conducted by Sudayasa et al⁽¹⁶⁾ which states that there is a relationship between Pokea clams consumption patterns and blood pressure in the coastal communities of the Pohara River, Sampara District. That is caused by differences in the processing of pokea clam meat by respondents. In a study conducted by Sudayasa et al⁽¹²⁾, most of respondents consumed Pokea clams meat by frying, while in this study, most respondents consumed pokea clam meat by boiling.

Repeated boiling can affect the meat content of Pokea clams. As stated by Yeni et al⁽¹⁰⁾ regarding the effect of boiling Pokea clams on the content of fatty acids and cholesterol, the content of fatty acids after boiling is relatively stable. Fresh and boiled clam meat is identified as having fatty acids consisting of Saturated Fatty Acid (SFA), Mono Unsaturated Fatty Acid (MUFA) and Poly Unsaturated Fatty Acid (PUFA). The highest total fatty acid content in fresh and boiled clam meat is SFA type of fatty acid which is dominated by palmitic acid. The total MUFA and PUFA content of fresh and boiled clam meat is higher than the SFA composition. MUFA and PUFA have an important role in reducing cardiovascular disease, type 2 diabetes, inflammatory diseases, and immune disorders. SFAs with a lower content have a role as triglycerides in the blood with a possibility of fatty acids suppress inflammation by inhibiting the biosynthesis pathway of leukotriene, which is unsaturated fatty acids that contain carbon released during the inflammatory process⁽¹⁰⁾.

Although in this study no relationship was found between consumption patterns of Pokea clams with increased levels of triglycerides in patients with hypertension, but there were more respondents in the case group who consumed less meat but experienced

an increasing blood pressure. These needs to get more attention considering there are some respondents who are still teenagers and have experienced increased blood pressure. The increasing blood pressure is not only influenced by the consumption pattern of pokea clam meat. Family history is one of the factors causing the increasing blood pressure in adolescents.

According to the research of Henuhili et al⁽¹⁷⁾, hypertension genes are dominant in every individual. Hypertension is in every generation. Even if someone does not inherit hypertension it will still be possible to have offspring who have hypertension. Inheritance of hypertension is not X-linked, meaning that genes on the genital chromosomes of either fathers or mothers can bequeath male or female offspring.

In addition, other factors that can also affect triglyceride levels are lifestyle such as lack of sports activities, lack of drinking mineral water, smoking, consuming alcohol and irregular eating patterns can result in higher levels of free fatty acids. The results of the bivariate analysis showed that there was no relationship between lipid consumption with triglyceride levels in hypertensive patients in Sampara District. According to Fentiana⁽¹⁸⁾, fat intake is the most dominant factor associated with obesity. Fat can affect health, including causing coronary heart disease, increased blood cholesterol levels and increased blood lipid levels.

Data from the measurements of height and weight of respondents in this study found the average body mass index is not normal (in the categories of less or more, and obesity) more than the normal category. However, in the results of interviews people do not like to consume foods that contain excess fat such as fried foods or coconut milk because many of the respondents are aged ≥ 35 years whose consumption patterns should be maintained, either those who have experienced complaints and those who have no complaints.

In line with research conducted by Hidayati⁽¹⁹⁾ which shows that there is no significant relationship between fat intake and triglyceride levels. Apart from fat intake, another thing that can increase triglyceride levels is an increase in carbohydrate intake wherein the formation of pyruvate and acetyl-CoA will cause an increase in the formation of fatty acids from acetyl-CoA. These fatty acids will be esterified with triphosphate which is produced from glycolysis and becomes triglycerides.

This research is inversely proportional to the research conducted by Nisa et al⁽²⁰⁾ that fat intake has a relationship with triglyceride levels ($\rho = 0.030$) and with a correlation coefficient of 0.299 which shows that increasing fat intake increases triglyceride levels. In accordance with the multivariate test, it was found that increasing 1 gram of fat intake would increase triglyceride levels by 0.311 mg/dL. These results are in line with previous research which states that fat intake is associated with triglyceride levels ($\rho = 0.001$) with each increase of 1 gram of fat/day will increase triglyceride levels by 0.109 mg/dL.

Although in this study there was no relationship between patterns of lipid consumption with triglyceride levels in hypertensive patients in Sampara District, but there are several other factors that influence the formation of triglycerides in the blood and can cause an increase in blood pressure. The results of the bivariate analysis showed that there was no relationship between carbohydrate consumption with triglycerides in hypertension in Sampara District.

The unrelated variables analyzed can be caused by blood pressure in addition to being influenced by consumption of Pokea clams and lipids, but can also be influenced by many factors. Another factor that can affect blood pressure is body mass index. Being overweight can increase the risk of hypertension five times higher than normal weight⁽²¹⁾.

Conclusion

There is no relationship between the consumption pattern of pokea clam meat (*Batissa violacea* var. *Celebensis* von Martens, 1897) and lipids with total cholesterol levels and triglyceride levels in hypertension patients in Sampara District. For future researchers, it is recommended to use a different research design from this study by adding and reviewing other variables, such as cross sectional or cohort studies by examining other factors to better support of the research results.

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References

1. Simumorang. Faktor-Faktor Yang Berhubungan Dengan Kejadian Hipertensi Pada Penderita Rawat Inap Rumah Sakit Umum Sari Mutiara Medan Tahun. *J Ilm keperawatan*. 2015;1(1).
2. Alifariki LO. Analisis Faktor Determinan Proksi Kejadian Hipertensi di Poliklinik Interna BLUD RSUD Provinsi Sulawesi Tenggara. *Medula*. 2015;3(1):214–23.
3. Kemenkes RI. Riset Kesehatan Dasar 2018. Jakarta; 2018.
4. Yoeantafara A, Martini S, Fakultas M, Masyarakat K, Airlangga U, Epidemiologi D, et al. Pengaruh Pola Makan Terhadap Kadar Kolesterol. *J MKMI*. 2017;13(4):304–9.
5. Badan Pusat Statistik Kabupaten Konawe. Kecamatan Dalam Angka Sampara 2017. Kabupaten Konawe: BPS Kab.Konawe; 2017.
6. Sugiharto. Faktor-Faktor Risiko Hipertensi Grade II Pada Masyarakat (Studi Kasus Di Kabupaten Karanganyar). Universitas Diponegoro; 2007.
7. Akuyam S., Aghogho U., Aliyu BA. Serum Total Cholesterol In Hypertensive Northern Nigerians. *Int J Med Med Sci*. 2009;1(3):73–4.
8. Roslizawaty, Rusli, Rani S., Suraidawati, Armansyah T. Z. Pengaruh Ekstrak Etanol Sarang Semut (*Myrmecodia* sp.) Lokal Terhadap Kadar Kolesterol Total Tikus Putih (*Rattus norvegicus*) Jantan Hiperkolesterolemia. *J Vet*. 2015;9(1).
9. Soleha M. Kadar Kolesterol Tinggi Dan Faktor-Faktor Yang Berpengaruh Terhadap Kadar Kolesterol Darah. *J Biotek Medisiana Indonesia*. 2012;1(2):85–92.
10. Yenni, Nurhayati, T., Nurjanah, Losung F. Kandungan Mineral, Proksimat dan Penanganan Kerang Pokea (*Batissaviolaceacelebensis* Marten 1897) dari Sungai Pohara Sulawesi Tenggara. In: *Prosiding Pertemuan I Imiah dan Seminar Nasional MPHPI*. Universitas Sam Ratulangi; 2011. p. 105-7.
11. Muzuni, Adi, D.A., Syarif S. Karakterisasi Fragmen Gen 18s Rrna Pokea (*Batissa Violacea Celebensis* von Martens, 1897) di Sungai Pohara Kecamatan Sampara Kabupaten Konawe. *J Biowallacea*. 2014;1(1):25–38.
12. Sudayasa P, Ruslan N, Kurniati I. Pengaruh Konsumsi Daging Kerang Pokea (*Batissa violacea*

- celebensis) Terhadap Tekanan Darah Pada Masyarakat Pesisir Pohara. 2017;515–22.
13. Septianggi, F.N., Tatik M. HSK. Hubungan Asupan Lemak dan Asupan Kolesterol dengan Kadar Kolesterol Total pada Penderita Jantung Koroner Rawat Jalan di RSUD Tugurejo Semarang. *J Gizi Univ Malang*. 2013;2(2):13–20.
 14. Gayet-Boyer C, Tenenhaus-Aziza F, Prunet C, Marmonier C, Malpuech-Brugere C, Lamarche B, et al. Is there a linear relationship between the dose of ruminant trans-fatty acids and cardiovascular risk markers in healthy subjects: results from a systematic review and meta-regression of randomised clinical trials. *Br J Nutr*. 2014 Dec;112(12):1914–22.
 15. Anis Prabowo, Weni Hastuti IMK. Hubungan Pola Makan dengan Peningkatan Kadar Kolesterol pada Lansia di Jebres Surakarta. *Motorik*. 2013;8(17):57–62.
 16. Sopiani, Selpia D., Herlina dan Saputra TH. Penetapan Kadar asam Lemak Bebas Pada Minyak goreng. *J Katalisator*. 2017;2(2).
 17. Henuhili V, Rahayu T, Nurkhasanah L. Pola Pewarisan Penyakit Hipertensi Dalam Keluarga Sebagai Sumber Belajar Genetika. In: *Prosiding Seminar Nasional Penelitian, Pendidikan dan Penerapan MIPA*. 2011. p. 242–7.
 18. Fentiana. Asupan Lemak Sebagai Faktor Dominan Terjadinya Obesitas Pada Remaja (16-18 Tahun) Di Indonesia (Data Riskesdas 2010). Universitas Indonesia; 2012.
 19. Diah O., Hidayati R. Hubungan Asupan Lemak Dengan Kadar Trigliserida Dan Indeks Massa Tubuh Sivitas Akademika Uny the Correlation Between Fat Intake, Triglyceride Levels, and Body Mass Index (Bmi) of the Academic Community From Yogyakarta State University. *J Prodi Biol*. 2017;6(1):25–33.
 20. Nisa, Fitria Zahrotun, Probosari, Enny., Fitrianti DY. Hubungan Asupan Omega-3 Dan Omega-6 Dengan Kadar Trigliserida Pada Remaja 15-18 Tahun. Universitas Diponegoro; 2017.
 21. Kautsar F, Syam A, Salam A. Obesity, Sodium and Kalium Intake and Blood Pressure of Students. *J MKMI*. 2014;10(4):187–92.

Modification of Ames Test According to Phenotype Features of Prototrophic *Escherichia Coli*

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Abstract

Background: Iraq is an oil country in addition to an agricultural economy so the using of pesticide has raised very dramatically to cater the food demands of increasing population. Thus, a continuous examination of pesticides is required. Ames test is a standard method for determining the carcinogenic compounds by induce back mutations in auxotrophic strain of *Salmonella typhimurium*- histidine negative (his⁻) and biotin-negative (bio⁻), but in our country-Iraq, this bacterial strain was unavailable in most time. However, this study designed to guess the possibility of employment prototrophic *Escherichia coli* according to phenotype features instead of *S. typhimurium*.

Method: A prototrophic *Escherichia coli* was sensitive to amikacin, erythromycin, chloramphenicol, ciprofloxacin, tobramycin and trimethoprim. The strain was exposed to different concentration of Chlorpyrifos (CPF) as a mutation inducer. The potentiality of mutagenesis of CPF was detected according to phenotype features using antibiotics susceptibility test (AST).

Result: Our result showed that the mutations were induced in some chromosomal genes of *E. coli* when exposed to CPF in high concentration 80-100%, while con. 10-70% were not. These genes encoded resistance to erythromycin, trimethoprim and tobramycin.

Conclusions: The modified Ames test can consider as a predictive tool for screening a potential carcinogenicity. The potential of genotoxic of the CPF has been detected.

Keywords: Mutagenic, carcinogenic, prototrophic *Escherichia coli*, chlorpyrifos.

Introduction

Our using and exposure to a wide diverse of chemical materials has increased significantly during the past decades. Oncological epidemiologists strongly suspected that the intrusion of these chemical compounds in the form of industrial pesticides, pollutants, food additives, hair dyes, cigarette smoke, and the like may play a influence role in the cause of malignant tumors in human¹.

Mutagenic chemical compounds are capable of causing cancers, and this interest has led to bulk of the programs of mutagenicity testing². Previous researches have revealed that some insecticides have mutagenic effectiveness in many biological test programs³. According to a genetic feature there is clear proof relationship between mutagenicity and carcinogenicity.

One study detected that approximately 90% of the chemical compounds demonstrated to be carcinogen are mutagen, they cause cancer by inducing mutations in somatic cells¹. Mutation may be caused in gene "point mutation" and this type of mutation was defined as "just a one base is altered or single or a relatively some bases are deleted or inserted", as large deletion or rearrangement of DNA as chromosomes break or rearrangement, or as gain or loss of whole chromosome⁴. These reports increased perception of the mechanisms of mutations and their function in cancer has stimulated efforts to identify environmental carcinogens agents that cause cancers⁴.

The observation that many carcinogens also are mutagens was the basis for development of the Ames test by Bruce Ames in the 1970. Dr. Bruce Ames and

his colleagues, studying the operon of histidine in *Salmonella typhimurium*, observed that histidine (-) auxotroph mutants were reverted to histidine (+) upon exposure to a mutagens⁵, so this test represent as a investigating method for the revealing of carcinogenic chemical compounds by testing the capability of chemical compounds to stimulate mutations in bacterial cell^{6,7}.

When exposed bacteria to a chemical agent and culturing in medium deficient-histidine, the average of back mutation (reversion) to prototrophic cell is detected by counting the number of bacterial colonies that are seen on the medium deficient-histidine^{6,8}. However, proving that a substance causes mutations in bacteria does not prove that it does so in human cells⁹, whereas some chemicals tested may not be mutagenic unless they are transformed into another, more active form. In animals, such transformations occur in the liver. Indeed, many known carcinogens are not actually carcinogenic compounds even they are altered by enzymes in the liver that function to destroy toxins and other materials that may be circulating in the blood. However, in some cases, these enzymes transform chemicals into more dangerous forms. For this reason, the extraction of a mammalian liver is added to the molten top-agar prior to plating the bacterial cells used in the Ames test (Fig. 1)⁵, however, several variations of the Ames test are possible⁸.

Chlorpyrifos (CPF): Chlorpyrifos (O,O-diet hylO-3,5,6-trichlor-2-pyridyl phosphorothioate; is a broad spectrum organophosphate insecticide used on animals, crops, and buildings, and in other placements, to inhibit and/or kill a many of pests, that including worms and insects¹⁰. In 1965 was first of introduce CPF into the market-place, has been used globally as a pesticides to control the harmful insects of agriculturally and in the homes¹¹. CPF acts on the nervous system of pest through inhibiting the acetylcholinesterase enzymes. World Health Organization WHO considered CPF is moderately hazardous to humans based on its acute toxicity¹². On the other hand, when humans exposure to high level of CPF that surpassing recommended amount has been related to persistent developmental disorders, neurological effects and autoimmune disorders¹³.

Materials Method

1. Overnight tryptic soy broth culture of prototroph *Escherichia coli* which resistant to (amikacin,

erythromycin, chloramphenicol, ciprofloxacin, tobramycin and trimethoprim).

2. Filter paper disks, sterile in Petri dish.
3. Muller Hinton agar.
4. 5 ml sterile tryptic soy broth in a test tube.
5. Chlorpyrifos in concentration 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% and 100%.

Procedure:

First Period:

1. For confirmation of *E. coli* sensitive to amikacin, erythromycin, chloramphenicol, ciprofloxacin, tobramycin and trimethoprim. Antibiotic susceptibility test (AST) were applied according to ((Schwalbe *et al.*, 2007 and Ferraro *et al.*, 2006)^{14,15}.
2. 0.1 ml of overnight culture *E. coli* were poured and spread on Muller Hinton agar, then leave at room temperature for 20 seconds.
3. With sterile forceps a sterile filter paper disk was placed perpendicularly at the center of the medium as shown in Figure 2.
4. With a sterile Pasteur pipette, enough of CPF were deposited just on the upper edge of the filter paper disk to saturate it, after that, the disk was pushed over with the pipette-tip onto the agar surface so it lies flat.
5. All four plates were incubated for 48 hours at 37°C.

Second Period:

1. The plates were examined.
2. When we observe a clear halo of revertant bacterial colonies surround the disk on the medium, within the inhibition zone, this may be due to mutations were occurred, Figure 3.
3. The scattered colonies were taken individually and cultured in new tryptic soy broth tube.
4. In new previous culture, the antibiotic susceptibility test was repeated, to confirmation if a mutation was accorded and to detect the site of mutation.
5. All the plates were incubated for 24 hours at 37°C.

Results

An application of our modified method to Ames test showed significant effect regarding the high

concentration of test compound CPF. Appearance of colonies within inhibition zone, may be indicator to obtain mutant strain. Furthermore, the number of apparent colonies relatively with concentration of CPF. However, the con. 10 to 70% of CPF were insignificant. Tab.1, present data of antibiotic susceptibility test (AST)

before and after exposure to different concentration of CPF.

In con. 80% and 90% *Escherichia coli* strain gained the ability to resistance to erythromycin and trimethoprim. In con. 100% gained the ability to resistance to erythromycin, trimethoprim and tobramycin.

Table 1. effective con. Of CPF according to modified method.

Antibiotics	Inhibition zone before exp./mm	Inhibition zone after exp./mm	CPF effect
	Co. 80%		
Amikacin	19/S	20/S	No
Chloramphenicol	18/S	18/S	No
Erythromycin	23/S	10/R	change
Ciprofloxacin	23/S	23/S	No
Tobramycin	16/S	17/S	No
Trimethoprim	19/S	1/R	change
Con. 90%			
Amikacin	19/S	19/S	No
Chloramphenicol	18/S	18/S	No
Erythromycin	23/S	11/R	change
Ciprofloxacin	23/S	23/S	No
Tobramycin	16/S	16/S	No
Trimethoprim	19/S	5/R	change
Con. 100%			
Amikacin	19/S	19/S	No
Chloramphenicol	18/S	19/S	No
Erythromycin	23/S	9/R	change
Ciprofloxacin	23/S	24/S	No
Tobramycin	16/S	7/R	change
Trimethoprim	19/S	3/R	change

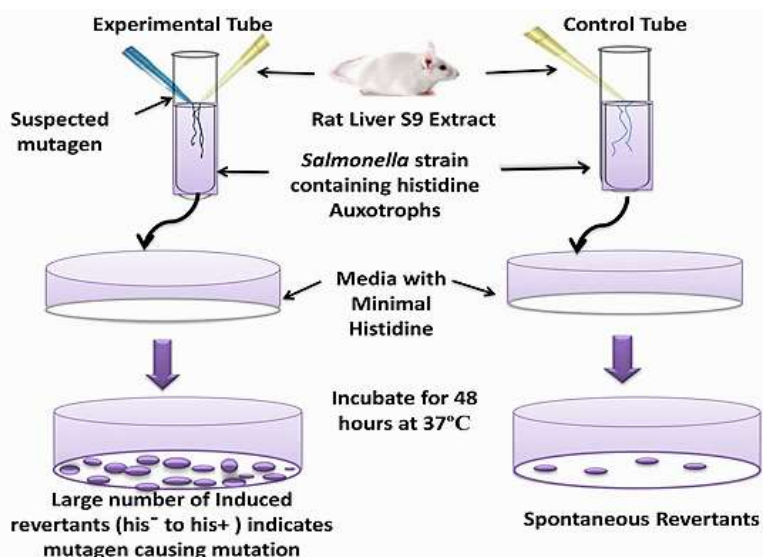


Figure 1. Genetic method for screening the mutagenicity in Salmonella strains⁵

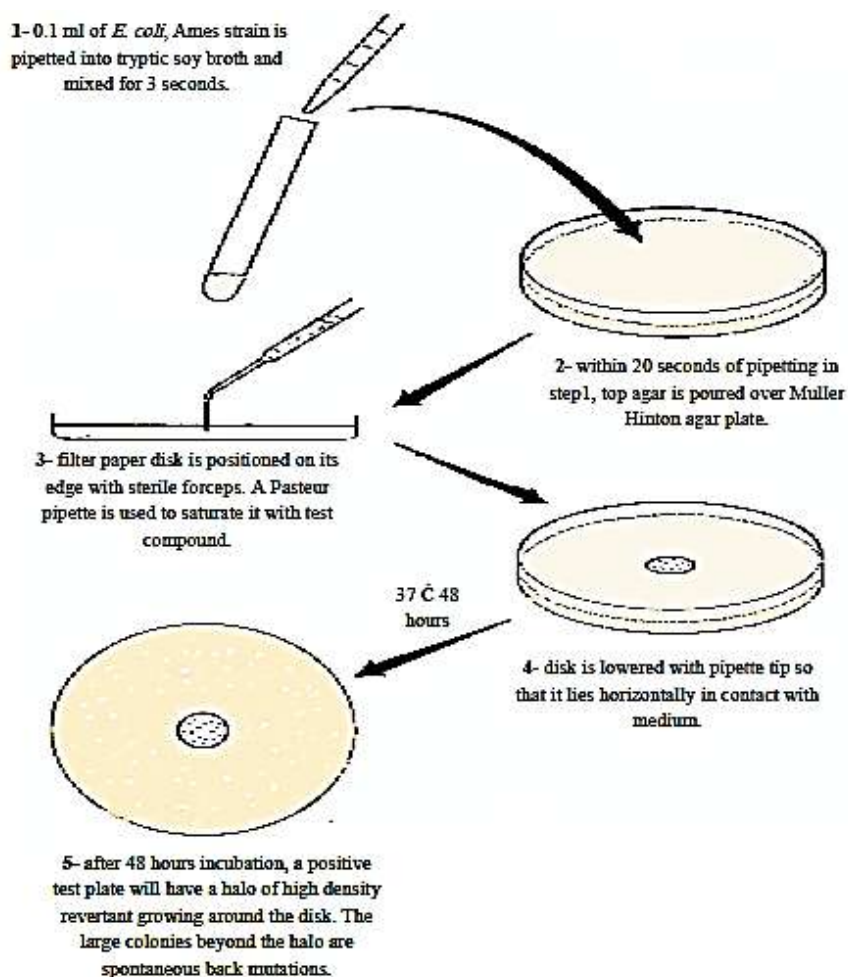


Figure 2. Procedure for performing a modified Ames⁶.

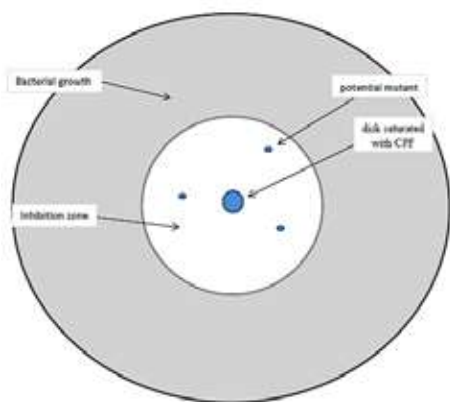


Figure 3. Illustrate the positive result of the modified Ames method.

Discussion

In our country (Iraq), some things were much difficult to obtain, due to wars and their results. One of

these is an auxotrophic strain of *Salmonella typhimurium* which employs in standard Ames test. Furthermore, in the last years, Iraq became open market to different unguaranteed materials and compounds, in addition, it is an agricultural economic so the using of pesticide has raised very dramatically to cater the food demands of increasing population. So that, we needed to modified method a test these compounds and passing this problem.

In our modified method, some steps of standard Ames test were ignored, such as using plates contain two layers of glucose–minimal salts agar and top agar. This traditional Ames test is quite fatigued and required long time for initial monitoring of mutagenic chemical compounds¹⁶. The Ames system has been continuously improved, such as the addition of *anr* mutation at the 48' mark of the *S. typhimurium* genomic map (strains TA1535, TA1537 and TA1538) to increase the membrane permeability to chemical compounds⁷.

(Boogaard et al. 2012)¹⁷, suggested modified Ames test as an indicator of the carcinogenicity of residual aromatic extract (RAE), and concluded that their modified Ames test can be used as a screening tool for assessing the potential carcinogenicity activity of RAEs. Since a cut-off value was determined to distinguish between carcinogenic and non-carcinogenic RAE samples. Their data demonstrate that RAEs with a mutagenicity index > 0.4 demonstrated potential carcinogenic activity to mouse skin following chronic exposure. RAEs with a mutagenicity index < 0.4 did not demonstrate a carcinogenic potential. However, the assay is not highly specific, which may result in a large number of false positives and identification of mutagens that are not necessarily carcinogens⁷.

The standard method to test chemical compounds for mutagenesis has been to measure the rate of back mutations in strains of auxotrophic bacteria. According to the Ames test a strains of *Salmonella typhimurium*, which is auxotrophic for “histidine negative” - (can not grow and be alive in the medium does not contain histidine)⁶. Furthermore, the *Salmonella* strain which applied in this test have various types of mutation in different genes at the operon of histidine, each of these mutations is engineered to be responsive to mutagenic-compounds that act by various mechanisms, since the mutations were designed in to these bacteria to make them more sensitive to a wide diverse of compounds⁴, while our method depending on inducing a new mutation in bacterial genomic, and measure its frequency. Our result revealed that *E. coli* strain gained the ability to resistance to erythromycin, trimethoprim and tobramycin, it seem that mutation may be happened in the genes responsible to for resistance to these antibiotics. however, these mutations may be accorded spontaneous¹. (Ameena S. 2010 and Hoeksema et al. 2019)^{18,19}, Proved that the genes administrator for to the following antibiotic resistance were located on the nucleotides of plasmid : ampicillin, amoxiclav, amoxicillin, cefixime, cephalaxine, cefotaxime, gentamycin, doxycyclin, nalidixic acid, rifampicin, nitrofurantoin, tetracycline and streptomycin. while the genes encoding resistance to the following antibiotics were located on the chromosomal nucleotides: chloramphenicol, erythromycin, amikacin, tobramycin, trimethoprim and ciprofloxacin. Furthermore, (Amira et al. 2018)²⁰, concluded that the genes related with resistance to macrolide antibiotic (*mphA*, *mrx*, *ereA*) were detected nine phenotypically resistant train *E. coli* to erythromycin and proved that the *dfiA* and *sul* genes

related with resistance to sulphonamides-trimethoprim were identified in 13 and 16 *E. coli* isolates, respectively.

In another hand, the genotoxic features of Chlorpyrifos have been reported in a different of tests in the previous years, but the study's results were not agree contradictory. Whereas there is increasing interest about the presence of genotoxin in the environments, the development of sensitive biomarker for identification of genotoxic influences in variety of organisms has gained importance, although, WHO presented report in specifications and evaluations for public health pesticides, and refer that CPF was non-mutagenic for organisms in low concentration, some studies confirmed that¹². The present study, modified Ames medium application test with the different concentrations of Chlorpyrifos revealed that a mutagenic-compound responsible with *E. coli* tester strain. Dose-quantity associate with increase in the number of revertant colonies of *E. coli* strains were reported. Furthermore, the number of spontaneous back mutations in negative control were less than all of the different treatment average of CPF. Several studies has been reported that CPF was genotoxic in *Chaannapuncteatus*. The exposure to 0.08 lg/l of Chlorpyrifos caused genital weakness in *Daphnia magna*¹¹. Additionally, (Kamilia et al. 2012)²¹, refer that CPF caused distortions in meiotic and mitotic chromosomes of mice as previously mentioned, the morphological distortions of sperms observed here might be because of stimulated modifications in testes DNA and sperm chromatin structures. These concepts of insecticide inflicted sperms toxicity may be supported by the high positive association observed between sperm-toxic and mutagenicity influences in mice.

Conclusion

This study refers to possibility of using a prototrophic *E. coli* strains *in vitro* instead of auxotrophic strain of *S. typhimurium* and application other method to detect a carcinogens, or the modified Ames test can consider as a predictive tool for screening a potential carcinogenicity. The potential genotoxic of the CPF has been detected.

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References

- 1) James G. Cappuccin and Chad Welsh Microbiology a Laboratory Manual. 11th ed. Pearson Education Limited. (2018).
- 2) Recep Liman. Mutagenicity and genotoxicity of dicapthon insecticide. Cytotechnology. 2014. 66:741–751.
- 3) Ajay Kumar, Kavita Sharma, Monika Tomar, Vinay Malik and Sudhir Kumar Kataria. Determination of Mutagenic Potential of Imidacloprid in Salmonella Typhimurium–TA 98 and TA 100 Following Bacterial Reverse Mutation Assay. International Journal of Biotechnology and Bioengineering Research. 2013. Volume 4, pp. 703-710.
- 4) Sebastian Tejs. The Ames test: a methodological short review. Environmental Biotechnology. 2008. 4, 7-14.
- 5) Joanne M. Willey, Linda M. Sherwood, Christopher J. Woolverton. Prescott's Microbiology. 9thed. The McGraw-Hill Companies, Inc. 2014.
- 6) Harold J. Benson. Microbiological Applications Laboratory Manual in general microbiology. 8th ed. The McGraw–Hill Companies. 2001.
- 7) Arriaga-Alba M., Montero_Montoya R., Javier J. Espinosa Aguirre. The Ames Test in Twenty-first Century. Research & Reviews: A Journal of Toxicology. 2012. Volume 2, Issue 1, Pages 23-37.
- 8) Michael J. Leboffe and Burton E. Pierce. Microbiology Laboratory Theory and Application. 3^{ed} ed. Morton Publishing Company, Inc. 2010.
- 9) Jacquelyn G. Black, Laura J. Black. Microbiology Principles and explorations. 7th ed. John Wiley & Sons, Inc. 2008.
- 10) Raed I. Lubbad. Long Term Toxicity of Chlorpyrifos and Diuron to Chickens and Rabbits. 2016. M.Sc. Thesis. The Islamic University–Gaza, Environmental Management and Monitoring. Gaza, Palestine.
- 11) Nobonita Deb and Suchismita Das. Chlorpyrifos Toxicity in Fish: A Review. Current World Environment. 2013. Vol. 8(1), 77-84.
- 12) World Health Organization (WHO). Specifications and Evaluations for Public Health Pesticides. CHLORPYRIFOS, O,O-diethyl O-3,5,6-trichloro-2-pyridyl phosphorothioate. 2012. online.
- 13) Keum Young Lee, Stuart E. Strand, and Sharon L. Doty. Phytoremediation of Chlorpyrifos by Populus and Salix. 2007. Int J Phytoremediation. 2012;14(1): 48–61.
- 14) Schwalbe, R., Moore, S.L., Goodwin, C.A. Antimicrobial Susceptibility testing protocols. CRC Taylor and Francis Group. 2007.
- 15) Ferraro, M.J., Jorgensen, H.J., Cullihan, R.D. Performance Standards for Antimicrobial disk susceptibility tests, approved standard. 9^{ed}. Formerly NCCLS. 2006.
- 16) Urvashi Vijay, Sonal Gupta, Priyanka Mathur, Prashanth Suravajhala, and Pradeep Bhatnagar. Microbial Mutagenicity Assay: Ames Test. Bio-protocol LLC.; 2018. Vol 8, Iss 06.
- 17) P. Boogaard, A. Hedelin, A. Riley, E. Rushton and M. Vaissiere. Use of the modified Ames test as an indicator of the carcinogenicity of residual aromatic extracts. 2012. CONCAWE Brussels December; 12/12.
- 18) Ameena S. M. Juma. Genetic Transformation in Antibiotic Resistant Escherichia coli O157:H7. 2010. Medical Journal of Islamic World Academy of Sciences; 18:2, 75-84.
- 19) Hoeksema M., Martijs J. Jonker, Stanley Brul and Benno H. ter Kuile. Effects of a previously selected antibiotic resistance on mutations acquired during development of a second resistance in Escherichia coli. 2019. BMC Genomics 20:284.
- 20) Amira A. Moawad, Helmut Hotzel, Heinrich Neubauer, Ralf Ehricht, Stefan Monecke et al. Antimicrobial resistance in Enterobacteriaceae from healthy broilers in Egypt: emergence of colistin-resistant and extended-spectrum β -lactamase-producing Escherichia coli. Gut Pathogens, 2018. BMC.; 10:39.
- 21) Kamilia Badrakhan Abdelaziz, Aida Ibrahim El Makawy, Ali Zain El-Abidin Abd Elsala, and Ahmed Mohamed Darwish. Genotoxicity of Chlorpyrifos and the Antimutagenic Role of Lettuce Leaves in Male Mice. 2012. Comunicata Scientiae.; 1(2): 137-145.

Central Venous and Arterial Gases Level Versus Lactate Clearance as an Indicator of Initial Resuscitation in Septic Patients in Intensive Care Unit

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Abstract

Objective: Aim of this study was to compare the central venoarterial carbon dioxide difference/arterial-central venous oxygen difference (P(va)CO₂/C(a-v)O₂) ratio versus lactate clearance as an indicator to evaluate the steps of initial resuscitation in septic patients.

Patients and Method: Our study was conducted in the ICU, Minia University Hospital. Eighty patients with severe sepsis or septic shock

Results: There was improvement in CVP, MAP, or Scvo₂ at T8 after early resuscitation with no significant differences between group 1 and group 2 and inside each group. There were no significant difference in P(v-a)CO₂/C(a-v)O₂ ratio at T0 and at T8 at group 1. However there was higher lactate level at T0 and exhibited significantly lower at T8 in group 2.

Conclusion: Further clinical trials are needed to conclusively establish lactate clearance as a resuscitation endpoint and an outcome measure to be targeted during the most proximal phases of severe sepsis and septic shock

Keywords: CVP; MAP; Scvo₂.

Introduction

Sepsis is one of the most common causes of death in the intensive care unit (ICU). It is difficult to be diagnosed due to multiple comorbidities and underlying diseases in these patients^[1, 2].

Sepsis is considered a complex syndrome characterized by presence of organ dysfunction mediated by different mechanisms of cell damage resulting in more than 30% mortality rate^[3,4]. Although

sepsis involve microvascular anomalies and constitute a central element of such organ dysfunction through decrease in oxygen supply and/or deficient utilization of the available oxygen^[5].

Severe sepsis and septic shock is a life-threatening condition for patients of intensive care unit (ICU)^[6,7]. Promoted practice for septic shock therapy is largely based on a study by Rivers et al. which developed a protocol known as early goal-directed therapy (EGDT)^[8].

The initial resuscitation of the septic patients includes anticipation for the need for fluid resuscitation, antimicrobials, and possibly vasoactive medications (vasopressors)^[9,10].

In a cellular hypoxia anaerobic carbon dioxide increases as hydrogen ions generated by anaerobic sources of energy are buffered by bicarbonate^[11]. Consequently, a rise in the respiratory quotient (VCO₂/

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VO₂ ratio) reflects the presence of global anaerobic metabolism^[12].

The P(v-a)CO₂/C(a-v)O₂ ratio is calculated from several parameters based on a known formula that mainly involves ScvO₂, hemoglobin (Hb), arterial oxygen saturation (SaO₂), and P(v-a)CO₂^[13]. Therefore, a simple and rapid method for identification of a high P(v-a)CO₂/C(a-v)O₂ ratio would be of substantial benefit, and the factors contributing to a high P(v-a)CO₂/C(a-v)O₂ ratio are worthy of consideration in the clinical setting^[14].

Sepsis is a disease characterized by hypercatabolism with increased demand for oxygen due to elevated consumption in tissue^[15]. Early therapy with optimization of blood volume, hemoglobin levels and/or use of inotropic agents favors the patient's prognosis^[16].

Despite questioning relating to the mechanisms of hyperlactatemia,^[17-19] this is a well-recognized instrument for diagnosing hypoperfusion and occult tissue hypoxia, and it is also used as a prognostic index among septic patients^[20]. However, although hyperlactatemia is generally measured in the arterial blood, the ideal collection site has not been clearly established^[21].

Patients and Method

Our study was conducted in the ICU, Minia University Hospital. Eighty patients with severe sepsis or septic shock were divided into two groups: group 1, resuscitated to normalize CVP, MAP, and P(va)CO₂/C(a-v)O₂ ratio; and group 2, resuscitated to normalize CVP, MAP, and lactate clearance. Whereas mortality was followed up for 28 days.

Inclusion Criteria:

- Septic adult patients who were sequentially admitted to ICU and required central venous catheters for resuscitation and met the criteria of sepsis were eligible for the study.
- Age: ≥ 18 to ≤ 65 years
- Sex: male and female

Exclusion Criteria:

- Patients less than 18 years or more than 65 years
- Patients who were unable to complete the assessment tools

- Patients with no relatives to sign the consent
- Patients admitted to intensive care unit not due to sepsis
- Patients had a contraindication to central venous catheterisation
- Pregnancy

Parameters to be assessed:

- The admission characteristics, pre-existing conditions and acquired complications in the intensive care unit will be recorded.
- The inclusion time (T₀) and study enrollment will be defined as the moment at which central venous pressure (CVP) monitoring begin after intensive care unit (ICU) admission.
- The demographic characteristics including the Acute Physiology and Chronic Health Evaluation II (APACHE II) score, the Sequential Organ Failure Assessment (SOFA) score, use of inotropes and type of organism.
- The global hemodynamic including HR, MAP, CVP, arterial, and central venous blood gas analyses were simultaneously performed on the T₀ and T₈.
- Measurements in this study included determination of the following variables: -Pao₂
- Arterial carbon dioxide tension (Paco₂) -central venous oxygen tension (Pvo₂) -central venous carbon dioxide tension (Pvco₂) -Sao₂, and Scvo₂ -The Hb and lactate level were measured from the arterial blood. -The arterial oxygen content (Cao₂) = $(1.34 \times \text{Sao}_2 \times \text{Hb}) + (0.003 \times \text{Pao}_2)$ -central venous oxygen content (Cvo₂) = $(1.34 \times \text{Svo}_2 \times \text{Hb}) + (0.003 \times \text{Pvo}_2)$ -arteriovenous oxygen content difference (C(a-v)O₂) -venoarterial CO₂ tension difference (P(v-a)CO₂) -P(v-a)CO₂/C(a-v)O₂ ratio -Lactate clearance rat = $(\text{T}_0 \text{ lactate} - \text{T}_8 \text{ lactate}) / (\text{T}_0 \text{ lactate}) \times 100\%$
- Prediction of ICU mortality at day 28.

Statistical Analysis: The patients were divided into 2 groups: group 1; P(v-a)CO₂/C(a-v)O₂ ratio group and group 2; Lactate clearance group. A descriptive analysis was performed. All data are expressed as the mean \pm SDs and medians (25th-75th percentiles) unless otherwise specified. Mann-Whitney tests were used to compare the groups in terms of the continuous variables, and χ^2 and Fisher exact tests were used to

compare the categorical variables between groups. Pairs of continuous variables were analyzed using linear regressions. All comparisons were 2 tailed, and $P < .05$ was required to exclude the null hypothesis. Statistical analyses were performed with the SPSS 13.0 software package (SPSS Inc, Chicago, Ill) and MedCalc 11.4.3.0 software (Mariakerke, Belgium).

Results

The relevant hemodynamic and global oxygen metabolic parameters at T0 and T8 for the LC and non-LC groups are shown in Tables 1 and 2, respectively. There was improvement in CVP, MAP, or Scvo₂ at T8 after early resuscitation with no significant differences between group 1 and group 2 and inside each group. There were no significant difference in P(v-a)CO₂/C(a-v)O₂ ratio at T0 and at T8 at group 1. However there was higher lactate level at T0 and exhibited significantly lower at T8 in group 2.

Table 1: Hemodynamic and related variables in group 1 at T0 and T8

Variables	T0	T8	P
HR (beats/min)	98 ± 27	99 ± 22	0.563
MAP (mm Hg)	89 ± 21	85 ± 14	0.512
CVP (mm Hg)	10 ± 3.5	9.7 ± 4	0.089
Scvo ₂ (%)	76 ± 9	75 ± 13	0.123
C(a-v)O ₂ (mm Hg)	3.48 ± 2.05	3.7 ± 1.6	0.132
P(v-a) CO ₂ (mm Hg)	6.4 ± 5.1	7.3 ± 4.5	0.978
P(v-a) CO ₂ /C(a-v)O ₂ ratio (mm Hg/mL)	1.87 ± 1.55	2.1 ± 1.0	0.538
No. of patients with NE (%)	20/34 (59)		0.797
NE dose (µg kg ⁻¹ min ⁻¹)	0.18 ± 0.25	0.32 ± 0.6	0.588

HR indicates heart rate; CVP, central venous pressure; MAP, mean arterial pressure; (P(v - a)co₂) veno-arterial gradient in carbon dioxide tension, (C(a - v)O₂) arteriovenous gradient in oxygen content; NE, norepinephrine, P value is significant if less than 0.05

Table 2. Hemodynamic and related variables in group 2 at T0 and T8.

Variables	T0	T8	P
HR (beats/min)	98 ± 22	92 ± 21	0.123
MAP (mm Hg)	90 ± 17	90 ± 15	0.215
CVP (mm Hg)	9 ± 3	8.5 ± 3	0.334
Scvo ₂ (%)	72 ± 11	77 ± 9	0.760
Lactate (mmol/L)	2.9 ± 2.2	1.3 ± 0.8	0.007*
No. of patients with NE (%)	28/50 (56)		
NE dose (µg kg ⁻¹ min ⁻¹)	0.15 ± 0.25	0.24 ± 0.31	0.904

HR indicates heart rate; CVP, central venous pressure; MAP, mean arterial pressure; NE, norepinephrine, * $P < 0.05$ is significant between T0 and T8 inside group 2

Discussion

Severe sepsis and septic shock are leading causes of death in the world [22]. mortality rate remains high in septic shock [23]. There is a need to test the prognostic value of factors that could be used for guiding therapy after the initial resuscitation.

The results of our study reported that a protocol targeting lactate clearance of at least 10% or more, as an evidence of adequate tissue oxygen delivery and a measurement of total body oxygen metabolism and was compared with the P(v-a)CO₂/C(a-v)O₂ ratio when resuscitating the septic patients at time of admission and 8 hours after the initial resuscitation.

Our results on P(v-a)CO₂/C(a-v)O₂ ratio demonstrated that, although the target indicator of the initial resuscitation of P(v-a)CO₂/C(a-v)O₂ ratio around 1.68 or low was achieved in 85% of patients in group 1, 45% mortality was recorded, with no statistically significant difference between survivors and nonsurvivors ($P > 0.05$).

Our results demonstrated that target indicator of lactate clearance of 10% or more was achieved in 70% of patients in group 2. On comparing it with P(v-a)CO₂/C(a-v)O₂ ratio as goals of the initial sepsis resuscitation, we found that targeting lactate clearance of at least 10%, as evidence of adequate tissue oxygen delivery and a measure of total body oxygen metabolism when resuscitating patients with severe sepsis and septic shock.

The present research showed discrepancy between lactate and P(v-a)CO₂/C(a-v)O₂ ratio as regards their correlation with mortality and, as we demonstrated, the target goal of lactate clearance of 10% or more was achieved in 70% of patients in group 1, but with a mortality of 30%. Hence, this group had 15% lower in-hospital mortality than those resuscitated to P(v-a)CO₂/C(a-v)O₂ ratio around 1.68 or low (30 vs. 45%, respectively), with a statistically significant difference.

In our study, basal lactate was significantly higher ($P < 0.05$) in nonsurvivors compared with survivors.

Monnet et al [24] also reported that the P(v-a)CO₂/C(a-v)O₂ ratio is predictive of increases in VO₂, but the Scvo₂ value is not. These authors demonstrated that a P(v-a)CO₂/C(a-v)O₂ ratio greater than 1.8 is predictive of VO₂ increases of more than 15% in response to increases in DO₂ when the Scvo₂ is greater than 70%.

The arterial lactate level is well known to reflect ongoing metabolism and serves as an indicator of anaerobic metabolism, and LC is associated with mortality in critically ill patients [25,26]. Although the use of LC is limited to a certain degree, it has generally been accepted for use as an indicator of oxygen debt in clinical practice, and LC is particularly well accepted for this purpose. Therefore, it was relatively reasonable to use LC as an indicator of anaerobic metabolism in our study. Thus, VO₂/DO₂ dependence has been considered to be a hallmark of tissue hypoxia and the activation of anaerobic metabolism [25,27], although it has been challenged because of the methodological limitations (mathematical coupling) in the VO₂/DO₂ relationship assessment [28].

Conclusion

Lactate clearance provide useful information for assessing the initial resuscitation of the septic patients in ICU after 8 hours, than P(v-a)CO₂/C(a-v)O₂ ratio. in addition to its simplicity in measurement away from miscalculation of P(v-a)CO₂/C(a-v)O₂ ratio assessment parameters. Further clinical trials are needed to conclusively establish lactate clearance as a resuscitation endpoint and an outcome measure to be targeted during the most proximal phases of severe sepsis and septic shock.

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References

1. Novosad SA, Sapiano MRP, Grigg C, et al. Vital signs: epidemiology of sepsis: prevalence of health care factors and opportunities for prevention. *Morb Mortal Wkly Rep*. 2016;65(33):864–869.
2. Vincent J-L, Rello J, Marshall J, et al. International study of the prevalence and outcomes of infection in intensive care units. *JAMA*. 2009;302(21):1303–1310.
3. D.C. Angus, T. van der Poll. Severe sepsis and septic shock. *N Engl J Med*, 369 (2013), pp. 840-851
4. D. Angus, C.A. Pereira, E. Silva. Epidemiology of severe sepsis around the world. *EndocrMetab Immune Drug Targets*, 6 (2006), pp. 207-212
5. M. Singer. Cellular dysfunction in sepsis. *Clin Chest Med*, 29 (2008), pp. 655-660
6. Jawad I, Luksic I, Rafnsson SB. Assessing available information on the burden of sepsis: global estimates of incidence, prevalence and mortality. *J Global Health* 2012; 2: 010404.
7. Levy MM, Artigas A, Phillips GS. Outcomes of the Surviving Sepsis Campaign in intensive care units in the USA and Europe: a prospective cohort study. *Lancet Infect Dis* 2012; 12: 919-924.
8. Rivers E, Nguyen B, Havstad S. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *New Eng J Med* 2001; 345: 1368-1377.

9. R.P. Dellinger, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012 Crit Care Med, 41 (2) (2013), pp. 580-637
10. J.L. Vincent, H. Gerlach. Fluid resuscitation in severe sepsis and septic shock: an evidence-based review Crit Care Med, 32 (11 Suppl.) (2004), pp. S451-S454
11. Gutierrez, G. A mathematical model of tissue-blood carbon dioxide exchange during hypoxia. Am J Respir Crit Care Med 2004;169:525-533. [12. Jakob, SM, Groeneveld, AB, Teboul, JL. Venous-arterial CO₂ to arterial-venous O₂ difference ratio as a resuscitation target in shock states? Intensive Care Med 2015; 41: 936-938.
13. He, H, Liu, D. Understanding the calculation of central venous-to-arterial CO₂ difference/arterial-central venous O₂ difference ratio. Shock 2017; 48: 690.
14. Mallat, J., Lemyze, M., Tronchon, L., Vallet, B. & Evenin, D. Use of venous-to-arterial carbon dioxide tension difference to guide resuscitation therapy in septic shock. World J Crit Care Med. 5(1), 47-56 (2016).
15. Ciarka A, De Backer D, Vincent JL. Lactic acidosis in the critically ill. Acta Clin Belg. 2000;55(6):295-9.
16. Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med. 2001;345(19):1368-77.
17. De Backer D. Lactic acidosis. Minerva Anesthesiol. 2003;69(4):281-4
18. Gutierrez G, Wulf ME. Lactic acidosis in sepsis: another commentary. Crit Care Med. 2005;33(10):2420-2.
19. Valenza F, Aletti G, Fossali T, et al. Lactate as a marker of energy failure in critically ill patients: hypothesis. Crit Care. 2005;9(6):588-93.
20. Bakker J, Gris P, Coffernils M, Kahn RJ, Vincent JL. Serial blood lactate levels can predict the development of multiple organ failure following septic shock. Am J Surg. 1996;171(2):221-6.
21. Shapiro NI, Howell MD, Talmor D, et al. Serum lactate as a predictor of mortality in emergency department patients with infection. Ann Emerg Med. 2005;45(5):524-8.
22. Le Gall JR, Lemeshow S, Saulnier F. A new Simplified Acute Physiology Score (SAPS II) based on a European/North American multicenter study. JAMA 1993; 270:2957-2963.
23. COITSS Study Investigators, Annane D, Cariou A, Maxime V, Azoulay E, Dhonneur G, Timsit JF, et al. Corticosteroid treatment and intensive insulin therapy for septic shock in adults: a randomized controlled trial. JAMA 2010; 303:341-348.
24. X. Monnet, F. Julien, N. Ait-Hamou, M. Lequoy, C. Gosset, M. Jozwiak, et al. Lactate and venoarterial carbon dioxide difference/arterial-venous oxygen difference ratio, but not central venous oxygen saturation, predict increase in oxygen consumption in fluid responders Crit Care Med, 41 (2013), pp. 1412-1420
25. J. Bakker, M. Coffernils, M. Leon, P. Gris, J.L. Vincent. Blood lactate levels are superior to oxygen derived variables in predicting outcome in human septic shock Chest, 99 (1991), pp. 956-962
26. M.A. Régnier, M. Raux, Y. Le Manach, Y. Asencio, J. Gaillard, C. Devilliers, et al. Prognostic significance of blood lactate and lactate clearance in trauma patients. Anesthesiology, 117 (2012), pp. 1276-1288
27. Z. Zhang, X. Xu. Lactate clearance is a useful biomarker for the prediction of all-cause mortality in critically ill patients: a systematic review and meta-analysis. Crit Care Med, 42 (2014), pp. 2118-2125
28. D.M. Yealy, J.A. Kellum, D.T. Huang, A.E. Barnato, L.A. Weissfeld, F. Pike, et al. A randomized trial of protocol-based care for early septic shock N Engl J Med, 370 (2014), pp. 1683-1693 [14]

Hematological Study and Estimation of Trace Elements in Patient with Thalassemia

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Abstract

Anemia is a deficiency of red blood cells which can be caused either by too rapid loss or by too slow production of red blood cells. Blood sample from thalassemia and normal were collected, serum analysis. The concentration of hemoglobin, white blood cell count was lower in-patient group than normal. The level of nickel, magnesium in serum of patient were $0.213 \pm 0.001 \mu\text{mole/L}$, $15.44 \pm 1.77 \mu\text{mole/L}$ While in normal 0.0321 ± 0.0035 and $13.34 \pm 1.92 \mu\text{mol/L}$ respectively

Keywords: Thalassemia, Serum, Nickel. hematology.

Introduction

Thalassemia is an inherited disorder by a normal hemoglobin, in normal hemoglobin, the number of α and β chain is equal, in thalassemia the number of these chains is not equal, this causes of the precipitation of the polypeptide chains leading to defective formation of RBCs⁽¹⁾. Thalassemia is problem of complex causes and is related with many factors, is an indicator of poor health and nutrition, hemoglobin is transfer in circulation with RBC⁽²⁾. The uptake of oxygen is affected by smoking and altitude and physiological factor and the body can alter blood volumes and hemoglobin concentrations to conciliate the necessity for oxygen.⁽³⁾

The aim of this study was to estimate hematological parameter in thalassemia Patients in comparing with healthy control.

Materials and Method

Thirty patients (15 males, 15 females) with thalassemia enrolled in this study with age from (30–42) years.

Data were collected from patient including name, gender, family history and other systemic diseases, while control group 20 (10 males, 10 females) and they were in healthy condition with age range from (30–45) years.

Sample of blood were collected from patient & healthy control for hematological parameters. Twenty μl of blood was added for 5 ml of Drabkin's solution, mixing and incubated for 5 min at 37°C and results were estimated by using Hb meter at 450 nanometers wavelength⁽⁴⁾. The content of trace element was determined by atomic absorption spectrophotometer⁽⁵⁾.

The results were analyzed using T-Test and level of significant at $p < 0.05$.

Result and Discussion

The present study describes that the number of thalassemia patient and normal group. The gender differences between male and female as a behavior, nutrition, lifestyle or stress, the present study was no significant $p < 0.05$ differences between male and female Table 1, the result contrast with result of Al-jifri 2017⁽⁶⁾.

Table 1: Age mean average in thalassemia and normal group

Sample	No. of Males	Mean Year	No. of Females	Mean Year	Total
Normal	10	37.1	10	36.6	20
Thalassemia	15	38.2	15	39.1	30

The result obtained indicated that very different between patient and control with different metals by using atomic absorption, there was significant decrease in concentration of nickel and magnesium in patient as compared with control. Table 2. The deficiencies of trace elements might be a contributing factor development of iron deficiency anemia in this study Table 2, show that there was significant decrease concentration of

nickel and magnesium among thalassemia patient as compared with control group, this result contrast with result of Abass in 2013⁽⁷⁾ and Gathwan in 2016⁽⁸⁾, they found the concentration of magnesium in saliva lower than in control group and Abd in 2017⁽⁹⁾ they found lower concentration of nickel and magnesium in anemic patient as compared with control.

Table 2: Nickel and magnesium comparison between patient and control (Mean ± SD)

Metal	Thalassemia Group (Mean±SD) µmole/L	Control Group (Mean±SD) µmole/L	P-value
Nickel	0.023 ± 0.001	0.032±0.0035	p<0.05
Magnesium	15.44±1.77	13.34 ± 1.92	p<0.05

In addition, there was significant decrease in concentration of hemoglobin and white blood cells count in blood of patient as compared with control Table 3 and this result contrast with result obtained in 2012 by Akinbami⁽¹⁰⁾.

Table 3: Total hemoglobin and White blood cells comparison between patient and control (Mean± SD)

Sample	Thalassemia Group (Mean±SD) µmole/L	Control Group (Mean±SD) µmole/L	P-value
HB (gm/100 ml blood)	9.73± 1.72	13.1± 1.91	p<0.05
Total WBC (cell/µL)	4.88±2.7	5.78± 2.1	p<0.05

In conclusion of this study the changes of hematological and metal parameter can be depended on in diagnosis of anemia.

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References

- Sernbulingar K., Sernbulingar P. Essentials of physiology for dental students. Jaypee Brothers Medical Publishers. USA. 2016.
- Christine A., Northrop C., David I. Biomarker and differentiation of anemia and their clinical usefulness. J. Blood medicine. 2013; 4: 11-22.
- United nations children’s fund, World Health Organization (WHO), iron deficiency anemia: Assessment, prevention and control; A guide for program managers. Geneva, Switzerland: WHO/NHD/01.3. 2001.
- Markarem, A. Clinical chemistry: Principles and techniques, 2nd. Edition, Hargeston, 1974; 1128–1135.
- Sunderman J., Marzouk R., Crisostomo A., Weatherby DR. Electrothermal atomic absorption spectrophotometry of nickel in tissue homogenates. Annals of Clinical and Laboratory Science, 1985; 15(4): 299-307.
- Al-Jiffri EH. Association between adipocytokine, systemic inflammation and oxidative stress biomarkers among type 2 diabetic patient. Advan. Res GastroenteroHepato. 2017; 5(4): 1- 6. DOI:10.19080/argh.2017.05.555669
- Abass SM. Surface properties of heat treated with different duration of titanium alloy dental implants. J College Dentis. 2013; 25 (3).

8. Gathwan KH., SuhaTA., ShathaKJ., Ali H. Some salivary constituents changes in anemic patients .Inter. J. Advance Res. Biol Sci. 2016; 3(3): 4-16.
9. AbdST., AbdullaWL., GathwanKH., JawadSK., Kadim MS.Estimation of some metals and hematological parameters in anemic patients in comparing to healthilysubject : A comparative study. Int JSci. Nature. 2017; 8(2): 193-196.
10. Akinbami A., Dosunmu A., AdedrinA., OshinaikeO., Adebola P., ArogundaceO. Haematological values in homozygous sickle cell disease in steady state and hemoglobin phenotypes AA controls in Lagos, Nigeria. BMC Res NotesAA 2012;doi: 10.1186/1756-0500-5-396.

Assessment of Survival and Function of Heterotopic Auto-transplanted Thyroid Tissue after Total Thyroidectomy for Non-toxic Multinodular Goiters

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Abstract

Background/Objective: Limited animal and human studies have shown function, albeit inadequate, of implanted thyroid tissue in muscles. This work aimed to ascertain results in a larger number of patients, finding practical method for implantation, studying the effect of changing weight of implant and effect of passage of time on its function. Method: Forty patients had total thyroidectomy for simple multinodular goiters. A piece of the excised gland was finely minced, mixed with saline as emulsion, and injected in thigh muscles. Twelve patients had 5-g implants, while 28 patients had 10-g implants. Four parameters were studied at 2 months, 6 months, and 12 months: technetium isotope uptake by the implant; thyroid stimulating hormone (TSH); free T3 (FT3); and free T4 (FT4). Results: All auto transplanted thyroid tissue survived and functioned. After 12 months, mean values (_ standard deviation) of isotope uptake, TSH, FT3, and FT4 of the 5-g implants were 0.44 _ 0.16%, 27.74 _ 30.4 UI/mL, 3.07 _ 1.10 pg/mL, and 1.01 _ 0.3 ng/dL, respectively. Those for the 10 g implants were 0.71 _ 0.20%, 22.78 _ 19.7 UI/mL, 3.92 _ 1.2 pg/mL, and 1.05 _ 0.3 ng/dL, respectively. Ten-gram implants showed significantly higher isotope uptake than 5-g. TSH, FT3, and FT4 significantly improved over the period of 1 year.

Conclusion: Injection of thyroid tissue suspension is a simple method for thyroid auto transplantation. TSH was elevated in the majority to maintain normal or near normal thyroid hormones. Ten-gram implants showed higher isotope uptake than 5-g, although this difference was not reflected by thyroid hormone profile. The implant seemed to function better with the passage of time from 2 months to 12 months.

Keywords: *Multinodular goiter; thyroid auto transplantation; thyroidectomy.*

Introduction

Whenever surgery is indicated for a simple multinodular goiter, the current trend is to do total thyroidectomy.^{1,2} Inevitably this makes the patient dependent on replacement therapy for life. Although

it seems relatively easy to control hypothyroidism by levo-thyroxine, from the patient's point of view, a daily dependence on it and regular visits to hospital to check hormone levels are burdensome. Other problems that may interfere with reaching a euthyroid status using replacement therapy are malabsorption³ and noncompliance of patients.⁴ The clinical application of transplantation in the endocrine field, by auto transplantation of endocrine organs for hormone replacement has already been established in the field of parathyroid surgery. Before applying the same principles on the thyroid gland in humans, studies have been done on animals. Autologous transplantations were found to be successful in 70% of cases and histological

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examinations showed normal thyroid architecture.⁵⁻⁸ Very few studies have addressed this issue in humans. The number of patients in each study was very small,⁹⁻¹² the largest study including only 15 patients.¹² Furthermore, the study methodology was not consistent.

The aims of the current work were to ascertain these results in a larger number of patients, find a practical method of ransplanting sizable thyroid tissue, and study the effects of changing weight of implant and passage of time on its function.

Patients and Method

This case series study was conducted at Minia University Hospital and included 40 patients with simple multi nodular goiters who were indicated for total thyroidectomy because of compression manifestations, and where nodularity extended to both lobes. Children, unwilling patients, and those who had any clinical or ultrasound suspicion of malignancy were excluded. Similarly, those with a family history of thyroid cancer and history of neck irradiation were excluded because they constitute a high risk of developing thyroid cancer. The study included 36 women and four men. Written informed consent was obtained from all patients, stressing the importance of regular follow up. Preoperative evaluation followed the same standard protocol and included a thorough history, examination, thyroid function tests, neck ultrasound, and fine-needle aspiration cytology of a dominant or suspicious nodule.

Total thyroidectomies were performed under general

anesthesia. During post excision hemostasis and closure a member of the operating team performed the auto transplantation preparation at a side table. The healthiest looking part of the thyroid was chosen. The slightest gross suspicion of malignancy led to termination of the implantation procedure. Intraoperatively, two patients were excluded from the study on gross picture suspicion of malignancy. Neither showed cancer on histological examination of postoperative paraffin sections.

The initial 12 patients received 5-g implants, while the remaining 28 received 10-g implants. The tissues to be transplanted were very finely divided using a pair of scissors and made into an emulsion by adding them to saline in a 20-mL syringe. This was attached to a 2.4 mm-caliber needle. A 3-mm incision was made in the anterolateral aspect of the middle third of the thigh. Through this incision the thyroid tissue emulsion was injected in 8e10 sites in the thigh muscles by changing the direction and depth of needle introduction.

Results

Apart from minor complications, postoperative courses were uneventful. Temporary recurrent laryngeal nerve occurred in one patient and resolved spontaneously in 4 weeks. Temporary hypoparathyroidism occurred in 11 patients and was controlled by oral calcium and vitamin D. The condition resolved within 3e7 weeks. There were no complications related to the auto transplantation site. None of the excised thyroids showed histological evidence of malignancy.

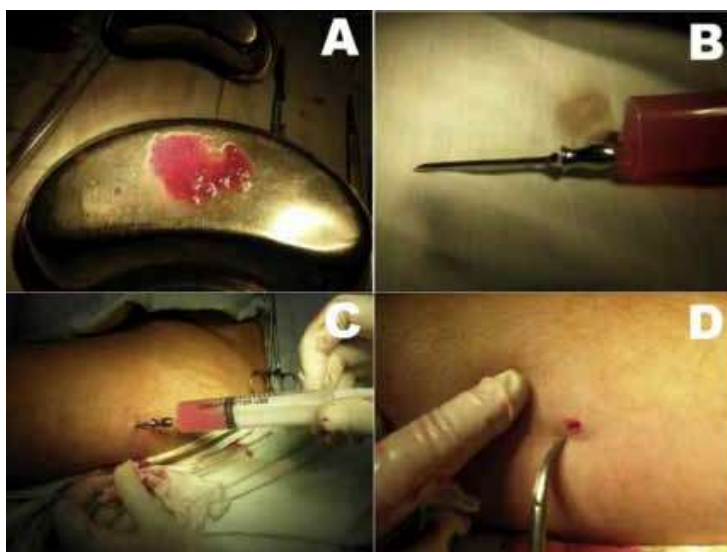


Figure 1 (A) Finely-minced thyroid tissue. (B) Emulsified thyroid tissue in saline, ready for injection. (C) Injection of the emulsion in the thigh. (D) The 3-mm incision after injection.

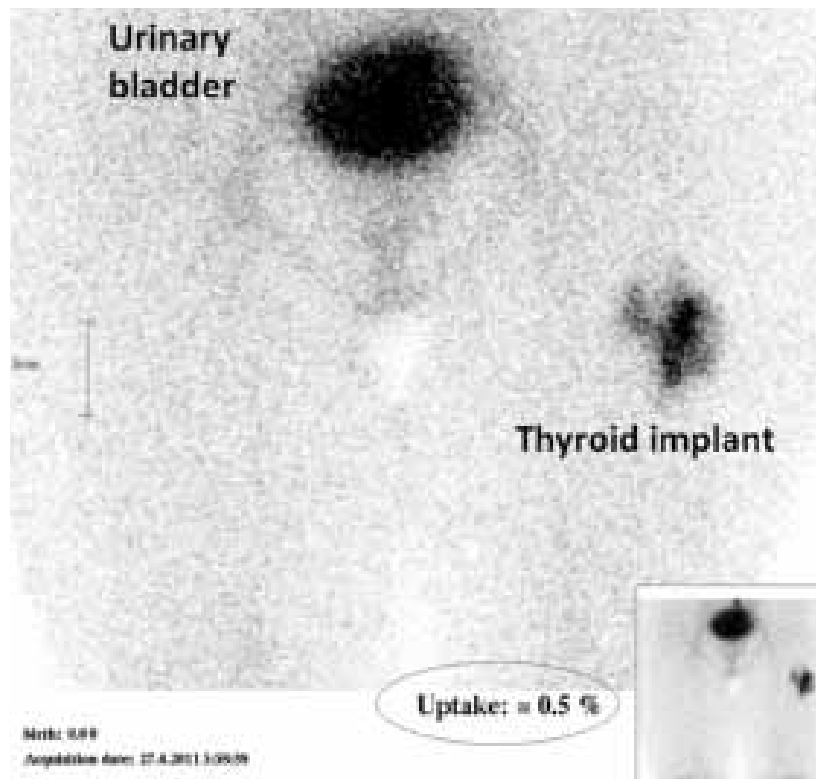


Figure 2: Normal isotope uptake (0.5%) by the implanted thyroid tissue in the left thigh

Table 1 ^{99m}Tc Uptake by the implant (n = 0.5–2%).

	5-g implants (12 patients)		10-g implants (28 patients)	
	Mean ± SD	% Patients achieving normal values	Mean ± SD	% Patients achieving normal values
2 mo	0.28 ± 0.16	8.3	0.44 ± 0.35	37
6 mo	0.28 ± 0.15	16.6	0.59 ± 0.27	73
12 mo	0.44 ± 0.16	41.6	0.71 ± 0.20	88

SD = standard deviation.

Table 2 Thyroid stimulating hormone levels (n = 0.4–4 UI/mL).

	5-g implants (12 patients)		10-g implants (28 patients)	
	Mean ± SD	% Patients achieving normal values	Mean ± SD	% Patients achieving normal values
Preop	2.26 ± 1.15		2.89 ± 1.22	
2 mo	49.56 ± 32	0	46.0 ± 26.2	0
6 mo	37.14 ± 29.6	0	37.04 ± 26.4	0
12 mo	27.74 ± 30.4	16.6	22.78 ± 19.7	3

SD = standard deviation.

Discussion

The purpose of heterotopic thyroid auto transplantation is to leave thyroid tissue in the body that might be able to avoid or reduce severity of post-thyroidectomy hypothyroidism in noncompliant patients. In the meantime, if recurrence occurs it would not be in the neck, thus avoiding compression on the trachea and avoiding dangerous reoperation in the neck. Reports on

its clinical application are very scarce in the literature, with few patients in each study. Furthermore, none of these studies focused on simple multinodular goiters; the majority were directed to Graves’ disease. The only well documented study that addressed this issue with a few multi nodular cases was that of Roy et al¹² who included eight multi nodular goiters among their studied 15 patients.

In the best documented technical description, that of Shimizu et al,¹¹ the workers implanted 2.5e3.5 g per patient with Graves' disease. For the current work, the implanted tissue was expected to be less active and hence at the start of the study 5-g implants were implanted for the first 12 patients. As functional results of these patients were found to be suboptimal, the weight of implanted tissue was raised to 10 g. The problem with implanting such sizeable amount of tissue was that many muscle pockets are made; they would be over-packed with the implanted thyroid tissue, a factor that may hinder the graft take. The procedure would also take an unacceptably long time. In 2000, Gauger et al¹³ described the technique of injecting parathyroid emulsion in the sternomastoid. Their technique was adopted in this work for thyroid tissue implantation using a 20-mL syringe with saline. This technique simplifies the implantation of sizeable tissues, in a short time (w15 minutes), and leaves a small, barely visible scar. With this technique all implants survived and functioned.

In the literature there is no previous mention of the effect of time passage on the function of thyroid auto transplant. In the current work, however, this point was investigated. Analysis of variance showed that the levels of FT3 and FT4 increased with time, and likewise TSH showed significant move towards normalization, i.e., reduction of its levels. Even though isotope uptake showed also a tendency towards elevation, it did not reach statistical significance.

Conclusion

Injection of thyroid tissue suspension is a simple method for thyroid autotransplantation. TSH was elevated in the majority to maintain normal or near normal thyroid hormones. Ten-gram implants showed higher isotope uptake than 5-g, although this difference was not reflected by thyroid hormone profile. The implant seemed to function better with the passage of time from 2 months to 12 months

Ethical Statement: The material has not been published anywhere. Authors of the manuscript have no financial ties to disclose and have met the ethical adherence.

Disclosure of Interest: The authors declare that they have no competing interests.

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or reporting of this research paper. All authors have read and approved the final version of the manuscript.

Conflict of Interest: None

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References

1. Moalem J, Suh I, Duh Q. Treatment and prevention of recurrence of multinodular goiter: an evidence-based review of the literature. *World J Surg.* 2008;32:1301e1312.
2. Agarwal G, Aggarwal V. Is total thyroidectomy the surgical procedure of choice for benign multinodular goiter? An evidence-based review. *World J Surg.* 2008;32:1313e1324.
3. Lips DJ, van Reisen MT, Voigt V, Venekamp W. Diagnosis and treatment of levothyroxine pseudomalabsorption. *Neth J Med.* 2004;62:114e118.
4. Sethi MJ, Parr M, Bhatia V. Management strategies for hypothyroidism in noncompliant patients: a case report and review of literature. *S. D Med.* 2008;61:368e369.
5. Shimizu K, Nagahama M, Kitamura Y, Igarashi T, Aida N, Tanaka S. Improvement of thyroid function after autotransplantation of cryopreserved thyroid tissue in rats: clinical application of the procedure to patients with persistent hypothyroid Graves' disease after thyroidectomy. *Thyroidol Clin Exp.* 1996;8:55e62.
6. Papaziogas B, Antoniadis A, Lazaridis C, et al. Functional capacity of the thyroid autograft: an experimental study. *J Surg Res.* 2002;103:223e227.
7. Ga'II, Miko' I, Furka I, Nagy D. Autotransplantation of cryopreserved thyroid tissue in dogs. *Magy Seb.* 2005;58:93e99 [in Hungarian].
8. Dobrinja C, Trevisan R, Trevisan G, Liguori G. Autotransplantation of thyroid tissue in rats. An experimental study. *Ann Ital Chir.* 2008;79:389e395.
9. Pushkar' NS, Makedonskaia VA, Utevskii AM, Chuiko VA, Karpenko LG. Autoimplantation of cryopreserved (-196 degrees C) thyroid gland parenchyma as a treatment method in postoperative hypothyroidism. *Probl Endokrinol (Mosk).* 1984; 30:42e46 [in Russian].

10. Okamoto T, Fujimoto Y, Obara T, Ito Y, Kodama T, Kusakabe K. Trial of thyroid autotransplantation in patients with Graves' disease whose remnant thyroid has unintentionally been made too small at subtotal thyroidectomy. *Endocrinol Jpn.* 1990;37: 95e101.
11. Shimizu K, Kumita S, Kitamura Y, et al. Trial of autotransplantation of cryopreserved thyroid tissue for postoperative hypothyroidism in patients with Graves' disease. *J Am Coll Surg.* 2002;194:14e22.
12. Roy PG, Saund MS, Thusoo TK, Roy D, Sankar R. Fate of human thyroid tissue autotransplants. *Surg Today.* 2003;33:571e576.
13. Gauger PG, Reeve TS, Wilkinson M, Delbridge LW. Routine parathyroid autotransplantation during total thyroidectomy: the influence of technique. *Eur J Surg.* 2000;166:605e609.

Somatic Manifestations of Depression in Patients of Nineva Province

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Abstract

Objective: To understand the somatic manifestations in patients with depression in Mosul area.

Method: In this study 234 patients with depression attending a civil psychiatric clinic in Mosul City in the period between 22nd of January 2017 to 22nd of November 2018 diagnosed according to the Diagnostic and Statistical manual of the American Psychiatric Association VIR (DSMVIR) as depression were examined for somatic manifestations, and any other medical disorders.

Results: Joints and muscles pain was the most common feature in the depressed patients, it was found in (52.1%) of the patients. Headache was the next common, (51%), followed by abdominal discomfort which was found in (47.8%) and chest pain in (44.4%), then the generalized weakness in (22.5%). Menstrual dysfunction was found in (33.8% of female patients) and sexual dysfunctions were found in (28.2% of male patients).

The higher incidence among females is due to the social roles of gender, the lower educational levels among females, and probably to avoid the stigma.

Conclusion: Identifying somatic manifestations among depressed patient is important in diagnosis, planning a successful management and in prognosis.

Keywords: *Depression, Somatic manifestation.*

Introduction

Depression is one of the most common psychiatric illness, most of these patient complaint from somatic manifestation formerly known as a somatoform disorder, is any mental disorder which manifests as physical symptoms that suggest illness or injury, but which cannot be explained fully by a general medical condition or by the direct effect of a substance, and are not attributable to another mental disorder (e.g. joint and muscle pain, headache, abdominal pain and chest pain)

Aim of the Study: To understand the somatic manifestations in patients with depression in Mosul area.

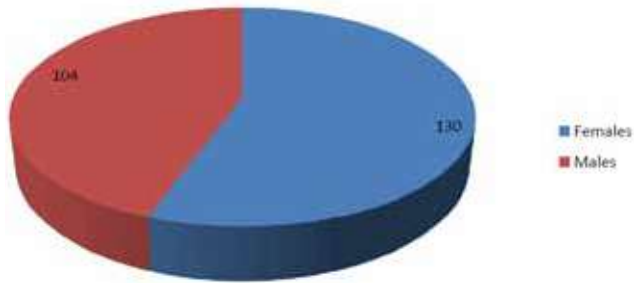
Patients and Method: 234 patients with depression

attending the private clinic in the period between 22nd of January 2012 to 22nd of November 2013 diagnosed according to the Diagnostic and Statistical Manual of the American Psychiatric Association VIR (DSMVIR) as depression were examined for somatic manifestations, and any other medical disorders. The results were analyzed using standard deviations and Chi square.

Results: During the 11 months 234 patients with depression were examined.

Gender: Most of the patients were 130 females and 104 males (55.5% and 44.5% respectively). There is no significant difference between the two ($p < 0.05$). Figure 1.

Gender



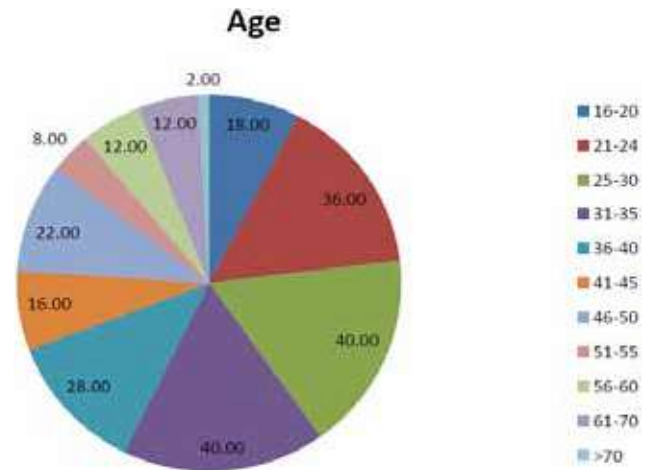
Age: Four patients were 16 years old and 2 patients around 70 years.

The other 228 patient's ages range between 17 and 67 years.

The table below shows the age groups according to No. of patients. Mean =35.63 SD=10.34

The difference is highly significant between the working age group (25-45y) and the non-working age group (16-24y and 46-70y) at P<0.05. Figure 2

Figure 2 Age:

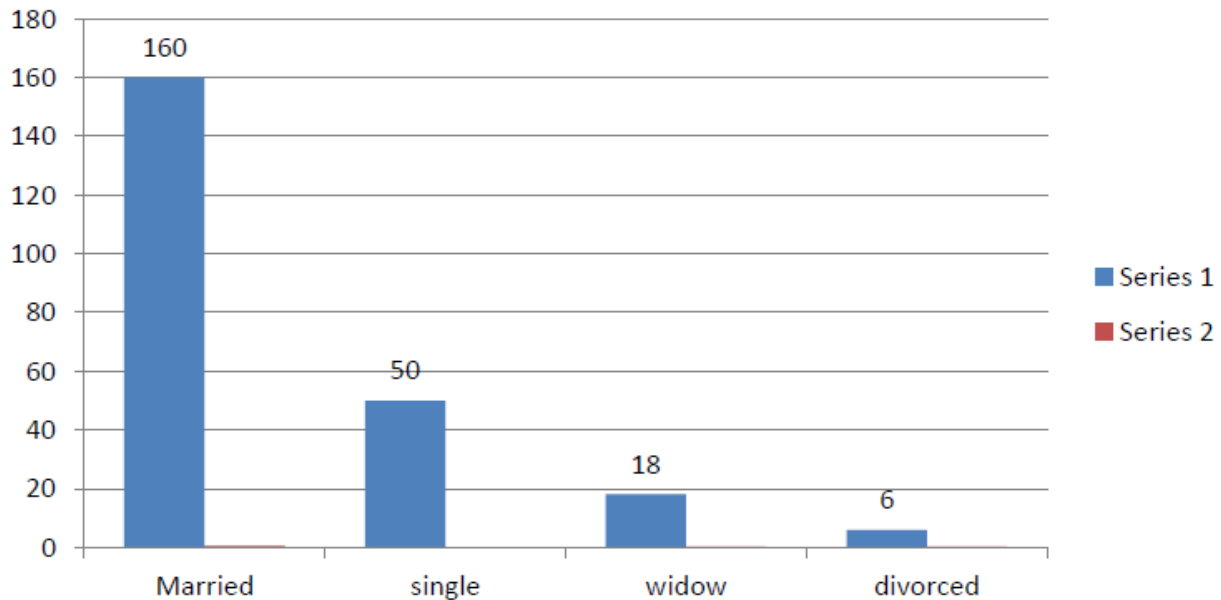


Marital State: The married patients were 160 (68.4%), fifty were single (21.4%), eighteen were widowed (7.7%) and the divorced were the least 6 patients representing (2.5%).

The difference between and married and other groups is highly significant. P<0.05. Figure 3

Figure 3 Marital State:

Marital State

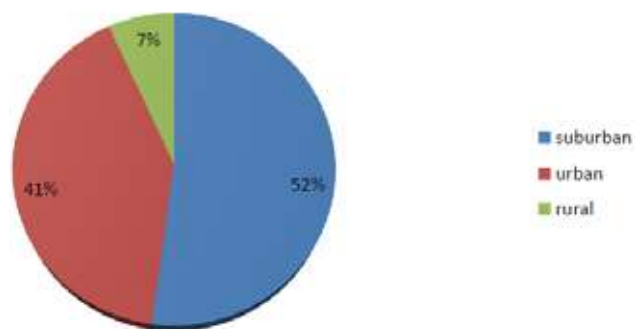


Residency and Education: Most of the patients (122) were from the suburban areas representing (52.1%), then the urban citizens 96 patients (41.1%), patients from rural areas were the least (16) representing

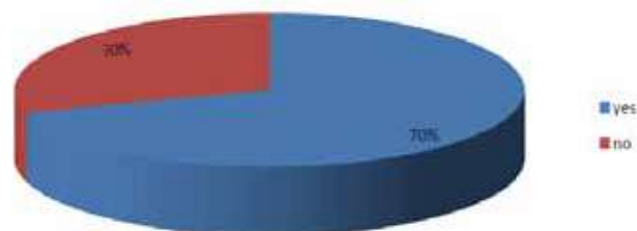
(6.8%).

With significant difference between urban and non-urban areas. P<0.05. Figure 4

Residency and education



Previous history



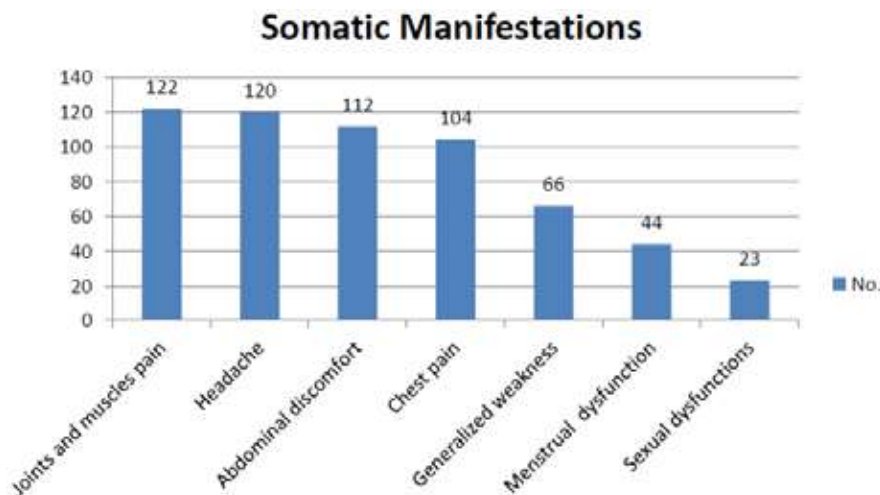
Previous History: Most of the patients (164) representing 70% had no previous history of depression while 70 (22 females and 48 males) patients representing (30%) had such history.

With significant difference between the two. $P < 0.05$.
Figure 5

Somatic Manifestations:

The somatic manifestations found in our patients are as follow: Joints and muscles pain was the most common feature in the depressed patients, it was found in 122 patients (52.1%). Headache was the next common, 120 patients (51%), followed by abdominal discomfort which was found in 112 patients (47.8%) and chest pain in 104 patients (44.4%), then the generalized weakness in 66 patients (22.5%). Menstrual dysfunction was found in 44 females (33.8% of female patients) and sexual dysfunctions were found in 23 males (28.2% of male patients). Figure 6

Figure 6 Somatic Manifestations:



Discussion

Headache abdominal pain musculoskeletal pain and sexual dysfunction are common in patients with depression, beside those patients with depression often present with somatic manifestations, usually seen by general practitioners and family doctors before psychiatrists [1].

Recognizing such patients in proper diagnosis and effectively treating them will improve their quality of life and may reduce their current excessive use of health care resources. Somatic symptoms identified by the general practitioner may be useful indicators for predicting major depression [2]. It is important to remember that depression is one of the leading health

burdens and usually the patient will present his illness with psychological and somatic complaints although in primary care somatic complaints dominate^[3].

Probably the primary health care unit is the ideal place to diagnose depression, but not uncommonly the somatic symptoms may lead to miss diagnosis^[4 & 5].

Some researchers showed that headache Musculoskeletal complaints and dizziness, gastrointestinal, cardiovascular and genitourinary symptoms are the most common somatic features in depression^[3].

The similar features are found in our study. Musculoskeletal complaints and headache the prominent somatic manifestations, usually the patient told about the distress caused by these symptoms and the inability to explain their causes.

While abdominal discomfort was explained as having irritable bowel syndrome, either by the patient himself, a medical staff, or sometimes by a physician. Commonly these patients were under treatment of irritable bowel syndrome and or even duodenal ulcer.

Chest pain or precisely discomfort, generalized weakness, menstrual dysfunction and sexual dysfunction, more or less were understood by the patients as direct effects of their low mood and bad temper^[6].

Depressive symptoms and syndromes are common in the medically ill, although they are frequently unrecognized and untreated^[5&9].

In our study 30% of the patients have comorbidity especially diabetes and it is known that depression is not uncommon among diabetic patients and the relationship between the two disorders is bidirectional^[7].

Most of the studies stated that incidence of depression is higher among females than males ^[3, 4, 6] in our study females outnumber males (130 vs. 104) although with no significant differences reflecting the transcultural variation, in expressing stress and psychiatric disturbances. Difficulties of the life during the years of war and the nature of stresses shared by the whole society may explain this point.

Somatic manifestations in depression seem to be more often in ages associated with social and occupational responsibilities. In this study the main bulk of patients fall in the age range of 25-45 years, maturity,

decline, life-cycle stage, survival, and historical trend play important role in depression in such ages. Other studies found somatic manifestations specially appetite change are more common among older patients^[8&9].

In Iraq residency reflects the socio-educational status, citizens of the cities usually of higher education and better economic facilities, although the life difficulties are more or less similar in both urban and non-urban areas.

Women are more frequently subjected to depression for genetic, hormonal and environmental causes^[10,11&12] beside that they have less chance for higher education than men, and this may explain why most of our patients with somatic manifestations are women from sub-urban areas.

Internal migration for security reasons could be considered as another cause.

Source of Funding: Self

Ethical Clearance: Not required

Conflict of Interest: None

References

1. Recognizing and treating the patient with somatic manifestations of depression - Depression in Special Patient Populations, Journal of Family Practice, Dec, 1996 by Jeffrey N. De Wester
2. J Affect Disord.; Epub Dec 6. Prediction of major depression in Japanese adults: somatic manifestation of depression in annual health examinations. Nakao M, Yano E. Department of Hygiene and Public Health, School of Medicine, Teikyo University, 2-11-1 Kaga, Itabashi, 2005, 173-8605.
3. The Importance of Somatic Symptoms in Depression in Primary Care. André Tylee, M.D., F.R.C.G.P., M.R.C. Psych. and Paul Gandhi, M.R.C. Psych. Prim Care Companion J Clin Psychiatry. 2005; 7(4): 167-176.
4. Christopher Dowrick (et,al), Br J Gen Pra Somatic symptoms and depression: diagnostic confusion and clinical neglect ct. 2005 November 1; 55(520): 829-830.
5. G Rodin and K Voshart . Depression in the medically ill: an overview. Am J Psychiatry 1986; 143:696-705

6. Ronald C. Kessler et al. Sex and depression in the National Comorbidity Survey I: Lifetime prevalence, chronicity and recurrence. *Journal of Affective Disorders* Volume 29, Issues 2–3, October–November 1993, Pages 85–96
7. Briana Mezuk, PHD1, William W. Eaton, PHD2, Sandra Albrecht, MPH1 and Sherita Hill Golden, MD, MHS34 Depression and Type 2 Diabetes Over the Lifespan. A meta-analysis. *Diabetes Care* 2008 Dec; 31(12): 2383-2390.
8. Mirowsky J, Ross CE. Age and depression. *J Health SocBehav.* 1992 Sep;33(3):187-205; discussion 206-12.
9. Zemore R, Eames N. Psychic and somatic symptoms of depression among young adults, institutionalized aged and noninstitutionalized aged. *J Gerontol.* 1979 Sep;34(5):716-22.
10. Ronald C. Kessler. Epidemiology of women and depression. *Next »Journal of Affective Disorders* 2003, 74, 5-13.
11. Rudolf E. Noble. Depression in women. *Metabolism - Clinical and Experimental* Volume 54, Issue 5, Supplement, 2005,49-52.
12. MM Weissman, M Olfson. Depression in women: implications for health care research. *Science* 11 August 1995. 26, 25-52.

Sex Determination in a Sample of Egyptian Population based on Outer and Medullary Metacarpal Measurements. A Multi-Detector Computed Tomographic Study

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Abstract

Prediction of sex from incomplete and decomposing skeletal remains is vital in establishing the identity of an unknown individual. The purpose of this study is to assess the applicability of outer and medullary parameters of third and fourth metacarpals using multi-detector computed tomography in sex determination in Egyptian population. All measurements showed significant sexual differences ($P < 0.05$). By simple discriminant analysis, mediolateral diameter of midshaft of the third metacarpal showed the highest percentage of accuracy (69%) in sex determination. This study concluded that metacarpals are useful bones for sex determination and also it imposes new forensic standards for determination of sex in Egyptian metacarpals using various discriminant formulae.

Keywords: Sex Determination; Metacarpals; Multi-detector Computed Tomography

Introduction

Sex determination is the classification of an individual as either male or female. To achieve an assignment of sex, anthropologists use biological characteristics that vary between both sexes [1].

The personal identification from extremities becomes very important in cases of mass disasters where there are a recovering hands separated from the body [2]. There extensive uses are because of the high incidence of recovery of these compact bones in both forensic and archaeological situations [3,4].

The real advance toward a more extensive and effective use of imaging techniques in forensic medicine

was prompted by the discovery of computed tomography (CT) due to its capability to provide 3D representation of the body structures in a few minutes [5].

The metacarpals are favored because they are the largest, remain complete in most damaged conditions and most easily identifiable bones of the hand [6]. Therefore, the aim of this study was to assess the relationship between the outer and medullary measurements of metacarpals and sex and to allow the sex of an individual to be diagnosed from these measurements in a sample of Egyptian population by using a multi-detector computed tomography (MDCT) scanning and developing a set mathematical models from discriminant function analyses.

Subjects and Method

This study was conducted on 200 patients (100 males and 100 females) with age ranged from 25 to 65 years at the Radiology Department of Minia University Hospital. These patients were subjected to MDCT for their third and fourth metacarpal bones of right hands. Patients with metacarpal fractures or deformities

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(acquired or congenital), skeletal immaturity, bone tumors, growth disorders, connective tissue diseases and previous orthopedic surgery of metacarpal bones were excluded from the study.

Axial cuts were taken on the Rt. hand including the metacarpals from MDCT and then reconstructed coronal and sagittal images were generated as well as the 3D reformatted images that were used to obtain the following measurements. The measurements have been modified from Basir [7] and Nathena et al. [8] as follow:

- Maximum metacarpal length (ML): Is described as the overall external dimension of a metacarpal in its longitudinal direction. Two transverse lines were first drawn touching the distal and proximal ends of the bone. The distance from the mid-point of the transverse line to the mid-point of the other line was taken to be the maximum metacarpal length.
- Medio-lateral diameter of mid shaft (MLDM): Is described as the widest part of mid shaft of the metacarpal in the transverse direction which was shown in medio-lateral view.
- Medullary length of the metacarpals (MdL): Two longitudinal lines were drawn touching the distal/

proximal dorsal aspect and the distal/proximal volar aspect respectively.

The collected data were coded, tabulated and statistically analyzed using SPSS program (Statistical Package for Social Sciences) software version 24. Descriptive statistics were done for numerical data by mean, standard deviation and minimum & maximum of the range.

Results

The mean age of tested cases was 49.01 years with standard deviation (SD) ±10.02. Descriptive statistics of different measurements of the right third and fourth metacarpals among all cases and independent-samples t test revealed highly significant increase in males when were compared with females (P < 0.05). Table 1 and Table 2.

Simple discriminant functional analysis for sex prediction using right third and fourth metacarpal measurements revealed that the highest accuracy was obtained with usage of MLDM of third metacarpal (69%).

Table 1: Descriptive Statistics and Independent-Sample t-Test of The Right Third Metacarpal Measurements in Male and Female

3 rd Metacarpal		Male	Female	P value
		N= 100	N= 100	
ML	Range	(62.6-68.8)	(62.8-65.8)	<0.001*
	Mean ± SD	66.1±0.93	65.4±0.72	
MLDPE	Range	(13.5-15.5)	(13.8-14.4)	<0.001*
	Mean ± SD	14.5±0.45	14.3±0.15	
MLDM	Range	(6-8.7)	(6.1-7.1)	<0.001*
	Mean ± SD	7.2±0.42	7±0.15	
MLDDE	Range	(15.5-18.5)	(16.5-17.5)	0.024*
	Mean ± SD	17.5±0.48	17.4±0.29	
MdL	Range	(44.8-48.8)	(45-46.8)	0.003*
	Mean ± SD	46.9±0.66	46.7±0.31	
NMdW	Range	(4.4-6.5)	(5-5.4)	0.001*
	Mean ± SD	5.5±0.38	5.4±0.06	
PMdW	Range	(9.1-10.5)	(9-9.8)	0.010*
	Mean ± SD	9.8±0.24	9.8±0.12	
DMdW	Range	(9.1-10.5)	(9.3-9.8)	0.001*
	Mean ± SD	9.9±0.23	9.8±0.10	

ML= Maximum metacarpal length, MLDPE= Medio-lateral diameter of proximal end, MLDM= Medio-lateral diameter of mid shaft, MLDDE= Medio-lateral diameter of distal end, MdL= Medullary length, NMdW= Narrowest medullary width, PMdW= Proximal medullary width, DMdW= Distal medullary width, *: P value is significant when P <0.05, N= number, SD= standard deviation.

Table 2: Descriptive Statistics and Independent-Sample t-Test of The Right Fourth Metacarpal Measurements in Male and Female

4 th Metacarpal		Male	Female	P value
		N= 100	N= 100	
ML	Range	(52.8-58.8)	(53-55.8)	<0.001*
	Mean ± SD	56±0.96	55.5±0.57	
MLDPE	Range	(11.8-14.4)	(12.8-13.1)	<0.001*
	Mean ± SD	13.3±0.48	13.1±0.06	
MLDM	Range	(5.5-7.2)	(5.5-6.2)	<0.001*
	Mean ± SD	6.3±0.35	6.2±0.11	
MLDDE	Range	(13.1-15.6)	(13.1-14.1)	<0.001*
	Mean ± SD	14.3±0.46	14.1±0.14	
MdL	Range	(41-44.3)	(40-42)	<0.001*
	Mean ± SD	42.2±0.56	41.8±0.42	
NMdW	Range	(4.1-5.6)	(4.4-4.6)	<0.001*
	Mean ± SD	4.7±0.31	4.6±0.04	
PMdW	Range	(7.3-9)	(7.6-7.7)	0.001*
	Mean ± SD	7.8±0.33	7.7±0.02	
DMdW	Range	(8-9.6)	(8.2-8.8)	0.001*
	Mean ± SD	8.6±0.32	8.5±0.07	

ML= Maximum metacarpal length, MLDPE= Medio-lateral diameter of proximal end, MLDM= Medio-lateral diameter of mid shaft, MLDDE= Medio-lateral diameter of distal end, MdL= Medullary length, NMdW= Narrowest medullary width, PMdW= Proximal medullary width, DMdW= Distal medullary width, *: P value is significant when P <0.05, N= number, SD= standard deviation.

Discussion

Sex determination is one of the crucial steps when it comes to establish an individual’s biological profile. A significant problem with relying on these bones is that they can be fragmented, damaged or poorly preserved which makes it necessary to search for new bones to identify the individual [9].

All the studied subjects were adult because sex differences become evident only after the end of puberty when the skeleton has completed its growth [10]. Sex differences in the shape, size and appearance of bones arise during development according to individual genetic markers and in response to sex hormones during puberty [11].

The current study is in acceptance with Navsa et al.[12] who conducted a study on 200 hand bones from sex-race group (50 white males, 50 black males, 50 white females and 50 black males) (age 21-80 years) from a South African population.

These results are in harmony with that of Eshak et al.[13] who measured the lengths (2D measurements) of

all metacarpal bones and the volumes (3D measurements) of the 2nd and 4th metacarpal bones from 122 Egyptian individuals (60 males and 62 females). They stated that males presented with significantly greater mean values than females for the lengths of metacarpal bones and the accuracy was ranged from 71.4% to 92.9%. They also proved that the 2nd & 5th metacarpals had the highest accuracy.

The mentioned results correspond with previous results of Khanpetch et al. [14] who used 249 skeletons (154 males and 95 females) from a Thai population. Six measurements were taken on each metacarpal, namely maximum length, medio-lateral base width, antero-posterior base height, medio-lateral head width, antero-posterior head height and mid-shaft diameter.

These results are consistent with the results of Singh et al. [15] who studied 143 metacarpals after obtaining x-ray of both hands from North Indian population sample.

The present results go with this of Ameri et al. [16] who investigated the possibility of estimating

gender using metacarpals dimensions in 200 Iranian adult persons (100 male and 100 female) without any background of specific disease. The length metacarpal was measured in millimeter and reported in ratio.

The current study comes in conjunction with what was mentioned by Kusec et al. [17] who conducted a morphometric analysis of six metacarpal bones (second, third and fourth of right and left hands) on hand radiographs of 434 male (aged between 19 and 86 years) and 549 female (aged between 19 and 79 years).

The reverse was found by Zanella & Brown [18] who estimated the applicability of discriminant function analysis comparing the correspondence results of the equations of previous studies based upon measurements from metacarpals. They used 23 adult cadavers and data were subjected to regression equations and linear discriminant analysis.

Conclusions

The present study proved that the right third and fourth metacarpals have a considerable value in predicting sex among Egyptian population by using discriminant function analysis. These will help in medico-legal cases for establishing the identity of an individual when only some remains of the body are found. This study has decreed new significant parameters of third and fourth metacarpals to be used in forensic medicine.

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References

1. Lesciotto KM & Doershuk LJ. Accuracy and reliability of the Klales et al. morphoscopic pelvic sexing method. *J. Forensic Sci.*, 2017;63(1):214-20.
2. Kanchan T & Krishan K. Anthropometry of hand in sex determination of dismembered remains - A review of literature. *J. Forensic Leg. Med.*, 2011; 18(1):14-7.
3. Mastrangelo P, De Luca S, Aleman I, et al. Sex assessment from the carpals bones: Discriminant function analysis in a, 20th century Spanish sample. *Forensic Sci. Int.*, 2011;206(1-3):216.e1-10.
4. Krishan K, Kanchan T, Asha N, et al. Estimation of sex from index and ring finger in a North Indian population. *Journal of Forensic and Legal Medicine*, 2013;20(5):471-9.
5. Willaume T, Farrugia A, Kieffer EM, et al. The benefits and pitfalls of post-mortem computed tomography in forensic external examination: A retrospective study of 145 cases. *Forensic Science International*, 2018; 286:70-80.
6. Mahakkanukrauh P, Khanpetch P, Prasitwattanseree S, et al. Determination of sex from the proximal hand phalanges in a Thai population. *Forensic Sci. Int.*, 2013;226(1-3):208-15.
7. Basir A. Metacarpal Morphology of the Singaporean Population (Bachelor of Science in Biomedical Engineering, Singapore University of Social Sciences, Singapore). Available from BME499 Capstone Project, 2008;pp.1-26 (H0402183).
8. Nathena D, Gambaro L, Tzanakis N, et al. Sexual dimorphism of the metacarpals in contemporary Cretans: Are there differences with mainland Greeks?. *Forensic Sci. Int.*, 2015;257:515.e1-8.
9. Gaya-Sancho B, Aguilera IA, Navarro-Munoz JJ, et al. Sex determination in a Spanish population based on sacrum. *Journal of Forensic and Legal Medicine*, 2018;60:45-9.
10. Rosing FW, Graw M, Marre B, et al. Recommendations for the forensic diagnosis of sex and age from skeletons. *Homo*, 2007;58(1):75-89.
11. DeSilva R, Flavel A & Franklin D. Estimation of sex from the metric assessment of digital hand radiographs in a Western Australian population. *Forensic Sci. Int.*, 2014;244:314.e1-7.
12. Navsa N, Steyn M & Iscan MY. Sex determination from the metacarpals in a modern South African male and female sample (Poster Presentation). University of Pretoria, Pretoria, South Africa, 2008. Retrived from <https://repository.up.ac.za/handle/2263/7406>.
13. Eshak GA, Ahmed HM & Abdel Gawad EA. Gender determination from hand bones length and volume using multidetector computed tomography: a study in Egyptian people. *J. Forensic Leg. Med.*, 2011;18(6):246-52.

14. Khanpetch P, Prasitwattanseree S, Case DT, et al. Determination of sex from the metacarpals in a Thai population. *Forensic Sci. Int.*, 2012;217(1-3):229e1-8.
15. Singh V, Kumar T & Mattoo MK. Metacarpal lengths & ratios as a marker of sexual dimorphism in population of Haryana and Jammu & Kashmir. A radiological study. *Journal of the Anatomical Society of India*, 2018;67(2): S33-6.
16. Ameri M, Ghorbani S, Ameri E, et al. Sex determination by the length ratio of metacarpals and phalanges: X-ray study on Iranian population. *Tehran Univ. Med. J.*, 2018;76(8):558-61.
17. Kusec V, Simic D, Chaventre A, et al. Age, sex and bone measures of the second, third and fourth metacarpal (Island of Pag, SR Croatia, Yugoslavia). *Collegium Anthropologicum*, 1988;12(2):309-22.
18. Zanella VP & Brown TM. Testing the validity of metacarpal use in sex assessment of human skeletal remains. *Journal of Forensic Sciences*, 2003;48(1):17-20.

Predicting Patient Survival after Pancreaticoduodenectomy for Malignancy Based on Histopathological Criteria

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Abstract

This Study Aimed to identify histopathological variables that might contribute to survival, mortality of patients, and serious complications after pancreaticoduodenectomy.

Patients and Method: This is prospective hospital based study that been done on all patients who underwent pancreaticoduodenectomy in National Liver Institute and Minia university hospital between the first of January 2015 till the end of December 2016. in the surgical department, National Liver Institute, Menoufiya University and Minia university hospital.

Results: We found that perineural infiltration and lymphovascular invasion were independently significant in multivariate analysis, the effects of combining them in terms of predicting longterm survival is very important. Smaller and well-differentiated tumours were associated with significantly better patient survival ($P < 0.03$ and $P < 0.01$, respectively). Positive lymph nodes were associated with reduced survival ($P < 0.003$).

Conclusion: The analyse the histopathological parameters influencing longterm patient survival after pancreaticoduodenectomy focusing on perineural infiltration and lymphovascular invasion as predictors of longterm survival.

Keywords: Pancreaticoduodenectomy; histopathological; tumours.

Introduction

Pancreatic malignancies overall are associated with poor longterm prognosis. Five-year survival rates following pancreatic resection for pancreatic adenocarcinoma remain low (<20%), even in large-

volume institutions. This cohort had a median follow-up of nearly 5 years and an actuarial survival of 27%, which is comparable with the recently published MD Anderson series. ⁽¹⁾.

Historically, pancreaticoduodenectomy (PD) has been associated with high rates of mortality and morbidity. The mortality rate was higher than 30%. Recently, several high-volume centers have reported markedly improved mortality rates, as low as 1–2%. Postoperative morbidity, however, remains common ⁽²⁾.

Pancreaticoduodenectomy is a therapy indicated for malignant diseases localized in the periampullary region, Furthermore, patients with benign lesions of this area in

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which a malignancy cannot be ruled out preoperatively may also benefit from this surgery⁽³⁾.

Aim of the Work: We aimed to assess prognosis and predict patient survival following pancreaticoduodenectomy based on lymphovascular invasion, perineural infiltration, lymph node status and lymph node ratio in patients candidate for Whipple operation for malignancy.

Patients and Method: Patients presented with pancreatic head mass or periampullary carcinoma candidate for whipple operation from January 2015 to December 2016, in the surgical department, National Liver Institute, Menoufiya University and Minia university hospital on .

This study included 40 patients of presented with pancreatic head mass or periampullary carcinoma candidate for whipple operation of either sex with age not less than 18 years old; operated by open exploratory maneuver through bilateral subcostal incision.

Operative Technique: All exploratory procedures were done under general anesthesia and naso-gastric tube was inserted to diminish the size of the stomach and to reduce the distension of small bowel. A Foley's urethral catheter was inserted to be removed in the recovery room.

Our technique utilizes a bilateral subcostal incision (Chevron incision). The liver and peritoneal surface is carefully examined to exclude the presence of metastatic disease, and intraoperative ultrasonography of liver and pancreas is performed. Adequate exposure is essential for proper Whipple's operation. Good retraction with self-retaining retractor makes assistant's hands free to help the surgeon during surgical procedure. Bipolar cautery, ligaseal, harmonic scalpel are of benefits including staplers to divide stomach and duodenum. Initial mobilization is done by reflecting the hepatic flexure and transverse colon downwards; then extended Kocherisation is done by lateral duodenal ligament which exposes SMV, IVC and aorta partly. Invasion or encasement of these vessels will prevent from proceeding with resection; just essential bypass will be sufficient. Middle colic vein when traced will help in identifying the SMV.

Gastrojejunostomy is done 20 cm distal to the hepaticojejunostomy as an antecolic anastomosis. As already stomach is transected with stapler earlier during

procedure, gastrojejunostomy is done using linear stapler device just proximal and posterior to the stapled line. Single layer 3-zero vicryl hand sewn anastomosis also can be done.



Fig. (1): Gastrojejunostomy anastomosis



Fig. (2): The specimen after removal

Statistical Analysis: All collected data were tabulated, graphed and mathematically analyzed. Numerical data expressed as mean±SD and categorical data were expressed as number and percent (%). T-student test was used to compare numerical data, and Chi-square test was used to compare categorical data. P-value was considered to be significant if it was less than 0.05

Results

This study included 40 patients presented with pancreatic head mass or periampullary carcinoma candidate for whipple operation of either sex with age not less than 18 years old; operated by open exploratory maneuver through bilateral subcostal incision from January 2015 to December 2016, in the surgical department, National Liver Institute, Menoufiya University and Minia university hospital.

****Multivariate analysis:**

****When all the significant histopathological parameters on univariate analysis were assessed using**

a multivariate regression model, perineural infiltration ($P < 0.03$) and lymphovascular invasion ($P = 0.05$) were the only independent factors prognostic for longterm survival.

****Prognostic modelling using perineural infiltration and lymphovascular invasion:** perineural infiltration ($P < 0.03$) and lymphovascular invasion ($P = 0.05$) were the only independent factors prognostic for longterm survival. As these two factors were

independently significant in multivariate analysis, the effects of combining them in terms of predicting longterm survival were analysed. The 40 patients with malignancies were divided into four categories consisting of those who were positive for both parameters, those who were positive for either one of the parameters and those who were negative for both. Figure 3 illustrates that patients who were negative for both parameters had significantly better survival than the other groups ($P < 0.0001$).

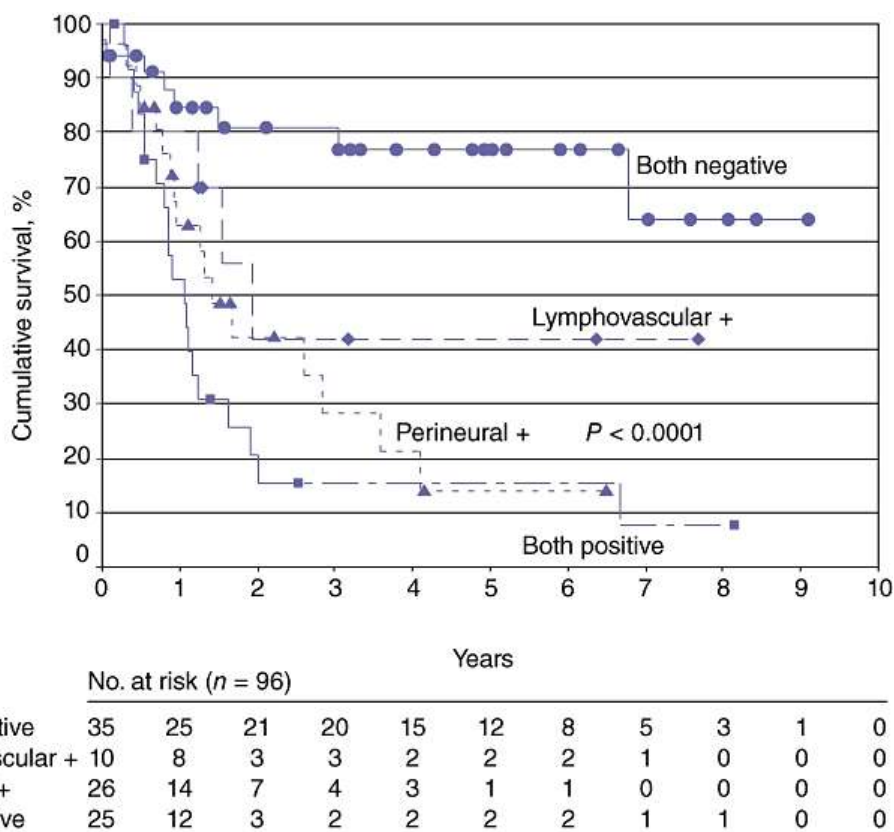


Figure 3: Cumulative patient survival in the presence or absence of perineural infiltration and lymphovascular invasion after resection. Survival is significantly improved if both features are absent on microscopic examination

Table (1): Five-year survival rates after pancreaticoduodenectomy for pancreatic malignancies in patients positive and negative for perineural infiltration and lymphovascular invasion (n= 40)

	Perineural –	Perineural +
Lymphovascular –	77%	14%
Lymphovascular +	42%	15%

Likewise, when these parameters were applied to patients with pancreatic adenocarcinoma, those who were negative for both parameters had an excellent actuarial 5-year survival of 71% compared with the other three groups

Discussion

We studied the effect of different variables on patient’s outcome within the first 6th months and first

two year survival after pancreaticoduodenectomy. The 6th month's time was chosen because the majority of the major complications and mortalities after pancreaticoduodenectomy have been reported to occur within this period.

Identification of key variables will be essential if improved clinically acceptable models are to be built in the future. Although many variables that are clinically assumed to be important in survival may not reach statistical significance in multivariable models, the ability to test the effect of clinically relevant variables will increase the face value of statistical prediction ⁽⁴⁾

The 5-year survival for patients who underwent pancreaticoduodenectomy for periampullary malignancies other than pancreatic adenocarcinoma was 61%. This result is also in line with previously published results for periampullary carcinomas, including a recently published series from Birmingham which reported an actuarial 5-year survival of 60% for ampullary carcinoma following resection. ⁽⁵⁾

Also the results of our study are agree with the results of the study done by Chen JW et al which shows that Patients who underwent resection had 1-, 3- and 5-year survival rates of 70%, 46% and 41%, respectively. The 1-, 3- and 5-year survival rates for periampullary cancers other than pancreatic adenocarcinoma were 83%, 69% and 61%, respectively; those for pancreatic adenocarcinoma were 62%, 31% and 27%, respectively ($P < 0.003$).⁽⁶⁾

In our study we confirmed that smaller and well-differentiated tumours were associated with significantly better patient survival ($P < 0.03$ and $P < 0.01$, respectively) and Positive lymph nodes were associated with reduced survival ($P < 0.003$) this is agree with the study done by⁽⁶⁾which confirms that Poor tumour differentiation ($P < 0.02$), tumour size >3 cm ($P < 0.04$), margin ≤ 2 mm ($P < 0.02$), nodal involvement ($P < 0.003$), were associated with poorer prognosis.

In our study we confirm that Smaller and well-differentiated tumours were associated with significantly better patient survival ($P < 0.03$)

In our study presence of histopathologically positive perineural infiltration and or lympho vascular invasion carries poor prognosis regard to survival this matches with the results of the study done by ⁽⁶⁾ which confirms that perineural infiltration ($P < 0.0001$) and lymphovascular invasion ($P < 0.002$) were associated

with poorer prognosis. In a multivariate analysis .

Conclusion: We concluded that The absence of malignant perineural infiltration and lymphovascular invasion was associated with highly significantly improved survival .

Ethical Statement: The material has not been published anywhere. Authors of the manuscript have no financial ties to disclose and have met the ethical adherence.

Disclosure of Interest: The authors declare that they have no competing interests.

Declaration of Authorship: All authors have directly participated in the planning, execution, analysis or reporting of this research paper. All authors have read and approved the final version of the manuscript.

Conflict of Interest: None

References

1. Katz MH, Wang H, Fleming JB, Sun CC, Hwang RF, Wolff RA, et al. Longterm survival after multidisciplinary management of resected pancreatic adenocarcinoma. *Ann Surg Oncol*. 2009;16:836–847.
2. Greenblatt DY, Kelly KJ, Rajamanickam V, et al. Preoperative Factors Predict Perioperative Morbidity and Mortality After Pancreaticoduodenectomy, *Ann Surg Oncol* 2011.
3. Pezzilli R, Falconi M, Zerbi A, et al. Clinical and Patient-Reported Outcomes After Pancreatoduodenectomy for Different Diseases A Follow-Up Study, *Pancreas* 2011; Volume 00, Number 00, Month 2011.
4. Noda H, Kamiyama H, Kato T, et al. Factors Influencing Improved Patient Outcomes after Pancreaticoduodenectomy - A Single Institute Experience of 209 Consecutive Patients in a Decade, *Hepato-Gastroenterology* 2012; 59:2310-2313.
5. Morris-Stiff G, Alabraba E, Tan YM, Shapely I, Bhati C, Tanniere P, et al. Assessment of survival advantage in ampullary carcinoma in relation to tumour biology and morphology. *Eur J Surg Oncol*. 2009;35:746–750.
6. Chen JW, Bhandari M, Astill DS, Wilson TG, Kow L, Brooke-Smith M, Toouli J, Padbury RT. *HPB* (Oxford). 2010 Mar;12(2):101-8.

Assessing Adverse Cardiac Effects of Direct Antiviral Agents in Hepatitis C Virus Infected Patients

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Abstract

Objective: To evaluate the effect of the direct antiviral agents (DAAs) which are recently involved in treatment of hepatitis C virus (HCV) patients on the cardiac function.

Patients and Method: The study conducted on one hundred subjects with hepatitis C virus (HCV) and treated with doses of sofosbuvir (SOF) plus daclatasvir (DCV) only or in addition to weight-based ribavirin (RBV) for 12 weeks. Level of human plasma B type natriuretic peptide (BNP), and left ventricular ejection fraction (LVEF) measured by echocardiography were evaluated to all subjects included before starting treatment and at the sixth week and after the twelfth week of the treatment.

Results: There were significant differences in levels of BNP and LVEF measurements through different times compared.

Conclusion: The patients included in the study with affected LVEF did not have heart failure symptoms. Statistically significant differences between parameters measured remained within the normal range.

Keywords: *Cardiotoxicity, hepatitis C virus, direct antiviral agents.*

Introduction

Chronic hepatitis C virus (HCV) infection affects more than 3% (170 million) of the world's population and is a major cause of liver cirrhosis and hepatocellular carcinoma.¹

National Egyptian health project survey held in 2015 which was performed to describe the prevalence of hepatitis C virus (HCV) infection. The study showed that in the 15–59-year age groups, the prevalence of HCV antibody was found to be 10.0% (95% CI 9.5–

10.5) and that of HCV RNA to be 7.0% (95% CI 6.6–7.4). In children, 1–14 years old, the prevalence of HCV antibody and HCV RNA were 0.4% (95% CI 0.3–0.5) and 0.2% (95% CI 0.1–0.3) respectively.²

Additionally, 3.7 million Egyptian citizens were suffering from chronic HCV infection in the age group 15–59 in 2015. The Egyptian government started a national project aiming to diagnose and cure HCV through whole Egypt.^{2,3}

Food and Drug Administration (FDA) has approved new regimens for HCV treatment involving direct-acting antivirals (DAAs) that target different steps in the HCV life cycle which created a breakthrough in HCV combatting.^{4,5}

The new DAAs include SOF, sold under the brand name sovaldi, which is recommended with some combination of ribavirin, peginterferon-alfa, simeprevir, ledipasvir and/or daclatasvir. The declared cure rates reached 30 to 97% depending on the type of hepatitis

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C virus involved. The pronounced side effects included feeling tired, headache, nausea, and trouble sleeping.^{6,7}

Lately, after the FDA announcement of the possible effect of DAAs on heart, ongoing surveillance of DAAs for cardiotoxicities may be beneficial, especially among patients at higher risk for cardiovascular disease.^{7, 8}

Aim of the Work: To study the possible cardiotoxic effects associated with direct antiviral agents (DAAs) used in HCV infected subjects treatment.

Patients and Method

Study design and population: This study was carried out over a period of 22 months; from 1st May 2017 till 31 th March 2019 on 100 subjects diagnosed as infected by hepatitis C virus (HCV) and treated with doses of SOF plus DCV only or in addition to weight-based RBV for 12 weeks. They were recruited from two centers in Minia governorate. These centers were the western medical center at Minia city and El-yom EL-wahed hospital at Samalout city. The study was conducted on Minia university hospital. Their ages were between 42-59 years. Both sexes were included in the study. History and clinical examination were recorded on a standardized report forms involved age, sex, vital signs and physical exams. They were 56 males and 44 females. Subjects were selected according to inclusion and exclusion criteria.

Inclusion Criteria: Patients diagnosed with HCV by positive polymerase chain reaction (PCR) and their ages ranged between 18- 60 years old.

Exclusion Criteria: Patients with Child's classification grade C cirrhotic patients, Hepatocellular carcinoma (HCC), except 6 months after intervention, or extra- hepatic malignancy except after two years of disease-free interval (in cases of lymphomas and chronic lymphocytic leukemia). Pregnant patients and patients unable to use effective contraception were excluded. Inadequately controlled diabetes mellitus (HbA1) patients and patients with liver disease other than HCV infection were excluded. Patients with QTc interval ≥ 450 ms or a personal or family history of torsades de pointe were excluded. Patients were excluded if their investigations included one of these findings: Platelet count $< 50,000/\text{mm}^3$, Creatinine clearance < 50 mL/min, serum creatinine ≥ 1.5 , and or human immunodeficiency virus (HIV) infection.

Method

It included transthoracic echocardiographs (TTEs), and B-type natriuretic peptide (BNP) levels. Parameters were assessed before beginning of the treatment (week 0), sixth week of the treatment (week 6), after ending the treatment (after week 12).

Human plasma B type naturetic peptide (BNP): For BNP (a sensitive marker of myocardial stress), one cm venous blood sample was collected from each subject in a syringe and was sent to the laboratory of clinical pathology, Minia University Hospital. The kits used were bought from Glory Science Company in China.

The patient's BNP level was considered normal if normal if less than 125 pg/ml.⁹

Left ventricular ejection fraction (LVEF): Assessing LVEF was done by echocardiographic studies which were performed using Echocardiography, MECANSET, High Class Trolley 3D 4D Color Doppler Ultrasound, CHINA. Each subject was examined in a semisupine left lateral position. Images were obtained at end expiratory apnoea and stored in cine loop format from three consecutive beats. All echocardiographic measurements were performed according to the recommendations of American Society of Echocardiography/European Association of Cardiovascular Imaging (ASE/EACVI) guidelines¹⁰ by a specialized cardiologist.

Left ventricular ejection fraction (LVEF) measurements were divided according to American Herat Association into 3 groups: normal 50%-70%, borderline: 41%-49%, reduced 40% or less.¹¹

Statistical Analysis: All data were checked, coded, entered, tabulated and analyzed by using SPSS (Statistical Package for Social Sciences) version 20.0 software. Statistical method included: Friedman test for non-parametric quantitative data and ordinal qualitative data between the different times. Wilcoxon signed rank test for non-parametric quantitative data and ordinal qualitative data between each two times. Descriptive method included: median and range were used to quantativedata. Qualitative data were summarized as number and percentage. $P < 0.05$ was considered significant and $P > 0.05$ was considered insignificant.

Results

Regarding BNP, there was high significant difference between BNP levels at week 0, week 6 and after week 12. There was high significant increase in frequency of abnormal BNP levels at week 6. The interquartile ranges of BNP at week 6 and after week 12 were less than 125 Pg/ml (Table 1).

Regarding LVEF measured by echocardiography. There was high significant increase in frequency of reduced LVEF at week 6 and after week 12. There were 6 cases with borderline LVEF and 15 cases with reduced LVEF at week 6. After week 12, there were 12 cases with borderline LVEF and 9 cases with reduced LVEF (Table 2).

Table (1): Showing BNP levels (Pg/ml) difference at week 0, week 6 and after week 12 of treatment regimen.

		At week 0	At week 6	After week 12	P value
		N=100	N=100	N=100	
BNP	Median	24.6 ^a	72.4 ^c	57.4 ^b	<0.001*
	IQR	(18.8-33.1)	(56.8-98.9)	(47.3-83.3)	
BNP	Normal	100(100%) ^a	88(88%) ^b	98(98%) ^a	<0.001*
	Abnormal	0(0%)	12(12%)	2(2%)	

Superscripts with small letters indicate significant difference between each two times., *: Significant level at P value < 0.05., IQR:interquartile range., N=number of cases.

Table (2): Showing LVEF difference at week 0, week 6 and after week 12 of treatment regimen

		At week 0	At week 6	After week 12	P value
		N=100	N=100	N=100	
Left ventricular ejection fraction	Normal	100(100%) ^a	79(79%) ^c	79(79%) ^b	<0.001*
	Borderline	0(0%)	6(6%)	12(12%)	
	Reduced	0(0%)	15(15%)	9(9%)	

Superscripts with small letters indicate significant difference between each two times, *: Significant level at P value < 0.05.

Discussion

Application of newly developed drugs on large scale of population may reveal unexpected adverse effects. DAAs cardiotoxicity may be evident when these drugs were recently introduced to markets as HCV curing agents. More accurate studies to monitor DAAs cardiotoxic effects were needed.⁸

The first report was published by Ahmad et al., who evaluated BNP retrospectively from frozen serum collected before and after treatment discontinuation, discovered increase in BNP in patients with severe and moderate systolic cardiomyopathy and in patients with normal LVEF. Abnormal BNP levels was recorded in 5 of 6 cases with LVEF< 30% and 4 of 8 patients with LVEF 30%-49%, and 2 of 20 cases with LVEF ≥50%; Although plasma BNP levels were raised over baseline, in most cases, were not significantly elevated above normal reference ranges. Most cases exhibited recovery

of cardiac function showed recovery in most cases after treatment discontinuation however, and no patients had elevated troponin levels. It was concluded that those biomarkers likely have little utility as screening method.⁸

Regarding LVEF, Ahmad et al. evaluated LVEF in 34 patients who received DAAs for approximately 1-6 weeks. Fourteen (39%) treated patients were noted to have LVEF <50%: 6 had LVEF <30% and 8 had LVEF 30%-50% at one or more evaluations in the 6-month period. Ahmad et al. considered that cardiac dysfunction was dose related as higher doses of DAAs were associated with higher incidence of cardiac dysfunction.⁸

The accepted explanation of different results in this study may be due to wide range difference in sample sizes and time of samples evaluation.

El-Adawy et al. in Egypt included 390 HCV infected patients divide into 4 groups of 4 different regimens of

DAAs. They observed significant elevation of BNP level in all groups of their study especially in the group of (SOF+DCV+ RBV) (P value <0.001). El Adway et al. evaluated cardiac function in by cardiac magnetic resonance (CMR), There was significant difference LV dysfunction especially in group received SOF, DCV and RBV group with P<0.001.¹²

Mazzitelli et al. who assessed cardiac dysfunction by longitudinal strain (GLS) in 82 patients received DAAs observed statistically significant worsening of GLS in the group of patients treated for 12 weeks; however, EF measured did not change significantly. Their results suggested that SOF based treatment could have a negative impact on cardiac function they recommended assessing biomarkers (such as TN-I, BNP, and micro-RNAs) for long term studies.¹³

On contrary, Biomy et al. study no significant differences in systolic and diastolic function parameters in patients between the beginning and after 6 months.¹⁴

But the difference in results could be easily explained by wide time range Biomy et al. used to assess patients. The results of the current study showed that the number of patients developed cardiac dysfunction decreased by time (15 cases of reduced LVEF at week 6 declined to 9 cases after week 12).

Pathological analysis made by Ahmad et al. of explanted heart of a case died during the research revealed diffuse elongation and thinning of ventricular cells accompanied by fine interstitial fibrosis, very limited areas of necrosis, and limited small areas of mononuclear inflammation. Severe biventricular dysfunction was not considered as the level of myocarditis was insufficient which was considered consistent with, but not diagnostic, of a toxic cardiomyopathy. As a result, Ahmad et al. changed the regimens for the next cases in their study.⁸

Pathological examination by Ahmed et al. also suggested mitochondrial dysfunction with minimal myonecrosis and myocardial injury.¹⁵

The first case of myo-pericarditis 3 days after initiating DAAs was reported by Schlegel et al. in a patient on DAAs. The patient was a 55 year old male with non is chemiocardiomyopathy and, normal blood pressure and no renal complications. The patients developed myo-pericarditis 3 days after initiating treatment. Endomyocardial biopsy showed with myopericarditis.¹⁶

The obvious from the current study results that there were some element of cardiac dysfunction that was going to improve after treatment discontinuation. Most of the means changes measured in this study were within normal range. Most of changes measured were at sub clinical level.

Ahmad et al. study showed that cardiac function was returning normal over time especially after the first 10 weeks after DAAs cessation.⁸ The transient effects discovered suggested that the cardiomyocytes injury is not permanent.

The actual mechanism is still unknown. Although some potential changes in cardiac energy utilization were proved, the mentioned studies revealed that DAAs were less possible to be a direct mitochondrial toxicant.¹⁷ In vitro studies showed that the effect of DAAs on human cardiomyocytes was associated with concentration- and time-related cytotoxicity.¹⁸ Direct effect of SOF should be considered. Additionally, a random effect, an effect of concomitant drugs, or an indirect effect of HCV eradication mediated by inflammatory changes may be accepted explanations.¹⁹ Concentration and time related cytotoxicity in human cardiomyocytes, in association with mitochondrial injury was proved.^{15,18}

Conclusion

From this study it could be concluded that most of the patients included in the study with affected LVEF did not have heart failure symptoms. Statistically significant differences between BNP and LVEF measured at different weeks were obvious but most of them remained within the normal range and none had significant abnormalities. The alteration of cardiac energy generation or utilization could be the exact cause of cardiotoxicity related to DAAs. Studies using different parameters would be helpful in assessing DAAs cardiotoxicity.

Ethical Clearance: Taken from ethical committee in El-Minia university hospital.

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Conflict of Interest: Nil.

References

1. Mohd Hanafiah K, Groeger J, Flaxman AD, Wiersma ST. Global epidemiology of hepatitis C virus infection: new estimates of age-specific

- antibody to HCV seroprevalence. *Hepatology*. 2013; 57:1333-1342.
2. Kandeel A., Genedy M., El-Refai S., Funk A. L., et al. The prevalence of hepatitis C virus infection in Egypt 2015: implications for future policy on prevention and treatment. *Liver International*. 2017; 37(1): 45-53.
 3. Kim D. D., Hutton D. W., Raouf A. A., Salama M., et al. "Cost-effectiveness model for hepatitis C screening and treatment: implications for Egypt and other countries with high prevalence." *Global public health*. 10(3): 296-317.
 4. DeClercq E. The race for interferon-free HCV therapies: a snapshot by the spring of 2012. *Rev Med Virol*. 2012; 22:392-411.
 5. Sherman RE, Li J, Shapley S, Robb M, Woodcock J. Expediting drug development—the FDA's new "breakthrough therapy" designation. *N Engl J Med*. 2013; 369:1877-1880.
 6. Food and Administration D. SOVALDI (sofosbuvir) prescribing information. 2014. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/204671s002lbl.pdf.
 7. Food and Administration D. FDA hepatitis update—important safety information: harvoni and Sovaldi. 2015. Available at <http://www.natap.org/2015/HCV/SVD20March15FINAL-1.pdf>.
 8. Ahmad T., Yin P., Saffitz J., Pockros P. J., et al. Cardiac dysfunction associated with a nucleotide polymerase inhibitor for treatment of hepatitis C. *Hepatology*. 2015; 62(2): 409-416.
 9. Januzzi J. L., van Kimmenade R., Lainchbury J., Bayes-Genis A., et al. NT-proBNP testing for diagnosis and short-term prognosis in acute destabilized heart failure: an international pooled analysis of 1256 patients: the International Collaborative of NT-proBNP Study. *European heart journal*. 2005; 27(3): 330-337.
 10. Lang R. M., Badano L. P., Mor-Avi V., Afilalo J., et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *European Heart Journal-Cardiovascular Imaging*. 2015; 16(3): 233-271.
 11. Wilcox J. E., Fonarow G. C., Yancy C. W., Albert N. M., et al. Factors associated with improvement in ejection fraction in clinical practice among patients with heart failure: findings from IMPROVE HF. *American heart journal*. 2012; 163(1): 49-56. e2.
 12. El-Adawy A. H., Altonbary A. Y., Hakim H., Bakr D. H., et al. Influence of different regimens of direct acting antiviral agents (DAAS) with or without ribavirin used for chronic hepatitis C treatment on the cardiac muscles in Egypt. *The Journal of Medical Research*. 2018; 4(4): 169-173.
 13. Mazzitelli M., Torti C., Sabatino J., D'Ascoli G. L., et al. Evaluation of cardiac function by global longitudinal strain before and after treatment with sofosbuvir-based regimens in HCV infected patients. *BMC infectious diseases*. 2018; 18:518.
 14. Biomy R., Abdelshafy M., Abdelmonem A., Abu-Elenin H., et al. Effect of Chronic Hepatitis C Virus Treatment by Combination Therapy on Cardiovascular System. *Clinical Medicine Insights: Cardiology*. 2017; 11: 1-9.
 15. Stoltz J. H., Stern J. O., Huang Q., Seidler R. W., et al. A twenty-eight-day mechanistic time course study in the rhesus monkey with hepatitis C virus protease inhibitor BILN 2061. *Toxicologic pathology*. 2011; 39(3): 496-501.
 16. Schlegel A., Kron P., De Oliveira M. L., Clavien P.-A., et al. Is single portal vein approach sufficient for hypothermic machine perfusion of DCD liver grafts? *Journal of hepatology*. 2016; 64(1): 239-241.
 17. VanVleet TR, Simic D, Horn KH. BMS-986094: transcriptional profiling in monkeys and mice [abstract 854]. Presented at the 53rd Annual Meeting and ToxExpo, Phoenix, AZ, March 24-27, 2014. *The Toxicologist*. 2014; 138:221.
 18. Kwagh J., Storck C., Shi H., Huang M., et al. BMS-986094: potential cytotoxicity in differentiated human cardiomyocytes. *The Toxicologist: Supplement to Toxicological Sciences*. 2014; Abstract no 856: 138-221.
 19. Zampino R., Marrone A., Restivo L., Guerrero B., et al. Chronic HCV infection and inflammation: clinical impact on hepatic and extra-hepatic manifestations. *World journal of hepatology*. 2013; 5(10): 528-540.

Allopurinol Versus Epinephrine in the Prevention of Post Endoscopic Retrograde Cholangiopancreatography (ERCP) Pancreatitis

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Abstract

This study was to evaluate and investigate the effects of using different drugs on reducing the frequency and severity of Post- ERCP pancreatitis. The study was done on 90 randomized patients with extrahepatic cholestasis and divided into three groups. Post ERCP pancreatitis was diagnosed by laboratory investigations, ultra-sonography and triphasic abdominal CT criteria of pancreatitis. The results of this study showed that there was a statistically significant difference in the percentage of knife precut between the studied groups. There was a statistically significant difference in the degree of post ERCP pancreatitis during comparison the control group with each studied drug group, in which allopurinol has a protective role in the occurrence of post ERCP pancreatitis by regression analysis. It is concluded to use allopurinol before ERCP procedure.

Keywords: ERCP, pancreatitis, knife precut, Allopurinol.

Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is one of the most commonly performed endoscopic procedures. The recent shift towards interventional uses of ERCP is largely due to the emergence of advanced imaging techniques, including magnetic resonance cholangiopancreatography and ultrasonography^[1].

ERCP is used primarily to diagnose and treat conditions of the bile ducts and main pancreatic duct, including gallstones, inflammatory strictures (scars), leaks (from trauma and surgery) and cancer^[2].

Complications of ERCP can be broadly divided into short-term (within 3 days of the procedure) and

long term (> 3 days after the procedure) complications. The reported incidence of ERCP-specific complications ranges from 5% to 40%, depending on the complexity of the procedure, the underlying diagnosis and patient comorbidities^[3].

According to Cotton's criteria, acute pancreatitis which occurs after ERCP is diagnosed in patients who experience abdominal pain after the procedure with a concomitant ≥ 3 fold increase in blood serum amylase activity that persists 24 hours after ERCP and who require hospitalization^[4,5].

Post ERCP pancreatitis is believed to be multi-factorial involving a combination of chemical, hydrostatic, enzymatic, mechanical and thermal factors. Although there is some uncertainty in predicting which patients will develop acute pancreatitis following ERCP, a number of risk factors acting independently or in concert have been proposed as predictors of post-ERCP pancreatitis^[6].

Allopurinol plays a part in the prevention of post-ERCP pancreatitis through the reduction of oxygen free radicals^[7]. Topical application of epinephrine on

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the papilla may reduce papillary edema by relaxing the sphincter of Oddi or by decreasing capillary permeability. They are also inexpensive drugs for prevention of post-ERCP pancreatitis^[8].

Patients and Method

Patients: This study was conducted on 90 randomized patients with extrahepatic cholestasis subjected to ERCP. The patients were selected from tropical medicine department and general surgery department of EL-Minia University hospital. The patients were selected for this study according to the following inclusion and exclusion criteria:-

Inclusion criteria:

The patients of either sex; male or female, of age range from 27-78 years old and had to have extrahepatic or intrahepatic biliary dilatation diagnosed by ultra-sonography and triphasic abdominal CT.

Exclusion Criteria: Patients with pancreatitis diagnosed by laboratory investigations, ultra-sonography and triphasic abdominal CT criteria of pancreatitis (e.g. enlargement of pancreas, inflammatory changes in pancreas and peripancreatic fat, ill-defined single peripancreatic fluid collection and two or more poorly defined peripancreatic fluid collections) were excluded.

The patients were divided into 3 groups as follow:

Group I (control group that included 30 patients): patients were not given any drugs before or after ERCP.

Group II (Allopurinol treated- group): included 30 patients, allopurinol (600mg) was taken orally one hour before ERCP. **Group III (Epinephrine- treated group):** included 30 patients were given 20 ml of 0.02% epinephrine sprayed on the papilla during ERCP.

Method: All patients in this study were subjected to the following:

1-Full history taking 2- Full clinical examination
3- Laboratory investigations serum amylase (normal 25-125 unit per liter) ^[9]. The serum amylase level was evaluated before ERCP and 6, 24, 48 hours post-ERCP. INR, total leucocytic count, random blood sugar, liver function tests, blood urea and serum creatinine.

Endoscopic retrograde cholangiopancreatography (ERCP) technique: Before ERCP, the patients were prepared by fasting at least 8-12 hours and instructed regarding the associated

medical history. They were instructed to stop concurrent used medication that lead to bleeding and correction of any bleeding tendency.

During ERCP, the patient lies on prone position and general anesthesia was performed under supervision of an anesthetist. ERCP was performed using Pentax EPM-3500, where side-viewing duodeno-scope is introduced to the stomach till the pylorus then passed to the duodenum and its papilla was visualized for mass or any abnormality.

Management was done according to the pathology as in case of calcular obstruction, stone extracted by ballon dilatation or mechanical lithotripsy followed by stent implantation. If large stone > 1cm, fragmentation of stone occurred by mechanical lithotripsy followed by stent implantation. After ERCP, the patients were followed up for possible complications by clinical examination and investigation.

Statistical Analysis: The data were analyzed by SPSS (statistical package for social sciences) program version 24. The significance of differences for parametric quantitative data was calculated by using One-way ANOVA test. Kruskal Wallis test was used for non-parametric data. Fisher exact test was used to calculate the significance of qualitative data between the five groups. Univariate and multivariate regression analysis were used for predicting pancreatitis. For all tests, $P < 0.05$ was considered significant.

Results

Diagnostic and therapeutic ERCP were done to all studied patients with obstructive jaundice. **Table 1** showed indications of ERCP in all studied patients, 10 (11.1%) patients had stricture (4 patients in group I, 2 patients in group II, 4 patients in group III), 51 (56.7%) patients had calcular obstructive jaundice (18 patients in group I, 17 patients in group II and 16 patients in group III). Malignant obstructive jaundice occurred in 29 (32.2%) patients. It was diagnosed as cancer pancreas in 20 patients (5 in group I, 7 in group II, 8 in group III)

Hepatic focal lesions occurred in 3 patients (one patient in group I, 2 in group II) and enlarged porta hepatis, para aortic and pre pancreatic lymph nodes in 6 patients (2 in group I, 2 patients in group II, 2 patients in group III). There was a statistically significant difference in diagnosis of causes of obstructive jaundice between studied groups (**table 1**).

Table 2 showed the details of ERCP procedure for all studied groups. The mean± SD of the procedure time in all groups was shown in this table. The least mean procedure time (min.) was in group II (12.5± 7.1) and the longest mean procedure time was in group III (20.1±9.3). All patients were received pre ERCP antibiotics. The least number of patients that underwent stone extraction was in group III (16 (55.53%) patients). The biggest number of patients was in group I (18 (60%) patients). Biliary stent insertion and biliary sphinctrotomy were done to all studied patients. Knife precut was done in 25 patients (9 in group I, 7 in group II and 9 in group III). There was a statistically significant difference in the percentage of knife precut between the studied groups.

Table 3 showed the incidence of post ERCP hyperamylasemia in control and all drug groups. It was found that there was no statistically significant difference in post ERCP serum amylase level at all different times in all groups. Epigastric pain occurred in 40 patients underwent ERCP (15 in group I, 12 in group II and 13 in group III). There was a statistically significant difference between all studied groups (P < 0.05) (**table 3**).

There was a statistically significant difference in the degree of post ERCP pancreatitis during comparison the

control group with each studied drug group, in which, the degree of pancreatitis is statistically significant decreased after drug intake. Group II showed the least number of patients that developed post ERCP pancreatitis (12 Patients only) (**table 3**).

Univariate regression analysis was done to factors associated with post ERCP pancreatitis, only precut and drug intake Before ERCP are statistically significant by regression analysis to predict the risk factors and protective factors of post ERCP pancreatitis. Precut ERCP was a risk factor for the development of post ERCP pancreatitis (OR was 10.5 and 95% confidence interval (CI) was 4.6-23.7. Drug intake before ERCP has a protective role (OR <1). It was noticed that Allopurinol was the best drug which can decrease the incidence of occurrence of post ERCP pancreatitis (OR= 0.362 & 95% CI was 0.074-2.121) (**table 4**). This finding was confirmed by multivariate regression analysis which revealed that combination of these 2 factors only that can predict or decrease the occurrence of pancreatitis (precut ERCP (OR= 22.3) which means it is a risky and drug intake especially Allopurinol that has the least OR in all drugs (OR=0.426) which also means it has a protective role in the occurrence of post ERCP pancreatitis (**table 5**).

Table (1): The ultrasonographic & abdominal triphasic CT and ERCP findings in all studied groups

Patients Groups		Group I (N=30)	Group II (N=30)	Group III (N=30)	P value
ERCP Findings					
Stricture		4 (13.3%)	2 (6.6%)	4 (13.3%)	0.01*
Calcular		18 (60%)	17 (56.6%)	16 (55.53%)	0.001*
Malignant	Hepatic focal lesion	1	2	0	0.01*
	Enlarged lymph nodes	2	2	2	0.01*
	Pancreatic mass (cancer head of pancrease)	5	7	8	0.001*

Fisher exact test for qualitative data between groups, *: Significant level taken at P value < 0.05

Table (2): Procedure details for all studied groups:

Groups Procedure Details	Placebo I	Allopurinol II	Epinephrine III	P value
	N=30	N=30	N=30	
Procedure time (min.)				
Mean±SD	15.6± 9.1	12.5± 7.1	20.1±9.3	0.252
Pre ERCP antibiotics	30(20%)	30(25%)	30(25%)	0.584
Stone Extraction	18 (60%)	17 (56.6%)	16 (55.53%)	0.487
Biliary stent insertion	30(20%)	30(25%)	30(25%)	0.435
Knife precut	9(30%)	7(23.3%)	9(30%)	0.001*
Biliary sphinctrotomy	30(20%)	30(25%)	30(25%)	0.276

Fisher exact test for qualitative data between groups *: Significant level taken at P value < 0.05

Table (3): Incidence of post ERCP hyperamylasemia, Epigastric pain and degree of post ERCP pancreatitis in all studied groups

Groups Parameters	Placebo I	Allopurinol II	Epinephrine III	P value
	N=30	N=30	N=30	
6h serum amylase level				0.676
Range	(37-1020)	(38-1150)	(53-1250)	
Mean ± SD	406.5±372.6	371.1±372	422.2±415.5	
Median	110	116.5	111.5	
24h serum amylase level				0.252
Range	(53-1170)	(51-1030)	(53-1080)	
Mean ± SD	465±438.3	366±357.6	436.2±426.9	
Median	101.5	111.5	111.5	
48h serum amylase level				0.104
Range	(53-1090)	(48-870)	(53-985)	
Mean ± SD	455.6±421.7	328.8±319.5	392.9±388.8	
Median	99	94.5	90	
Epigastric pain				0.028*
No	15(50%)	18(60%)	17(56.7%)	
Yes	15(50%)	12(40%)	13(43.3%)	
Degree of pancreatitis				
Absent	16(53.3%)	18(60%)	17(56.7%)	0.001*
Mild	0(0%)	6(20%)	0(0%)	
Moderate	8(26.7%)	4(13.3%)	10(33.3%)	
Severe	6(20%)	2(6.7%)	3(10%)	

Kuskal Wallis test for non-parametric quantitative data between the five groups, *: Significant level taken at P value < 0.05

Table (4): Univariate regression analysis of factors associated with post ERCP pancreatitis

Factors	PEP		Univariate analysis		P value
	No	Yes	OR	95% CI	
	N=51 (56.7%)	N=39 (43.3%)			
Age					0.321
>60 year	19 (37.2%)	17(43.6%)	0.347	0.124-0.303	
<60 year	32 (62.7%)	22(56.4%)			
Sex					0.365
Male	22(43.1%)	15(38.5%)	0.456	0.312-1.345	
Female	29(56.9%)	24(61.5%)			
Biliary sphinctrotomy					0.467
Yes (90 patients)	51 (56.7%)	39(43.3%)	0.347	0.453-0.675	
Precut ERCP					<0.001*
N0.: 25(27.8%)	3 (12%)	22(88%)	10.5	4.6-23.7	
Drug	Allopurinol				0.01*
	Yes (30)	18(35.3%)	12(30.8%)	0.362	
	Epinephrine				0.795
Yes (30)	17(33.3%)	13(33.3%)	0.874	0.316-2.418	

PEP: post ERCP pancreatitis OR: Odds Ratio CI: Confidence Interval, *: Significant level taken at P value < 0.05

Table (5): Multivariate regression analysis of factors associated with post ERCP pancreatitis

Factors		PEP		Multivariate analysis		P value
		No	Yes	OR	95% CI	
		N=51 (56.7%)	N=39 (43.3%)			
Precut ERCP No.: 25(27.8%)		3 (12%)	22(88%)	22.3	8.2-25.6	<0.001*
Drug	Allopurinol Yes (30)	18(35.3%)	12(30.8%)	0.426	0.25-2.98	0.01*
	Epinephrine Yes (30)	17(33.3%)	13(33.3%)	0.815	0.232-2.861	0.549

PEP: post ERCP pancreatitis OR: Odds Ratio CI: Confidence Interval, *: Significant level taken at P value < 0.05

Discussion

ERCP is a direct contrast technique of the pancreaticobiliary system. It is useful in the diagnosis and management of diseases involving the pancreas and bile ducts such as stones, benign and malignant strictures and developmental anomalies. Also, intra-hepatic bile duct pathologies can be treated by ERCP using occlusion cholangiography. Pathology in the gallbladder and cystic duct abnormalities can be visualized by ERCP^[12].

The major complication of an ERCP is the development of pancreatitis which can occur in up to 5% of all procedures. This may be self-limited and minor but may need hospitalization and rarely to be life-threatening. Those at additional risk for pancreatitis are younger patients, females, procedures that involve cannulation or injection of the pancreatic duct, patients with previous post-ERCP pancreatitis and those with sphincter of Oddi dysfunction^[13].

The pathophysiology of PEP is not well explained. Mechanical, hydrostatic, chemical, cytokine, oxidative, enzymatic, allergic, thermal and microbiological factors have all been discussed as being its causes. PEP may result from mechanical trauma which causing injury to the papilla or pancreatic sphincter and leading to swelling of the pancreatic duct and obstruction to the flow of pancreatic enzymes^[14,15].

Post-ERCP pain with marked elevation of serum amylase and/or lipase especially when the values are greater than 1,000 IU/L, it is strongly suggestive of pancreatitis. In cases of diagnostic doubt especially when severe pancreatitis is predicted, radiologic imaging should confirm the diagnosis. Early recognition of post-ERCP pancreatitis may be possible by evaluating

serum amylase or lipase within a few hours of the procedure^[16,17].

The degree of pancreatic inflammation and serum hyperamylasemia was decreased after pretreatment with allopurinol in pancreatography induced pancreatitis^[18].

Post-ERCP pancreatitis should be managed and treated as other causes of acute pancreatitis. This is sometimes complicated because it is difficult to distinguish mild from severe disease during the early stages of the disease. In acute pancreatitis, close monitoring for signs of organ dysfunction is essential^[19].

It was found that there was no statistically significant difference in post ERCP serum amylase level at all different times in all groups. Epigastric pain occurred in 40 patients underwent ERCP (15 in group I, 12 in group II and 13 in group III). There was a statistically significant difference between all studied groups (P < 0.05).

Univariate regression analysis was done to factors associated with post ERCP pancreatitis. Precut ERCP was a risk factor for the development of post ERCP pancreatitis (OR was 10.5 and 95% confidence interval (CI) was 4.6-23.7. Drug intake before ERCP has a protective role (OR <1). It was noticed that Allopurinol and Epinephrine can reduce the incidence of occurrence of post ERCP pancreatitis but allopurinol was preferred than epinephrine in this study to decrease the incidence of occurrence of post ERCP pancreatitis (OR= 0.362 & 95% CI was 0.074-2.121).

Contrary to the results of the current study is that mentioned by **Kamal et al.**^[20] who reported that the incidence of PEP in indomethacin alone group was

6.4% as compared to 6.7% in the combination group. Severe PEP was found in 12% versus 16% of patients in the indomethacin alone and combination groups respectively. The combination of papillary spray of epinephrine and rectal indomethacin does not reduce the incidence of PEP compared to rectal indomethacin alone in high risk patients.

On the other hand, **Xu et al.** [21] studied 941 subjects undergoing diagnostic ERCP and demonstrated a reduction in PEP incidence by epinephrine which sprayed directly on the papilla at the time of ERCP. Prevention of PEP was occurred through relaxation of the sphincter of oddi and reduction of papillary edema by decreasing capillary permeability.

The results of this current study were agree with that mentioned by **Akshintala et al.** [22] who studied the beneficial effect of epinephrine in the prevention of PEP. Topical epinephrine could reduce the risk of PEP by 75% compared to controls on sensitivity analyses (OR 0.25, 95% CI 0.06-0.66).

The present study is against with **Hatamia et al.** [23] who stated that 66 patients were randomized to the epinephrine group (group A), 68 cases to the indomethacin group (group B) and 58 individuals to the indomethacin-epinephrine group (group C). They concluded that the single application of epinephrine and the combination of epinephrine and indomethacin significantly reduced the risk of PEP.

General measures for prevention of PEP includes proper training of endoscopist, maintaining proficiency, adequate disinfection, avoidance of diagnostic ERCP, avoidance of repeated cannulation and injection of PD, careful use of electrocautery and avoidance of balloon dilation especially in higher risk patients such as younger patients who are anicteric [24].

The present results were not agree with this of **Mosler et al.** [25] who analyzed 701 patients. They were randomized to receive either allopurinol or placebo 4 hours and 1 hour before ERCP. The overall incidence of pancreatitis was 12.55%. It occurred in 12.96% of patients in the allopurinol group (and in 12.14% of patients in the control group. Prophylactic oral allopurinol did not reduce the frequency or the severity of post-ERCP pancreatitis.

There was significant reduction of post-ERCP pancreatitis by allopurinol (OR= 0.362 & 95% CI was

0.074-2.121) when compared to epinephrine which in disagreement with those of **Romagnuolo et al.** [26] who studied 586 subjects. The crude PEP rates were 5.5% (allopurinol) and 4.1% (placebo) (95% confidence interval 2.1%-4.8%).

The results of the current study are not in accordance with the study of **Bai et al.** [27] who showed no significant difference in the incidence of post-ERCP pancreatitis between allopurinol treated and allopurinol untreated groups (8.9 vs. 9.7%, P=0.68, RR 0.86, 95% CI 0.42-1.77).

The current study is agree with **Katsinelos et al.** [28] who showed that the frequency of acute pancreatitis was significantly lower in the allopurinol vs the placebo group. The protective effect of allopurinol was also apparent in the diagnostic ERCP and the biliary sphincterotomy subgroups when the frequency of post-ERCP pancreatitis was analyzed after stratification by procedure.

Conclusion

Owed to our results in this current work, it is concluded that acute pancreatitis is the most common complication after ERCP. Also, it is concluded that precut ERCP was a risk factor for the development of post ERCP pancreatitis and administration of allopurinol can decrease the incidence of PEP. And so, it is advised to give allopurinol before ERCP and make further scientific researches to find another drugs that can ameliorate post ERCP pancreatitis.

Ethical Statement: The material has not been published anywhere. Authors of the manuscript have no financial ties to disclose and have met the ethical adherence.

Disclosure of Interest: The authors declare that they have no competing interests.

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Conflict of Interest: None

References

1. Silveira ML, Seamon MJ, Porshinsky B, et al. Complications Related To Endoscopic Retrograde Cholangiopancreatography: A Comprehensive

- Clinical Review. *J. Gastrointest. Liver Dis.* 2009; 18(1):73-82.
2. Siddiqui UD, Hawes RH. Chronic Pancreatitis. In Chandrasekhara V, Elmunzer BJ, Khashab M and Muthusamy VR. (EdS.). *Clinical Gastrointestinal Endoscopy* (3rd ed.) (pp.686-98), 2019; London, England: Elsevier.
 3. Nandasena M, Lakmal C, Pathirana ., et al. Endoscopic retrograde cholangio pancreatography (ERCP) - a novel risk factor for conversion of laparoscopic cholecystectomy. *HPB.* 2018; 20(2): S739.
 4. Cotton PB, Garrow DA, Gallagher J, et al. Risk factors for complications after ERCP: a multivariate analysis of 11,497 procedures over 12 years. *Gastrointest. Endosc.* 2009; 70(1):80-8.
 5. Lubowska-Pajak E, Kolomecki K. Assessment of pharmacological prophylaxis for acute pancreatitis following ERCP in patients with choledocholithiasis. *Pol. Przegl. Chir.* 2015; 87(12):620-5.
 6. Chapman CG, Waxman I, Prachand VN. Endoscopic and Minimally Invasive Therapy for Complications of Pancreatitis. In Yeo CJ (Ed.). *Shackelford's Surgery of the Alimentary Tract* (8th ed.) (pp.1113-26), 2019; Philadelphia, United States: Elsevier.
 7. Abbasinazari M, Mohammad Alizadeh AH, Moshiri K, et al. Does Allopurinol Prevent Post Endoscopic Retrograde Cholangio-Pancreatography Pancreatitis? A Randomized Double Blind Trial. *Acta Medica Iranica.* 2011; 49(9):579-83.
 8. Maranki J, Yeaton P. Prevention of Post-ERCP Pancreatitis. *Curr. Gastroenterol Rep.* 2013; 15(11):352.
 9. Ribeiro A, Goel A. The Risk Factors for Acute Pancreatitis after Endoscopic Ultrasound Guided Biopsy. *Korean J. Gastroenterol.* 2018; 72(3):135-40.
 10. Balthazar EJ, Robinson DL, Megibow AJ, et al. Acute pancreatitis: value of CT in establishing prognosis. *Radiology.* 1990; 174(2):331-6.
 11. Choi HW, Park HJ, Choi SY, et al. Early Prediction of the Severity of Acute Pancreatitis Using Radiologic and Clinical Scoring Systems with Classification Tree Analysis. *AJR Am. J. Roentgenol.* 2018; 211(5):1035-43.
 12. Kapral C, Muhlberger A, Wewalka F, et al. Quality assessment of endoscopic retrograde cholangiopancreatography: results of a running nationwide Austrian benchmarking project after 5 years of implementation. *Eur. J. Gastroenterol. Hepatol.* 2012; 24(12):1447-54.
 13. Begley S, Clarke T. FDA knew devices spread fatal 'superbug' but does not order fix. Reuters. Viewed 10 February 2017. Retrived from [https://www.reuters.com/article/us-usa-ucla-devices/u-s-fda-knew-devices-spread-fatal-superbug-but-does-not-order-fix idUSKBN0LO02Q20150220](https://www.reuters.com/article/us-usa-ucla-devices/u-s-fda-knew-devices-spread-fatal-superbug-but-does-not-order-fix-idUSKBN0LO02Q20150220).
 14. Sagi SV, Schmidt S, Fogel E, et al. Association of greater intravenous volume infusion with shorter hospitalization for patients with post-ERCP pancreatitis. *J. Gastroenterol. Hepatol.* 2014; 29(6):1316-20.
 15. El Hajj II, Sherman S. Unexplained Acute Pancreatitis and Acute Recurrent Pancreatitis. In Baron TH, Kozarek RA and Carr-Locke DL (EdS.). *Ercp* (3rd ed.) (pp.486-98), 2018; London, England: Elsevier.
 16. Badalov N, Tenner S, Baillie J. The Prevention, recognition and treatment of post-ERCP pancreatitis. *JOP.* 2009; 10(2):88-97.
 17. Thiruvengadam NR, Forde KA, Chandrasekhara V, et al. Lowering the risk of post-ERCP pancreatitis. *Gastrointestinal Endoscopy.* 2017; 85(3):688-9.
 18. Cao WL, Yan WS, Xiang XH, et al. Prevention Effect of Allopurinol on Post-Endoscopic Retrograde Cholangiopancreatography Pancreatitis: A Meta-Analysis of Prospective Randomized Controlled Trials. *PLOS ONE.* 2014; 9(9):e107350.
 19. Jacobson BC, Vander Vliet MB, Hughes MD, et al. A prospective, randomized trial of clear liquids versus low-fat solid diet as the initial meal in mild acute pancreatitis. *Clin. Gastroenterol. Hepatol.* 2007; 5(8):946-51.
 20. Kamal A, Akshintala VS, Talukdar R, et al. A Randomized Trial of Rectal Indomethacin and Papillary Spray of Epinephrine versus Rectal Indomethacin Alone for the Prevention of Post-Ercp Pancreatitis in High Risk Patients. *Gastrointestinal Endoscopy.* 2017; 85(5): AB78-9.
 21. Xu LH, Qian JB, Gu LG, et al. Prevention of post-endoscopic retrograde cholangiopancreatography pancreatitis by epinephrine sprayed on the papilla. *J. Gastroenterol. Hepatol.* 2011; 26(7):1139-44.
 22. Akshintala VS, Hutfless SM, Colantuoni E, et al. Systematic review with network meta-analysis:

- pharmacological prophylaxis against post-ERCP pancreatitis. *Aliment. Pharmacol. Ther.* 2013; 38(11-12):1325-37.
23. Hatami B, Kashfi SMH, Abbasinazari M, et al. Epinephrine in the Prevention of Post-Endoscopic Retrograde Cholangiopancreatography Pancreatitis: A Preliminary Study. *Case Rep. Gastroenterol.* 2018; 12(1):125-36.
24. Sharma K, Sharma M, Narang S, et al. Post ERCP pancreatitis: a endoscopist's night mare! an insight with literature review. *Journal of Liver Research, Disorders & Therapy.* 2016; 2(5):119-22.
25. Mosler P, Sherman S, Marks J, et al. Oral allopurinol does not prevent the frequency or the severity of post-ERCP pancreatitis. *Gastrointestinal Endoscopy.* 2005; 62(2):245-50.
26. Romagnuolo J, Hilsden R, Sandha GS et al. Allopurinol to prevent pancreatitis after endoscopic retrograde cholangiopancreatography: a randomized placebo-controlled trial. *Clinical Gastroenterology and Hepatology.* 2008; 6(4):465-71.
27. Bai Y, Gao J, Zhang W, et al. Meta-analysis: allopurinol in the prevention of postendoscopic retrograde cholangiopancreatography pancreatitis. *Aliment. Pharmacol. Ther.* 2008; 28(5):557-64.
28. Martinez-Torres H, Rodriguez-Lomeli X, Davalos-Cobian C et al. Oral allopurinol to prevent hyperamylasemia and acute pancreatitis after endoscopic retrograde cholangiopancreatography. *World Journal of Gastroenterology.* 2009; 15(13):1600-6.

Role of SWI in Early Detection of Hemorrhagic Transformation in Acute Cerebral Ischemia

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Abstract

Background: The advent of new magnetic resonance imaging (MRI) techniques has improved acute stroke diagnosis. Susceptibility weighted imaging (SWI) has an important role in the management of cerebrovascular strokes.

Patients and Method: The study was conducted upon 50 patients clinically diagnosed with cerebro-vascular strokes and referred to department of radio-diagnosis, Faculty of Medicine, Minia University. Computed tomography (CT) was done at first then magnetic resonance imaging was performed on a 1.5T Philips MR system using conventional MRI sequences as fluid attenuated inversion recovery (FLAIR), T2-weighted, T1-weighted and advanced sequences as susceptibility-weighted imaging (SWI) with the parameters including slice thickness, voxel size, field of view (FOV) and matrix,. They were done after the approval of ethical committee of our institution. Informed written consents were taken from the patients or their relatives.

Results: In our study, we found that 35 patients presented with acute non hemorrhagic infarction even on SWI and 15 patients presented with hemorrhagic infarction noted in SWI. Only ten of those patients with hemorrhagic infarction detected in CT. We found that detection rate of hemorrhage in SWI sequence was (100%). Detection rate of hemorrhage in CT was (33.3%). In SWI as regarding detection of different signs of acute ischemic strokes we found that of hemorrhage was (88%), detection rate of prominent cortical veins in vicinity of infarct was (62%) and detection rate of dark vessel sign was 6%. Comparative studies between them were done revealed that hemorrhage was the most important sign detected at SWI.

Conclusion: From this study we concluded that new imaging SWI MRI modality is a valuable MRI sequence in imaging hemorrhagic transformation in ischemic stroke.

Keywords: MRI, SWI, DWI, stroke, infarction.

Introduction

Stroke or cerebrovascular accident (CVA) is a clinical term which represent a sudden neurological

insult persisting for more than 24 hours as a sequel of an alteration of normal blood supply to the brain. Stroke is the third leading cause of mortality worldwide with significant morbidity rate among survivors. In hemorrhagic stroke, bleeding occurs directly into the brain parenchyma. The usual mechanism is thought to be leakage from small intra-cerebral arteries damaged by chronic hypertension. Imaging of stroke is used to differentiate ischemic from hemorrhagic stroke, arterial from venous infarction and to distinguish anterior and posterior circulation strokes. ⁽¹⁾ Non-contrast head CT (NCCT) is the first-line diagnostic test for emergency evaluation of acute stroke due to its speed

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of imaging, widespread availability and low cost. In CT small infarcts are less likely to be visible and detect parenchymal hemorrhage with near 100% accuracy only within 5–7 days of stroke. From this point of view, magnetic resonance imaging (MRI) is increasingly being used in the diagnosis and management of acute ischemic stroke and is sensitive and relatively specific in detecting changes that occur after such strokes. Magnetic resonance can detect acute hemorrhage within ischemic area through the first six hours. ⁽²⁾ Routine MR sequences remain specific for hemorrhage in 90% of patients. ⁽³⁾ In the remaining 10% detection of hemorrhage may be difficult as low signal caused by haemosiderin not visible on spin echo T2 MR and other sequences vary in their sensitivity to the presence of haemosiderin. So it is imperative to use new imaging technique as susceptibility weighted imaging (SWI). It is a magnetic resonance (MR) technique that is exquisitely sensitive to paramagnetic substances such as deoxygenated blood, blood products, iron and calcium. Susceptibility weighted imaging (SWI) used to assess ischemic area in patients with acute ischemic infarction based on elevation of deoxy-hemoglobin to oxy-hemoglobin ratio in venous system of the ischemic brain tissue with hypo-perfusion which contributes to the magnetic susceptibility difference between veins and the surrounding ischemic brain tissue. ^(4,5) Deoxy-hemoglobin within the veins lead to visualization of prominent vein (which appear hypointense) over the affected cerebral hemisphere on susceptibility-weighted imaging (SWI) called prominent vein sign. This property accounts for the blood oxygen level dependent (BOLD) effect. ⁽⁶⁾ Susceptibility-weighted imaging can detect spontaneous hemorrhagic transformation of ischemic stroke earlier than CT scans as it is more sensitive in detecting minute amount of hemorrhage within infarction than CT. ^(7,8) However, the ability of SWI to detect recurrent hemorrhage has not been assessed. It detects microbleed which may be a marker for patients at risk for intra-cerebral hemorrhage. Early detection of bleeding within ischemic area is very important as hemorrhage is a contraindication to the use of anticoagulant and thrombolytic therapy in the acute stroke setting. Also SWI used to assess intravascular clots as it detects thrombus within intracranial artery which appear dilated and hypointense in comparison with the other side giving what is called blooming artifact. SWI sequences also have the potential to assess tissue viability. ^(9,10) Assessment of ischemic penumbra is essential for predicting evolution or deterioration in patients with acute ischemic infarction. ⁽¹⁰⁾

Aim of the work: The aim of this study is to assess the role of susceptibility-weighted imaging in assessment of hemorrhagic transformation in patients with acute ischemic infarction.

Patients and Method

Study design and population: In a prospective study 30 patients with clinically diagnosed to have acute stroke were included diagnosed in neuropsychiatry department and they were referred to department of radio-diagnosis, Faculty of Medicine, Minia University. The study was done between October 2018 to September 2019. The examination was done after the approval of ethical committee of our institution. Informed written consents were taken from the patients or their relatives

Inclusion and exclusion criteria

Inclusion criteria:

- All patients included in this study were diagnosed clinically having acute stroke.
- Age older than 18 years.
- Stroke symptoms lasting >1 hour.
- National Institutes of Health Stroke Scale (NIHSS) score is more than 4.

Exclusion criteria: General contraindications to MRI as the presence of any paramagnetic substances such as pacemakers, metallic clips or claustrophobic patients were excluded from the study. Patients with an NIHSS score less than or equal to 4 were excluded.

Method

CT scanning: CT was performed with a CT HiSpeed 16 slice scanner (GE Medical Systems, Milwaukee, WI) in the hospital emergency department using the non helical scanning technique: 120 KV, 300 mA, 1-second scanning time, and 5 mm section thickness.

MRI technique: MR imaging was performed using 1.5 Tesla MR Scanner (Ingenia, Philips Healthcare, Netherlands). All patients were imaged in the supine position using standard quadrature head coil. The MRI examination was conducted on the brain including the following MRI sequences; Axial T1 images utilizing the following parameters: repetition time (TR) of 800 msec/echo time (TE) of 30 msec, slice thickness of 5 mm, (NSA) 3, matrix 512x 512, gap 1–2 mm, flip angle=90 ° and FOV = 230mm. Axial T2 weighted images utilizing

the following parameters: repetition time (TR) of 4800 msec/echo time (TE) of 110 msec, slice thickness of 5 mm, number of signal averages (NSA)=3, matrix 512x 512, gap 1–2 mm, flip angle=90 ° and field of view (FOV)= 230mm. Axial FLAIR images utilizing the following parameters: repetition time (TR) of 6000 msec/echo time (TE) of 140 msec, slice thickness of 5 mm, (NSA) 3, matrix 512x 512, gap 1–2 mm, flip angle=90 ° and FOV = 230mm. Axial SWI images utilizing the following parameters: repetition time (TR) of 43 msec/echo time (TE) of 25 msec, slice thickness of 3 mm, matrix 300x300, gap 1–2 mm, flip angle=20 ° and FOV = 230mm.

Data processing and image interpretation: The images were transformed to Philips 881030 Intelli-Space IX/LX Workstation. They were evaluated as following:

Image interpretation: All patients were imaged by CT and evaluated for presence of hemorrhage within infarct areas and evidence of early ischemic changes (EIC) (using stroke window width of 30HU and center level of 35 HU) which was defined by the presence of one or more of the following findings: sulcal effacement, hyperdense MCA/basilar artery sign, basal ganglia/subcortical hypodensity and loss of gray-white differentiation. Then patients had MRI using conventional sequences to evaluate site, size and extension of infarct area as well as signal intensity at different pulse sequences. Presence or absence of infarction using SWI and other sequences as well as type of hemorrhage either macro-hemorrhage (more than 50% of infarct area) or pitechial hemorrhage (less than 50% of infarct area) were assessed. Detection of dark vessel and prominent cortical veins in vicinity of infarct area was also done using MRIcro software to assess venous structures in 5 consecutive sections around the level of the lateral ventricles from just above the level of basal ganglia to the highest section because these sections include most of the cerebral vein. Bilateral venous voxel counts were computed and the asymmetry index (ratio of voxel numbers of cerebral veins between the ipsilateral and contralateral side) was calculated. Each infarct area in each patient appears in CT was correlated with its similar on SWI.

Statistical analysis: Statistical analysis was performed using the SPSS software for Windows v. 20 (SPSS Inc., Chicago, IL). Tests of significance (Repeated

measures ANOVA, Cochran’s Q tests, Kappa statistics and ROC Curve analysis). P-values less than 0.05 (5%) was considered to be statistically significant. Mean, standard deviation (\pm SD) and range for parametric numerical data, while median and inter-quartile range (IQR) for non-parametric numerical data. Frequency and percentage of non-numerical data.

Results

Our study included 50 patients with acute stroke diagnosed in our neurological department. The mean age of all patients was (36.24) years and as regarding gender of the patients (84%) of patients were females and (16%) were males. Total of 35 patients had no acute hemorrhage even on SWI and 15 patients had hemorrhagic infarction. Ten of those patients with hemorrhagic infarction detected in CT and 5 patients of those patients with hemorrhagic transformation detected in SWI and not in CT. We found that detection rate of hemorrhage in SWI sequence was (100%). Detection rate of hemorrhage in CT was (66.6%). Comparative studies between CT and SWI sequences revealed significant increase in sensitivity and specificity of detection of hemorrhage in SWI sequence with highly significant statistical difference ($p < 0.001$) as in (table I). In SWI as regarding detection of different signs of acute ischemic strokes we found that of hemorrhage was (88%), detection rate of prominent cortical veins in vicinity of infarct was (62%) and detection rate of dark vessel sign was 6%. Comparative studies between different sign in SWI was done revealed that SWI had significant increase in sensitivity and specificity of detection of hemorrhagic transformation over detection of other signs with highly significant statistical difference ($p < 0.0001$) as in table II. No significant difference was found in detection of intravascular clot in SWI in comparison with CT ($p > 0.05$).

Table I: detection of hemorrhagic transformation in ischemic stroke in CT in comparison to SWI using Roc-curve analysis:

	AUC	P value	SE
Hemorrhagic transformation in SWI	0.987	<0.0001	0
Hemorrhagic transformation in CT	0.497	0.015	0.032

SE= Standard Error, AUC= Area under curve, ROC =Receiver

operating characteristic.

Table II: Comparison between different signs of ischemic stroke in SWI in 30 patients with ischemic stroke:

Variable	Detection rate of dark vessel sign	Detection rate of prominent cortical vein	Detection rate of hemorrhage	Cochran's Q test
				P value
SWI	(6%) ^^	(62)^^	(88%) ^^	= 0.097 #

^^% per total of 15 patients, # Cochran's Q test.



Figure 1: Axial CT image of same patient show right sided subacute infarction with no definite hemorrhage noted.



Figure 2: Axial SWI shows blooming signal seen at right parietal region denote hemorrhage .

Discussion

SWI is as an important sequence that detect critical information as regarding hemorrhagic transformation and intravascular clot of ischemic stroke. It has demonstrated advantages over conventional MRI sequences and

CT imaging in detection of hemorrhagic events in the vicinity of infarction due to its exquisite sensitivity to paramagnetic substances such as deoxyhemoglobin. SWI venography allows clear visualization of cerebral veins. Shortly after arterial occlusion in patients with acute stroke, there is an increase in deoxyhemoglobin and a decrease in oxyhemoglobin within cerebral veins leads to a signal drop along the course of cerebral veins on SWI venography. SWI venography may thus provide the oxygen metabolic information about ischemic brain tissue by the noninvasive estimation of blood oxygen level. (11) The acknowledgment of this lead to a revolution in detection of hemorrhagic transformation in ischemic stroke and increased interest in SWI. Our study aims to assess presence of hemorrhage in patients with ischemic stroke using different MRI sequences including SWI and CT imaging. Most of our patients were females (84%).

We are in agreement with several authors as Deepti Naik and Sanjaya Viswamitra Studies who reported that SWI was an important sequence in detection of hemorrhagic transformation in infarct area over CT and other MRI sequences. Chronic hemorrhages in a patient with stroke may reflect the vulnerability of the vascular system and has been suggested as a predictor for future bleed particularly in patients undergoing thrombolytic therapy. We agree with Haacke EM and Tang J et. al. study who stated that SWI can demonstrate venous changes at an infarct which appear as multiple prominent hypointense veins in the vicinity of infarct.

Conclusion

Finally, in our study we were in agreement with the findings reported by the other studies regarding the great value of SWI in assessment of ischemic stroke. SWI has the ability to identify several parameters such as hemorrhage which may be of prognostic value in making therapeutic decisions. Based on our study, future implementation of adding the SWI sequence beside the conventional MR sequences as a routine modality in

patients with ischemic stroke is important.

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References

1. Wardlaw JM, Lewis SC, Dennis MS,s (1998) Is visible infarction on computed tomography associated with an adverse prognosis in acute ischaemic stroke? *Stroke* 29:1315-1319.
2. Wardlaw JM. What pathological type of stroke is it? In: Warlow CP, et al, eds. *Stroke, a practical guide to management*, 2nd ed. Oxford: Blackwell Science (in press). NOTES In depth and comprehensive coverage of brain imaging in stroke set out in a practical and logical order with lots of examples. There are important additions to the second edition so read that in preference to the first, as there has been an explosion of information on neuroimaging since the first edition appeared.
3. Wardlaw JM, Statham PFX (2000) How often is haemosiderin not visible on routine MRI following traumatic intracerebral haemorrhage. *Neuroradiology* 42:81-84.
4. Hermier M, Nighoghossian N. Contribution of susceptibility-weighted imaging to acute stroke assessment. *Stroke* 2004;35:1989-94.
5. Mittal S, Wu Z, Neelavalli J, et al. Susceptibility-weighted imaging: technical aspects and clinical applications, part 2. *AJNR Am J Neuroradiol* 2009;30:232-52.
6. Patel MR, Edelman RR, Warach S. Detection of hyperacute primary intraparenchymal hemorrhage by magnetic resonance imaging. *Stroke*. 1996;27:2321–2334.
7. Nighoghossian N, Hermier M, Adeleine P, Blanc-Lasserre K, Derex L, Honnorat J, Philippeau F, Dugor JF, Froment JC, Trouillas P. Old microbleeds are a potential risk factor for cerebral bleeding after ischemic stroke. A gradient-echo T2*-weighted brain MRI study. *Stroke*. 2002;33:735–742
8. Hermier M, Nighoghossian N, Derex L, Bertheze`ne Y, Blanc-Lasserre K, Trouillas P, Froment JC. MRI of acute post-ischemic cerebral hemorrhage in stroke patients: diagnosis with T2*-weighted gradient-echo sequences. *Neuroradiology*. 2001; 43:809–815
9. Gro`hn OH, Kauppinen RA. Assessment of brain tissue viability in acute ischemic stroke by BOLD MRI. *NMR Biomed*. 2001;14:432-440.
10. Kavec M, Gro`hn OHJ, Kettunen MI, Silvennoinen MJ, Penttonen M, Kauppinen RA. Use of the spin echo T2 BOLD in assessment of misery perfusion at 1.5 T. *MAGMA*. 2001;12:32-38. 15.
11. Lee JM, Vo KD, An H, Celik A, Lee Y, Hsu CY, Lin W. Magnetic resonance cerebral metabolic rate of oxygen utilization in hyperacute stroke patients. *Ann Neurol*. 2003;53:227–232.

Risk Factors for Pediatric Intensive Care Admission among Asthmatic Children in Aseer, South-West Saudi Arabia

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Abstract

Background: The burden of childhood asthma continues to rise with increasing rates of asthma prevalence, severity, and death. Asthma is the one of the most chronic pediatric disorder and is frequent caused for hospitalization and pediatric intensive care unit (PICU) admissions.

Objective: To determine risk factors for PICU admission in children with asthma.

Patients and Method: The study used a retrospective case-control design. The cases included children admitted to the PICU and controls were children admitted to the hospital general ward.

Results: A total of 320 charts of asthmatic children were reviewed: 72 (22.5%) admitted to the PICU and 248 (77.5%) admitted to the general ward. Univariate analysis indicated that asthmatic children admitted to PICU were more likely to be older ($p<0.001$), have longer asthma duration ($p<0.001$), higher use of: inhaled corticosteroids ($p<0.0001$), cromolyn ($p=0.03$), long acting β_2 agonists ($p=0.001$), and poor adherence to treatment ($p=0.002$). However, multivariate analysis revealed that longer duration of asthma ($p=0.03$), use of inhaled corticosteroids ($p=0.01$), and non-compliance with therapy ($p=0.02$) were associated with an increased risk of PICU admission. **Conclusions:** this study identified a significant number of risk factors associated with PICU admission. Early recognition could help to develop preventive strategies, improve efficacy of treatment and reduce admission to PICU.

Keywords: Asthma, Risk factors, Children, Pediatric intensive care.

Introduction

Bronchial asthma is a common and potentially serious health problem globally, with estimated 300 million affected individuals, with great variation between countries¹. The incidence and prevalence of asthma have increased during the last 20 years^{2,3}. Asthma is considered one of the most common chronic disorders in

the Kingdom of Saudi Arabia as 2 million Saudis suffer from asthma⁴. It imposes a substantial burden on family, health care services, and society as a whole⁵.

Asthma can cause episodic coughing, wheezing, shortness of breath, chest tightness and exacerbations that sometimes require urgent health care services and may be fatal. Around 30% of asthmatic exacerbations attended to the emergency department of a hospital require hospitalization and up to 20% require intensive care management^{6,7}. In the past two decades, hospital admissions for asthma have been increasing despite improved knowledge about the disease and the availability of better treatment modalities. Severe acute asthma in children is associated with substantial morbidity and may require Pediatric Intensive Care Unit (PICU) admission. Understanding the risk factors

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for hospitalization for asthma is important for treating and reducing their effects on society⁸. This study was designed to determine the potential risk factors for PICU admission in Saudi children with asthma.

Patients and Method

We performed a retrospective case-control study at the Abha Private Hospital, Abha, South-west Saudi Arabia between January 2014-December 2018.

Study Design: The inclusion criteria were as follows: all children aged 2-14 years who admitted to the PICU with acute asthma which was previously diagnosed by pediatricians or pulmonologists before PICU admission were eligible as cases. The admission criteria to PICU were clinically predefined and did not change during the study period. They included respiratory failure, imminent exhaustion, no clinical benefit after continuous nebulization of bronchodilator drugs, and/or the need for mechanical ventilation. The control group included patients aged 2-14 years diagnosed with asthma who admitted to the General Pediatric Ward of the Hospital with an acute asthma exacerbations. Controls were recruited during the same period of the study.

The Exclusion Criteria: Patients younger than 2 years were excluded because bronchiolitis an acute wheezing illness occurring mainly in children younger than 2 years, closely resembles asthma and may affect our data. Patients admitted to the Hospital whose diagnosis code changed to non-asthma during hospitalization also were excluded. Children who had not been diagnosed with asthma prior to their admission and presented with their first asthmatic attack were excluded from the study because defining controls would not be feasible.

Materials

The medical records of patients and controls were reviewed and the following information extracted: Demographic variables: age, gender, number of siblings, and consanguinity. Disease variables: age at first symptoms of asthma, duration of the disease, previous admission to the PICU, and family history of asthma. Variables related to medications: inhaled/oral corticosteroids, cromolyn, long-acting β_2 agonists, leukotriene receptors antagonists, and compliance to therapy. Variables related to exposure and atopy: history of parental smoking, inhaled allergens, eczema and presence of pets in the home.

Statistical Analysis: Data were analyzed using the Statistical Software Package SPSS 19 (SPSS, Inc., Chicago, IL). Quantitative data were presented as mean+ standard deviation (SD), while qualitative data were demonstrated as frequency and percent (%). Differences between cases and controls were analyzed by Student's *t*-test for continuous normally distributed variables. Categorical data were assessed by chi-square test. The dependent variable was PICU/General Pediatric Ward admission. Variables found to be significant on univariate analysis were subsequently evaluated by multiple logistic regression. For all analysis, statistical tests were two-sided, and $p < 0.05$ was regard as significant.

Results

A total of 320 asthmatic children were enrolled in the study: 72 (22.5%) were admitted to PICU, and 248 (77.5%) to the General Pediatric ward. The mean age was statistically older in patients who admitted to PICU than in those who admitted to the General Pediatric ward (6.3 ± 0.4 vs 4.6 ± 0.3 respectively, $p < 0.001$). Females were preponderance in both groups but this finding was statistically non significant. Cases and controls were matched in terms of breast fed for 6 months, number of siblings, and first degree consanguinity (table 1).

Disease characteristics and risk factors in the two groups are shown in (table 2). Disease features: the duration of asthma was significantly longer in the PICU group than in the General Pediatric Ward group (25.1 ± 0.2 months vs 21.0 ± 0.7 months respectively, $p < 0.001$). Parental smoking and exposure to inhaled allergens were significantly reported more frequently in the group with PICU admission, $p < 0.05$.

Medications: significant differences between the two groups were noticed including higher use of inhaled corticosteroids ($p < 0.0001$), cromolyn ($p = 0.03$), and long acting β_2 agonists ($p = 0.001$) in the PICU group. More patients in the PICU group had poor compliance with therapy (40.3% vs 22.2%, Odds ratio (OR) = 2.36, Confidence interval (CI) (1.35-4.13), $p = 0.002$). Other factors: asthmatic children who admitted to PICU had more frequent prior admissions to the PICU ($p = 0.0003$).

Multivariate analysis (table 3) revealed that longer duration of the disease ($p = 0.03$), use of inhaled corticosteroids ($p = 0.01$), and non-compliance with therapy ($p = 0.02$) were significantly associated with an increased risk for admission to the PICU compared to the General Pediatric Ward.

Table 1: Demographic characteristics of asthmatic patients admitted to PICU and General Pediatric ward

Characteristics	PICU (n = 72)	General Ward (n = 248)	OR (95% CI)	p-value
Age (Year) ^a	6.3 ± 0.4	4.6 ± 0.3	1.30 (1.78-1.61)	< 0.001
Gender^b				
Male	30 (41.7)	106 (42.7)	0.95 (0.56-0.61)	0.9
female	42 (58.3)	142 (57.3)		
Breast-fed 6 months ^b	29 (40.3)	102 (41.1)	0.97 (0.57-1.65)	0.8
Number of siblings^b				
> 4	22 (30.6)	75 (30.2)	1.01 (0.57-1.79)	0.9
< 4	50 (69.4)	173 (69.8)		
First-degree consanguinity ^b	32 (44.4)	106 (42.7)	1.07 (0.63-1.81)	0.7

^aValues are means + SD, ^bNumber (%), OR: odds ratio; 95% CI: confidence interval, PICU: pediatric intensive care unit

Table 2. Disease characteristics and risk factors in patients admitted to PICU and General Pediatric ward

Risk factors	PICU (n = 72)	General Ward (n = 248)	OR (95% CI)	p-value
Disease features				
Age at first symptoms of asthma (Year) ^a				
Duration of asthma (month) ^a	3.1 ± 0.1	3.2 ± 0.5	1.6 (0.01-0.21)	0.09
Family history of asthma ^b	25.1 ± 0.2	21.0 ± 0.7	3.1 (4.26-3.93)	<0.001*
Exposure and atopy ^b	18 (25.0)	52 (20.9)	1.2 (0.67-2.32)	0.4
Parental smoking	31 (43.1)	75 (30.2)	1.74 (1.01-2.99)	0.04*
Inhaled allergens	24 (33.3)	40 (16.1)	2.60 (1.43-4.70)	0.002*
Pet cat	15 (20.8)	57 (22.9)	1.91 (0.96-3.79)	0.06
Eczema	31 (43.1)	95 (38.3)	1.2 (0.71-2.07)	0.5
Medication^b				
Inhaled corticosteroids	38 (52.8)	41 (16.5)	5.6 (3.18-9.99)	<0.0001*
Oral corticosteroids	9 (12.5)	15 (6.0)	2.2 (0.92-5.30)	0.07
Long acting β_2 agonist	17 (23.6)	22 (8.9)	3.17 (1.57-6.38)	0.001*
Cromolyn	12 (16.7)	20 (8.1)	2.28 (1.05-4.92)	0.03*
Non-compliance with therapy	29 (40.3)	55 (22.2)	2.36 (1.35-4.13)	0.002*
Co-morbidities^b				
GERD	4 (5.6)	11 (4.4)	1.26 (0.39-4.10)	0.6
Previous admission to PICU^b	10 (13.9)	5 (2.0)	7.83 (2.58-23.76)	0.0003*

^aValues are means + SD, ^bNumber (%), OR: odds ratio; 95% CI: confidence interval, GERD: gastroesophageal reflux disease; PICU: pediatric intensive care unit, *Significant *p* value

Table 3: Significant risk factors on multivariate analysis

Factors	OR (95% CI)	p-value
Duration of asthma	2.17 (1.23-4.30)	0.03
Use of inhaled corticosteroids	3.01 (1.48-5.90)	0.01
Non-compliance with therapy	1.46 (1.01-1.07)	0.02

OR: odds ratio; 95% CI: confidence interval

Discussion

The impact of childhood asthma on the health care system is considerable. As one of the most chronic

diseases of children, bronchial asthma is frequently caused for emergency room visits and hospital admission³. An admission to PCU with asthma is potentially life threatening and is a recognized risk factor for subsequent death⁹.

This retrospective study was conducted to identify risk factors for PICU admission. Our study showed that asthmatic children who were admitted to the PICU were significantly older than those who admitted to the General Pediatric Ward. Children in the PICU group were approximately 2 years older than the control group.

The possible explanation may be due to the severity of the asthmatic attack and PICU admission were related to a longer duration of asthma in older children and perhaps the development of remodeled airways. This explanation is supported by the longer history of asthma in children with PICU admission. Many studies reported a longer duration of asthma in children admitted to ICU suggesting a link between asthma duration and severity that may account for the findings¹⁰⁻¹². Female gender was pronounced as a risk factor for hospitalization and readmission in studies conducted by Nunez et al¹³ and Kargar et al¹⁴. In our study although there was a female preponderance but statistically was non-significant.

Previous admission to the PICU was higher in group admitted to the PICU and the difference was statistically significant ($p = 0.0003$). This finding is consistent with previous studies that reported previous admission to emergency department and PICU were also linked to hospital readmission¹⁵⁻¹⁷. However, other studies did not reported significant differences.^{10,13} Parental smoking and inhaled allergens have adverse influences on asthma and hospital admission¹⁸. In the present study, parental smoking and exposure to inhaled allergens were significantly reported more frequently in children with PICU admission ($p < 0.05$). This confirms the previous reports in which a history of exposure to smoking and being in continuous contact with allergens have been known as risk factors for morbidity, asthma severity, and hospitalization for asthma¹⁹⁻²¹.

Atopy is a recognized risk factor for severe asthma¹. We found that eczema was not linked to PICU admission possibly because of small patients number. Serum IgE levels provide a quantitative definition of atopy and may have been a better measure to use, but serum IgE were not recorded in a sufficient number of patients files for analysis.

In their systemic review, Alvarez et al²² reported that the use of inhaled corticosteroids measured in a dose-independent fashion did not significantly increase or decrease the risk for near fatal and fatal asthma in adults. Some studies in children observed that inhaled corticosteroids prophylaxis is effective controlling symptoms and reducing hospitalization and death²³⁻²⁵. These findings are in contrast to our results. The difference would be explained by greater severity of asthma and non-compliance with therapy in the PICU group. Similar findings were noted in a comparable study of asthmatic adults²⁶. Similarly, the higher numbers of patients

receiving treatment with long acting β_2 agonists, the use of asthma management plans, and asthma management by a respiratory specialists are factors likely to be related to asthma severity and PICU admission¹². Differences between the routine patient care, respective guidelines for treatment of asthma, age and other characteristics of the patients complicate the comparisons between these studies.

Our study noted that asthmatic children admitted to PICU were significantly had poor compliance with therapy. This finding is consistent with several studies that have suggested that poor adherence with asthma management predisposes asthma patients to more severe attacks and death¹². The barriers to adherence to asthma management may be the medications (steroids), the patients, their families, and physicians^{27,28}.

Previous admission to emergency department, general Ward and PICU admissions were linked to higher hospital readmission in studies by Lasmar et al¹⁶, Visitsumthorn et al¹⁷ and Kargar et al.¹⁴ In the present study, previous admission rate to PICU was higher in group admitted to PICU and the difference was statistically significant ($p = 0.0003$). After multivariate analysis, 3 risk factors remained significant for PICU admission in children with asthma. These included, longer duration of the disease, use of inhaled corticosteroids, and non-compliance with therapy.

A limitation of the present study is that we used a retrospective study design, with information collected from the medical records. For this reason, several variables could not be analyzed reliably such as quality of the home, and instructions by a specialized nurse.

In conclusion, this study identified duration of asthma, use of inhaled corticosteroids, and non-compliance with therapy as significant risk factors for PICU admission in Saudi children with asthma. Future prospective standardized studies are needed to validate these results. Early identification of children at risk for PICU admission may result in development of preventive strategies, improvement of efficacy of treatment and thus in a reduction of PICU admission for asthma.

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References

1. Global initiative for asthma: Global strategy for asthma management and prevention. Global initiative for asthma website 2019; <http://www.ginasthma.org/>.
2. Gupta RS, Weiss KB: The 2007 national asthma education and prevention program asthma guidelines: accelerating their implementation and facilitating their impact on children with asthma. *Pediatrics* 2009; 123 (3): 193-198.
3. Al Frayh AR, Shakoor Z, Gad El Rab MO, Hasanain SM: Increased prevalence of asthma in Saudi Arabia. *Ann Allergy Asthma Immunol* 2001; 86 (3): 292-296.
4. Horaib YF, AlAmri ES, Alanazi WF, Sharahili EA, Alolayah AM, Alrobian MA. The prevalence of asthma and related risk factors among the children in Riyadh, Saudi Arabia. *The Egyptian Journal of Hospital Medicine* 2018; 70 (6): 965-973.
5. Newacheck PW, Halfon N. Prevalence, impact and trends in childhood disability due to asthma. *Arch Pediatr Adolesc Med* 2000; 154: 287-293.
6. Morell F, Genover T, Munoz X, Garcia-Aymerich, Fereer J, Cruz MJ. Rate and characteristics of asthma exacerbations: the ASMAB I study. *Arch Bronconeumol* 2008; 44: 303-311.
7. Morell F, Genover T, Benaque E, Picado C, Munoz X, Cruz MJ. Incidence and characteristics of asthma exacerbations in Barcelona (ASMAB II). *Arch Bronconeumol* 2009; 45: 550-555.
8. Kuo, Craig TJ. A retrospective study of risk factors for repeated admissions for asthma in a rural/suburban university hospital. *J Am Osteopath Assoc* 2001;101(5): 14-17.
9. Masoli M, Fabian D, Holt S, Beasley R. The global burden of asthma: executive summary of the GINA Dissemination Committee report. *Allergy* 2004; 59(5): 469-478.
10. Belessis Y, Dixon S, Thomsen A, Duffy B, Rawkinson W, Henry R et al. Risk factors for an intensive care unit admission in children with asthma. *Pediatr Pulmonol* 2004; 37: 201-209.
11. Bratton SL, Odetola FO, McColeagan JB, Cabana MD, Levy FH, Keenan HT. Regional variation in ICU care for pediatric patients with asthma. *J Pediatr* 2005; 147(3): 355-361.
12. Lyell PJ, Villanueva E, Burton D, Freezer NJ, Bardin PG. Risk factors for intensive care in children with acute asthma. *Respirology* 2005; 10(4): 436-441.
13. Nunez B, Fiorentino F, Kersul A, Belda S, Garcia S, Gutierrez C et al. Characteristics of asthma patients admitted to an intermediate respiratory care unit. *Arch Bronconeumol* 2013; 49(4): 146-150.
14. Kargar Maher MH, Habibi P, Bilan N. Clinical predictors of intensive care unit admission for asthmatic children. *Int J Pediatr* 2015; 3: 713-716.
15. Alshehri MA, Almegamesi TM, Alfrayh AS. Predictors of short-term hospital readmissions of asthmatic children. *J Family Community Med* 2005; 12(1): 11-17.
16. Lasmar LM, Camargo PA, Goulart EM, Sakurai E. Risk factors for multiple hospital admissions among children and adolescents with asthma. *J Bras Pneumol* 2006; 32 (5): 391-399.
17. Visitsunthorn N, Lilitwat W, Jirapongsananuruk O, Vichyanond P. Factors affecting readmission for acute asthmatic attacks in children. *Asian Pac J Allergy Immunol* 2013; 31(2): 138-141.
18. Martin AJ, Campbell D, Gluyas PA, Coates JR, Ruffin RE, Roder DM, et al. Characteristics of near-fatal asthma in childhood. *Pediatr Pulmonol* 1995; 20: 1-8.
19. Sporik R, Platts-Mills TA, Cogswell JJ. Exposure to house dust mite allergen of children admitted to hospital with asthma. *Clin Exp Allergy* 1993; 23: 740-746.

20. Miles J, Cayton R, Ayres J. Atopic status in patients with brittle and non-brittle asthma: A case-control study. *Clin Exp Allergy* 1995; 25: 1074-1082.
21. Salamzadeh J, Wong ICK, Hosker HSR, Chrystyn H. A logistic regression analysis of predictors for asthma hospital re-admissions. *Iran J Pharm Res* 2003; 2: 5-9.
22. Alvarez GG, Schulzer M, Jung D, Fitzgerald JM. A systemic review of risk factors associated with near-fatal and fatal asthma. *Can Respir J* 2005; 12(5): 265-270.
23. Bames PJ. Inhaled glucocorticoids for asthma. *N Engl J Med* 1995; 332: 868-875.
24. Macarthur C, Caplin C, Parkin PG, Feldman W. Factors associated with pediatric asthma readmissions. *J Allergy Clin Immunol* 1996; 98(5): 992-993.
25. Minkovitz CS, Andrews JS, Serwint JR. Rehospitalization of children with asthma. *Arch Pediatr Adolesc Med* 1999; 153(7): 727-730.
26. Martin AJ, Campbell DA, Gluyas PA, Coates JR, Ruffin RE, Roder DM et al. Characteristics of near-fatal asthma in childhood. *Pediatr Pulmonol* 1995; 20(1): 1-8.
27. Conn KM, Halterman JS, Fisher SG, Yoos HL, Chin NP. Parental beliefs about medications and medication adherence among urban children with asthma. *Ambul Pediatr* 2005; 5(5): 306-310.
28. Modi AC, Lim CS, Yu N, Geller D, Wagner MH, Quittner AL. A multi-method assessment of treatment adherence for children with cystic fibrosis. *J Cyst Fibrosis* 2006; 5(3): 177-185.

Evaluation the Prevalence of Association between Cranial Congenital Fetal Anomalies and Extra-Cranial Congenital Fetal Anomalies

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Abstract

The purpose of this study evaluated the Percentage of association between cranial congenital fetal anomalies and extra-cranial congenital fetal anomalies. Patients and method: The study conducted for two years in Minia University Fetomaternal Unit 2018-2019, We examined 2091 cases referred to us from all Minia regions because of congenital anomalies risk, 263 cases detected carrying different types and numbers of anomalies. Results: The number of congenital anomalies in this study was 263 with percentage (12.5%) but when these number of congenital anomalies linked to all Antenatal care cases that attached to Minia University hospital in two years with average number (40,000) cases in two years we found percentage was (0.65%). In this study the top affected system was the central nervous system with percentage 32.7%, then the renal system 18.6%, then the cardiovascular system 14.8%, then the chest 8%, then the musculoskeletal system 7.2% then hydrops fetalis 6.5% followed by GIT 5.7% then the neck 5.3%, followed by face which was the least prevalent Anomalies which the percentage was 1.1%. Conclusions: We found that CNS was the most common system affected and the most rare system affected was the face. The ratio of congenital anomalies in Minia Governorate was 0.65% Which was less than the global percentage.

Keywords: Prevalence, Cranial, Anomalies, CNS.

Introduction

Congenital fetal anomalies are structural or functional aberration from normal Including metabolic abnormalities, present postnatal. These abnormalities may be a result of defective embryogenesis or intrinsic defects in the development process. Birth defects can be single or included in A Syndromic manner also may be a leading cause of the neonate disability or even mortality.⁽¹⁾

Antenatal care designed mainly for Detection of congenital fetal anomalies. Healthy baby outcome postnatally a leading indication to use ultrasound in pregnancy. Risk factors for congenital anomalies are multifactorial, they include advanced maternal age, previously anomalous baby, family history of birth abnormalities, consanguinity, maternal diseases, drug abuse, infections as viral infections and Ionized radiation exposure. The detection of birth defects can be

the cornerstone of regional health records for future use in the preventive programs.⁽²⁾

The control of genetic linked abnormalities should be based on A Well integrated and comprehensive plane, including the best possible curative and prevention measures like community education screening programs, genetic counseling, and the availability of early detection measures. Efficient Screening programs (registries and databases) and continued investment in genetic research are the cornerstone of any successful public health intervention, particularly in low-resource communities.⁽³⁾

Prenatal screening using the ultrasound for detection the fetal anomalies should be started at 12-14 and 18-22 weeks of pregnancy. Although routine fetal anomalies scan if very helpful in detection of fetal anomalies but there are limitations to detect every anomaly, as not all anomalies are evident at these scan

age when the ultrasound tool had been used, also the scan itself is operator dependant and widely based on the available efficient machines. Some fetuses are difficult to be scanned clearly, because of many reasons as oligohydramnios or maternal obesity⁽⁴⁾

Patients and Method

Study design: cross sectional observational prospective study **Setting:** Al-Minya University maternity hospital, Department of Obstetrics and Gynaecology, Fetomaternal unit which is a tertiary governorate maternity hospital that covers 9 local areas with people about 5.5 millions and these hospital accept referral from all governorate hospitals. Time and sample size : The study extends from may 2017 to may 2019(2 years). **Methodology:** The study will be conducted according the general ethics and principles that approved by the department committee. **Step 1**

Ascans survey for those patient that referred for Cranial anomalies which will include the following items:

Skull Examination of integrity and normal shape, and measurement of biparietal diameter and head circumference. **Brain** Examination of cerebral ventricles, choroid plexuses, midbrain, posterior fossa (cerebellum and cisterna magna), and measurement of the anterior and posterior horns of the lateral ventricles. **Face** Examination of the profile, orbits and upper lip **Neck** Measurement of nuchal fold thickness. **Spine** Examination both longitudinally and transversely. **Heart** Examination of rate and rhythm, four-chamber view, and outflow tracts. **Thorax** Examination of the shape of the thorax, the lungs and diaphragm **Abdomen** Examination of the stomach, liver, kidneys, bladder, abdominal wall and umbilicus, and measurement of abdominal circumference. **Limbs** Examination of the femur, tibia and fibula, humerus, radius and ulna, hands and feet (including shape and echogenicity of long bones and movement of joints), and measurement of femur length. **Step 2 Categorizing the patient into 2 main group** Group 1 includes patients with isolated cranial anomalies Group 2 includes those which show any extra cranial anomalies association with cranial anomalies. **Step3** Compare between group 1 and group 2 to detect the percentage of association collectively. **Step 4** Each cranial anomaly will be compared with each extracranial anomaly to detect the percentage of association. Each association will be linked with the patient age and gestational age also baby gender.

The collected data were coded, tabulated and statistically analyzed using SPSS program (Statistical Package for Social Sciences) software version 24. Descriptive statistics were done for numerical data by mean, standard deviation and minimum & maximum of the range. Analyses were done for parametric quantitative variables between the two groups using independent sample *t* test. Simple, multiple and multiple stepwise discriminant functional analyses were used to determine the equations that predict the sex using different metacarpal internal measurements.

Results

This study was conducted at Al-Minya University maternity hospital, Department of Obstetrics and Gynaecology, Fetomaternal unit which is a tertiary governorate maternity hospital that covers 9 local areas with people about 5.5 millions and these hospital accept referral from all governorate hospitals from May 2017 to may 2019.

Group 1 includes patients with isolated cranial anomalies Group 2 includes those which show any extracranial anomalies association with cranial anomalies.

Table (1): Affected Systems

		N=263
Affected System	Hydrops	17(6.5%)
	CNS	86(32.7%)
	Chest	21(8%)
	CVS	39(14.8%)
	Musculoskeletal	19(7.2%)
	Renal	49(18.6%)
	GIT	15(5.7%)
	Face	3(1.1%)
	Neck	14(5.3%)
Anomaly		
	Hydrops	17(6.5%)
	Ventriculomegally	37(14.1%)
	Anaencephally	25(9.5%)
	Intracranial Hge	1(0.4%)

		N=263
	Dandy's Waler	4(1.5%)
	Isolated Vecmis hypoplasia	2(0.8%)
	Encephalocele	10(3.8%)
	Holoprosencephally	3(1.1%)
	Spina bifida	4(1.5%)
	Lung hypoplasia	21(8%)
	cardiomegally	14(5.3%)
	VSD	22(8.4%)
	Ebsteinanomaly	1(0.4%)
	Single AV coral	1(0.4%)
	RT sided aplasia	1(0.4%)
	Hypochondroplasia	17(6.5%)
	Talibus	2(0.8%)
	Bilateral renal agenesis	17(6.5%)
	Potter-1	20(7.6%)
	Bilateral hydronephrosis	10(3.8%)
	Post urethral valve obstruction	2(0.8%)
	Gastrochiasis	2(0.8%)
	Examphalus major	8(3%)
	Duedenal atresia	5(1.9%)
	Cleft lip	3(1.1%)
	cystic hygroma	14(5.3%)
	Oro-pharengal mass	0(0%)
	fetal goiter	0(0%)
	Hiatus hernia	0(0%)
	Multicystic kidney	0(0%)

Table (2): Systems of associated anomaly

		N=85
Systems of Associated Anomaly	<i>Hydrops</i>	20(23.5%)
	CNS	12(14.1%)
	Chest	10(11.8%)
	CVS	4(4.7%)
	Musculoskeletal	7(8.2%)
	Renal	14(16.5%)
	GIT	9(10.6%)
	Face	3(3.5%)
	Neck	6(7.1%)
		N=85
Associated anomaly	<i>Hydrops</i>	20(23.5%)
	Ventriculomegally	3(3.5%)
	Anaencephally	0(0%)
	Intracranial Hge	0(0%)
	Dandy's Waler	5(5.9%)
	Isolated Vecmis hypoplasia	0(0%)
	Encephalocele	0(0%)
	Holoprosencephally	3(3.5%)
	Spina bifida	1(1.2%)
	Lung hypoplasia	10(11.8%)
	cardiomegally	0(0%)
	VSD	3(3.5%)
	Ebsteinanomaly	0(0%)
	Single AV coral	0(0%)
	RT sided aplasia	1(1.2%)
	Hypochondroplasia	6(7.1%)
	Talibus	1(1.2%)
	Bilateral renal agenesis	3(3.5%)
	Potter-1	5(5.9%)
	Bilateral hydronephrosis	3(3.5%)
	Post urethral valve obstruction	2(2.4%)
	Gastrochiasis	0(0%)
	Examphalus major	1(1.2%)
	Duedenal atresia	2(2.4%)
Cleft lip	2(2.4%)	
cystic hygroma	5(5.9%)	
Oro-pharengal mass	1(1.2%)	
fetal goiter	1(1.2%)	
Hiatus hernia	6(7.1%)	
Multicystic kidney	1(1.2%)	

Table (3): Affected systems in details

		N=263	Anomaly	N (%)
Affected System	Hydrops	17	Hydrops	17(100%)
	CNS	86	Ventriculomegally	37(43%)
			Anaencephally	25(29.1%)
			Intracranial Hge	1(1.2%)
			Dandy’s Waler	4(4.7%)
			Isolated Vecmis hypoplasia	2(2.3%)
			Encephalocele	10(11.6%)
			Holoprosencephally	3(3.5%)
			Spina bifida	4(4.7%)
	Chest	21	Lung hypoplasia	21(100%)
	CVS	39	cardiomegally	14(35.9%)
			VSD	22(56.4%)
			Ebsteinanomaly	1(2.6%)
			Single AV coral	1(2.6%)
			RT sided aplasia	1(2.6%)
	Musculokeletal	19	Hypochondroplasia	17(89.5%)
			Talibus	2(10.5%)
	Renal	49	Bilateral renal agenesis	17(34.7%)
			Potter-1	20(40.8%)
			Bilateral hydronephrosis	10(20.4%)
Post urethral valve obstruction			2(4.1%)	
GIT	15	Gastrochiasis	2(13.3%)	
		Examphalus major	8(53.3%)	
		Duedenal atresia	5(33.3%)	
Face	3	Cleft lip	3(100%)	
Neck	14	cystic hygroma	14(100%)	

Discussion

These study designed to outline the prevalence of congenital anomalies through advanced Ultrasound fetal scan of referred cases of high suspicious in Minia Governorate that located in the north of upper Egypt to set up the start of the first regional register of congenital anomalies in our governorates such baseline data will be apart of planning and evaluation programs.

The frequency of congenital anomalies in this study was 263/2091 with percentage (12.5%) but when these number of congenital anomalies linked to all Antenatal care cases that attached to Minia University hospital in two years with average number (40,000) cases in two years with percentage (0.65%) this results do not match with the global incidence of prevalence of Congenital anomalies which is between (3-5%)(5) also this prevalence not match with other Egypt previous regional

studies like Giza that was found (3.17%)(6), Alexandria was found (1.6%)(7).

However a study that had been carried out in Turkey and included 22 University hospitals was found the total prevalence (3.65%)(8).

The higher frequency in live borns in Egypt may be due to either inclusion of all minor anomalies in the study or inclusion of fetal anomalies in stillbirth(9).

In this study the most common affected system is the central nervous system with percentage 32.7% followed by the renal system 18.6% followed with the cardiovascular system 14.8%, followed by the chest 8% followed by the musculoskeletal system 7.2% followed by hydrops fetalis 6.5% followed by GIT 5.7% followed by neck 5.3% followed by face which is the least prevalent anomalies with percentage 1.1%.

Our results disagree with ⁽⁴⁾ that show the most common affected system is the musculoskeletal 16.66% and the least represented anomaly is neck 4.1% .

Our results agree in the common and least represented anomalies but differ in percentage with ⁽¹⁰⁾ that show the most common affected system is the CNS 26.5% and the least represented anomaly is face 1.5%.

Our results disagree with ⁽¹¹⁾ that show the most common affected system is the CNS 30% and the least represented anomaly is GIT 3%

Conclusion

We concluded that CNS was the most frequent system affected and the least system affected was the face.

Declarations

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References

1. Rosano A et al. Infant mortality and congenital anomalies from 1950 to 1994: an international perspective. *Journal of epidemiology and community health* 2000;54:660-6.
2. Kalter H et al. Congenital malformations: etiologic factors and their role in prevention (first of two parts). *The New England journal of medicine* 1983;308:424-31.
3. WHO. Control of Genetic Diseases (Executive Board EB116/3). The World Health Organization, 2005 Geneva
4. Francine, R., Pascale, S., & Aline I a, H. Congenital anomalies: prevalence and risk factors. *Universal Journal of Public Health*, 2014; 2(2),58-63.
5. Göynümer FG, Kepkep K, Yetim G, Tuncay Y, et al. Doğumlarda Majör Konjenital Anomalilerin Retrospektif Analizi (Retrospective analysis of major congenital anomalies at birth). *Perinatol. Dergisi*; 2005; 13:31-34.
6. Temtamy SA, Abdelmeguid N, Mazen I, Ismail SR, Kassem NS, Bassiouni R. A genetic epidemiological study of malformations at birth in Egypt. *East Mediterr Health J* 1998;4(2):252-9.
7. Ansary MK. A genetic study of congenital malformations in a sample of newborns in Shatby University Maternity Hospital, Alexandria (Thesis). Alexandria, Egypt, University of Alexandria;1995.
8. Tunçbilek E. Clinical outcomes of consanguineous marriages in Turkey. *Turk. J. Pediatr.* 2001; 43:277-279
9. Shawky RM, El Sedfy HH, Abolouz SK, Labatia GY. Prevalence of congenital malformations in a thousand consecutive Egyptian liveborn. *Egypt J Med Hum Genet* 2001;2(1):43-53
10. Shawky, R. M., & Sadik, D. I. Congenital malformations prevalent among Egyptian children and associated risk factors. *Egyptian Journal of Medical Human Genetics*, 2011;12(1).
11. Tomatır, A. G., Demirhan, H., Sorkun, H. C., Köksal, A., Özerdem, F., & Cilengir, N. Major congenital anomalies: a five-year retrospective regional study in Turkey. *Genetics and Molecular Research*, 2009; 8(1),19-27.

The Effect of Type 2 Diabetes Mellitus and Treatment Regimens on the Success of Drug Resistant Tuberculosis Treatment in 2014-2018 in Riau Province

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Abstract

The immune-compromised condition due to type 2 diabetes mellitus (T2DM) can increase the risk of treatment failure in patients with drug resistant-tuberculosis (DR TB). This study aims to determine the effect of T2DM and treatment regimen on the success of DR-TB treatment in Riau Province in 2014-2018.

The design of this study was retrospective cohort using data of DR TB which were recorded in 01 DR TB form, 03 DR TB form, DR TB medical records and e TB manager at the DR TB referral hospital of Arifin Achmad Regional General Hospital and 7 sub-referral hospitals in Riau Province in 2014-2018. The independent variables were the type 2 DM and treatment regimen. The covariate variables were demographic factors namely, age, sex, marital status, occupation, education, residence category, clinical factor of previous TB treatment history, and medication adherence. The dependent variable was the success of DR TB treatment. The samples of this study were 146: 50 samples of exposed group (T2DM) and 96 samples of non-exposed group (Non T2DM). The survival analysis was used for data analysis. The results showed that 54.79% patients were successfully treated. The probability of 50% success of treatments in both T2DM and nonT2DM using old regimen (conventional method) occurred on the 729th day. While, the probability of 50% treatment success in both T2DM and Non T2DM groups using new regimen (STR/ shorter regimen) occurred faster on the 272th day.

The risk of T2DM group with the new regimens in the treatment of DR-TB was 10.66 times (95% CI 3.23-35.12). Whereas, the treatment on NonT2DM group with old regimen with marital status that was controlled showed a significant statistic value with value $p < 0.001$.

Conclusion: The use of new regimen accelerated the healing time and increased the successful treatment of patients with T2DM with DR TB.

Keywords: Type 2 diabetes mellitus (T2DM), regimen, drug-resistant tuberculosis (DR-TB).

Introduction

Drug-resistant tuberculosis (DR-TB) still has been a major public health problem globally, including in Indonesia. Indonesia is at the 7th position of countries with the most common cases of DR-TB. Data show there are 23,000 new cases of rifampicin-resistant TB

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(RR-TB) or multi-drug resistant TB (MDR-TB) with additional resistance to isoniazid surfaces every year globally.⁽¹⁾

Treatments of drug-resistant tuberculosis (DR TB) are considered to be successful when treatment results show that the patients are cured and the treatments are complete. On the other hand, treatments of DR TB are considered to be unsuccessful when treatment results show that the patients are uncured, die, drop out of taking drugs, losing in follow-up and are not evaluated⁽²⁾. The success rate of DR-TB treatment in Indonesia (patients are cured and the treatments are complete) is still considered low. Compared to the success target of DR TB treatment that must be achieved in 2020, that is 90%⁽³⁾, the results of treatment in 2016 showed that only 48% patients were cured⁽⁴⁾. Control of DR-TB must be conducted through thorough treatment and quick comprehensive action supported by strong political policies and decent regional budget⁽⁵⁾. The increase of DM cases extremely influence the failure of DR-TB treatments⁽⁶⁾.

The prevalence of T2DM continues to increase in developing countries including Indonesia. T2DM on adults occurs approximately 90-95% of all DM cases⁽⁷⁾. The influence of T2DM towards the success of TB-RO treatment was caused by longer time to conversion, drug side effect and drug interaction⁽⁷⁾⁽⁸⁾⁽⁹⁾. The DR-TB treatment became more difficult because DM can cause changes in oral absorption, reduce the binding of drug proteins in the body, and the renal insufficiency and fatty liver cause the impaired clearance of drugs that brought about longer treatment time, ≥ 20 months⁽¹⁰⁾. Pharmacologically the interaction of DR TB drugs and DM drugs causes a low success in the treatment of patients with T2DM of DR TB⁽¹¹⁾. The implementation of T2 DM of DR-TB treatment is more difficult because there is an interaction of DR TB and DM drugs resulting suboptimal drug concentration. Therefore, the treatment success is less likely to be achieved⁽²⁾.

Since the beginning of January 2014 until the end of September 2017, the treatment of DR-TB in Riau Province used the old regimens or conventional method with the intensive period at least 8 months and 12-month of follow-up phases. Since October 2017 up to present time, the treatment in Riau Province has been using a new blend of regimens with an intensive period of 4-6 months and 5-month of follow-up phases. STR is usually used for 9 to 11 months treatment and it is shorter than

the old regimens⁽¹²⁾⁽¹³⁾. The use of new regimens was able to accelerate the final conversion of sputum culture and the treatment success⁽¹⁴⁾⁽¹⁵⁾.

There is only a few research on the influence of T2DM and treatment regimens on the success of DR- TB treatment. The purpose of this study is to determine the effect of T2DM and treatment regimens on the success of DR-TB treatment in Riau Province in 2014-2018.

Materials and Method

Material: The type of data collected in this study is secondary data about demographic data namely, age, sex, marital status, occupation, education, residence category, clinical factors of T2DM status, history of previous TB treatments, medication adherence and treatment regimens.

The method of data collection was determined by the researchers and enumerators who had received previous training. Data was collected at the DR-TB referral hospital and DR-TB sub-referral hospitals by the researchers involving enumerators to ensure the data validity and to prevent data bias.

The data that had been collected was processed manually as well as by computers through the stages of data checking, coding, data entry and processing and cleaning data. Data analysis was made using STATA version 15 with a survival analysis. The outcome in this study was in the form of the treatment starting time until the success of DR-TB treatment.

Research Method: This study used a quantitative research with retrospective cohort through DR TB secondary data of Riau Province in 2014-2018. Samples were taken from all adult ≥ 30 years old DR TB patients who underwent treatments at a DR TB referral hospital of Arifin Achmad Regional Hospital and 7 DR TB sub-referral hospitals in Riau Province in 2014-2018. This study used secondary data of DR TB 03, DR-TB 01, medical records and *e TbManager* of patients from the DR TB referral hospital of Arifin Achmad Regional Hospital and 7 DR TB sub-referral hospitals in Riau Province in 2014-2018.

Sample population of 216 respondents were all TB RO patients who underwent treatments at the DR-TB referral hospital of Arifin Achmad General Hospital and 7 DR-TB Sub-Referral Hospitals in Riau Province. The subjects of this study 146 respondents, were ≥ 30

years old DR-TB patients who underwent treatments at the DR-TB referral hospital of Arifin Achmad General Hospital and 7 DR-TB sub-referral hospitals in Riau Province. Since the beginning of the DR-TB treatment

program in 2014 until February 2018, there were 146 DR-TB patients whose end of treatments had been identified.

Results

Frequency distribution based on Type 2 DM and treatment regimen on the success of treatments

Table 1: Frequency distribution based on Type 2 DM and treatment regimens on event status (The Success of DR-TB Treatment) in 2014-2018 in Riau Province

No	Variable	Sensor		Success of Treatment (Event)		Total	P
		n= 66 (45, 20%)		n=80 (54, 79%)		n= 146 (100%)	
		N	%	N	%	n	%
1.	DM Status and regimen						
	• Non DM and old regimen	29	19,86	42	28,76%	71	48,63
	• DM and old regimen	21	14,38	15	10,27%	36	24,65
	• Non DM and new regimen	6	4,10	19	13,01%	25	17,11
	• DM and new regimen	10	6,84	4	2,73%	14	9,57

Based on the table above, among 146 patients, 80 patients (54.79%) were successfully treated and 66 patients (45.21%) were unsuccessfully treated. 71 patients (48.63%) were not in Type 2 DM and they were treated using old regimens. In the univariate analysis, it was found that the success of treatments using old regimens on DR-TB patients with nonT2DM was higher than treatments using old regimens on DR-TB patients with T2DM (28.76% vs. 10.27%). Whereas,

treatments using new regimens on DR-TB patients with nonT2DM were more successful than treatments using new regimens on DR-TB patients with T2DM (13.01% vs. 2.73%).

Final Model of Multivariate Survival of Effect of Type 2 DM and regimens on the success of DR-TB treatments.

Table 2: Results of Final Model of Effect of Type 2 Diabetes Mellitus and treatment regimens on the success of DR-TB treatments in Riau Province in periods of 2014-2018

No	Variable	Coef (B)	SE	P value	HR Adj	95% CI
1.	Status DM and regimen					
	• Non T2DM/old regimen	-	-	-	-	ref
	• T2DM/old regimen	0,02	0,32	0,93	1,02	0,54-1,92
	• Non T2DM/new regimen	1,95	2,24	<0,001	7,06	3,79-13,16
	• T2DM/new regimen	2,36	6,48	<0,001	10,66	3,23- 35,12
3.	Marital Status					
	• Married	-	-	-	-	Ref
	• Not Married	0,52	0,57	0,12	1,69	0,86-3,31
	• Widow/Widower	0,49	0,87	0,35	1,64	0,57-4,65

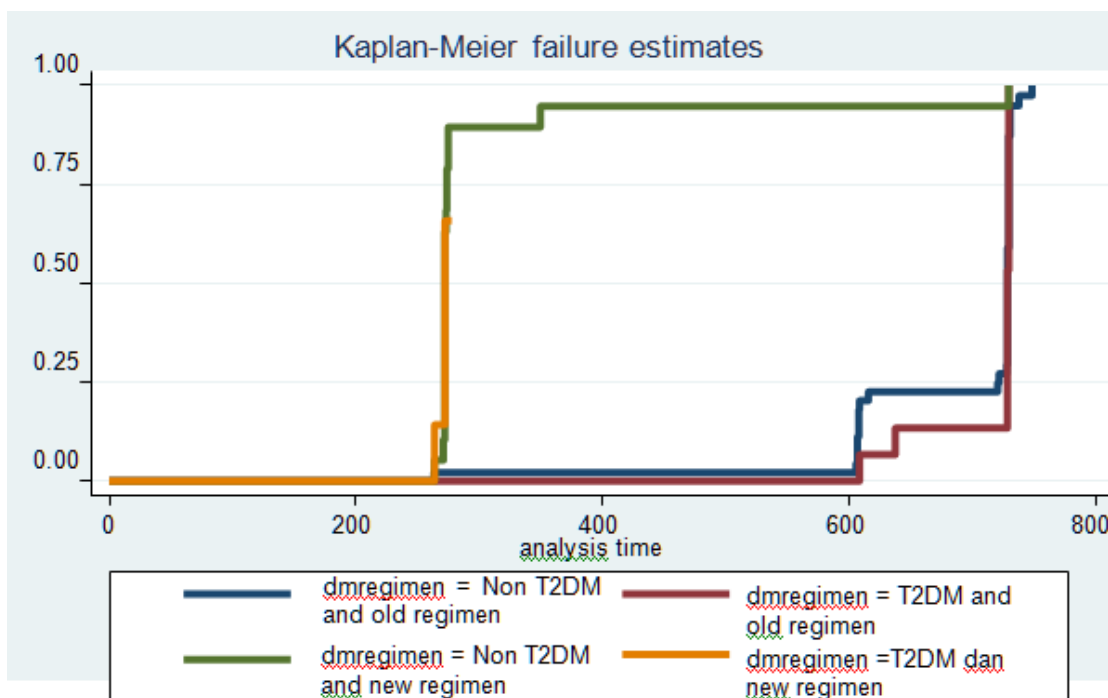
Based on the table above, the probability of successful DR-TB treatments on T2DM group using new regimens was 10.66 times higher (95% CI 3.23-35.12) compared

to the Non T2DM group using old regimens after marital status is controlled with statistically significant at p value <0.001. Probability of successful treatments on T2DM

group using new regimens is bigger than probability of successful treatments on Non T2DM group using new regimens and T2DM group using old regimens.

Influence of type 2 DM and treatment regimens on the success of DR-TB treatment: The 50% probability of treatment success on T2DM and non

T2DM patients using the old regimen occurred on the 729th day. Whereas, the 50% probability of treatment success on T2DM and non T2DM patients using new regimens occurred more quickly on the 272th day as shown in the figure 2.



The Figure of Kaplan Meier Survival Analysis shows that DR-TB treatments on T2DM and Non T2DM patients using old regimens have a longer median survival level than DR-TB treatments on T2DM and Non T2DM patients using new regimens (729 days vs. 272 days).

Discussion

There are several weaknesses in this study that affected the results of the study, such as information bias. The limitation of this study is that information bias may occur due to incomplete and inaccurate data recording on DR-TB 01, DR-TB 03, medical record records and data of e TB manager which was filled out by the staffs of DR-TB referral general hospital and sub referral hospitals.

The strength of this study is that the study can examine the sequence of causal events where causes precede effects so that the temporal time relationship

can be assessed. Time survival can be included in a cohort study with survival analysis so that time can be taken into account on all samples until observations are finalized. In this study, the T2DM factors and the regimens precede the effect on an event status (treatment success) so that the effect of causality on the results of this study is relatively good.

The time element shows that the treatment adherence decreases in DR-TB patients using old regimens that influence the side effects of the drug taken⁽¹¹⁾. DR-TB patients who also have DM have greater risk of undergoing treatment compared to DR-TB with non T2DM⁽²⁾. The late conversion from T2DM status also results in the increase of treatment time⁽¹⁶⁾.

The treatment of DR TB patients both with T2DM and NonT2DM groups using new regimens is significantly more successful compared to that of DR-TB patients in T2DM group and NonT2 DM groups

using old regimens. The research results in 9 African countries showed that new regimens were very effective in increasing the success of DR-TB treatment by 77.4% to 91.8%⁽¹⁷⁾⁽¹⁸⁾. Based on research in Jakarta, the success of treatment using old regimens was 39.8% and using new regimens was 48.9%⁽¹⁸⁾. However, this study did not consider the exposure status of T2DM or NonT2DM.

The management of DM control is very important in observing the severity and adequate treatment response on DR-TB patients who also suffer T2DM⁽²⁰⁾⁽²¹⁾. The low adherence of T2DM patients who undergo the DR-TB treatments can affect the success and duration of the treatments. A good collaboration of DR-TB and T2DM programs needs to be made to improve the success of DR-TB treatment on T2DM patients and to reduce the burden of DR-TB among DM patients and the burden of DM patients among DR-TB patients⁽²⁾⁽¹⁷⁾.

Observational studies performed in countries that implemented new treatment regimens (STR) i.e. in Bangladesh, Benin, Burkina Faso, Burundi, Cameroon, Central Africa, Congo, Nigeria, Switzerland and Uzbekistan showed that the success rate of STR treatment was 84% (95% CI; 70-87%). Meanwhile, the success rate of treatment using long-term standard regimens only reached 62% (95% CI; 53% -70%). The use of new regimens/STR became a potential effort to shorten treatment time and to make treatment simpler and more effective⁽¹⁸⁾⁽⁵⁾⁽²²⁾⁽¹⁵⁾. The limitation of this study is that this study cannot see the effect of group of serious-categorized T2DM patients or group of mild-categorized T2DM patients and the treatment regimens on the successful DR-TB treatment.

Conclusion

This study proved that DR-TB treatment on DR-TB patients in T2DM group and nonT2DM group using new regimens resulted in a greater chance of successful treatment and a faster recovery time than DR-TB treatment using old regimens.

Conflict of Interest: None

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References

1. WHO. Global Tuberculosis Report 2018. Geneva, Switzerland: WHO; 2018.
2. Lin Y, Harries A, Critchley J A, Owiti P, Dejgaard A, Kumar AMV, Crevel R DR. Management Of Diabetes Mellitus Tuberculosis, A guide to The Essential Practise. First Edit. Paris: International Union Against Tuberculosis and Lung Disease; 2019.
3. WHO. Global Tuberculosis Report 2015. Switzerland; 2015.
4. WHO. Global Tuberculosis Report 2019. Vol. 66, WHO. Switzerland: WHO; 2019. 37–39 p.
5. Reid MJA, Arinaminpathy N, Bloom A, Bloom BR, Boehme C, Chaisson R, et al. The Lancet Commissions Building a tuberculosis-free world: The Lancet Commission on tuberculosis. The Lancet Commissions. 2019;393:1331–84.
6. dooley et al. Tuberculosis and diabetes mellitus;convergence of two epidemics. Lancet Infect dis. 2009;9(12):737–46.
7. ADA. Standard of medical care in diabetes 2018. USA: ADA; 2018.
8. Salindri AD, Kipiani M, Kempker RR, Gandhi NR, Darchia L, Tukvadze N, et al. Diabetes Reduces the Rate of Sputum Culture Conversion in Patients With Newly Diagnosed Multidrug-Resistant Tuberculosis. Open Forum Infectious Dis. 2014;1–10.
9. Baker MA, Harries AD, Jeon CY, Hart JE, Kapur A, Lönnroth K, et al. The Impact of Diabetes on Tuberculosis Treatment Outcomes: A Systematic Review. BMC Med [Internet]. 2011;9(1):81. Available from: <http://www.biomedcentral.com/1741-7015/9/81>
10. Latif A, Ghafoor A, Wali A, Fatima R, Haq M, Yaqoob A, Abdullah Z, Najmi H. Union I. Did Diabetes Mellitus Affect Treatment Drug-Resistant Tuberculosis Patients in Pakistan from 2010 to 2014? Public Heal Action. 2018;I(1):14–9.
11. Kang Y, Kim S, Jo K, Kim H, Park S, Kim T, et al. Impact of Diabetes on Treatment Outcomes and Long-Term Survival in Multidrug-Resistant

- Tuberculosis. *Respiration*. 2013;86:472–8.
12. Pontali E, Raviglione MC, Migliori GB. Regimens to treat multidrug-resistant tuberculosis: past, present and future perspectives. 2019; Available from: <http://dx.doi.org/10.1183/16000617.0035-2019>
 13. Piubello A, Ait-khaled N, Caminero JA. *Field Guide For The Management Of Drug Resistant Tuberculosis*. Paris, Perancis: International Union Against Tuberculosis And Lung Disease; 2018.
 14. Al-Temimi A, Nizam M, Hassan Y, Aziz N., Asmani MF., Abdullah I. Re-challenging treatment plan for multidrug-resistant tuberculosis in diabetic patient: A case report. *Asian J Pharm Clin Res* [Internet]. 2019;12(2):11–4. Available from: <http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L2001560646%0Ahttp://dx.doi.org/10.22159/ajpcr.2019.v12i2.24772>
 15. Cheepsattayakorn A CR. Shorter Treatment Regimens for Multidrug-Resistant Tuberculosis: A Great Challenge. *EC Pulmonology Respir Med*. 2017;4:196–205.
 16. Gadallah MA, Mokhtar A, Rady M, El-moghazy E, Fawzy M, Khalil S. ScienceDirect Prognostic factors of treatment among patients with multidrug-resistant tuberculosis in Egypt. *J Formos Med Assoc* [Internet]. 2015;1–7. Available from: <http://dx.doi.org/10.1016/j.jfma.2015.10.002>
 17. Trebucq A, Schwoebel V, Kashongwe Z, Bakayoko A, Kuaban C, Noeske J, Hassane S, et al. Treatment outcome with a short multidrug-resistant tuberculosis regimen in nine African countries. *Int J Tuberc Lung Dis*. 2018;22(November 2017):17–25.
 18. Sotgiu G, Migliori GB. Effect of the short-course regimen on the global epidemic of multidrug-resistant tuberculosis. *Lancet Respir Med* [Internet]. 2017;5(3):159–61. Available from: [http://dx.doi.org/10.1016/S2213-2600\(16\)30432-5](http://dx.doi.org/10.1016/S2213-2600(16)30432-5)
 19. Frana E. Perbedaan Hasil Pengobatan TB Multi Drug Resistant (TB MDR) Antara Metode Standar Konvensional dan Metode Standar Jangka Pendek Di Indonesia Tahun 2017. Indonesia; 2019.
 20. Park SW, Shin JW, Kim JY, Park IW. The effect of diabetic control status on the clinical features of pulmonary tuberculosis. *Eur J Clin Microbiol Infect Dis*. 2012;31:1305–10.
 21. Leung C, Yew WINGW, Mok THYW, Lau KAMS, Wong CHIF, Chau CHIH, Chan CHIK, et al. Effects of diabetes mellitus on the clinical presentation and treatment response in tuberculosis. *Respirology*. 2017;22(January):1225–32.
 22. Foundation D, Sans M. Shorter & cheaper regimen to treat multidrug-resistant tuberculosis: A new hope. *Indian J Med Res*. 2017;146(September):301–3.

Role of Vitamin C in Endothelial Dysfunction in Patients with Type 2 Diabetes Mellitus Introduction

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Abstract

Background: To investigate the relationship between ascorbic acid level in serum and anti-oxidant parameters in blood with type 2 diabetes mellitus patients.

Patients and Method: The study was conducted on 85 subjects, 25 as a control and 60 with type 2 diabetes

Results: The current study was done in the period between January 2016-December 2018. The study included 60 patients with type 2 DM. The duration of diabetes ranged from one month to 240 month with mean 74.2±64.8

Conclusion: T2-DM patients with more severe diabetic nephropathy had lower vitamin C levels

Keywords: Type 2 diabetes mellitus; Vitamin C; endothelial dysfunction.

Introduction

In severe Oxidative stress (OS) cell damage may occur due to the low expression of antioxidant enzymes, is particularly sensitive to reactive oxygen and nitrogen species (RONS) ⁽¹⁾. These molecules may act on different substrates in the insulin intracellular signaling cascade, causing cell damage ⁽²⁾.

This process is probably the common event for DM-2 complications with the hyperglycemia being the probable biochemical key involved in the induction of such pathways ⁽³⁾. For Monnier & Colette ⁽⁴⁾, both the activation of the OS and the excessive glycation of proteins caused by hyperglycemia appear as important components in the emergence of diabetic complications.

Aim of the Study: To investigate the relationship between ascorbic acid level in serum and anti-oxidant parameters in blood with clinical, and duplex findings of brachial artery of patients with type 2 diabetes mellitus.

This prospective Cross sectional case control study was conducted in the period between (from January 2016-December 2018) at MINIA university hospital from the out-patient clinic.

The included subjects of the current study were 85 subjects: 63 females and 22 males and their ages ranged from 41-72 years old.

Group 1: The control group (25 volunteers) will be selected as healthy participants of matched age and gender having no past history of any chronic medical illnesses.

Group 2: Sixty (60) diabetic type 2 patients will be included among those attained to the MINIA university hospital out-clinic.

- Patients with other chronic medical illnesses,
- Those with secondary diabetes or other endocrinal

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pathologies.

- Mental health problems (senile dementia and Alzheimer's disease, among others) will be excluded, as they configure vulnerable groups, beyond the scope of this study.

Laboratory studies; Duplex study; Echocardiography.

Statistical Studies: The collected data were coded, tabulated, and statistically analyzed using SPSS program (Statistical Package for Social Sciences) software version 25.

The level of significance was taken at (P value < 0.05).

Results

Table 1: Echocardiographic parameters comparative analysis:

		Control	DM	P value
		N=25	N=60	
Ejection fraction of left ventricle	Range	(59-78)	(59-76)	0.678
	Mean ± SD	65.4±4.9	65±4.2	
left ventricular diameter in diastole	Range	(3.1-5.1)	(3.2-6.3)	0.034*
	Mean ± SD	4.3±0.6	4.6±0.6	
left ventricular diameter in systole	Range	(2.1-3.5)	(2.1-3.7)	0.060
	Mean ± SD	2.8±0.4	2.9±0.4	
Left ventricle hypertrophy	Yes	0(0%)	9(15%)	0.053
	No	25(100%)	51(85%)	

In this table:

1. **The Ejection fraction of left ventricle** was ranged from (59-78), the mean was 65.4±4.9 in control, while in Diabetic group the range was (59-76) and the mean was 65±4.2.
2. **Left ventricular diameter in diastole** ranged from (3.1-5.1cm), the mean was 4.3±0.6 in control, while in Diabetic group the range was (3.2-6.3cm) and the mean was 4.6±0.6.
3. **Left ventricular diameter in systole** was ranged from (2.1-3.5cm), the mean was 2.8±0.4, while in Diabetic group the range was (2.1-3.7cm) and the mean was 2.9±0.4.
4. **Left ventricle hypertrophy was found 15% in diabetic, while not in 85% of diabetic group.**
5. As shown in this table regarding **Echocardiographic parameters**. There were statically significant difference between control and diabetic group regarding to **left ventricular diameter in diastole**.

Discussion

Persistent hyperglycaemia in diabetes mellitus increases the production of reactive oxygen species

(ROS) and activates mediators of inflammation as well as suppresses antioxidant defense mechanisms, ultimately contributing to oxidative stress which leads to endothelial dysfunction (ED) in diabetes. Furthermore, there is increasing evidence that ROS, inflammation and fibrosis promote each other and are part of a vicious connection leading to development and progression of CVD and kidney disease in diabetes⁽⁵⁾.

In the current study; 35% of diabetic patients showed manifestations of peripheral ischemia and 30% of them showed diabetic retinopathy (P <0.001). They showed raised Systolic B.P. and diastolic B.P. highly significantly level (P=0.009 & P<0.04 respectively) than control.

Endothelial dysfunction is one of the initial key steps in atherosclero-genesis in diabetic subjects. Several risk factors, such as hypertension, dyslipidaemia, inflammation, oxidative stress, and AGEs, are associated with atherosclerosis and micro- and macro-vascular pathologies⁽⁶⁾. The mechanism of endothelial dysfunction (ED) in type 2-DM may be due to increased inactivation of endothelium-derived nitric oxide by oxygen-derived free radicals⁽⁵⁾.

Relationships between oxidativestress markers and antioxidants, point to vitamin C as a potential prognostic indicator of diabetic microangiopathy. All patients with long-standing diabetes used oral hypoglycemic drugs or insulin or both, and most of them were taking antihypertensive and cholesterol-lowering drugs, they showed the highest imbalance between the antioxidant status and increased concentrations of oxidative damage markers^(5,7).

In the current study; plasma levels of ascorbate, SOD, catalase and glutathione were highly significantly decreased, while plasma lipid peroxidation levels were highly significantly raised in patients' group than those of control (P= 0.001). Urinary ACR, plasma total cholesterol and LDL were highly significantly raised in patients' group than that of control group (P= 0.001). The Plasma TG was insignificantly raised in diabetic patients' group (P=0.67).

These results agreed with those of⁽⁸⁾whoshowed that T2-DM patients with the highest Urinary ACR (greater than 300 mg/g) had the lowest levels of vitamin C and the highest urine albumin concentration. They found also that vitamin C levels correlated negatively with serum creatinine, urine albumin and UACR. Overall they concluded that T2-DM patients with more severe diabetic nephropathy had lower vitamin C levels.

Concentration of vitamin C was significantly lower in patients with metabolic syndrome (MS) than in the control group. Gender and age did not affect either the mean concentrations of vitamin C.⁽⁶⁾

In Type-2 DM, reduced serum antioxidant activity correlates with worsened glycemic control. Increased oxidative stress and low vitamin C levels were correlated with severity of diabetic neuropathy. SOD and vitamin C prevent the rapid inactivation of NO by superoxide anion ⁽⁷⁾.

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References

1. Bandeira SDM., Guedes,GDS., Fonseca LSD., Pires, AS., Daniel P. Gelain, A., Characterization of Blood Oxidative Stress in Type 2 Diabetes Mellitus Patients: Increase in Lipid Peroxidation and SOD Activity.Oxid Med Cell Longev. 2012; 2012: 819310.
2. Evans JL, Maddux BA, Goldfine ID. The molecular basis for oxidative stress-induced insulin resistance. Antioxidants and Redox Signaling. 2005; 7(7-8):1040–1052.
3. Brownlee M. Biochemistry and molecular cell biology of diabetic complications. Nature. 2001; 414(6865):813–820.
4. Monnier L, Colette C.Glycemic variability: should we and can we prevent it? Diabetes Care. 2008; 31(supplement 2):S150–154.
5. Yuan, T., Yang, T., Chen, H., Fu, D., Hu, Y., Wang, J., ... & Xie, X. New insights into oxidative stress and inflammation during diabetes mellitus-accelerated atherosclerosis. Redox biology;2018)
6. ADONI, Naveed A.; ABUSAID, Ghassan H.; FUJISE, Ken. Inflammation and heart diseases. In: Inflammation, Lifestyle and Chronic Diseases: The Silent Link. CRC Press, 2016. p. 157-182.]
7. Kamodyová, N., Červenka, T., & Celec, P. Salivary markers of oxidative stress in oral diseases. Frontiers in cellular and infection microbiology, 2015; 5, 73.]
8. HEERSPINK, Hiddo JL; RABELINK, Ton; DE ZEEUW, Dick. Pathophysiology of Proteinuria: Albuminuria as a Target for Treatment. In: Chronic Renal Disease. Academic Press, 2020. p. 211-224.]

Effectiveness of Providing Self-Management Education to Deal With Emesis Gravidarum on Decreasing Nausea Vomiting Pregnancy (NVP) at Private Practice Midwives Puskesmas IV Denpasar Selatan Work Area

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Abstract

Data shows that 50-90% of pregnant women experience nausea in the first trimester. Excessive gravida emesis will gain weight into hyperemesis gravidarum and can disrupt the mother's metabolism including dehydration, weight loss, alkalosis, and hypokalemia. Non-pharmacological therapy is a type of complementary therapy that can be used as an intervention to treat nausea including hypnotherapy, acupressure, acupuncture, relaxation, and therapy. Self-management is regulating personal activities to live a better and healthier life. Emesis gravidarum self-management education adopts the concept of Corbin and Straus in Kate and Halsted (2003), which is outlined in a module that aims to enable pregnant women to educate themselves to be able to regulate their own lives, set goals, and provide self-reinforcement in dealing with nausea, vomiting experienced. The purpose of this study was to determine the effectiveness of providing self-management education to deal with emesis gravidarum on decreasing Nausea Vomiting Pregnancy (NVP). This is an analytical study with a pre-experimental research design (quasi-experiment design) with one group pre-test-post test design. This study was conducted at Private Practice Midwives (hereafter: PMB) Puskesmas IV Denpasar Selatan Work Area. The population of this study was pregnant women who came to PMB in the work area of Puskesmas IV Denpasar Selatan. The sample of this study was pregnant women who experienced nausea and vomiting in the first trimester who met the inclusion criteria where the sampling technique in this study was accidental sampling. Analysis of the data in this study was conducted t-test to test the differences between the two pre and post-test distributions before self-management education was given and after the providing of self-management education was faced with emesis gravidarum. The results of the study showed that the average value of PUQE 24 hours before the self-management module was given was 9.5, the standard deviation value was 2.591, the minimum and maximum values were 6.0-14.0. The average value of PUQE-24 hours after the self-management module was given was 7.1, the standard deviation value was 2,273 with minimum and maximum values of 3.0-12.0. The conclusion of giving self-management module is effective to decrease nausea and vomiting in first-trimester pregnant women.

Keywords: *First-trimester pregnant women, emesis gravidarum, self-management education.*

Introduction

Pregnancy is the growth and development of the fetus in intra-uteri starting from conception and ending until the beginning of labor. The process of pregnancy causes changes in the body of the mother. These changes are largely due to the influence of hormones, for instance the hormones estrogen and progesterone. Increased hormones estrogen and progesterone in the body cause

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physiological discomfort in the mother such as nausea, vomiting, fatigue, and enlargement of the breast. The process of pregnancy causes various changes in the entire body system such as cardiovascular, respiratory and gastrointestinal systems influenced by the pregnancy hormone HCG (Chorionic Gonadotropin Hormone)¹.

Physiological adaptations to the gastrointestinal system cause discomfort in the form of nausea and vomiting. Pregnant women who have this will experience interference with their activities. Psychologically, nausea and vomiting during pregnancy affect more than 80% of pregnant women and have a significant effect on the quality of life².

Nausea and vomiting are one of the earliest, most common and most stressful symptoms in early pregnancy. About 50 - 90% of pregnant women experience nausea in the first trimester and about 25% of pregnant women experience nausea and vomiting problems. Nausea and vomiting most often occur in young pregnancies from the 6th week after the first day of the last menstruation. 50% of pregnant women who experience nausea and vomiting can overcome at the age of 14 weeks and 90% can overcome until the age of 22 weeks³. Nausea and vomiting during pregnancy, known as morning sickness, occurs in the first trimester of pregnancy and some continue until the second trimester. The frequency of occurrence of morning sickness is not only in the morning but can be daytime even at night⁴.

According to the Lacase report of 367 pregnant women, 78.47% experienced nausea and vomiting that occurred in the first trimester; 52.2% experienced mild nausea and vomiting, 43.3% experienced moderate nausea and vomiting and 2.5% experience severe nausea and vomiting. In the second trimester, most pregnant women still experienced nausea and vomiting by 40% with the following details 63.3% experienced mild nausea and vomiting, 35.9% experienced moderate nausea and vomiting, 0.8% experienced severe nausea and vomiting.

Excessive emesis of gravidarum will become hyperemesis gravidarum which can disrupt the mother's metabolism, dehydration, weight loss, alkalosis, and hypokalemia. Impact on the fetus such as abortion, LBW, premature birth, and malformation in newborns⁵.

Most pregnant women who experience nausea and vomiting in the community use pharmacological therapy. Some just left alone. The use of pharmacology

for pregnant women needs to be considered because there are changes in pharmacokinetics and pharmacodynamics of drugs during pregnancy⁶. Non - pharmacological therapy, type of complementary therapy that can be used to treat nausea such as hypnotherapy, acupressure, acupuncture, relaxation, and therapy.

Nausea and vomiting during pregnancy are mild disorders; this condition can be overcome by self-control. In addition to self-control, nausea and vomiting can also be overcome by creating behaviors to reduce complaints⁷. Handling of nausea and vomiting in pregnant women needs to be done to improve maternal health status, one of them is by creating behaviors to reduce complaints. Creating behavior for a healthy life according to the patient's condition is part of self-management⁸.

Emesis gravidarum self-management education adopts the concept of Corbin and Straus in the 7th, which is outlined in the form of a module that aims to enable pregnant women to educate themselves to be able to regulate their own lives, set goals and provide self-reinforcement in dealing with nausea and vomiting experienced

Material and Method

This study was held at PMB Puskesmas IV Denpasar Selatan's Work Area; six PMB in total. The design used in this study was a quasi-experimental with one group pretest-posttest design. The type of data collected is secondary data, obtained from the visitation register of pregnant women at PMB, Puskesmas profiles and primary data obtained directly from interviews with respondents about the characteristics, knowledge, and data on the level of nausea and vomiting. The instrument used was a questionnaire to determine the characteristics of respondents, and a questionnaire (PUQE-24 hours) to measure the severity of nausea and vomiting. The pregnant women as the respondents were provided self-management modules and standard operating procedures to deal with emesis gravidarum. The population in this study was all pregnant women who had antenatal visits in PMB Puskesmas IV Denpasar Selatan work area in 2018. The sample of this study was pregnant women who experience nausea and vomiting who visited and met the study inclusion criteria. Criteria for inclusion; first-trimester pregnant women who experience nausea and vomiting are willing to be respondents and have not experienced complications in pregnancy. Exclusion

criteria are first-trimester pregnant women who experienced complications, hyperemesis gravidarum, and gastritis. The sampling technique used was accidental sampling, by taking respondents who happened to be present or at the time of the study. This was conducted for four months in BPM Region Puskesmas IV Denpasar Selatan. Severity measurement of nausea and vomiting on pregnant women with a questionnaire (PUQE-24 hours) was carried out twice; first, before being given self-management education (pretest) and second, two weeks after giving self-management education (posttest) modules. Data analysis used Paired T-test with a 95% confidence interval and a significance level of $P < 0.05$.

Findings: The results of the analysis in this study are as follows:

Table 1: Frequency Distribution of Nausea and Vomiting before Providing the Self-Management Module at PMB Puskesmas IV Denpasar Selatan working area in 2019

No.	Nausea and vomiting	Frequency (f)	Percentage (%)
1	No symptoms	-	-
2.	Mild	10	25
3.	Moderate	22	55
4	Severe	8	20
	Total	40	100

Source: Primary Data Research in 2019

Based on table 1 shows that from 40 respondents before providing self-management module; 10 respondents (25%) showed mild symptoms, and 8 respondents (20%) showed severe symptoms, almost half of the respondents, 22 people (55%) showed moderate symptoms.

Table 2: Frequency Distribution of Nausea and Vomiting after Providing the Self-Management Module at PMB Puskesmas IV Denpasar Selatan work area in 2019

No.	Nausea and vomiting	Frequency (f)	Percentage (%)
1	No symptoms	3	7.5
2.	Mild	16	40
3.	Moderate	21	52.5
4	Severe	-	-
	Total	40	100

Source: Primary Data Research in 2019

Table 2 shows that from 40 respondents after providing self-management module; 3 respondents (7,5%) showed no symptoms of nausea and vomiting, almost half of respondent; 16 people (40%) showed mild symptoms, and more than half respondents; 21 people (52,5%) showed moderate symptoms, and no respondent showed severe symptoms.

Table 3: Pregnancy Unique Quantification of Emesis and Nausea (PUQE)-24 hours Score Before and After Providing Self-Management Module at PMB Puskesmas IV Denpasar Selatan Work Area in 2019

Variable	Mean	SD	Minimum	Maximum
Pretest	9,5	2,591	6,0	14,0
Posttest	7,1	2,273	3,0	12,0

Based on table 3 the mean of PUQE-24 hours before providing self-management module is 9.5, SD is 2,591, minimum and maximum are 6,0-14,0. Mean of PUQE-24 hour after providing self-management module is 7,1, SD is 2,273, minimum and maximum 3,0-12,0

Wilcoxon test was used due to not eligible data for parametric test

Table 4: Wilcoxon Signed Ranks Test

Ranks				
		N	Mean Rank	Sum of Ranks
Post_Modul - Pre_Modul	Negative Ranks	31 ^a	16.00	496.00
	Positive Ranks	0 ^b	.00	.00
	Ties	9 ^c		
	Total	40		

a. Post_Modul < Pre_Modul, b. Post_Modul > Pre_Modul, c. Post_Modul = Pre_Modul

Test Statistics	
	Post_Modul - Pre_Modul
Z	-4.886 ^b
Asymp. Sig. (2-tailed)	.000

a. Wilcoxon Signed Ranks Test, b. Based on positive ranks.

Based on table 4 shows that *Asymp. Sig.(2-tailed)* with error rate 0.5%;p-value (0.000), ($p < 0.05$) So the H_0 is declined and H_a is accepted. This means there is effectiveness in providing self-management module to decrease nausea and vomiting.

Discussion

The results of this study illustrate the tendency for a decrease in PUQE-24 scores from before and after providing the module. The mean PUQE-24 score decreased by 2 points, 9.5 with a standard deviation of 2.591 before treatment, and 7.1 with a standard deviation of 2.273 after treatment. The results of statistical analysis with the Wilcoxon test showed the number of 31 respondents (76%) had decreased PUQE-24 scores with p-value =0,000. This proves that there is a significant effect on providing self-management modules on dealing with morning sickness. Kohen et al. (2005) categorize the severity of nausea and vomiting in pregnancy into 3 categories. The score of 0-3 has no symptoms, the score of 4-6 is mild, the score is 7-12 moderate, and the score is ≥ 13 severe categories.

Based on the characteristics of the frequency of morning sickness, before treatment there were 25% of respondents experiencing mild nausea and vomiting, 55% experienced moderate nausea and vomiting, and 20% of respondents who experienced severe nausea and vomiting. After treatment, respondents who did not experience nausea and vomiting (7.5%), those who experienced mild nausea and vomiting became 40%, and those who experienced moderate vomiting nausea 52.5%. Wilcoxon statistical test results showed a significant difference between PUQE scores before giving morning sickness self-management modules and after administration. This shows that there is an effect of morning sickness self-management module on the decrease in the frequency of nausea and vomiting in pregnant women. Value $p = 0,000$ so that it can be concluded that this self-management module is effective in dealing with morning sickness in pregnant women.

The use of morning sickness self-management module to decrease the frequency of nausea and

vomiting in pregnant women was only investigated by Latifah L (2014) where the results of the study showed that differences in the pretest and posttest values were analyzed using the Wilcoxon test, so that a significance value : 0,000 ($p < 0.05$) was obtained⁹. There is a difference in the PUQE score before and after giving the morning sickness self-management module. The morning sickness self-management module is effective in dealing with morning sickness in pregnant women. The previous study did not measure respondents' prior knowledge and used a minimum of 30 respondents.

The self-management module has been applied to several independent treatments for cardiovascular disease and schizophrenia. Self-management treatment method have been investigated for their effects on chronic diseases such as cardiovascular disease, diabetes mellitus, chronic obstructive pulmonary disease, and schizophrenia. Diabetic patients who follow the self-management program are shown to have significantly improved their clinical conditions (decreased blood sugar), can achieve self-care targets, and are satisfied with health care⁹. Research on the chronic obstructive pulmonary disease (PPOM) has also shown equally positive results. Patients who participated in the self management program experienced a decrease in the severity of the disease by 39.8%, a decrease in the number of hospital visits by 57.1%, a decrease in the number of visits to the doctor incidentally by 58.9%, and a decrease in visits to the emergency department by 41%¹⁰.

Self-management is one of the most common terms used in health promotion and patient health education. Self-management is very useful for patients, especially patients with chronic diseases where only patients who can be responsible for the treatment of the disease daily during his illness. Patients with chronic diseases besides experiencing physical disorders, usually also experience psychological disorders and well-being. Therefore, self-management programs often focus on improving self-perspective and patient welfare⁷.

Morning sickness self-management module contains several interventions to overcome nausea and vomiting during pregnancy, including the consumption of ginger drinks, food management, gradual mobilization during the morning, acupressure, and relaxation. Several studies have proven that ginger products which can be in the form of drinks or extracts are proven to overcome nausea and vomiting during pregnancy¹². McKinney

et al. (2009) mentioned that eating arrangements by eating small but frequent portions, avoiding oily foods, consuming more protein compared to carbohydrates, and separating eating and drinking can reduce the incidence of nausea and vomiting during pregnancy¹¹. Wentorf and Dykes (2001) and Artika (2006), found that acupressure by suppressing the P6 point (Neiguan point) was significant in reducing nausea and vomiting during pregnancy¹³. During the study, there were no respondents who complained about the difficulty in implementing the tasks and recommendations in the morning sickness self-management module.

Conclusion

Providing Self-Management Education to Deal Emesis Gravidarum Effective on Decreasing Nausea Vomiting Pregnancy (NVP) at PMB Puskesmas IV Denpasar Selatan Work Area

Conflict of Interest: None

Source of Funding: This study is funding by Grant Research for Beginner Lecturer Ministry of Research and Technology Higher Education

Ethical Clearance: Have got the letter of ethical eligibility from the research ethics committee of the Faculty of Medicine of Udayana University/Sanglah Hospital Denpasar with a letter number:1193/UN14.2.2.VII.14/LP/2019

References

1. Hani,Ummi,dkk. Midwives Service on Physiology Pregnancy. Jakarta : Salemba Medika; 2011
2. Hollyer et al. The use of CAM by women suffering from nausea and vomiting during pregnancy. BMC complementary and alternative medicine. Obtained on June 20th, 2017 from <http://www.biomedical.com/1472-6882/2/5/prepub>.
3. Kia, P.Y., Safajou, F.,Shahnazi, M. & Nazemiyeh, H. The effect of Lemon Inhalation Aromatherapy on Nausea and Vomiting of Pregnancy: A Double-Blinded, Randomized Controlled Clinical Trial. Iranian Red Crescent Medical Journal. 2014 March 16 (3) :e14360.
4. Runiari, Nengah. Nursery Service on Client with Hiperemesis gravidarum. Jakarta: Salemba Medika; 2010
5. Mazzotta, P., & Magee, LA. A risk-benefit assessment of pharmacological and nonpharmacological treatments for nausea and vomiting of pregnancy. *PubMed*, 59(4).2000; 781-800
6. Ward, S.K., & Hisley, S.M. Maternal child nursing care optimizing outcomes for mothers, children, & families. Philadelphia: F.A. Davis Company; 2009
7. Kate, R.L., & Halsted, R.W. Self-management education: History, definition, outcomes, and mechanism. *Ann Behav Med*.2003; 1-7.
8. Latifah, L., Setiawati N & Hapsari, E.D. Self management module efektif dalam mengatasi morning sickness pada ibu hamilJKP; 2017
9. Buml, B.M., & Garret, D.G. Patient self-management program of diabetes: First-year clinical, humanistic and economic outcomes. *Journal of American Pharmacists Association*. 2005; 130-137
10. Bourbeau, J., Julien, M., Maltais, F., Rouleau, M., Beaupré, A., & Bégin, R. Reduction of hospital utilization in patients with chronic obstructive pulmonary disease. *Arch Intern Med*. 2003; 585-591.
11. McKinney, E.S., James, S.R., Murray, S.S., & Ashwil, J.W. Maternal-child nursing (3rd ed.). St. Louis, Missouri: Saunders Elsevier; 2009
12. Saswita., Dewi, YI & Bayhakki. Effectiveness of Drinking Ginger in reducing emesis gravidarum in first trimester pregnant women : *Journal Ners Indonesia*, 1(2); 2011
13. Werntoft, E., & Dykes, A.K. Effect of acupressure on nausea and vomiting during pregnancy. A randomized, placebocontrolled, pilot study. *J Reprod Med.*, 46(9). 2001; 835-9

Detection of Single Nucleotide Polymorphisms in IL-1B gene in Iraqi Patients with Hepatitis B

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Abstract

Host genetic factors play an important role in the pathogenesis of hepatitis B virus (HBV) infection. However, the role of interleukin 1 receptor, type I (IL-1B) gene in HBV infection and breakthrough infection in people remains unclear. The aim of this study was to detect a SNP in IL-1B in HBV infection in Iraqi people.

Keywords: Nucleotide, Hepatitis B, Polymorphisms.

Introduction

Hepatitis B virus (HBV) infection, a viral infection spreading through the blood and body fluids, is a global health problem affecting more than 2 billion people globally (Liaw and chu CM,2009). Worldwide 240 million people are infected with chronic hepatitis B virus (CHB), resulting in an estimated 650000 death each year. Almost 80-90% of people infected during the first year of life and 30-50% of people infected before the age of 15 develop chronic infection respectively. The infection with HBV < 5% of them will develop chronic infection and 20-30% of chronic infected patients will develop cirrhosis and/or liver cancer ⁽¹⁾.

Hepatitis B vaccine (HB vaccine) has been approved for preventing transmission of HBV since 1982. At present, HB vaccine has been added into the national immunization program in almost all countries⁽²⁾. Without immunoprophylaxis, about 90% of people infected by their mother with hepatitis B antigen (HBsAg) and with high viral load would develop chronic HBV infection⁽²⁾. China used to be a hyper endemic region for HBV infection. To raise the coverage rate of HB vaccine, the Chinese government has provided all people with recombinant HB vaccine free of charge since 2002. Vaccination with a three dose provide long term protection⁽³⁾. It was reported that the prevalence of HBsAg in china was decreased⁽⁴⁾. In addition the infants born of HBsAg positive mothers have been able to receive hepatitis B immunoglobulin (HBIG) within 24 hours after birth for free since 2010⁽⁵⁾. HBV breakthrough infection is influenced by immunological factors, viral

factors, environmental factors and host genetic factors ⁽⁶⁾. Host genetic factors play an important role in the pathogenesis of HBV infection ¹². A number of studies have reported the associations between HBV infection outcomes and polymorphisms ¹¹. Being involved in the inflammatory cytokine network, interleukin-1 family (IL-1 family) plays an important role in the pathogenesis of HBV infection. IL-1 family includes: IL-1A, IL-1B, IL-18, IL-33, IL-36, IL-37, and IL-38 et al ¹³. Genetic variants in IL-1 family (such as IL-1B and IL-18) were reported to be associated with persistent HBV infection or HBV clearance⁽⁷⁾ demonstrated that the polymorphisms of the promoter region of the IL-18 gene at position ₆₀₇ and ₁₃₇ were closely associated with susceptibility to CHB ¹⁴. ^(8,9) indicated that another IL-1 family member, IL-1B gene polymorphisms, were associated with the clinical outcomes of HBV infection in Eastern Indian population ¹². We aimed to explore the association IL-1B, single-nucleotide polymorphisms (SNPs) and breakthrough infection of HBV in children through a case-control study^(10,11).

Materials and Method

DNA extraction that used in this study:

Approximately (2ml) of blood was taken from each patient by sterile syringe and places EDTA tubes.

1. Each blood sample was placed into 15 ml tube.
2. Cell lysis solution was added to the sample about 6 ml.
3. Blood and cell lysis were mixed together by

inverting the tubes several times and incubate them for 10 minutes in room temperature.

4. Samples were centrifuged at 10000 rpm for 20 minutes.
5. The supernatant was discarding by using a pipette to avoid losing the pellet.
6. Add 2 ml of nucleic lysis buffer to the samples.
7. The mixtures were mixed by inversion.
8. Then 2 ml of protein precipitation solution was added then vortex the samples for 20 seconds.
9. Centrifuged the samples at 10000 rpm for 10 minutes.
10. After the centrifugation, the supernatant were transfer to new tubes that contain Isopropanol about 2 ml.
11. The mixtures were centrifuged at 10000 rpm for 20 minutes.
12. Then discarded the supernatants and add 2 ml of 70% ethanol.
13. Centrifuged the sample again at 10000 rpm for 10 minutes.
14. Aspirated the ethanol and dry the pellet for 10–15 minutes.
15. The final step is (100µl) of DNA rehydration was added to the samples and storage them overnight at 4 °C
16. At the next day the samples were taken to estimate the DNA concentration by Nanodrop.

Blood Samples: The samples were collected from Medical City Hospital in Baghdad, using EDTA tubes and sterile syringe which consist of 50 patients (20 controls, 30 patients). The samples were transferred to the laboratory for DNA extraction.

Amplification of DNA by PCR technique:

Specific primers and their preparation: There are variant SNPs in the *IL-1B* gene that examined and used in this study .

One pairs of specific primers were provided by (Alpha DNA–Canada) for detection of SNPs in *IL-1B* gene. The details of these primers which including sequence and their gene locations are presented in table (1). Which provided in lyophilized form and dissolved in sterile distilled water to have the final concentration of 10 pmol/µl

Table (1): The details of this primer

Primer	Sequence
IL-1B	CTCATCTGGCATTGATCTGG (FORWARD) GGTGCTGTTCTCTGCCTCGA (REVERSE)

Then amplified the gene with PCR program that contain (Initial Denaturation at 95°C for 5 minute, Denaturation at 94°C for 30 seconds, Annealing temperture at 60°C for 30seconds, Extension at 72°C for 1 minute and final extension at 72°C for 7 minutes).

The quantity and amplification size of PCR product were confirmed by Agarose gel electrophoresis of 5 µl of amplified DNA on 2% Agarose gel (1 hour and 0.5 X Tris Borate Buffer). The gels stained with Ethidium bromide and visualized by U.V transilluminator and then were imaged by gel documentation system. The specific size of PCR products were estimated by comparing with the ladder bench top PCR markers (100bp) . There were some problems appeared on the gel such as:

1. Primer dimer
2. Unspecific product.

The suitable solution for avoiding these problems by using optimization PCR reaction which consist:

1. Changing in annealing temperatures: That means using different temperatures less than the original temperature (58°C less than 60°C) and three temperatures more than the original (62°C, 64°C, 66°C more than 60°C), to know at which temperature that the primer work well and can give a sharp band as shown in table(2)
2. Using 0.7 µl of primer volume instead of 1µl illustrated in PCR master mix (optimization).

Table (2): Shows Optimization PCR Programme

Steps	Temperatures	Time
Initial denaturation	95°C	5 min (35 cycle)
Denaturation	94 °C	30 sec.
Annealing	55°C	45 sec.
	57°C	
	59°C	
	61°C	
	63°C	
Extension	72 °C	1 min
Final extension	72 °C	7 min

3. Changing in time of annealing temperature by using 45 sec. instead of 30 sec.

Then the quantity and amplification size of PCR product were confirmed by Agarose gel electrophoresis of 5 µl of amplify DNA on 2% Agarose gel (1 hour and 0.5 X Tris Borate Buffer). The gel stained with Ethidium bromide which visualize the PCR product by U.V trans illuminator and then were imaged by gel documentation system. The specific size of PCR products were estimated by comparing with the ladder bench top PCR markers (100bp).

Results

Fifty human blood samples were collected from Medical City Hospital in Baghdad province, from consisting of 30 samples infected with hepatitis B that

have different ages ranged between 20-35 years. The samples were extracted by miniprep kit for frozen blood.

The amplification of IL-1B gene was done using specific PCR which is couple of specific primers. In the first PCR experiment, a standard concentration of 10 Pmol of each primer, 100 ng of template DNA was added and 35 cycles were preformed. The PCR yield were bands of the desired product so; all reaction components were kept at the same concentration as indicated in figure (1). Concerning molecular genetic studies, hepatitis B is one of the most extensively studied in patients and attention has been given to liver with special focus on the *IL-1B* gene.

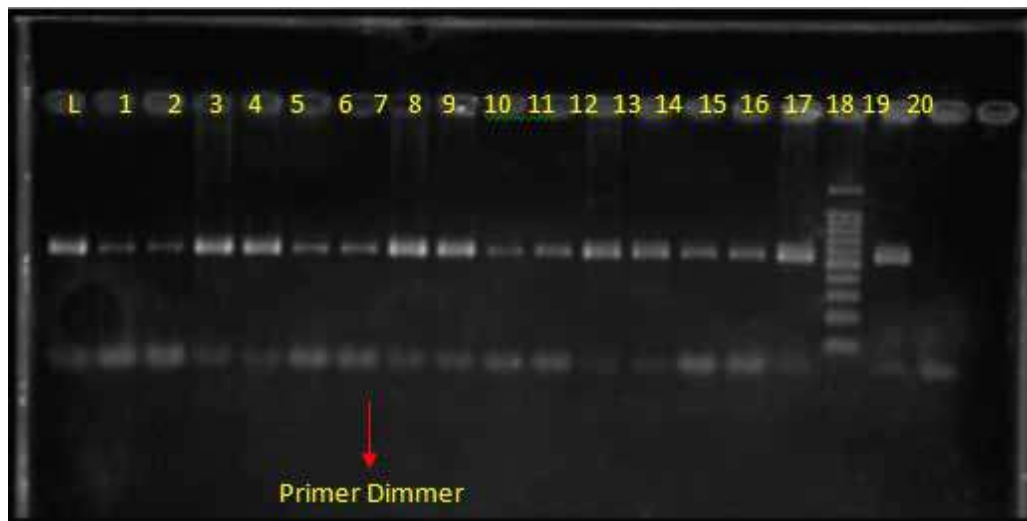


Figure (1): Agarose gel electrophoresis of the IL-1B gene in DNA samples by specific PCR.

The achieving balance between reaction components is optimization of conditions were done by using different runs to improve the performance of the method as indicated in figure (2).

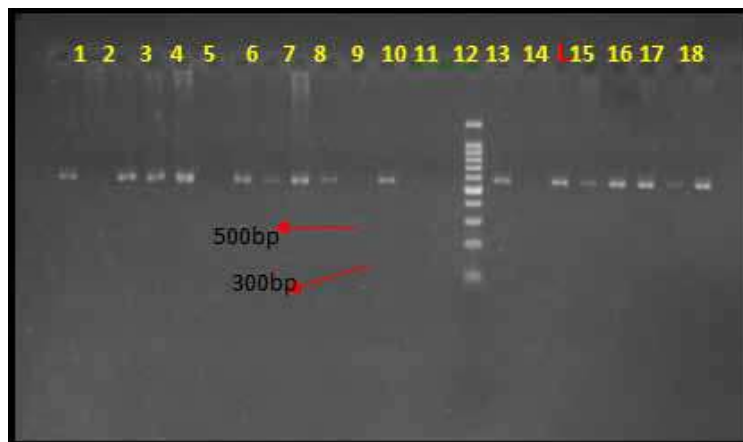


Figure (2): Agarose gel electrophoresis of the IL_1B gene in DNA samples after optimization reaction of general PCR.

From all these experiment we found that there is a SNP in all the patients which leading to have hepatitis B which concern from the symptoms of the disease.

Discussion

Hepatitis B is the most important infectious diseases in china. In recent years, genetic factors such as cytokine and human leukocyte are reported to play important role in HBV infection. in the present study we evaluated whether the genetic variant of IL-1B could influence HBV infection in people. The results showed that strong significant differences were found in the distribution of genotypes for polymorphisms of IL-1B gene SNP. In the present study we identified one SNP in IL-1B.

Conclusion

This study provides further evidence to confirm that genetic factors may play important roles in breakthrough infection of HBV in Iraqi patients. Our results suggest that the SNP in IL-1B gene is probably a risk factor for immune response, leading to breakthrough infection of HBV in Iraqi patients still needs further investigation based on a large population.

Source of Funding: Self

Ethical Clearance: Not required

Conflict of Interest: None.

References

1. Biswas A, Panigrahi R, Pal M, De BK, Chakrabarti S, Ghosh MK, et al. Association of Interleukin-1 beta and Gene Polymorphisms with Liver Pathogenesis in Hepatitis B Virus Infection among Eastern Indian Population. *J ClinExpHepatol* 2013;3:281–7.
2. Cui F, Luo H, Wang F, Zheng H, Gong X, Chen Y, et al. Evaluation of policies and practices to prevent mother to child transmission of hepatitis B virus in China: results from China GAVI project final evaluation. *Vaccine* 2013;31(Suppl 9): J36–42.
3. Ding Y, Sheng Q, Ma L, Dou X. Chronic HBV infection among pregnant women and their infants in Shenyang, China. *Virology* 2013;10:17.
4. Ferreira SC, Chacha SG, Souza FF, Teixeira AC, Santana RC, Deghaide NH, et al. IL-18, TNF, and IFN-gamma alleles and genotypes are associated with susceptibility to chronic hepatitis B infection and severity of liver injury. *J Med Virol* 2015;87:1689–96.
5. Gusatti CS, Costi C, de Medeiros RM, Halon ML, Grandi T, Medeiros AF, et al. Association between cytokine gene polymorphisms and outcome of hepatitis B virus infection in southern Brazil. *J Med Virol* 2016.
6. Li C, Ji H, Cai Y, Ayana DA, Lv P, Liu M, et al. Serum interleukin-37 concentrations and HBeAg seroconversion in chronic HBV patients during telbivudine treatment. *J Interferon Cytokine Res* 2013;33:612–8.
7. Li F, Wang Q, Zhang L, Su H, Zhang J, Wang T, et al. The risk factors of transmission after the implementation of the routine immunization among children exposed to HBV infected mothers in a developing area in northwest China. *Vaccine* 2012;30:7118–22. 6.
8. Liang X, Bi S, Yang W, Wang L, Cui G, Cui F, et al. Reprint of: Epidemiological serosurvey of Hepatitis B in China? declining HBV prevalence due to Hepatitis B vaccination. *Vaccine* 2013;31(Suppl 9):J21–8.
9. Liaw YF, Chu CM. Hepatitis B virus infection. *Lancet* 2009;373:582–92. 2. Komatsu H, Inui A. Hepatitis B virus infection in children. *Expert Rev Anti Infect Ther* 2015;13:427–50. 3.
10. Ni YH, Chen DS. Hepatitis B vaccination in children the Taiwan experience. *PatholBiol (Paris)* 2010;58:296–300.
11. Palomo J, Dietrich D, Martin P, Palmer G, Gabay C. The interleukin (IL)-1 cytokine family—Balance between agonists and antagonists in inflammatory diseases. *Cytokine* 2015;76:25–37.

The Relationship between the Consumption Pattern of Pokea Clam and Protein with LDL and HDL Levels in Patients with Hypertension

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Abstract

Introduction: This study aims to determine the relationship between the consumption pattern of pokea clam and protein with LDL and HDL levels in patients with hypertension.

Method: This study used an observational analysis method with a case control study design. Research location in the area of the Sampara District. The number of samples was 60 people consisting of 30 case samples and 30 control samples using purposive sampling technique. The data was taken using a questionnaire pokea clam consumption pattern, Semi-Quantitative Food Frequency Questionnaire (FFQ-SQ) questionnaire and blood pressure data using mercury sphygmomanometer. Result of the data obtained were processed by analysis of Chi-Square test data with a value of $p < 0.05$ accompanied by an Odd Ratio value.

Results: Statistical analysis showed that the relationship between pokea clam consumption patterns ($p=0,604$; OR=1,408) and protein consumption patterns ($p=0,218$; OR=2,051) with LDL levels. Statistical analysis showed that the consumption patterns of pokea with HDL levels (OR= 1.259, $p=0.704$) and protein consumption patterns with HDL levels (OR=0.889, $p=0.839$).

Conclusion: There were no correlation between pokea clam consumption pattern and protein with LDL and HDL levels in hypertensive patients of Sampara District.

Keywords: *Batissa violacea ceebencus*, LDL, HDL, Hypertension, Pokea clam, Protein

Introduction

Pokeaclam (*Batissaviolaceacelebensis*, von Martens 1987) is bivalves that live in several rivers in Southeast Sulawesi. It has special characteristic compared to similar species from other regions. The typical characteristics of pokea clam can be seen from the morphological and ecological conditions of the origin waters⁽¹⁾. Compared

with the same genus, Pokea clam has more shape form and live at very low salinity. Meat of Pokea clam is used as a comestible containing protein by the people of Sampara District, Konaweregency⁽²⁾.

Pokeaclam or *Batissaviolaceavar. celebensis*, von Martens, 1897 is bivalves belonging to the Corbiculidae family, and it is one of the main types of freshwater clam located in the Southeast Sulawesi region⁽²⁾. A kind of Pokea clam is scattered in several large islands in Indonesia such as (West Papua, Sumatra, Sulawesi, Java). Pokeaclam spread out in Sulawesi especially in Southeast Sulawesi waters, and it is mainly in large rivers such as the Pohara River, Lasolo River, Roraya River, Laeya River⁽³⁾.

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Based on Yenni et al’s research on proximate analysis of pokea clam meat, showed that meat of pokea clam contain protein 50.48%, 6.86% of fat, 29.13% of carbohydrate, 5.53% of fiber, and 2.70% of water. Based on its dry weight, pokea clam contain the highest levels of protein which is more than 50%, medium fat content more than 5%, and carbohydrate content more than 20%. The nutritional content of Pokea clam is equivalent to several types of mollusca. It is empirically believed to be a prodisiac, increase reproductive vitality, treat fever, jaundice, and reduces blood pressure or overcome hypertension⁽¹⁾.

The incidence of hypertension ranked first in the 10 highest of non-communicable diseases in Southeast Sulawesi, compared to acute respiratory infections cases. Hypertension ranked third most diseases in Kendari City⁽⁴⁾⁽⁵⁾.

Pokea clam meat has macro content in the protein form (50.48%), fat (6.86%), carbohydrate (29.13%), ash (10.67%), fiber (5.53%), and water (2.70%). Protein consists of 9 essential amino acids and 11 non-essential amino acids. Fat divided into cholesterol, triglycerides and phospholipids also contains 27 types of fatty acids consisting of 12 types of SFA, 6 types of monounsaturated fatty acids or MUFA and 9 types of polyunsaturated fatty acids or other PUFA. The other form contained in Pokea clam is cholesterol but in lower level than in the chicken’s meat. Micro content of Pokea clam in the form of Phosphorus (P) Selenium (Se) Copper (Cu) Zinc (Zn) Cobalt (Co) Chrome (Cr) Iron (Fe)⁽¹⁾⁽⁶⁾.

Protein, fat and cholesterol content in the Pokea clam, and sources of protein and lipids (triglycerides, cholesterol, phospholipids) from other foods will enter the body. Lipids in blood plasma that insoluble in plasma fluid need to be modified by protein to be able transported into the blood circulation. Cholesterol, triglycerides and phospholipids bind to proteins and this bond is called apoprotein. Apolipoprotein plus lipids becomes lipoprotein. Lipids (cholesterol, triglycerides, and phospholipids) and proteins with apoprotein are the basic ingredients for the formation of lipoprotein, in the form of high density lipoprotein (HDL), Low Density Lipoprotein (LDL), very low density lipoprotein (VLDL), intermediate density lipoprotein (IDL) use to carry out its function as a carrier of cholesterol from peripheral tissues to the liver⁽⁷⁾.

Material and Method

The type of research is observational analytic with a case-control study design conducted in March-August 2019, in the District of Sampara. Using a purposive sampling technique, 60 respondents is selected consisting of 30 case samples and 30 control samples. Data source of hypertension patients obtained from the Sampara Health Center. Confirm of blood pressure is measured with sphygmomanometer. The research instrument was in the form of pokea clam meat consumption pattern, Semi-Quantitative Food Frequency Questionnaire (FFQ-SQ). LDL and HDL levels were measured through venous blood collection and examined at the Prodia Kendari clinical laboratory.

Findings:

Table 1: Distribution of Sample Frequency by Gender, Age, Low Density Lipoprotein, Consumption Pattern of Pokea Clam Meat, and Protein Consumption Pattern

Respondent Characteristics	Respondent Category				Total	
	Control		Case		n	%
	n	%	n	%		
Gender						
Male	3	5	10	16,7	13	21,7
Female	27	45	20	33,3	47	78,3
Age						
18-25 Years old	3	5	3	5	6	10
26-35 Years old	9	15	9	15	18	30
36-45 Years old	13	21,7	13	21,7	26	43,3
46-55 Years old	5	8,3	5	8,3	10	16,7

Respondent Characteristics	Respondent Category				Total	
	Control		Case		n	%
	n	%	n	%		
Pokea Clam Consumption Pattern						
Enough	11	18,3	6	10	17	28,3
Less	19	31,7	24	40	43	71,7
Protein Consumption Pattern						
High	22	36,7	17	28,3	39	65
Low	8	13,3	13	21,7	21	35
Low Density Lipoprotein						
Optimal	22	36,7	21	35	43	71,7
Not optimal	8	13,3	9	15	17	28,3
High Density Lipoprotein						
Normal	8	26,6	11	36,6	19	31,6
Low	22	73,3	19	63,3	41	68,3

Table 2: Analysis of the Relationship between Consumption Patterns ofPokeaclam Meat, Protein Consumption Pattern, and Low Density Lipoprotein in Sampara District

Consumption Pattern of Pokea	Low Density Lipoprotein						p value	OR	95% CI	
	Optimal		Not Optimal		Amount				LL	UL
	n	%	n	%	n	%				
Enough	13	21,7	4	6,7	17	28,3	0,604	1,408	0,38	5,147
Less	30	50	13	21,7	43	71,7				
Consumption Pattern of Protein										
High	30	50	9	15	39	65	0,218	2,051	0,647	6,501
Low	13	21,7	8	13,3	21	35				

Table 3: Analysis of the Relationship between Consumption Patterns ofPokeaclam Meat, Protein Consumption Pattern, and High Density Lipoprotein in Sampara District

Consumption Pattern of Pokea	High Density Lipoprotein						p value	OR	95% CI	
	Normal		Low		Amount				LL	UL
	n	%	n	%	n	%				
Enough	6	10	11	18,3	17	28,7	0,218	2,051	0,647	6,501
Less	13	21,7	30	50	43	71,7				
Consumption Pattern of Protein										
High	12	20	27	45	39	65	0,839	0,889	0,286	2,762
Low	7	11,7	14	23,3	21	35				

Discussion

In this study, there is no relationship between consumption patterns of PokeaClam meat with levels of LDL. This can be caused by the processing method of pokeaclam before consumption. In general, people are more likely to process pokeaclam by boiling, although there are also some respondents processingpokeaclam meat by frying or sautéing⁽⁸⁾. According Purwaningsih

et al ⁽⁹⁾ that the effect of processing by steaming, boiling without salt and boiling with salt on red-eye snails (Cerithideaobtusa) causes a decrease in macro and micro mineral content, except for the content of sodium and magnesium processed by boiling with the addition of salt.

This study is not in line with previous studies which found that there was a relationship between

consumption patterns of pokea clam meat ($p = 0.002$ and $OR = 5.06$) with blood pressure in the Sampara District community⁽¹⁰⁾. The study stated, fried Pokeaclam meat can affect the incidence of hypertension.

Protein intake functions are primarily as a catalyst, a carrier, activator, regulator of genetic expression, neurotransmitter, structural booster, immune booster and for growth⁽¹¹⁾. In statistical test found there are no significant differences between the mean levels of LDL and HDL, in patients with level of adequacy protein mild deficit and more. If the level of protein adequacy is calculated based on the nutritional adequacy rate (RDA) compared to the level of protein adequacy based on actual needs, then the distribution of samples in the category of protein deficit adequacy level becomes more⁽¹²⁾.

The results of this study indicate that there is no relationship between protein consumption patterns with LDL levels in the District of Sampara. This is caused by the fulfillment of fiber intake in the community of Sampara District. According to Samudra⁽¹²⁾ that fiber has an important role in reducing blood cholesterol level. Consuming at least 28 grams of fiber per day can reduce cholesterol levels up to 15-19%. Epidemiological study that examines entire fiber states that there is a relationship between fiber intake and total cholesterol levels because the mechanism of fiber has an ability of lowering blood cholesterol. Some studies show that soluble fiber can reduce LDL levels without reducing HDL cholesterol levels.

The results of this study are not in line with research conducted by Safitri⁽¹³⁾ who found a correlation between soy protein consumption with serum cholesterol levels with a weak negative patterned correlation. It is proven by the statistical test results which obtained p value of 0.048 ($p < 0.05$). That is caused soy is not only rich in vegetable protein but also contains dietary fiber, thus increasing total daily fiber consumption and decreasing fat consumption. One example is in 100 grams of BDD (edible weight) fried *Tempe* containing 9.7 grams of dietary fiber.

Most of the people of Sampara tend to consume foods rich in vitamin A, vitamin E contain in many grains, nuts and fruits including beans, brown rice, white rice, bread, peanuts, green beans, bananas and others. It is known that vitamin E can modulate the activity of the enzyme nitrite oxide synthase 3 gene in producing nitrite oxide (NO). NO itself is a compound that can

cause vascular relaxation released by endothelial blood vessels. Vitamin E works as an antioxidant because it is easily oxidized, vitamin E will be taken up by LDL thereby improving endothelial function by reducing LDL sensitivity to the oxidation process, so as to increase the amount of NO production⁽¹⁴⁾.

Pokeaclam (*Batissaviolaceacelebensis*) are a type of freshwater clam located in the Pohara River. The kind of this Freshwater clam are consumed by many people in the Sampara District area in the form of satay, boiled clam meat, stir-fried clam meat and so forth. Pokeaclam are rich in carbohydrates, fats and proteins⁽⁸⁾. Based on studies of fat and carbohydrate content in pokea clam meat when it enters the body, it will be absorbed in the intestine, and then it is brought into extra hepatic tissue or fat tissue and undergoes hydrolysis. The results of this hydrolysis are then carried to the liver by LPL enzymes through capillaries and chylomicrons as lipid transport to enter the liver which will be synthesized into HDL and VLDL. Then VLDL is converted into IDL and LDL to distribute LDL cholesterol to tissue cells and then LDL cholesterol will be transported back to the liver by HDL and will be secreted into bile acids⁽¹⁵⁾.

Cholesterol in LDL contains the most cholesterol which is about 45% of all types of lipoproteins, so it can be said that LDL is the main carrier of cholesterol in the blood. The body's tissue cells receive cholesterol from LDL cholesterol, but the amount of cholesterol the cells can receive or absorb is limited. Consuming saturated fats or foods contains many cholesterol can increase LDL levels in the blood⁽¹⁶⁾.

Table 3 shows the normal group the HDL content with the consumption of pokeaclam in the normal category only 6 respondents (10%) and the low group in the HDL level were 13 respondents (21.7%). This situation can be caused by many things; one of it is physical activity.

The physical activity can be in the form of sports and activities carried out on a daily basis that can reduce the risk of cardiovascular disease⁽¹⁷⁾. The results are also in line with the description of the population in the Sampara District area that has a source of livelihood as a farmer which is majority in Sampara District. This illustrates that most of Sampara's community is in lower classes, and have a lot of physical activity⁽¹⁸⁾.

Besides physical activity, another factor that has an influence is daily eating patterns. Food consumed will

undergo metabolic processes in the body and produce an energy or Adenosine Triphosphate (ATP). ATP is formed in the body in accordance with the needs of the body itself, but in its formation the food consumed is not all converted to ATP but can be stored in the form of cholesterol. Increasing physical activity is carried out, so that more ATP is needed and will make a little formation of total cholesterol, Low Density Lipoprotein (LDL) and increased High density Lipoprotein (HDL)⁽¹⁹⁾.

Based on data of this research shows that some of the respondents in the study did not carry out physical activity on a regular basis, with the most category being female respondents as housewives (IRT). This can be one of the factors that cause no increasing in HDL levels. In this study not all of the respondents who did regular exercise for example such as aerobics, in other words there is a possibility that this situation could affect HDL cholesterol levels in respondents who did not experience an increasing.

Adequate or good nutritional intake can increase HDL levels in the body if accompanied by adequate exercise. A study conducted by Maulida in (20) said that regular exercise such as aerobic exercise for 6 months could significantly increase HDL cholesterol levels. This routine exercise will improve the function of ApoA-1 as a receptor of HDL to help reduce cholesterol in the blood vessels to the liver⁽²⁰⁾.

This is in line with the results of this study that showed there is no relationship between protein consumption patterns with HDL levels in patients with hypertension in the Sampara sub-district. The Chi square test results obtained p-value of 0.839 ($p > 0.05$). Based on Table 5, the results obtained are normal groups of cholesterol levels in high protein consumption patterns that are 12 respondents (20%) and in normal groups HDL levels of low protein consumption patterns in 7 respondents (11.7%) which show no relationship between protein consumption patterns with HDL levels in patients with hypertension in the Sampara District area.

Conclusion

There is no relationship between the consumption pattern of pokeaclam meat (*Batissaviolacea* var. *Celebensis* von von Martens, 1897) and proteins with low density lipoprotein (LDL) and high density lipoprotein (HDL) in patients with hypertension in the coastal areas of Sampara district.

Conflict of Interest: In this study there is no conflict of interest.

Source of Funding: This research uses private funds.

Ethical Clearance: This study has received an ethics permit from the Health Research Ethics Commission from Halu Oleo University with number: 492/UN29.20/PPM/2019.

References

1. Yenni, Nurhayati, T., Nurjanah, Losung F. Kandungan Mineral, Proksimat dan Penanganan Kerang Pokea (*Batissaviolacea celebensis* Marten 1897) dari Sungai Pohara Sulawesi Tenggara. In: Prosiding Pertemuan I Imiah dan Seminar Nasional MPHPI. Universitas Sam Ratulangi; 2011. p. 105-7.
2. Bahtiar. Kepadatan dan Distribusi Kerang Pokea (*Batissaviolacea celebensis* Martens, 1897) pada Substrat Berbeda di Sungai Pohara Sulawesi tenggara. 2012.
3. Bahtiar. Pertumbuhan, Kematian dan Tingkat Eksploitasi Kerang Pokea (*Batissa violacea* var. *celebensis*, vonMarten 1897) pada Segmen Muara Sungai Lasolo Sulawesi Tenggara. *Mar Fish.* 2016;7(2):137-47.
4. Tenggara DKPS. Profil Kesehatan Sulawesi Tenggara Tahun 2016. Kendari: Dinkes Kesehatan; 2017.
5. Badan Pusat Statistik. Kota Kendari dalam Angka 2017. Kendari: BPS Kendari; 2017.
6. Yenni. Pengaruh Perebusan Terhadap Kandungan Gizi Kerang Pokea (*Batissaviolacea celebensis* Martens 1897) dan Aktivitas Antioksidannya. Institut Pertanian Bogor; 2012.
7. Jim E. Metabolisme Lipoprotein. *J Biomedik.* 2013;149-56.
8. Sudayasa, I Putu, Hartati B. Family Nutrition Improvement Effort Though Nutrition Management of Pokea Clam Based on Enviromental Health. *J Pengabdian Kpd Masy (Indonesian J Community Engag.* 2019;5(2):222-36.
9. Purwaningsih, Sri., Salamh, Ella., Mirlina N. Pengaruh Pengolahan Terhadap Kandungan Mineral Keong Matah Merah (*Cerithidea Obtusa*). IPB; 2011.

10. Sudayasa, P., Halim, HAN., Purnama, ANS., Ruslan N. Pengaruh Konsumsi Daging Kerang Pokea (*Batissa violacea celebensis*) Terhadap Tekanan Darah pada Masyarakat Pesisir Pohara. In Kendari; 2017.
11. Goldman PS, Tran VK, Goodman RH. The multifunctional role of the co-activator CBP in transcriptional regulation. *Recent Prog Horm Res.* 1997;52:103–20.
12. Samudra B. Hubungan Antara Gaya Hidup dan Konsumsi Pangan dengan Profil Lipid Darah pada Pasien Dislipidemia di RSPAD Gatot Soebroto Jakarta. Institut Pertanian Bogor; 2015.
13. Safitri, S., Tjiptaningrum, A., Anggraini, I, D., Ayu, R P. Hubungan Konsumsi Protein Kedelai Serta Konsumsi Serat Makanan Dengan Kadar Kolesterol Total Pada Pasien Puskesmas Kedaton Bandar Lampung. Universitas Lampung; 2017.
14. Ekawati E. Pengaruh Konsumsi Vitamin E dengan Ekspresi Gen eNOS3: Alternatif Diet Penderita Hipertensi berdasarkan Nutrigenomik. 2017;
15. Yudi D. Pengaruh Susu dan Jahe Terhadap Kadar Kolesterol Total pada Wanita Hiperkolesterolemia. *J Gizi Indones.* 2016;89–95.
16. Soliman GA. Dietary Cholesterol and the Lack of Evidence in Cardiovascular Disease. *Nutrients* [Internet]. 2018 Jun 16;10(6):780. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/29914176>
17. Sunu, U.F.S., Permadi, G. F. Hubungan Antara Aktifitas Fisik dan Angka Kecukupan Gizi Makronutrien Terhadap Rasio Kolesterol Total/HDL Pada Masyarakat Pedesaan. *J Farm Sains dan Komunitas.* 2017;
18. Badan Pusat Statistik Kabupaten Konawe. Kecamatan Dalam Angka Sampara 2017. Kabupaten Konawe: BPS Kab.Konawe; 2017.
19. Zuhroiyyah S. Hubungan Aktifitas Fisik dengan Kadar Kolesterol Total, Kolesterol Low Density Lipoprotein dan Kolesterol High Density Lipoprotein pada Masyarakat jatiningor. 2017.
20. Maulida K. Perbedaan Kadar Kolesterol LDL dan HDL Sebelum dan Setelah Pemberian Sari Bengkuang (*Pachyrrhizus erosus*) pada Wanita. *J Nutr Coll.* 2014;

The Correlation between GPX-1 Serum and Hearing Threshold of SLE Patient Post Prednisone Therapy

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Abstract

Introduction: Systemic Lupus Erythematosus (SLE) is a disease characterized by the involvement of antibodies in the immune system-mediated inflammation, including the auditory system. One of the things that causes hearing loss in SLE is the occurrence of vasculitis and the process of oxidative stress which results in decreasing the activity of Glutathione Peroxidase (GPx) which is one of the important antioxidants in the human body against ROS. Provision of Prednisone therapy in SLE patients with hearing loss will improve hearing. It is expected that there will be an increase in GPx-1 levels along with hearing improvement in SLE patients with hearing loss after receiving prednisone.

Objective: To determine the correlation of hearing threshold with changes of serum GPx-1 levels in systemic lupus erythematosus patients who receiving prednisone therapy.

Method: A comparative analytic study conducted with pre-post design which analyzed the correlation between elevated serum GPx-1 levels and hearing threshold of SLE patients receiving prednisone therapy.

Results: This study found significant changes in GPx-1 levels after SLE patients with hearing loss received prednisone therapy. Comparison of serum GPx-1 levels of SLE patients who experience sensorineural hearing loss before and after prednisone therapy. The statistical test used is the Wilcoxon test and significant if p value <0.05. Comparative test of GPx-1 levels showed a significant number (p <0.001) with increase difference about 3.69U/g Hb. There is significant correlation between the increased serum GPx-1 levels with a decreased hearing threshold shown at high-frequency frequencies at 10,000 Hz and 14,000 Hz (p <0.05).

Conclusion: There is a correlation between improved hearing threshold in increased serum GPx-1 levels in patients receiving prednisone therapy.

Keywords: GPx-1, Hearing Loss, Oxidative Stress, Prednisone, ROS, SLE

Introduction

Systemic Lupus Erythematosus (SLE) related to the deposition of autoantibodies and the formation of immune complexes that cause tissue damage.¹ SLE occurs due to disruption of immune regulation which causes an increasing of excessive autoantibodies causing disruption of the reticulo-endothelial system which eliminates antigen-antibody complexes.²

As many 10,6% of SLE cases from Sardjito Hospital Yogyakarta from 2015 to 2016, about 10.5% of SLE cases from Rheumatology Department of Internal Medicine Hasan Sadikin Hospital in Bandung (RSHS) in 2015.² Mutiara in 2012 conducted a study at the Department of Rheumatology Internal Medicine RSHS Bandung and found 6 of 23 LES patients (26%) had sensorineural, symmetrical, and bilateral hearing loss. There were two people had mild-degree hearing loss and four people moderate-degree hearing loss.^{3,6}

ROS has one or more unpaired atoms and ROS is produced when oxidative metabolism occurs in the body.^{8,9}GPx-1 enzyme is widely found in all cell parts such as cytosol, mitochondria and peroxisomes. In the cochlea, GPx-1 has very high activity in cortical organs, spiral ganglion, vascularis stria, spiral ligaments and supporting cells.^{8,9,17}In SLE patients, The decreasing of GPx activity can cause destruction of antioxidant enzyme activity and increase ROS production and oxidative stress occurrence.^{8,9}

Management of hearing disorders in SLE since 60 years ago is corticosteroids.¹¹Prednisone is the preferred because they have an anti-inflammatory mechanism through the inhibition of the phospholipase enzyme that converts phospholipid into arachidonic acid.¹² In 2015, Cavaleriu study showed a significant decrease in MDA levels of SOD and GPx.¹³Currently at RSHS Bandung, the management of low-grade SLE is giving prednisone oral 0.5 mg/KgBW/day in accordance with the SLE management therapy protocol.¹⁴

This study aims to determine the correlation of hearing threshold with changes of serum GPx-1 levels in systemic lupus erythematosus patients who receiving prednisone therapy.

Method

The design of this study was a comparative analytic study with pre-post design that analyse the relationship between increased serum GPx-1 levels and hearing status of SLE patients receiving prednisone therapy in 19 samples. The study was conducted from May 2018 to July 2018 in Hasan Sadikin Hospital. The Inclusion criteria of sample were patient with Mild-degree SLE, Age ranged and patient 18-50 years old, patient had Type-A Timpanogram in both ear but exclusion criteria were patient with noise exposure (*NIHL*), patient with congenital malformation in ear, head trauma and hearing disorder and had hypertension story. The statistical test used is the Wilcoxon test and significant if p value <0.05.

Findings: Study about the correlation between serum GPx-1 levels and hearing status of LES patients who received prednisone therapy had been conducted with sequential study sampling according to patient arrival. The number of subjects were 120 people and were mild-degree SLE patients from May 2018 to June 2018. After screening, 19 subjects were taken. Subject characteristics included gender, age, and no complaint

of vertigo and tinnitus during history taking.

Table 1:Characteristic of Study Subject

Variable		Number
1. Age (Years)		
Mean (SD)	33.9 (8.6)	
Range	22 - 48	
2. Gender		
Female		19 (100%)
3. Additional Complaint		
Vertigo		5 (26.31%)
Tinitus		4 (21.05%)
Vertigo and Tinitus		9 (47.30%)

All study subjects were SLE patients who complained of hearing loss. Based DPOAE examination, 19 subjects were referred before prednisone therapy and after prednisone therapy, 18 subjects were pass with 1 subject were still referred.

The bold number indicates a significant p value in statistical tests. In the right ear, it is found to be significant at low and high frequencies, except in the frequency of conversation (1000 Hz, 2000 Hz, 4000 Hz). But in left ear, it is found to be significant except in the frequency 250 Hz, 1000 Hz, 2000 Hz.

Information about the number of study subjects with sensorineural-type hearing loss before and after prednisone therapy. McNemar test, one of the nonparametric statistical tools, used to test the differences between two groups of study subjects to measure GPx-1 levels and hearing status before and after prednisone therapy with a significant p value of <0.05.

Majority subjects experienced hearing loss on the right ear at high frequency before prednisone therapy with a value of p <0.05. While on the left ear, Majority subjects, in right ear, as many as 17 people (89.5%) experienced hearing loss at frequency of 14,000 Hz and in left ear as many as 15 people (78.9%) at a frequency of 12,500 Hz and 47.4% at a frequency of 11,200 Hz with meaningful statistical value (p = 0.016). The results of the statistical comparative test of GPx-1 levels showed significant value (p<0.001) with the difference in increase about 3.69 U/g Hb. The mean level of GPx-1 before therapy is 1.92 with mean level of GPx-1 after therapy is 5.61 U/gHb.

The correlated Between DPOAE result With Increase Of Gpx-1 Serum Value. In the right ear, it is

found to be not significant in the frequency 500 Hz, 2000 Hz, 4000 Hz, 8000 Hz, 9000 Hz, 11,200 Hz, 12,500 Hz. But in left ear, it is found to be not significant in all frequencies.

Discussions

Productive age considered to be exposed to sunlight and ultraviolet light. High exposure to cigarette smoke and the reproductive system that is still productive are risk factors for weighting SLE at a young age. A meta-analysis study from At Stadio and colleagues in 2017 said that the highest age of SLE patients from all over the world is 20-49 years and in Asia the age range is 20-39 years.⁴

All study subjects were young adult women. Abbasi said that SLE can affect men and women of all ages but 90% of people diagnosed with SLE are women.⁷ Female incidence is around 90% of the total SLE patients. This is related to the estrogen hormone which is known to increase the expression of the immune system while androgens work to suppress the expression of the immune system.^{1,3,4} Estrogen activates polyclonal B cells resulting in excessive autoantibody production in SLE patients.⁵

In this study, complaints of tinnitus, vertigo and 47% complained of both. In some literature, sensorineural hearing loss occurs in SLE patients accompanied by disturbances of balance and other internal ear disorders.¹ That is similar with study conducted by Maciaszczyk and colleagues who found an increase in the prevalence of inner ear disorders such as vertigo and tinnitus in SLE patients who experienced sensorineural hearing loss. In the inner ear, high-frequency auditory stimuli are transduced to the tip of the cochlear basal and low-frequency stimuli occur at the apical end. Endolymphatic hydrops processes that increase the stiffness of the structure vibrate the inner ear and cause dysfunction of the outer hair cells.^{1,4,5,7}

The patient's hearing threshold with sensorineural hearing loss decreased between the frequency of conversation to high frequency, similar to the symptoms that occur at presbycusis, namely hearing loss in SLE patients at high frequencies.^{10-12,13} DPOAE examination is used to confirm hair cell damage in the study subject and one of the examination method that can be used to determine cochlear hair cell function objectively.

In the right ear of 12 frequencies examined, there were 9 frequencies that increased in intensity, especially at high frequencies, which was indicated by a meaningful statistical test, where the value of $p < 0.05$. In the left ear 8 frequencies that experience improvement are indicated by a significant statistical test. This is consistent with the study conducted a study at the Polyclinic Rheumatology Department RSHS Bandung and obtained 6 people (26%) from 23 SLE patients experiencing sensorineural, symmetrical, and bilateral hearing impairments.⁶ Characteristics of internal ear disease due to autoimmune diseases are described as progressive, bilateral, sensorineural type usually occurs in high frequency, the majority attacks young adults and is associated with vestibular complaints.^{5,13} This is related to the accumulation of immune complexes in the auditory arteries reducing the diameter of blood vessels by decreasing blood flow. This reduction in blood flow induces an oxygen deficit followed by the release of oxidative molecules responsible for damage to hair cells. Hair cell damage in the basal part of the cochlea, decreases the auditory function in capturing high notes.¹³

The anti-inflammatory and immunosuppressive effects given are considered to provide maximum results against improvement of the hearing threshold.¹¹ In this study the preferred drug was prednisone.¹² The dose used in various studies is 1 mg/KgBW for 4 weeks with a maximum dose of 60 mg/day obtained hearing improvement as in the study of Mutiara, Wijana, and Anggraeni on 26 SLE patients with sensorineural hearing loss given prednisone for 4 weeks. After administering therapy for 4 weeks, 24 patients experienced improvement in hearing to normal and 4 patients did not experience improvement. Prednisone has a mineralocorticoid effect that plays an important role in endolymphatic homeostasis and maintains endococcal potential. Prednisone improves hearing by interfering mineralocorticoid receptors that improve endolymphatic homeostasis.¹¹ In addition, Prednisone increases blood flow in the cochlea, reduces vascular stria degeneration, and has antioxidant effects.¹¹

From 19 subjects in the right ear, 16 people (84.2%) experienced sensorineural hearing loss at a frequency 14,000 Hz, 17 people (89.5%) at frequency 12,500 Hz and 15 people (78, 9%) at frequency 11,200 Hz and all three are measurements before being given prednisone therapy. After 4 weeks of therapy there were 12 people

experiencing improved hearing in the right ear at a frequency of 14,000 Hz, 16 people at frequency 12,500 Hz, and 10 people at a frequency of 11,200 Hz in the right ear, and in the left ear a statistically significant improvement was only shown in frequency 11,200 Hz.

All study subjects experienced an increase in GPx-1 levels accompanied by hearing improvements after both total and partial treatment with an average increase of 3.69 U/gHb. GPx-1 examination selected in this study because it is one of the most dominant cellular antioxidants in the defense process against ROS when oxidative stress reaction occurs in the cochlea. In the cochlea, GPx-1 activity will increase in the cortical organ area, vascular stria and spiral ganglion.^{8,9} The main risk factor for microvascular damage is due to a decrease in GPx-1 levels during atrophy of the vasculature stria. In addition, the increased ROS oxidative stress in sensorineural hearing loss could suppresses GPx-1 production which is natural antioxidant.⁹

The correlation between improvement in hearing and an increase in GPx-1 levels in blood in SLE patients. From this study, it was found that the right ear had more significant improvement in hearing threshold than in the left ear, which was shown by the number of subjects and improved hearing-threshold difference. However, statistically, a significant correlation occurred at a frequency of 10,000 Hz and 14,000 Hz in the right ear which meant a relationship between the function of increased hearing and an increase in the level of GPx-1 in the blood dominated in the right ear even though it did not occur at all frequencies.

Conclusion

There is an increase in GPx-1 levels accompanied by increased hearing in SLE patients who experience sensorineural hearing loss after receiving prednisone therapy, especially in high frequency.

Conflict of Interest: There was no conflict of interest in this study.

Ethical Clearance: The ethical clearance is granted from KEPK, Dr. Hasan Sadikin General Hospital, Bandung

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References

1. Batuecas-Caletrio A, Del Pino-Montes J, Cordero-Civantos C, Calle-Cabanillas MI, Lopez-Escamez JA. Hearing And Vestibular Disorders In Patients With Systemic Lupus Erythematosus. 2013; 22:437–42.
2. Direktorat Jenderal Pencegahan dan Pengendalian Penyakit Tidak Menular. Kementerian Kesehatan RI. Pedoman Pengendalian Penyakit Lupus Erythematosus Sistemik. ISSN 2442-7659. 2016
3. Yu C, Gershwin ME, Chang C. Diagnostic Criteria For Systemic Lupus Erythematosus: A Critical Review. Elsevier J Autoimmun. 2014; 48(49):10–3.
4. Di Stadio A, Ralli M. Systemic Lupus Erythematosus and Hearing Disorders: Literature Review and Meta-Analysis of Clinical and temporal Bone Findings. 2017; 45(5): 1470-80.
5. Maciaszczyk K, Durko T, Waszczykowska E, Polguy AE, Pajor A. Auditory Function In Patients With Systemic Lupus Erythematosus. Elsevier. Auris Nasus Larynx. 2011; 38(11):26-32.
6. Abbasi M, YazdiZ, Kazemifar AM, Baksh ZZ. Hearing Loss In Patients With Systemic Lupus Erythematosus. Global Journal Of Health Science. 2013; 5(5):102-6.
7. Shah D, Mahajan N, Sah S, Nath SK, Paudyal B. Oxidative Stress and Its biomarkers in Systemic Lupus Erythematosus. Journal of Biomedical Science. 2014;21-3.
8. Majumder P, Duchon MR, Gale JE. Cellular glutathione content in organ of Corti and its role during ototoxicity. Frontiers in cellular Neuroscience. 2015; 9:143
9. Mutiara I, Anggreini R, Wijana. The Effect of Giving Prednisone on Hearing Status Systemic Lupus Erythematosus Patients. Tesis. Bandung: Faculty of Medicine Univesitas Padjajaran. 2013.
10. Cavaleriu BD, Martu DV, Hritcu L, Manolachel OR, Radulescu LM. Idiopathic Sudden Hearing Loss: Oxidative Status Before And After Corticoid Treatment. Arch. Biol. Sci. 2015; 67(4):1297-1302.
11. Kasjmir YI, Handono K, Wijaya LK, Hamijoyo L, Albar Z, et al. Diagnosis and Management of Systemic Lupus Erythematosus. Indonesian Rheumatology Association. ISBN 978-979-3730-16-5. 2011.

12. Lasso de la Vega M, Villarreal IM, Lopez Moya J, Ramon Garcia-Berrocal J. High Frequency Audiometry Can Diagnose Sub-Clinic Involvement In A Seemingly Normal Hearing Systemic Lupus Erythematosus Population. *Acta Oto-Laryngologica*. 2016: 1651-2251.
13. Malky AG. An analysis of ototoxicity in children: Audiological detection, clinical practice and genetic susceptibility. London: University College London (UCL). 2014.

Leptospirosis Associated with Environmental Risk Factors: A Systematic Review

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Abstract

This article aimed to summarize environmental risk factors that can cause leptospirosis in human. Leptospirosis is one of the zoonotic diseases. Zoonotic diseases are infectious diseases of animals that cause diseases when transmitted to humans. The bacteria that cause leptospirosis are *Leptospira*. *Leptospira* is pathogenic bacteria that are transmitted from animals to humans, directly or indirectly. Leptospirosis mainly found in the human who comes into contact with the urine of infected animals, urine-contaminated surface water, and soil in the environment or drinking water and food that contaminated with *Leptospira*. This review retrieved articles from four science databases, namely ProQuest, Scopus, Pubmed, and ScienceDirect. A systematic review was conducted using a predefined protocol based on PRISMA. The searching process utilizes three main keywords that include leptospirosis, risk factors, and humans in various combinations. During the initial search from four science databases (ProQuest, Scopus, Pubmed, and ScienceDirect), there were 506 articles retrieved. During the screening process, 59 articles excluded due to duplication, 403 articles excluded based on title and abstract incompatibility with inclusion criteria, 14 articles excluded due to not match of article content with inclusion criteria, and seven articles excluded because of the ineligibility with the study. In the final screening process 23 articles were chosen to be analyzed. This review found the environmental risk factors that cause leptospirosis in humans are flooding, sanitation, household environment, and the presence of animal reservoir. Prevention is needed by improving the environment and dealing with flood problems properly.

Keywords: *Infectious disease; Leptospirosis; risk factors; environment; human.*

Introduction

Leptospirosis is one of the zoonotic diseases. Zoonotic diseases are infectious diseases of animals that cause diseases when transmitted to humans. It spread to humans by ticks, mosquitoes, fleas, or contact with animals infected^(1,2). The bacteria that cause leptospirosis are *Leptospira*⁽¹⁾. *Leptospira* is pathogenic bacteria that are transmitted from animals to humans, directly or

indirectly. The bacteria enter the body through cuts or abrasion on the skin, or the mucous membrane of the mouth, nose, and eyes^(1,3). Leptospirosis mainly found in the human who comes into contact with the urine of infected animals, urine-contaminated surface water, and soil in the environment or drinking water and food that contaminated with *Leptospira*^(1,3).

There are so many factors that can increase the incidence of leptospirosis, such as behaviour, geographic, demographic, socio-economic, and environment. Factors related to socio-economic, sanitation and risky behaviour showed a consistent pattern of being associated with increased leptospirosis risk⁽⁴⁾. There have been many studies that have been conducted on the risk factor of leptospirosis in humans. However, there is still little research that focuses on environmental factors.

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This article aims to summarize ecological risk factors that can cause leptospirosis in humans

Method

Search Strategy: Data sources taken from four science databases, namely ProQuest, Scopus, Pubmed, and ScienceDirect, were published last ten years. A systematic review was conducted using a predefined protocol based on PRISMA⁽⁵⁾. The searching process utilizes three main keywords that include leptospirosis, risk factors, and humans in various combinations.

Inclusion and Exclusion Criteria: All scholarly articles published last ten years, written in English, subject with at least one of the following terms (public health, environmental science, and medicine), full-text, the open-access journal included. Review articles, outbreak reports, case reports, brief communication, systematic review, and articles that not discuss environmental factors excluded.

Data Extraction and Management: All articles were identified base on title and abstract by two reviewers. Data selected from eligible studies included first authors, title, study period, published, country, design study, method, independent variable, and outcome related to risk factors (Odds Ratio). Data synthesis will be planned using narrative synthesis. Environmental risk factors divided into related to water and unrelated to water. The risk factor related to water is all risk factors that cause leptospirosis through water contaminated by *Leptospira* bacteria. Risk factors unrelated to water are variables that cause leptospirosis originating from contaminated environments other than water. Such as soil, food, and other environmental conditions that can increase the risk of leptospirosis. The Odds Ratio (OR) value will be analyzed based on statistical analysis. OR value will find out how much the risk of these variables can increase the incidence of leptospirosis.

Result

Articles Characteristics: A total of 506 eligible articles were obtained from four databases using inclusion and exclusion criteria (Proquest: 266, Pubmed: 60, Scopus: 121, and ScienceDirect: 59 articles). During the screening process, 59 articles excluded based on duplicate, 403 articles excluded based on title and abstract, 14 full-text articles excluded because of research reason (review, case report, outbreak report, brief communication, systematic review, and not

written in English), seven articles excluded because of ineligibility (not discuss environmental factors) with the study. In the final process, 23 articles were chosen to be analyzed.

Based on 23 articles that have been analyzed, it is known that the most study period was carried out in 2010 (n=4) and published in 2014 (n=5) and 2018 (n=5). Of the 23 articles, five articles conducted in Brazil. In the eligible articles, 11 articles using a cross-sectional study, six articles using case-control study and the other articles using cohort, ecological, retrospective study, and experimental study. Most of the eligible articles using questionnaires, Geographic Information System (GIS), and laboratory test (Microscopic Agglutination Test) to collecting data and using secondary data to be analyzed.

Risk Factors: There is an environmental risk factor related to water and unrelated to water. Of the 23 eligible articles were analyzed, 11 articles found the association between environmental risk factors related to water with leptospirosis incidence. The risk factor consists of working in waterlogged fields (OR=4,6)⁽⁶⁾, flooding(OR=3,35)⁽⁷⁾, access to water(OR=2,79)⁽⁸⁾, cleaning clogged sewer (OR=3,82)⁽⁷⁾, contact with sewage water(OR=2,83)⁽⁷⁾, drinking water in public tap(OR=6,51)⁽⁹⁾, agricultural worker(OR=1,8)⁽⁹⁾, exposed in stagnant water(OR=2,01)⁽⁹⁾, detected with cattle urine(OR=1,2)⁽¹⁰⁾, unsafe water (OR=1,82)⁽¹¹⁾, and rainfall (OR=13,77)⁽¹²⁾.Based on risk factors related to water, rainfall has the most significant effect on leptospirosis disease. An area that has high rainfall has 13,8 times greater risk of leptospirosis than an area with low rainfall.

Environmental risk factor related to water analyzed in 19 eligible articles. The risk factors consist of storage of cow dung in or surrounding house, residence in the house-made up of cow dung, a household with the access of food to rodent (OR 3)⁽⁶⁾, built-up area⁽¹³⁾, high coverage of grassland tenure⁽¹³⁾, heavy sabulous clays in the soils⁽¹³⁾, and a wet climate⁽¹⁴⁾. Also, the risk factor include the socio-economic problem⁽¹⁴⁾, presence of *Rattus norvegicus* feces (OR=4,95)⁽⁸⁾, presence of positive pathogenic *Leptospira* (OR=4,15)⁽¹⁵⁾, rodent burrow(OR==2,80)⁽⁸⁾, un-plastered walls (OR=2,71)⁽⁸⁾, presence of garbage dumping in the farm (OR=2,40)⁽¹⁵⁾, having higher numbers of piggeries around the home, the higher density of piggeries above the house, contact with mud, contact with garbage, the living below-median altitude of the village, living at lower altitudes, dwelling

near water bodies, outdoor labour, living on clay soil (OR=3,11)⁽¹⁶⁾ etc.

Discussion

Leptospirosis is an endemic disease in several regions, especially in the tropics and subtropics area^(1,17). Leptospirosis may present with a wide variety of clinical manifestations. These may range from mild flu-like illness to a serious and sometimes fatal disease. The common symptoms in leptospirosis are icterus (jaundice). Many risk factors can increase the incidence of leptospirosis. These factors consist of the environment, behaviour, individual characteristics, medical history, socio-economic, topography, demographics, access to health service, etc.^(6,13,14,18). Environmental risk factors consist of risk factor related to water and unrelated to water. The risk factor that related to water that has a significant association with leptospirosis is flooding. In the rainy season and flood, the incidence of leptospirosis usually increases and endemic⁽¹⁷⁾. Rainfall is one factor that can increase the incidence of leptospirosis. This is because the high rainfall intensity causes inundation and flooding in some flood-prone areas. Flooding can be contaminated by *Leptospira* bacteria. Flooding has a very important role in the transmission of leptospirosis in epidemic and endemic areas⁽¹⁹⁾. Flood causing material losses and also cause various health problems. Flooding is a medium for spreading leptospirosis through water contaminated with *Leptospira* bacteria and entering the human body through wounds⁽¹⁹⁾. In a study stated that a confirmed leptospirosis outbreak in Guyana occurred after severe flooding⁽²⁰⁾. In flood-prone areas, the community has a risk of leptospirosis because the community makes contact with water, either by cleaning puddles, submerged in puddles, and through mud carried by floods.

Risk factors unrelated to water consist of sanitation, household environment, and the presence of an animal reservoir. Poor hygiene, like the presence of cow dung landfills surrounding houses and contact with garbage, can increase the incidence of leptospirosis^(6,7). An animal-like reservoir rat contaminated litter. The urine contaminated garbage and entering the human body through wounds and food. People who come into contact with waste and don't apply healthy living behaviours such as washing hands with soap and not using personal protective equipment when making contact with garbage will be a risk for leptospirosis. Contact with waste is related to occupational environment and leptospirosis⁽²¹⁾.

The household environment is an important transmission determinant in urban slum areas⁽²²⁾. House environment like un-plastered walls can cause leptospirosis disease⁽⁸⁾. This environment is because rodent, especially rats as reservoir animal, can enter the house and contaminate food or direct contact with the human. Owning a farm around a house can increase the presence of *Leptospira* bacteria. *Leptospira* bacteria can survive in soil and reservoir animals like goats, cow, in a farm can contaminated soil around the house⁽²³⁾. Therefore the house environment is important to note. The controlling house environment will be able to help reduce the incidence of leptospirosis. Other than that, environmental improvement is very necessary, especially in the slums area that is endemic to leptospirosis. Controlling the house is to reduce morbidity and mortality.

In addition, the home environment also affects the presence of rat. The environment around the house that is not clean and moist becomes a habitat that is preferred by rats. House conditions that are not impermeable to rats will make it easier for rats to enter the house. one example of the condition of a house that is not impermeable as the un-plastered walls. Houses that un-plastered walls can increase the incidence of leptospirosis. Where people who live in houses where un-plastered walls have a risk of 2.71 greater than people who live in houses that have plastered walls⁽⁸⁾. Another example of a home environment that can increase leptospirosis is living in an agricultural area. The agricultural area is one of the rat habitats. Moist and muddy farming areas are the place that rats like to live and breed. One species of rats that have habitat in agricultural areas is *Rattus norvegicus*⁽²⁴⁾.

There are many kinds of animals that carry the *Leptospira* bacteria, such as cattle, pigs, goats, buffalos, horses, dogs, rodents and wild animals⁽³⁾. Pigs are one of the animals that can also cause leptospirosis. People at risk are pig farmers. Apart from direct contact with animals infected with *Leptospira* bacteria, leptospirosis can also enter the human body through livestock meat infected with leptospirosis. Therefore, it is very important to control the health of livestock. Rodents recognized as the most common reservoir leptospirosis in human. A study shows that out of 128 patients who displayed leptospirosis like symptoms, 70% reported having seen a rodent in their houses and 29,6% of them owned dogs⁽²⁵⁾. A rat infestation has a significant association with leptospirosis. Exposure to rodent urine is associated with

acute leptospirosis. Humans that exposed to rodent are having 1,7 time higher risk for severe leptospirosis than those who are not detected (26).Based on the result of a systematic review, it estimated that the animal reservoir of leptospirosis is cattle, pig, cow, rodent, and rat. These animals can cause leptospirosis in human through urine, faeces, and direct contact with an infected animal.

For the future research is needed meta-analysis to identify the environmental risk factor with using Odds Ratio (OR)And carried out research based on continents. So we get an overview of risk factors that affect leptospirosis in each continent.

Conclusion

Many factors influence the incidence of leptospirosis, especially in terms of the environment. Flooding, sanitation, household environment, and the presence of animal reservoir have a significant association with leptospirosis

Ethical Clearance: Ethical approval was not required

Conflict of Interest: No conflict of interest

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References

1. World Health Organization. Human Leptospirosis: Guidance for Diagnosis, Surveillance and Control [Internet]. Geneva: World Health Organization; 2003. iii. Available from: https://apps.who.int/iris/bitstream/handle/10665/42667/WHO_CDS_CSR_EPH_2002.23.pdf;jsessionid=409A63D77E5B29922E817B7731BADE27?sequence=1
2. Core AB, Kumrah A, Program AI, Service CDCD, Program EI, Program ID, et al. The National Center for Emerging and Zoonotic Infectious. Available from: https://www.cdc.gov/ncezid/pdf/ncezid_brochure_2012.pdf
3. Centers for Disease Control and Prevention. Leptospirosis Fact Sheet for Clinicians. Cdc. 2018.
4. Mwachui MA, Crump L, Hartskeerl R, Zinsstag J, Hattendorf J. Environmental and Behavioural Determinants of Leptospirosis Transmission: A Systematic Review. PLoS Negl Trop Dis [Internet]. 2015;9(9). Available from: <https://www.scopus.com/inward/record.uri?eid=2-s2.0-84943196151&doi=10.1371%2Fjournal.pntd.0003843&partnerID=40&md5=4b4ee214c2a52b4f48b4f87829e9c39b>
5. Moher D, Liberati A, Tetzlaff J, Altman DG, Altman D, Antes G, et al. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement (Chinese edition). J Chinese Integr Med. 2009;7(9):889–96.
6. Desai KT, Patel F, Patel PB, Nayak S, Patel NB, Bansal RK. A case-control study of epidemiological factors associated with leptospirosis in South Gujarat region. J Postgrad Med. 2016;62(4):223–7.
7. Felzemburgh RDM, Ribeiro GS, Costa F, Reis RB, Hagan JE, Melendez AXTO, et al. Prospective Study of Leptospirosis Transmission in an Urban Slum Community: Role of Poor Environment in Repeated Exposures to the Leptospira Agent. PLoS Negl Trop Dis [Internet]. 2014;8(5). Available from: <https://www.scopus.com/inward/record.uri?eid=2-s2.0-84901779232&doi=10.1371%2Fjournal.pntd.0002927&partnerID=40&md5=e6227425cf8c5fe2cab8134d4eb63328>
8. Costa F, Ribeiro GS, Felzemburgh RDM, Santos N, Reis RB, Santos AC, et al. Influence of household rat infestation on leptospira transmission in the urban slum environment. Small PLC, editor. PLoS Negl Trop Dis [Internet]. 2014 Dec 4 [cited 2019 May 6];8(12):e3338. Available from: <http://dx.plos.org/10.1371/journal.pntd.0003338>
9. Prabhakaran SG, Shanmughapriya S, Dhanapaul S, James A, Natarajaseenivasan K. Risk factors associated with rural and urban epidemics of leptospirosis in Tiruchirappalli district of Tamilnadu, India. J Public Heal. 2014;22(4):323–33.
10. Maze MJ, Cash-Goldwasser S, Rubach MP, Biggs HM, Galloway RL, Sharples KJ, et al. Risk factors for human acute leptospirosis in northern Tanzania. PLoS Negl Trop Dis. 2018 Jun;12(6):e0006372.
11. Meny P, Menéndez C, Ashfield N, Quintero J, Rios C, Iglesias T, et al. Seroprevalence of leptospirosis in human groups at risk due to environmental, labor or social conditions. Rev Argent Microbiol [Internet]. 2019; Available from: <http://www.sciencedirect.com/science/article/pii/S0325754119300069>

12. Matsushita N, Ng CFS, Kim Y, Suzuki M, Saito N, Ariyoshi K, et al. The non-linear and lagged short-term relationship between rainfall and leptospirosis and the intermediate role of floods in the Philippines. *PLoS Negl Trop Dis* [Internet]. 2018;12(4). Available from: <https://www.scopus.com/inward/record.uri?eid=2-s2.0-85046370739&doi=10.1371%2Fjournal.pntd.0006331&partnerID=40&md5=6d2e15bbe7ab7215d36ed5066103468b>
13. Rood EJJ, Goris MGA, Pijnacker R, Bakker MI, Hartskeerl RA. Environmental risk of leptospirosis infections in the Netherlands: Spatial modelling of environmental risk factors of leptospirosis in the Netherlands. *PLoS One* [Internet]. 2017 Oct;12(10). Available from: <https://search.proquest.com/docview/1955030461?accountid=17242>
14. Vitale M, Agnello S, Chetta M, Amato B, Vitale G, Bella CD, et al. Human leptospirosis cases in Palermo Italy. The role of rodents and climate. *J Infect Public Health* [Internet]. 2018 Mar [cited 2019 May 6];11(2):209–14. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1876034117301983>
15. Binti Daud A, Mohd Fuzi NMH, Wan Mohammad WMZ, Amran F, Ismail N, Arshad MM, et al. Leptospirosis and workplace environmental risk factors among cattle farmers in northeastern Malaysia. *Int J Occup Environ Med* [Internet]. 2018 Apr;9(2):88–96. Available from: <https://www.scopus.com/inward/record.uri?eid=2-s2.0-85045620385&doi=10.15171%2Fijoem.2018.1164&partnerID=40&md5=5cdc9472d41f507f8b8eacac18bf579>
16. Lau CL, Dobson AJ, Smythe LD, Fearnley EJ, Skelly C, Clements ACA, et al. Leptospirosis in American Samoa 2010: Epidemiology, environmental drivers, and the management of emergence. *Am J Trop Med Hyg* [Internet]. 2012;86(2):309–19. Available from: <https://www.scopus.com/inward/record.uri?eid=2-s2.0-84857024561&doi=10.4269%2Fajtmh.2012.11-0398&partnerID=40&md5=1e542e062a4b556928df7b1ea817e0a4>
17. Haake, David A and Levett PN. Leptospirosis in Human. Vol. 387, PubMed Central. 2015. 65–97 p.
18. Prabhakaran SG, Shanmughapriya S, Dhanapaul S, James A, Natarajaseenivasan K. Risk factors associated with rural and urban epidemics of leptospirosis in Tiruchirappalli District of Tamilnadu, India. *J Public Health (Bangkok)* [Internet]. 2014 Aug;22(4):323–33. Available from: <https://search.proquest.com/docview/1546078875?accountid=17242>
19. Kawaguchi L, Sengkeopraseuth B, Tsuyuoka R, Koizumi N, Akashi H, Vongphrachanh P, et al. Seroprevalence of leptospirosis and risk factor analysis in flood-prone rural areas in Lao PDR. *Am J Trop Med Hyg*. 2008;78(6):957–61.
20. Dechet AM, Parsons M, Rambaran M, Mohamed-Rambaran P, Florendo-Cumbermack A, Persaud S, et al. Leptospirosis Outbreak following Severe Flooding: A Rapid Assessment and Mass Prophylaxis Campaign; Guyana, January–February 2005. *PLoS One* [Internet]. 2012 Jul;7(7). Available from: <https://search.proquest.com/docview/1325396574?accountid=17242>
21. Waitkins SA. Leptospirosis as an occupational disease. *Br J Ind Med*. 1986;43(11):721–5.
22. Maciel EAP, de Carvalho ALF, Nascimento SF, de Matos RB, Gouveia EL, Reis MG, et al. Household transmission of *Leptospira* infection in urban slum communities. *PLoS Negl Trop Dis*. 2008;2(1).
23. Wynwood SJ, Graham GC, Weier SL, Collet TA, McKay DB, Craig SB. Leptospirosis from water sources. *Pathog Glob Health*. 2014;108(7):334–8.
24. Hausser J, de Roguin L. *Rattus norvegicus*. *Säugetiere der Schweiz/Mammifères de la Suisse/Mammiferi della Svizzera*. 2013;283–7.
25. Romero-Vivas CME, Cuello-Pérez M, Agudelo-Flórez P, Thiry D, Levett PN, Falconar AKI. Cross-sectional study of *Leptospira* seroprevalence in humans, rats, mice, and dogs in a main tropical seaport city. *Am J Trop Med Hyg* [Internet]. 2013 Jan 9 [cited 2019 May 6];88(1):178–83. Available from: <http://www.ajtmh.org/content/journals/10.4269/ajtmh.2012.12-0232>
26. Maze MJ, Cash-Goldwasser S, Rubach MP, Biggs HM, Galloway RL, Sharples KJ, et al. Risk factors for human acute leptospirosis in northern Tanzania. *PLoS Negl Trop Dis* [Internet]. 2018 Jun;12(6). Available from: <https://search.proquest.com/docview/2070854729?accountid=17242>

Comparative Study of the Effect of Chronic Aluminium Chloride Administration on the Expression of Endothelial Nitric Oxide Synthase in Rat Brain

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Abstract

Background: Aluminium chloride (AlCl₃) is a known potent environmental neurotoxic agent causing progressive neurodegenerative changes in the brain. Increasing evidence suggests that oxidative stress is strongly related to AlCl₃ neurotoxicity. Endothelial nitric oxide synthase (eNOS) is a form of the nitric oxide (NO) synthases family.

Aim of the Work: The current study was carried out to investigate the profile of the expression of eNOS in different brain regions following chronic aluminium chloride administration.

Materials and Method: Twelve adult male albino rats were divided equally into two groups. Group I was the untreated control, group II was given AlCl₃ (100 mg/kg body weight) orally daily for 42 days. At the end of the experiment, rats were killed by decapitation under anaesthesia. The brains were removed and processed for immunohistochemistry using antibody raised against eNOS.

Results: By comparison to the untreated control, AlCl₃-treated rats showed significant (P<0.001) increase of eNOS expression in capillaries of cerebral cortex, hippocampus and cerebellum. In addition, there was significant (P<0.001) increase of eNOS expression in hippocampus when compared to cortex and cerebellum.

Conclusion: These data provide further evidence that chronic exposure to aluminium chloride potentiates oxidative stress with subsequent NOS induction in different brain regions with more hippocampal affection.

Keywords: Aluminium chloride, neurotoxicity, eNOS, oxidative stress, brain, hippocampus.

Introduction

Aluminium (Al) is considered as the most abundant metal in the earth's crust⁽¹⁾. It is found in salt, corn,

yellow cheese, tea, herbs, spices, some cosmetics, aluminium containers and drinking water⁽²⁾. Al induces neurodegeneration by increasing Fe accumulation and reactive oxygen species production in different brain regions⁽³⁾. There are many reports of decreased performance on cognitive examinations of aluminium-exposed industrial workers, indicating that aluminium contributes to neurodegeneration⁽⁴⁾. Aluminium chloride (AlCl₃) has been documented to have negative effects on the behavior of Wistar rats⁽⁵⁾. The daily intake of aluminium is reported to be approximately 10–20 mg from food additives, medicines such as antacids,

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cooking utensils and deodorants⁽⁶⁾. Al exacerbates brain oxidative damage⁽⁷⁾, causes neuro-inflammation and induces amyloid- β and neurofibrillary tangles deposition. In addition, it exacerbates oxidative stress caused by iron and other metals, and has been shown to induce apoptosis⁽⁸⁾. The hippocampus is considered as one of the earliest brain region affected by $AlCl_3$ ⁽⁹⁾.

Materials and Method

Animals: A total of 12 adult male albino rats (200 gm) were used in this study.

Materials: Aluminum chloride ($AlCl_3$), anti-endothelial nitric oxide synthase (**anti-eNOS**) (polyclonal rabbit antibody) (Catalog Number N3893) was obtained from Sigma Aldrich Company, Egypt.

Experimental Protocol: The protocol of this study has been approved by the ethical committee of Faculty of Medicine, Minia University. In this study 12 adult male albino rats weighing 200 gm and of 6 weeks were housed in clean plastic cages for two weeks before study. They were fed standard laboratory diet and were allowed free access to water.

Animals were randomly divided into two equal groups (6 rats each): **Group I:** received distilled water by a gastric tube for 42 days and served as control. **Group II:** received 100 mg/kg body weight/day of $AlCl_3$ ⁽¹⁰⁾ which dissolved in water by a gastric tube for 42 days.

Sampling and Histological Study: All rats were sacrificed at the end of this experiment by decapitation, the brains were obtained then sagittally divided into 2 hemispheres using a sharp blade in order to obtain cortical, cerebellar and hippocampal tissues for immune-histological studies.

Immunohistochemical staining for anti-endothelial nitric oxide synthase (anti-eNOS): The immunocytochemical staining was performed using anti-eNOS which is a polyclonal rabbit antibody. Immunohistochemistry was performed on formalin-fixed, paraffin-embedded tissue. 5 μ m brain sections were cut for immune-labelling. The procedure was done according to the manufacture instructions. Briefly, sections were deparaffinized in xylene, rehydrated in descending grades of alcohol then immersed in 0.1% hydrogen peroxide for 15 minutes in order to block the endogenous peroxidase activity. Then the sections were washed by phosphate buffer then incubated in an

ultra-vision block for 5 minutes at room temperature to block the non-specific background staining. The primary antibodies anti-eNOS were diluted at 1:100 in antibody diluent. Sections were incubated in the primary anti-eNOS antibody 15 minutes at room temperature. The reaction was visualized using; Ultravision one detection System, HRP Polymer & DAB Plus Chromogen. After completion of the reaction, counter staining was done using hematoxylin and dehydrated by passing through ascending concentrations of alcohol then cleared by xylene. Cover slip using permanent mounting media is put at last⁽¹¹⁾.

The changes in the immunohistochemical reaction in different brain regions of the treated animals were detected through a comparative examination of the corresponding tissues of the normal control animals.

Morphometric Analysis: The cerebral cortex, cerebellum and hippocampus were examined using bright field microscopy. Image analysis software; Image J (<http://rsbweb.nih.gov/ij/>; NIH, Bethesda) was used to assess eNOS immunopositivity under 40 high power field. Immunopositivity was assessed by measuring the surface area covered by the positive staining. The analysis is automated and was performed by the software. In each animal six sections with 250 μ m distance in between were used for measuring the area fraction of eNOS immunoreactivity.

Statistical Analysis: Quantitative data has been analyzed using SPSS (IBM Corp. Released 2010. Windows, Version 20.0). The mean and standard error (SE) was calculated for each group. Values were expressed as means \pm SE. One-way analysis of variance (ANOVA) test was used to detect significant differences between different groups, followed by the use of Tukey-Kramer as a post hoc test. The results were considered statistically significant when the p-values were <0.05 .

Results

Immunohistochemical staining for anti-endothelial nitric oxide synthase (anti-eNOS):

The positive immunoreactivity appeared as brown cytoplasmic staining of the immunoreactive cells.

A. Control Group (Group I): Sections of the control group displayed faint eNOS immunoreaction in the endothelial cells of the hippocampal blood capillaries (Figure 1).

B. Aluminium chloride (AlCl₃) (Group II): This group showed strongly positive eNOS immunoreaction in the endothelial cells of blood capillaries of cerebral cortex (Figure 2A), cerebellum (Figure 2B) and hippocampus (Figure 2C).

Morphometric analysis of area fraction of eNOS:

There was a significant increase in the area fraction of eNOS immunopositivity in cerebral cortex, cerebellum and hippocampus of AlCl₃ group compared to the control group (p <0.001). Comparing eNOS expression in these regions, we noticed significant increase in the hippocampus when compared to cerebral cortex and cerebellum (all p <0.01) (Table 1).

Table 1: The area fraction of eNOS immunopositivity in the studied groups.

Groups	Mean ±SD	P-value
Control group	0.82± 0.1	
Cerebral cortex of AlCl ₃ group	1.8± 0.1	<0.001 ^{c*}
Cerebellum of AlCl ₃ group	1.5± 0.1	<0.001 ^{c*} <0.109 ^{cc}
Hippocampus of AlCl ₃ group	2.2± 0.3	<0.001 ^{c*} <0.010 ^{cc*} <0.001 ^{cer*}

^cversus the control group, ^{cc}versus the cerebral cortex of AlCl₃ group and ^{cer}versus cerebellum of AlCl₃ group, *p ≤ 0.05 is significant.

Discussion

Aluminium (Al) is considered as an environmental factor which contributes neurodegenerative disorders. Occupational exposure of Al can occur through diet by food processing and storage in aluminium vessels, foil and cans, drinking water, medicines such as antacids, vaccines and cosmetics. The population who expose routinely to Al may have higher chances of neurotoxicity⁽¹²⁾. The repeated exposure to Al could cause severe oxidative stress and pathological changes. It acts as a pro oxidant and with continuous exposure, it accumulates in hippocampus, cortex and other different brain regions, where it induces reactive oxygen species (ROS) formation and result in oxidative damage⁽¹³⁾.

In our study, the intensity of staining of eNOS immunoreaction increased in the capillary endothelium of different brain regions in AlCl₃ group as compared to control group and the maximum affection was noticed in hippocampal capillaries.

Some studies found increased activation of eNOS in

neurodegenerative diseases⁽¹⁴⁾. It is documented that the activity of eNOS was elevated in spinal cord injury⁽¹⁵⁾ streptozotocin induced diabetes⁽¹⁶⁾.

However, other studies demonstrated a significant negative correlation between capillary expression of eNOS and extent of brain pathological changes⁽¹⁷⁾.

Nitric oxide (NO) is formed by a family of NO synthases (NOS)⁽¹⁸⁾. Three isoforms of NOS have been identified as: endothelial NOS (eNOS), inducible NOS (iNOS) and neuronal NOS (nNOS). In addition to NO, it is reported that NOS can produce superoxide anion. This phenomenon is called NOS uncoupling as superoxide production mainly occurs if NOS is not coupled with its substrate⁽¹⁹⁾. Superoxide is documented to have a prominent role in mediating neuronal dysfunction in addition to learning and memory deficits of AlCl₃ toxicity⁽²⁰⁾. During oxidative stress, superoxide and its derived oxidants production induce eNOS uncoupling leading to the formation of eNOS-derived superoxide instead of NO⁽¹⁴⁾. Chronic traumatic encephalopathy (progressive neurodegenerative disease) is recently reported to cause excessive superoxide production by eNOS uncoupled in the endothelial cells. These superoxides can react with the NO formed by microglia or astrocytes forming peroxynitrite, which in turn can increase phosphorylated tau expression in neurons⁽²¹⁾. Oxidative stress results from imbalance between oxidation and antioxidant system which occurs due to excessive production of free radical molecules as ROS and NO or depletion of antioxidant components⁽²²⁾⁻⁽²³⁾ reported strong correlation between memory dysfunction and oxidative stress in the hippocampus. Some studies eNOS inhibition caused reduction of BBB disruption⁽²⁴⁾. Several studies documented BBB breakdown in AlCl₃ toxicity leading to loss of neuronal connectivity, synaptic dysfunction and neurodegeneration⁽²⁵⁾. Some studies revealed that aluminium concentration increases in the cerebral cortex and hippocampus of rat with aluminium chloride neurotoxicity and the aluminium concentration is reported to be more in hippocampus when compared to cerebral cortex⁽²⁶⁾.

Conclusion

These data provide further evidence that chronic exposure to aluminium chloride potentiates oxidative stress with induction of eNOS with subsequent increase of oxidative stress and neuronal cell degeneration in different brain regions with maximal affection of hippocampus.

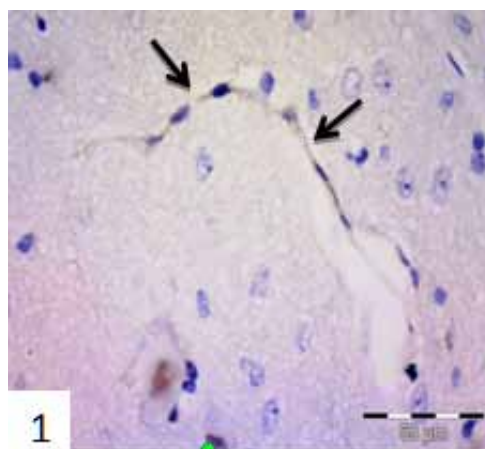


Figure 1: A representative photomicrograph in rat brain of the control group showing faint immune reaction of eNOS in the endothelial cells of a longitudinal blood capillary (arrows). AlCl₃ group (B) showing strongly positive eNOS expression in the endothelial cells of numerous longitudinal blood capillaries (arrows) as compared to control group. Inset is cross section in blood vessels.

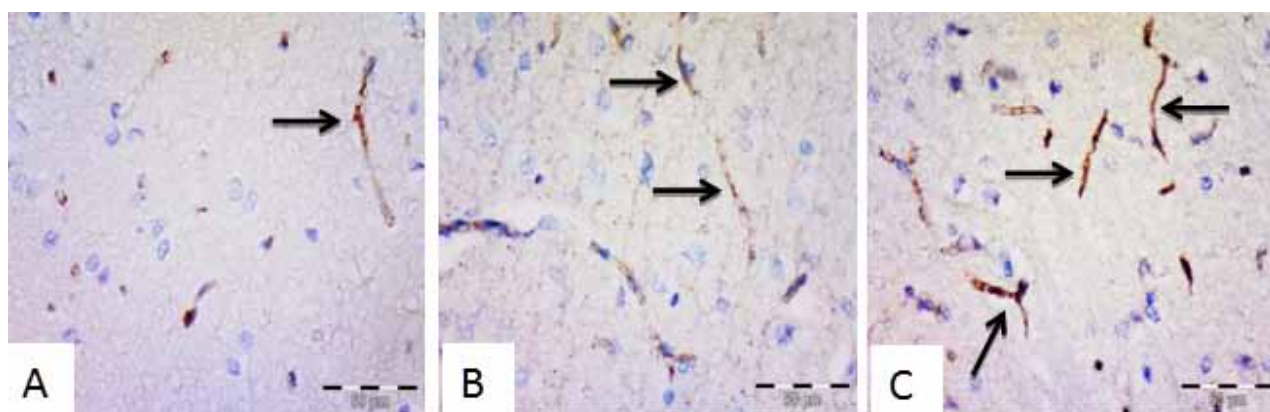


Figure 2: Representative photomicrographs in rat brain of the AlCl₃ group showing positive eNOS expression in the endothelial cells of the blood capillaries (arrows) in cerebral cortex (A), cerebellum (B) and hippocampus (C). Notice increase number and intensity of staining of capillary endothelium in hippocampus (C).

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References

1. Majumdar AS, Nirwane A, Kamble R. Coenzyme Q10 abrogated the 28 days aluminium chloride induced oxidative changes in rat cerebral cortex. *Toxicology international*. 2014;21(2):214.
2. Yokel RA, McNamara PJ. Aluminium toxicokinetics: an updated minireview. *Pharmacology & Toxicology: MiniReview*. 2001;88(4):159-67.
3. Wu Z, Du Y, Xue H, Wu Y, Zhou B. Aluminum induces neurodegeneration and its toxicity arises from increased iron accumulation and reactive oxygen species (ROS) production. *Neurobiology of aging*. 2012;33(1):199. e1-. e12.

4. Al-Otaibi SS, Arafah MM, Sharma B, Alhomida AS, Siddiqi NJ. Synergistic Effect of Quercetin and α -Lipoic Acid on Aluminium Chloride Induced Neurotoxicity in Rats. *Journal of toxicology*. 2018;2018.
5. Buraimoh A, Ojo S, Hambolu J, Adebisi S. Behavioural endpoints of adult wistar rats, following aluminium chloride exposure. *British Journal of Pharmacology and Toxicology*. 2011;2(5):273-6.
6. Thirunavukkaras S, Upadhyay L, Venkataraman S. Effect of manasmitra vatakam, an ayurvedic formulation, on Aluminium-induced neurotoxicity in rats. *Tropical Journal of Pharmaceutical Research*. 2012;11(1):75-83.
7. Becaria A, Bondy SC, Campbell A. Aluminum and copper interact in the promotion of oxidative but not inflammatory events: implications for Alzheimer's disease. *Journal of Alzheimer's Disease*. 2003;5(1):31-8.
8. Kumar A, Dogra S, Prakash A. Protective effect of curcumin (*Curcuma longa*), against aluminium toxicity: Possible behavioral and biochemical alterations in rats. *Behavioural brain research*. 2009;205(2):384-90.
9. Alawdi SH, El-Denshary ES, Safar MM, Eidi H, David M-O, Abdel-Wahhab MA. Neuroprotective effect of nanodiamond in Alzheimer's disease rat model: a pivotal role for modulating NF- κ B and STAT3 signaling. *Molecular neurobiology*. 2017;54(3):1906-18.
10. Lakshmi B, Sudhakar M, Prakash KS. Protective effect of selenium against aluminum chloride-induced Alzheimer's disease: behavioral and biochemical alterations in rats. *Biological trace element research*. 2015;165(1):67-74.
11. Cemek M, Kağa S, Şimşek N, Büyükokuroğlu ME, Konuk M. Antihyperglycemic and antioxidative potential of *Matricaria chamomilla* L. in streptozotocin-induced diabetic rats. *Journal of natural medicines*. 2008;62(3):284-93.
12. Ribes D, Colomina M, Vicens P, Domingo J. Effects of oral aluminum exposure on behavior and neurogenesis in a transgenic mouse model of Alzheimer's disease. *Experimental Neurology*. 2008;214(2):293-300.
13. Mundugaru R, Narayana SKK, Ballal SR, Thomas J, Rajakrishnan R. Neuroprotective Activity of *Garcinia pedunculata* Roxb. ex Buch.-Ham. Fruit Extract Against Aluminium Chloride Induced Neurotoxicity in Mice. *Indian journal of pharmaceutical education and research*. 2016;50(3):435-41.
14. Massaad CA, Amin SK, Hu L, Mei Y, Klann E, Pautler RG. Mitochondrial superoxide contributes to blood flow and axonal transport deficits in the Tg2576 mouse model of Alzheimer's disease. *PLoS one*. 2010;5(5):e10561.
15. Jiang ZS, Pu ZC, Hao ZH. Carvacrol protects against spinal cord injury in rats via suppressing oxidative stress and the endothelial nitric oxide synthase pathway. *Molecular medicine reports*. 2015;12(4):5349-54.
16. Gürpınar T, Ekerbiçer N, Uysal N, Barut T, Tarakçı F, Tuğlu MI. The effects of the melatonin treatment on the oxidative stress and apoptosis in diabetic eye and brain. *The Scientific World Journal*. 2012;2012.
17. Provias J, Jeynes B. The role of the blood-brain barrier in the pathogenesis of senile plaques in Alzheimer's disease. *International Journal of Alzheimer's Disease*. 2014;2014.
18. Liu Y, Lu X, Xiang F-L, Poelmann RE, Gittenberger-de Groot AC, Robbins J, et al. Nitric oxide synthase-3 deficiency results in hypoplastic coronary arteries and postnatal myocardial infarction. *European heart journal*. 2012;35(14):920-31.
19. Luo S, Lei H, Qin H, Xia Y. Molecular Mechanisms of Endothelial NO Synthase Uncoupling. *Current Pharmaceutical Design*. 2014;20(22):3548-53.
20. Massaad CA, Washington TM, Pautler RG, Klann E. Overexpression of SOD-2 reduces hippocampal superoxide and prevents memory deficits in a mouse model of Alzheimer's disease. *Proceedings of the National Academy of Sciences*. 2009;106(32):13576-81.
21. Shin N, Kim H-g, Shin HJ, Kim S, Kwon HH, Baek H, et al. Uncoupled Endothelial Nitric Oxide Synthase Enhances p-Tau in Chronic Traumatic Encephalopathy Mouse Model. *Antioxidants & Redox Signaling*. 2018.
22. Massaad CA, Klann E. Reactive oxygen species in the regulation of synaptic plasticity and memory. *Antioxidants & redox signaling*. 2011;14(10):2013-54.
23. Postu PA, Noumedem JA, Cioanca O, Hancianu M, Mihasan M, Ciorpac M, et al. *Lactuca capensis* reverses memory deficits in A β 1-42-induced an

- animal model of Alzheimer's disease. *Journal of cellular and molecular medicine*. 2018;22(1):111-22.
24. Han F, Shirasaki Y, Fukunaga K. Microsphere embolism-induced endothelial nitric oxide synthase expression mediates disruption of the blood-brain barrier in rat brain. *Journal of neurochemistry*. 2006;99(1):97-106.
25. Sweeney MD, Sagare AP, Zlokovic BV. Blood-brain barrier breakdown in Alzheimer disease and other neurodegenerative disorders. *Nature Reviews Neurology*. 2018;14:133.
26. Chacko A, Ittiyavirah SP. Neuroprotective effect of against aluminium-induced *Gracilaria corticata* neurotoxicity in the hippocampus and cerebral cortex of rat brain: Biochemical and histological approach. *Asian Journal of Pharmacy and Pharmacology*. 2019;5(3):604-13.

Nutritional Evaluation on High Protein Supplement Diet by Biological Assay in Wistar Rat

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Abstract

Enteral nutrition is the best way to feed or supplement the diet when gastrointestinal tract functions of patients are partially or totally preserved. Whenever total enteral nutrition is needed, it represents the only source of nutrients for patients. Thus, it is mandatory to ensure that high biological value proteins are included in enteral formula.

Objective: To investigate the nutritional effectiveness of protein blend constituted intended to be used in enteral nutrition products.

Materials and Method: 27 male Wistar rats, with initial body weight of 60±5 g, were divided into three groups and fed for 28 days with: Group A were fed ONS-ST, Group B were fed ONS-HP, and Group C were fed ONS-PF. Enteral diet was fed 30 g./day during 4 weeks and consumption was recorded every day. Observation on body weight and food consumption were determined during the Study. Growth study (PER and NPRR) and digestibility study (TD, BV and NPU) were calculated. **Results:** The obtained results for growth study and digestibility indicated that the supplement prepared with local food was a good protein source, especially when protein-mix was added. Experimental (Group B) and standard (Group A) had similar values for all analysed indices (PER, NPRR, TD, BV and NPU). These indices were also similar Group C, but lower than experimental and standard groups.

Conclusion: The nutritional effectiveness of ONS-HP versus ONS-ST when administered for 4 weeks to rats were compared. There were no differences between the ONS-HP group and ONS-ST group in body weight and nitrogen balance. Additionally, there were no adverse effects associated with administration of ONS-HP. These results suggest that ONS-HP is as nutritionally effective as ONS-ST, and as useful for nutritional management as conventional enteral nutrition formulas, even in a lower administration volume.

Keywords: Nutritional Evaluation, High Protein, Supplement diet, Biological Assay, Wistar Rat.

Introduction

Enteral nutrients are widely used for nutritional supplementation in patients after surgery and in patients who have long-term difficulty with oral ingestion, due to factors such as sequelae of stroke, neurological intractable diseases, and severe motor and intellectual disabilities⁽¹⁻⁵⁾. Approved enteral nutrition formulas are designed to satisfy the daily vitamin and mineral requirements of adults consuming approximately 1,500 kcal/day in Thailand. Therefore, patients who require long-term nutrient administration and who have low activity, with maintenance energy requirements of approximately 1,200 kcal/day, need to adjust their

intake volume to meet the recommended daily caloric intake. However, such adjustment may result in deficiency of some vitamins or trace elements⁽⁶⁻⁸⁾. It has also been reported that deficiency may result from administration of enteral nutrition formulas that do not contain trace elements (iodine, selenium, chromium, and molybdenum) newly categorized as essential in "Thai Dietary Reference Intakes (Thai DRIs)⁽⁹⁻¹³⁾.

In addition to these nutritional management issues, the following goals must be met in clinical practice: reduction of volume to lower the risk of aspiration, securing time for rehabilitation by shortening administration time, and use of oral nutritional

supplements for nutritional treatment⁽¹⁴⁻¹⁸⁾. Therefore, a high-concentration enteral nutrition formula that allows efficient ingestion of energy and nutrients in smaller volumes is required. In this study, ONS-HP and ONS-ST were administered to Wistar Rats for 4 weeks, and their effects on nutritional status were compared to evaluate the nutritional effectiveness of ONS-HP.

Material and Method

- 1. Enteral diet formulas:** ONS-HP and ONS-ST were prepared at Queen Sirikit Heart Center, Faculty of Medicine, Khon Kaen University, Thailand. The composition of each enteral diet formula is shown in Table 1.
- 2. Animals and Experimental Diets:** Male Wistar rats (n = 27), 6-weeks old were provided by Northeast Laboratory Animal Center (NELAC), Khon Kaen University, Thailand. All the assays described in the present work adhered to the Principles of Animal Care and were approved by Institutional Animal Care and Use Committee of Khon Kaen University (IACUC-KKU). The rats were fed commercial laboratory chow and were allowed drinking water ad libitum for about 3 days before the experiments began.

The animals were individually housed in stainless-steel cages in the animal house at a constant temperature (23°C ± 2°C) and humidity (30-60%), on a 12-h light/12-h dark cycle (lights on at 07:00 a.m.). All animals were weighed daily at 08:00 a.m. At that time, the water and the non-ingested food were weighed and withdrawn from the cages; the new food was weighed and offered to the animals in a specific receptacle inside the cages. During the remaining time, the animals received food and water ad libitum. As such, this schedule ensured that animals of all groups had the same time of feeding.

Rats were divided into three groups: Control group were fed ONS-ST, Experiment group were fed ONS-HP, and Basal group were fed ONS-PF. Enteral diet was fed 30 g/day during 4 weeks and consumption was recorded every day.

- 3. Analysis of Physiological Parameters:** Diet, carcass, and feces were analyzed for nitrogen (N) content according to the method described by⁽¹⁹⁾. All parameters were determined following the method described by⁽²⁰⁾.

Protein efficiency ratio (PER) was extrapolated

by relating the weight gained to the amount of protein eaten-up, see equation 1.

$$PER = \frac{\text{Increase in body weight (g)}}{\text{Weight of protein consumed (g)}} \quad \dots(1)$$

The net protein Ratio (NPR) was calculated estimating the body weight differences between the test group and the basal (protein free) group, using equation 2.

$$NPR = \frac{\text{weight gain on test diet (g)} - \text{weight loss on basal diet (g)}}{\text{protein ingested by the test group (g)}} \quad \dots(2)$$

The true digestibility (TD) was determined based on the nitrogen that was eaten-up and fecal nitrogen using equation 3.

$$TD = \frac{\text{Nitrogen Intake} - (\text{Fecal Nitrogen output on test group} - \text{Fecal Nitrogen output on basal group})}{\text{Nitrogen Intake}} \times 100 \quad \dots(3)$$

The biological value (BV) was using equation 4.

$$BV = \frac{\text{Nitrogen retained (g)}}{\text{Nitrogen absorbed (g)}} \times 100 \quad \dots(4)$$

The Net Protein Utilization (NPU) was using equation 5.

$$NPU = \frac{BV \times TD}{100} \quad \dots(5)$$

- 4. Experimental Design:** The growth, and digestibility studies were carried out using the Completely Randomized Design (CRD). Rats were randomly assigned to the treatments based on their weights. The results are expressed as means ± SD. Statistical analysis was performed using one-way ANOVA. The frequency of recorded fecal conditions in each group was calculated and a DMRT test was conducted. P values less than 0.05 were considered statistically significant.

Results and Discussions

Analysis of Physiological Parameters: The biological assay comprised weight gain (g) by estimating animals feed consumption (g) (Table 2), feed efficiency, protein quality indexes, Protein Efficiency Ratio (PER), Net Protein Ratio (NPR) True Digestibility (TD) rates, Biological Value (BV) and Net Protein Utilization (NPU) (Table 3), derived from the experimental diets with chemical composition described in Table 1.

There was no significant difference in the initial

animal weight for the three diet groups since no difference was above 0.50 g. However, during the experiment, the animals of control group (ONS-ST) had a significant increase in body weight. Further, when compared the animals of the group fed on ONS-HP also weight more increased than fed on ONS-ST (Table 2). On the other hand, the basal group (ONS-PF) had a constant weight loss till the 14th day of the experiment. Weight gain in Wistar rats of the ONS-HP group reached 49.70±0.94 g. on the 14th day and 166.80±2.19 g. on the 28th day, whereas ONS-ST animals had a weight gain of 44.60±0.71 g. (14th day) and 96.20±4.31 (28th day) (Table 2).

Nitrogen Balance: Results had no difference among the experiment and standard groups when compare to the protein efficiency ratio (PER). Among the groups treated, no difference at (p < 0.05) was observed in the net protein utilization (NPU). Also, there was no significant difference in the net protein ratio (NPR) among the groups treated (p < 0.05). The true digestibility (TD) of the experimental animals had no observable differences among the groups treated at p < 0.05. The biological values (BV) of all the groups were significantly different from each other with the reference diet.

To explore the details of protein nutritional status, the nitrogen balance was assessed period, from Day 7 to Day 13. Nitrogen intake was about 180 mg higher in the ONS-HP group than in the ONS-ST group, and fecal nitrogen excretion was higher in the ONS-HP group than in the ONS-ST group (Table 3). The biological value and nitrogen retention rate were not significant difference during in the ONS-HP and ONS-ST group. Results show that digestibility of ONS-HP is lower than that of ONS-ST due to the former having a higher concentration of anti-nutrition factors, which decrease digestibility. However, a good quality protein mixture provides good digestibility and adequate proportions of total nitrogen and essential amino acids, not synthesized by the organism (21).

Conclusion

Weight is often used to measure nutritional status because it is strongly influenced by the changes of food and nutrient conditions. It will go down with decreasing food and nutrient intake (10), and at the time of food intake and nutritional conditions fulfilled, the weight will increase to normal weight. In the present study, the

effectiveness of a novel highly concentrated enteral nutrient, ONS-HP, was compared to that of an approved one, ONS-ST, in rats. There was a significant between-group difference in weight gain in the ONS-HP group. Several studies have reported that dietary fiber causes hypertrophic changes increases fecal volume in rats, without causing toxicity (22). The water-soluble dietary fiber which is present in ONS-HP, may therefore have caused the increased weight in the ONS-HP group.

In regard to nitrogen balance, the biological value and nitrogen retention rate were significantly higher in the ONS-HP group than the ONS-ST group. It has been reported that differences in protein content among enteral nutrition formulas are associated with differences in urinary nitrogen excretion in rats, and that the biological value and nitrogen retention rates change in relation to these differences (23-25). Therefore, the differences in the biological value and nitrogen retention rates in the present study may be attributable to the use of two enteral nutrition formulas with different protein content.

In summary, the nutritional effectiveness of ONS-HP versus ONS-ST when administered for 4 weeks to rats were compared. There were no differences between the ONS-HP group and ONS-ST group in body weight and nitrogen balance. Additionally, there were no adverse effects associated with administration of ONS-HP. These results suggest that ONS-HP is as nutritionally effective as ONS-ST, and as useful for nutritional management as conventional enteral nutrition formulas, even in a lower administration volume.

Table 1: Composition of the diets (% w/w). Control(ONS-ST); Experimental(ONS-HP) and Basal (ONS-PF)

Ingredients	Diets/Groups		
	ONS-ST	ONS-HP	ONS-PF
Casein 1	12.50	-	-
Salt mixture 2	5.00	5.00	5.00
Vitamin mixture 2	1.00	1.00	1.00
Soybean oil	8.00	8.00	8.00
Choline	0.04	0.04	0.04
Cellulose	1.00	1.00	1.00
Corn starch	72.46	51.00	84.96
Protein-Mix	-	25.96	-

¹Casein contained 80.00% w/w protein, ²According to AOAC, 1975

Table 2. Weight evolution and feed ingestion of recently-weaned rats fed on control diet (ONS-ST), experiment diet (ONS-HP) and compare diet (ONS-PF).

Diet Group	14 Days			28 Days		
	Weight gain (g)	Food Intake (g)	Protein Intake (g)	Weight gain (g)	Food Intake (g)	Protein Intake (g)
ONS-ST	44.60±0.71 ^a	137.40±2.83 ^a	14.49±0.49 ^a	96.20±4.31 ^b	311.30±1.47 ^{ns}	32.81±0.97 ^{ns}
ONS-HP	49.70±0.94 ^a	142.60±5.18 ^a	15.60±0.52 ^a	166.80±2.19 ^a	313.50±4.86 ^{ns}	34.30±1.32 ^{ns}
ONS-PF	-10.40±0.65 ^b	64.90±3.44 ^b	0.55±0.07 ^b	-	-	-

Different letters in each column indicate significant difference at $p < 0.05$.

Table 3. Nitrogen balance by biological assay in rats

Diet Group	Nitrogen (mg)			PER	NPR	TD	BV	NPU
	Intake	Urine	Fecal					
ONS-ST	2,317.76±3.88 ^a	231.85±3.67 ^a	201.41±0.31 ^a	2.02±0.56	3.87±0.86	94.04±0.51	91.93±0.97	86.45±1.21
ONS-HP	2,496.16±2.91 ^a	359.46±2.44 ^a	237.56±1.98 ^a	3.14±0.32	4.12±0.21	92.93±0.67	86.78±0.63	80.65±0.87
ONS-PF	88.32±4.87 ^b	43.33±0.27 ^b	62.34±0.14 ^b	-	-	-	-	-

Results except nitrogen intake are shown as the mean ± SD (n = 9/group). Statistical significance was determined using one-way ANOVA ($p < 0.05$).

Ethical Clearance: Taken from Institutional Animal Care and Use Committee of Khon Kaen University, Record No. IACUC-KKU-78/62.

Source of Funding: Agricultural Research Development Agency (Public Organization), government organization.

Conflict of Interest: We have no conflicts of interest to disclose.

References

- Weimann A, Braga M, Harsanyi L, Laviano A, Ljungqvist O, Soeters P, et al. ESPEN Guidelines on Enteral Nutrition: Surgery including Organ Transplantation. *Clinical Nutrition*. 2006;25(2):224-44.
- Arends J, Bodoky G, Bozzetti F, Fearon K, Muscaritoli M, Selga G, et al. ESPEN Guidelines on Enteral Nutrition: Non-surgical oncology. *Clinical Nutrition*. 2006;25(2):245-59.
- Weimann A, Braga M, Carli F, Higashiguchi T, Hübner M, Klek S, et al. ESPEN guideline: Clinical nutrition in surgery. *Clin Nutr*. 2017; 36:623-50.
- Kumode M, Nagae A. Management of nutrition in children or persons with severe motor and intellectual disabilities. *The Journal of Japanese Society for Parenteral and Enteral Nutrition*. 2012; 27:1175-82. (In Japanese).
- Mihara C, Katada F, Bretón I, Planas M, Schneider SM, Burgos R. Nutritional support in neurological diseases. *The Journal of Japanese Society for Parenteral and Enteral Nutrition*. 2011; 26:899-915. (In Japanese)
- Tanaka S-I, Miki T, Hsieh S-T, Kim J-I, Yasumoto T, Taniguchi T, et al. A Case of Severe Hyperlipidemia Caused by Long-term Tube Feedings. *Journal of Atherosclerosis and Thrombosis*. 2003;10(5):321-4.
- Toyoda M, Saito A, Fukuyo N, Togashi N, Kanno J, Fujiwara I, et al. A case report of severely-retarded child with vitamin D deficient rickets caused by complex factors. *Japanese Journal of Pediatrics*. 2010; 63:1039-44.
- Ishii S, Tanaka Y, Asagiri K, Kobayashi H, Asakawa T, Takagi A, et al. A case of neutropenia and anemia due to copper deficiency during enteral nutrition management. *Journal of Japanese Society of Clinical Nutrition*. 2010; 31:90-3.
- Kusunoki J, Saito T, Ogino M, Sakai F, Maeda T. Deficiency of trace elements and vitamin in degenerative neurological disease. *Kitasato Medicine*. 2002; 32:119-31.
- Kimura A, Arizono Y, Maeda J, Matsubasa T, Shinohara M. Selenium administration to the long-

- term enteral feeding children with developmental disability. *The Journal of the Japan Pediatric Society*. 2003; 107:61-4.
11. Masumoto K, Nagata K, Uesugi T, Nakashima K, Nakashima K, Oishi R, et al. Selenium deficiency in a child receiving long-term home enteral nutrition using elemental diet. *The Journal of Japanese Society for Parenteral and Enteral Nutrition*. 2007; 22:195-9.
 12. Owari M, Kosumi T, Nakajima S, Soh H, Yonekura T, Fukuzawa M. A retrospective study of selenium density in neurologically impaired children with long-term enteral tube feeding. *Japanese Journal of Nutritional Assessment*. 2010; 27:175-8.
 13. Shiga K, Kodama H, Kaga F, Izumi Y, Nakamoto N, Fujisawa C. Hypothyroidism caused by iodine deficiency and iodine levels in enteral formulas. *Pediatrics International*. 2011;53(4):501-4.
 14. Kudo M, Tanaka Y. Aspiration. In: *Types and Selection of Enteral Nutrients*. Fuji Medical Publishing, Osaka, Japan, 2005; p. 120-4.
 15. Okada S. Nutrition management guidance in tube feeding. *Community-Based Rehabilitation*. 2015; 10:42-6.
 16. Ikeda K, Kimura Y, Iwaya T, Noda Y, Ito N, Kimura T, et al. ONS for postoperative malnourished patients with esophageal cancer. *The Journal of Japanese Society for Parenteral and Enteral Nutrition*. 2008; 23:617-21.
 17. Kikuchi T, Ogawa S, Yamamoto H, Saitou Y, Okabe M, Shirayama T, et al. Nutrition management of the elderly person in the home medical care. *The Journal of Japanese Society for Parenteral and Enteral Nutrition*. 2013; 28:1057-64.
 18. Hiki N. Enteral nutritional management for cancer patients. *The Journal of Japanese Society for Parenteral and Enteral Nutrition*. 2015; 30:923-6.
 19. Official method of analysis of the association of official analytical chemists. *Analytica Chimica Acta*. 1991;242:302.
 20. Heywood V, Casas A, Ford-Lloyd B, Kell S, Maxted N. Conservation and sustainable use of crop wild relatives. *Agriculture, Ecosystems & Environment*. 2007;121(3):245-55.
 21. Boye J, Wijesinha-Bettoni R, Burlingame B. Protein quality evaluation twenty years after the introduction of the protein digestibility corrected amino acid score method. *British Journal of Nutrition*. 2012;108(S2).
 22. Konishi F, Oku T, Hosoya N. Hypertrophic effect of unavailable carbohydrate on cecum and colon in rats. *Journal of Nutritional Science and Vitaminology*. 1984;30(4):373-9.
 23. Yoshida Y, Ogawa Y, Takahashi Y, Kawamura Y, Ishitsuka S, Hashimoto A, et al. Nutritional effect of MCT-SS, a new enteral nutrient, in rats. *The Clinical Report*. 1993; 27:42594273.
 24. Takahashi Y, Ogawa Y, Yoshida Y, Kawamura Y, Hashimoto A, Ishitsuka S, et al. Nutritional effect of MCT-SS in small intestine resected rats. *The Clinical Report*. 1993; 27:4275-87.
 25. Hayashi N, Nakamura T, Yoshiwara D, Ishii T, Takeshita Y. Experimental evaluation of a liquid enteral nutrition OSN-001 on the nutritional usefulness in small intestine resected rats—comparison with MCT-SS. *Clinical Pharmacology and Therapy*. 1996; 6:231-41.

The Impact Using Healthy Training Method to Develop Some Physical Abilities and Integrated Skills Performances of Futsal for the Deaf and Mute

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Abstract

We have noticed in the recent years that there is a clear improvement in the practice level of football in general and Futsal in particular, which consider the product of the scientific development of modern multi-purpose training method, which all world countries seek to prepare their trainers in a scientific way to aim of improving their athletes to reach the international levels, Scientific research is the best method which to check of the various scientific theories in the sports field and benefit from them to serve and develop sport.

In view of the development of science and knowledge in many sports fields, including football, the game has received a large share of the attention researchers, which reflected on the development of play styles, plans and laws that contributed to give aesthetic in the players performance and increase the enthusiasm of the public, and from among those method is Futsal, which is one of the game method being a basic pillar for its development, as well as its skills, plans, events and unexpected positions in the game works to excite everyone and excitement towards practice and viewing because of the ease of law and small stadium space, the small of players number and similar of the basic skills with the football skills (Soccer), which led to practice by a large number of players.'

Keywords: Deaf, Mute, Integrated skills.

Introduction

It was explained by⁽¹⁾ that explains that the skill performances in the football game means all the necessary and purposeful movements that lead to a specific purpose within the framework of the football law, whether those movements with ball or without the ball, and the player's proficiency is determined by the level of his handling of the ball and how to run and control The mastery of basic skills and the players ability to control and use the ball efficiently is the first basis to implement the plans, whether offensive or defensive, whenever the proficiency level of the player higher for the skill performance whenever high his value in the team, football is a collective educational sport requires that each player's performance complement the performance of the rest of his teammates, and this also applies on the basic skills till became each team fully diversified in the performance level of its players

and thus become a good level of team. Also⁽²⁾ agrees that there is a clear and abbreviated division of the skill performances with the ball are:

1. Individual (single) performances
2. Composite performance (integrated)

The only skill performances are performed individually and have a definite beginning and end, the effect and the introductory movement role in accomplishing the main duty of the skill are evident, These skills appear in the player's performance of the control skill on the ball (suck, mute, receipt), the side glide, throw ball out of bounds, passes, free kicks and corner and penalty.

Composite skill performances: They represent models of different forms of a set of individual skill performances that merged with each other and overlap

their end stages to form the beginning of the next skill performed by the player in a particular game position to achieve a specific goal according to his requirements. The motor activity of the football player is not only a single skill, but a set of individual skills that merged to become a multi-skill performance that is connected and interdependent among them, where the distinguished players direct to integrate process and melting individual skills inside the only integrate skill such as control the ball and running then pass where this includes integrated skills, ie abbreviated in terms of total time and the total area to perform thus become more connected performance⁽³⁾. There are some skill performances that depend mainly on the technique and technical style of performances and some other skills depend on the player's ability to respond to external stimulants related to others in actual competition situations and this is what happens in football as we note the emergence of some players are highly skilled in training but fail to show the same superior level during matches because they are unable to respond properly to different playing situations⁽⁴⁾.

After conducting an analytical study to identify the most important of these composite skill performances (integrated), a number of (10) composite skill performances are:

1. The Direct pass from the movement (running).
2. Receiving and passing (receiving and passing from movement).
3. Receiving then run the ball and then pass.
4. Receiving then dribbling and passing.
5. Receiving with dribbling and passing.
6. Receiving with dribbling then running the ball and passing.
- 7 - Receiving then running the ball then dribbling then passing.
8. Receiving then dribbling then running the ball then passing.
9. Receiving then running the ball then dribbling then run and pass.
10. The same previous skill sentences but ending with the correction⁽⁵⁾.

It is clear from the above that the physical preparation is an important pillar and an essential duty in Futsal and the modern football requires high capacity, where the

players movement on the playground requires a great deal of physical abilities, in addition to the ability of accomplishing and control the ball throughout the periods of dealing with the ball, and to achieve the futsal's player the highest level of performance during the matches the player must be considered a completely physical preparation in the light of playing the game. because the good preparation of physical players has a closely related to his mastery of the basic skills of the game and makes him perform competitions in a distinctive way because the skill and planning performance depends largely on the Physical competence of the player due to many factors, including the game nature, the game time, the size of the stadium space and the large duties lies on the player.

Research Problem: The studying process of any problem requires extensive knowledge and especial realization of the problem type and basing on scientific grounds aimed at reaching the player to the highest levels, and in order to reach the player to high levels of sports in the performance of sports activities in general and futsal in particular, it requires a high level of skill performance and physical abilities, Through the researchers experience in the futsal training field have noticed that there is a very obvious weakness in physical and skills abilities of the players, and may be the reason is not to rely on scientific training programs to develop the physical qualities and skills and using the correct scientific evaluation for address these problems, therefore, the researchers see the need to develop effective training programs with using training means (Pleomorphic) and circular and cross training in order to develop some of the physical and skills abilities of futsal players for the deaf and mute.

Research Importance: The importance of the research is to identify the impact of the various training method (Pleomorphic, circular, cross) in the development of some physical abilities and integrated skills of futsal players, and through the reference research and access to Arabic and foreign studies within the researchers' knowledge limits, it was found that there are no studies have the various training method to develop some physical abilities and integrated skills of the players of the Paralympic Committee in Maysan province of futsal, this prompted the researchers to try to identify the impact of these method on the futsal players in Maysan and the relation of physical and developing the skill side of the players, which are clearly affecting the level of their performance while playing in the league.

Research Objective: The research aims to develop some of the physical abilities and skills performance of futsal players through:

1. Identify the impact of using the different training method to develop the physical abilities of the futsal players.
2. Identify the impact of using the various training method to develop the skills performance of the futsal players.

Research Hypotheses:

1. There are statistically significant differences between the pre-measurement and post-measurement of the members of the experimental group in favor of post-measurement in the development of special physical abilities of the futsal players.
2. There are statistically significant differences between the pre - measurement and post-measurement of the members of the experimental group in favor of post-measurement in the development of the skill performance of the futsal players.

Biometric Training Mean: It is a training method through which a sudden lengthening (ie, decentralized contraction) which precedes the maximum central contraction where the muscle is lengthened and shortened and helps to develop and improve the explosive capacity, and this type depends on the muscle rubber to give them great kinetic energy, and plyometric exercises are divided into (exercises related to the limb) Lower body and upper limb) and may be performed by using or without tools and include (partridge, jump, leap) and other free exercises, which is a sudden lengthening of the muscle and then followed by shortening them⁽⁶⁾.

Cross Training Method: It means doing different things for a lot of people. For some, it may mean the effect of training one side of the body on the other, for others it is an activity used to give active rest from an organized training program, for some, it means using things related to the main activity to avoid the negative results in organized training.

Circular Training Method: It is a regulation of physical effort to achieve a state of adaptation, where it operates through a predetermined path, with a group of activities and performances of the momentary stop at each training station to perform a specified number of repetitions of exercises, free activities, tools or weights according to a specific system.

Futsal: It is the term used internationally for the game, which is derived from the Spanish and Portuguese language and is an abbreviation word of (football) which means football in Spanish and the word (sala) its internal meaning to be the term is football for the halls, and this term is an alternative to the previous term, which is called five-way football. (21)

Research Methodology: The researcher used the experimental method to design two experimental groups and the other controlled by using pre and post measurements to suit the type and nature of the research.

Research Fields:

The Human Field:

1. **Research population:** The research population is represented by (44) players of the Paralympic Committee in Maysan governorate of futsal for the season 2017-2018
2. **Research sample:** The research sample was selected by deliberate random method from the players of the Paralympic Committee in the Maysan province of futsal for the season 2017-2018 and the number (30) were divided into two groups (control group, experimental group) The number of each group (15) players were taken into account in the selection of the sample in accordance with the following conditions.

Sample selection conditions:

1. Age between 15 and 17 years.
2. The player's height and weight shall be Proportional with the stage of the age under study.
3. Hearing degree should be 91 decibels (deep loss).
4. Free from diseases that effect of performance.
5. To be committed and continuing in training without interruption.
6. Paralympic Committee officials agree to conduct the experiment on the players.

Spatial Field: The application of scientific transactions to calculate the validity and reliability of the test and the proposed program of the basic research sample on the stadium of the closed hall in the Technical Institute of Technology in Maysan

Time Domain:

1. Scientific transactions were applied to calculate

the validity and reliability of the test on Saturday, 4/11/2017

2. The test was repeated on Tuesday 14/11/2017
3. Pre- tests were applied on Thursday 23/11/2017
4. The basic study of the proposed program was conducted on Sunday 26/11/2017 until Wednesday 24/1/2018
5. The tests were conducted on Thursday 25/1/2018.

Conflict of Interest: Nil

Source of Funding: Self

Ethical Clearance: Not required

References

1. Abdullatif A Aljuboury. Introduction of fibrin adhesive system (tissucol) in periodontal surgery;part ii: clinical pocket reduction and attachment regeneration. Mustansiria DJ 2005; 1(2):108-119
2. Prato GP, De paoli S, Clauser C, Bartolucci E. On the use of a Biologic Sealing system (tissucol) in periodontal surgery. Int J periodontrestorat Dent 1983;3(4):48-60
3. Abdullatif A Aljuboury. Periodontitis its prevalence among chronic periodontitis patients with cohort incentive condition. Must DG2006;3(1):45-60
4. Abdullatif A Aljuboury, Hadeel M. Experimental gingivitis in overweight subjects, clinical and microbiological study. J Bagh Coll Dent 2011;23(1):51-54
5. Tomas I. M, Melisa S. G, Flavio C.E, et.al. Culture and Characterization of Mesenchymal Stem Cells from Human Gingival Tissue. Periodontol, 2010;81:917-925.
6. Sudo K, Kanno M, Miharada K, et al. Mesenchymal progenitors able to differentiate into osteogenic, chondrogenic, and/or adipogenic cells in-vitro are present in most primary fibroblast-like cell populations. Stem Cells 2007;25:1610-1617.

Histopathological Findings in Patients with Abnormal Uterine Bleeding

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Abstract

Background: Uterine bleeding, which affects a woman between menstrual periods, indicates several hormonal phenomena, which are uterine bleeding outside regular menstrual periods, usually associated with menstruation without ovulation, which is usually the cause of uterine bleeding. The purpose of this study was to describe the prevalence of the AUB among Mosul women.

Methodology: Study design: A prospective study was applied in the Mosul city, Iraq. All cases of abnormal vaginal bleeding procured between October, 2018 and October, 2019, at Al-khanssa teaching hospital, in Mosul city, Iraq. A total of 152 cases were included in the study. For each case, representative slides were reviewed and the pattern of uterine histopathological changes identified and classified according to age groups.

Results: Total of (233) women abnormal uterine bleeding was studied from October 2018 to October 2019. Women' age ranged from 15-55 years. Structural cause of chronic abnormal uterine bleeding consisted of 35.42% of cases, whereas nonstructural cause of chronic abnormal uterine bleeding consisted of 64.58% of cases. Ovulatory dysfunction was the most common finding among women with chronic AUB, accounting for (57.7%) cases. Polyp was found in (16.2%) women, Leiomyoma in (12%) patients, Adenomyosis in (4.94%) patients, Endometrial in (2%) patients, malignancy and hyperplasia in (1.9%) women, and Coagulopathy in (1%) women. The highest rate of Ovulatory dysfunction was belonged to age 25-29 years (19.9%).P prevalence was recorded at the highest rate among women belonged to age (40-44).The prevalence of A & L increased by the age. The prevalence rate was 42.3% among women aged (40-44)(45-49) years respectively. The majority occurrence of AUB found in women belonged to age group()years and those who were multiparous.

Conclusion: The study concluded that our college students still need intensive training in critical thinking and problem solving techniques, and that the teachers of training and teaching should follow advanced method of teaching their students.

Keywords: AUB, Bleeding, Uterine.

Introduction

Abnormal uterine bleeding (AUB) is a significant

clinical entity. AUB and its sub group, heavy menstrual bleeding (HMB), are common conditions affecting 14-25% of women of reproductive age^(1,2) and may have a significant impact on their physical, social, emotional and material quality of life⁽³⁾. AUB is mainly caused by an imbalance in the sex hormone balance in a woman's body, which is due to a combination of factors such as polycystic ovary syndrome (POCS), Endometriosis, and Uterine polyps. Chronic AUB was defined as 'bleeding from the uterine corpus that is abnormal in

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volume, regularity and/or timing that has been present for the majority of the last 6 months⁽⁴⁾. AUB may be the symptom of endometrial carcinoma in 8–50% of cases.^(5,6) Adenocarcinoma of the endometrium is often preceded by proliferative precursor lesions “endometrial hyperplasia”. Thus, early accurate diagnosis and proper treatment of endometrial hyperplastic lesions are essential to prevent progress to endometrial cancer and preclude unwarranted hysterectomy without definitive diagnosis.⁽⁷⁾

Aim of the Study: The purpose of this study was to describe the prevalence of the AUB among Mosul women.

Method

Ethical Considerations: This study was approved by the Council of College of Nursing at University of Mosul, Iraq. Study participants were not exposed to harm in any ways whatsoever. Anonymity, privacy and dignity of student were prioritized. No any conflicts of interests and no any advantages were given to the student. Formal Consent was obtained from the student before the study and the protection of them were ensured.

Study Design: A prospective study was applied in the Mosul city, Iraq.

Study Sample: All cases of abnormal vaginal bleeding procured between October, 2018 and October, 2019, at Al-khansa teaching hospital, in Mosul city, Iraq. A total of 152 cases were included in the study.

Procedure: The cases were classified according to age and causes For each case into three category. The first category includes women with AUB because of non-structural causes includes (Secretory endometrium, Proliferative endometrium, Atrophic endometrium, Disordered proliferative endometrium, Decidual

reaction Hormonal imbalance). The second category includes patients with abnormal uterine bleeding due to structural causes (Endometrial polyp, Endometritis, Low grade endometrial hyperplasia, Endometrial carcinoma, Pregnancy-related conditions and Cervical lesions). The third category includes women reproductive age (< 40 years), women of latter reproductive age or perimenopausal age (40-55 years), and finally postmenopausal women (55 years and older)

Statistical Analysis: Data was entered in Microsoft excel 2010 for graphical representation and managed in statistical package for the social sciences (SPSS) version 19. Analysis was done in the form of percentages and proportions and represented as tables where necessary.

Results

Total of (233) women abnormal uterine bleeding was studied from October 2018 to October 2019. Women’ age ranged from 15-55 years. Structural cause of chronic abnormal uterine bleeding consisted of 35.42% of cases, whereas nonstructural cause of chronic abnormal uterine bleeding consisted of 64.58% of cases. Ovulatory dysfunction was the most common finding among women with chronic AUB, accounting for (57.7%) cases. Polyp was found in (16.2%) women, Leiomyoma in (12%) patients, Adenomyosis in (4.94%) patients, Endometrial in (2%) patients, malignancy and hyperplasia in (1.9%) women, and Coagulopathy in (1%) women. The highest rate of Ovulatory dysfunction was belonged to age 25-29 years (19.9%).P prevalence was recorded at the highest rate among women belonged to age (40-44).The prevalence of A & L increased by the age. The prevalence rate was 42.3% among women aged (40-44)(45-49) years respectively. The majority occurrence of AUB found in women belonged to age group()years and those who were multiparous.

Table (1): Distribution of abnormal bleeding according to types

Types	No	%
Polyp	42	18.03
Adenomyosis	15	6.44
Leiomyoma	36	15.45
Malignancy and hyperplasia	10	4.29
Coagulopathy	8	3.43
Ovulatory dysfunction	112	48.07
Endometrial	10	4.29
Total	233	100

Table (2): Distribution of abnormal bleeding according to types and age.

Types/age	15-19y	20-24y	25-29y	30-34y	35-39y	40-44y
Polyp	0%	0%	18%	22%	27%	33%
Adenomyosis	0%	0%	1%	2%	43%	54%
Leiomyoma	0%	0%	0%	0%	46%	54%
Malignancy and hyperplasia	0%	0%	0%	0%	33%	67%
Coagulopathy	12.6%	14.4%	23.9%	20.2%	18.6%	10.3%
Ovulatory dysfunction	22%	20%	25%	12%	11%	10%

Discussion

In the present study the finding shown that the ovulatory dysfunction is most common case (48.07%). Ovulatory dysfunction can contribute to the genesis of AUB, generally manifesting as a combination of irregular timing of bleeding and inconsistent quantity of flow (AUB), which in some cases results in HMB⁽⁸⁾. "In many regions, particularly (but not limited to) the USA, ovulatory disorders comprised the huge cases encompassed by the now-discarded term "DUB." Disorders of ovulation may present as a spectrum of menstrual abnormalities ranging from amenorrhea, through extremely light and infrequent bleeding, to episodes of unpredictable and extreme HMB requiring medical or surgical intervention. Some of these manifestations relate to the absence of predictable cyclic progesterone production from the corpus luteum every 22–35 days, but in later reproductive years many relate to unusual "disturbed" ovulations, which have been labeled as "luteal out-of-phase" events"^(9,10).

Polyp consisted (18.03%) of the cases in the current study. There seems to be little controversy regarding the inclusion of endometrial and endocervical polyps. These epithelial proliferations comprise a variable vascular, glandular, and fibromuscular and connective tissue component and are often asymptomatic, but it is generally accepted that at least some contribute to the genesis of AUB⁽¹¹⁾. The lesions are usually benign but a small minority may have atypical or malignant features^(12,13). A similar incidence was found by Gopalan U (1.1%), Muzaffar M et al (1.2%), Khan S et al (0.6%), and (1.3%) Baral R et al.^(14,15,16,17)

Furthermore, the study finding revealed that Leiomyoma consisted (15.45%) of cases. Benign fibromuscular tumors of the myometrium are known by several names, including "leiomyoma," "myoma," and the frequently used "fibroid." "Leiomyoma" is generally

accepted as the more accurate term and was selected for use in the present system. The prevalence of these lesions (up to 70% in Caucasians and up to 80% in women of African ancestry⁽¹⁸⁾, their spectrum of size and location (subendometrial, intramural, subserosal, and combinations of these), and the variable number of lesions in a given uterus require that they be afforded a separate categorization in the system. Like polyps and adenomyosis, many leiomyomas are asymptomatic, and frequently their presence is not the cause of AUB. Furthermore, leiomyomas have widely varying rates of growth, even in a single individual⁽¹⁹⁾. Previous studies had indicated that AUB caused by AUB-L was more severe and the incidence is 14%-25%.^(19,20) However, our study has found that the bleeding pattern of women with AUB-L was mainly HMB, which accounted for 51% and 44% of length-period prolongation, and the menstrual cycle was regular. Previous study suggested that uterine myoma and endometrial causes of bleeding are associated with increased surface area and brittleness of the blood vessels, resulting in endovascular blood flow increase to overcome platelet aggregation.^(22,23) In addition, AUB-L was associated with age.^(24,25) The study found that the incidence of AUB-L increased with age, reaching a peak between 45 and 49 years.

Conclusion

Abnormal uterine bleeding is one of the most common health problems facing women and a change their quality of life. In Mosul, this problem wasn't previously highlighted only through this study, which concluded that

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References

1. World Health Organization multicenter study on menstrual and ovulatory patterns in adolescent girls. II Longitudinal study of menstrual patterns in the early postmenarcheal period, duration of bleeding episodes and menstrual cycles. World Health Organization Task Force on Adolescent Reproductive Health. *J Adolesc Health Care* 1986;7:236–44. (Level II-2).
2. Hickey M, Balen A. Menstrual disorders in adolescence: investigation and management. *Hum Reprod Update* 2003;9:493–504.
3. Department of gynecology, endocrinology group of gynecology of Chinese medical association. Diagnostic and treatment guidelines for abnormal uterine bleeding. *Zhong Hua Fu Chan Ke Za Zhi* 2014;49:801–6.
4. Practice bulletin no. 128: diagnosis of abnormal uterine bleeding in reproductive aged women. *Obstet Gynecol* 2012;120:197–206.
5. Liu Z, Doan QV, Blumenthal P, et al. A systematic review evaluating health-related quality of life, work impairment, and health care costs and utilization in abnormal uterine bleeding. *Value Health* 2007;10:173–82.
6. Kazemijalish H, Ramezani Tehrani F, Behboudi-Gandevani S, et al. A Population-based study of the prevalence of abnormal uterine bleeding and its related factors among iranian reproductive-age women: an updated data. *Arch Iran Med* 2017;20:558–63.
7. Cote I, Jacobs P, Cummings D. Work loss associated with increased menstrual loss in the United States. *Obstet Gynecol* 2002;100:683–7.
8. Matteson KA, Raker CA, Clark MA, et al. Abnormal uterine bleeding, health status, and usual source of medical care: analyses using the Medical Expenditures Panel Survey. *J Womens Health (Larchmt)* 2013;22:959–65.
9. Munro MG, Critchley HO, Fraser IS. FIGO Menstrual Disorders Working Group The FIGO classification of causes of abnormal uterine bleeding in the reproductive years. *Fertil Steril* 2011;95:2204–8. 2208 e1-3.
10. Hale GE, Hughes CL, Burger HG, Robertson DM, Fraser IS. Atypical estradiol secretion and ovulation patterns caused by luteal out-of-phase (LOOP) events underlying irregular ovulatory menstrual cycles in the menopausal transition. *Menopause* 2009;16(1):50–9.
11. Hale GE, Manconi F, Luscombe G, Fraser IS. Quantitative measurements of menstrual blood loss in ovulatory and anovulatory cycles in middle- and late-reproductive age and the menopausal transition. *Obstet Gynecol* 2010;115(2 Pt 1):249–56.
12. Lieng M, Istre O, Sandvik L, Qvigstad E. Prevalence, 1-year regression rate, and clinical significance of asymptomatic endometrial polyps: cross-sectional study. *J Minim Invasive Gynecol* 2009;16(4):465–71.
13. Anastasiadis PG, Koutlaki NG, Skaphida PG, Galazios GC, Tsikouras PN, Liberis VA. Endometrial polyps: prevalence, detection, and malignant potential in women with abnormal uterine bleeding. *Eur J Gynaecol Oncol* 2000;21(2):180–3. (12) Shushan A, Revel A, Rojansky N. How often are endometrial polyps malignant? *Gynecol Obstet Invest* 2004;58(4):212–5.
14. Gopalan U, Rajendiran S, Karnaboopathy R. Study of endometrial histopathology in women with abnormal uterine bleeding. *Int J Reprod Contracept Obstet Gynecol*. 2017;6(3):824-8.
15. Muzaffar M, Akhtar KAK, Yasmin S, Rahman M, Iqbal W, Khan MA. Menstrual irregularities with excessive blood loss: A Clinico-Pathological Correlation. *J Pak Med Assoc*. 2005;55:486-9.
16. Khan S, Hameed S, Umer A. Histopathological pattern of endometrium on diagnostic D and C in patients with abnormal uterine bleeding. *Annals King Edward Medical Univ*. 2011;17(2):166-70.
17. Baral R, Pudasaini S. Histopathological pattern of endometrial samples in abnormal uterine bleeding. *J Pathol Nepal*. 2011;1:13-6.
18. Day Baird D, Dunson DB, Hill MC, Cousins D, Schectman JM. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. *Am J Obstet Gynecol* 2003;188(1):100–7.
19. Davis BJ, Haneke KE, Miner K, Kowalik A, Barrett JC, Peddada S, et al. The fibroid growth study: determinants of therapeutic intervention. *J Womens Health (Larchmt)* 2009;18(5):725–32.
20. Munro MG. Classification of menstrual bleeding disorders. *Rev Endocr Metab Disord* 2012;13:225e34.

21. Stewart EA, Nowak RA. Leiomyoma-related bleeding: a classic hypothesis updated for the molecular era. *Hum Reprod Update* 1996;2:295e306.
22. Weiss G, Maseelall P, Schott LL, et al. Adenomyosis a variant, not a disease? Evidence from hysterectomized menopausal women in the Study of Women's Health Across the Nation (SWAN). *Fertil Steril* 2009;91:201–6.
23. Dueholm M. Transvaginal ultrasound for diagnosis of adenomyosis: a review. *Best Pract Res Clin Obstet Gynaecol* 2006;20:569–82.
24. Bergholt T, Eriksen L, Berendt N, et al. Prevalence and risk factors of adenomyosis at hysterectomy. *Hum Reprod* 2001;16:2418–21.
25. Ali İrfan Güzel, Burak Akselim, Selçuk Erkılınç, et al. Risk factors for adenomyosis, leiomyoma and concurrent adenomyosis and leiomyoma. *J Obstet Gynaecol Res* 2015;41:932–7.

Nutritional Education Regarding Ante Natal Care: Improving Knowledge, Attitudes, and Behaviors of Health Cadres

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Abstract

Background: Health cadres have a significant role in helping improve the health of pregnant women. Therefore, providing education supported by comprehensive tools to increase cadres' competence and knowledge of ante natal care (ANC) for pregnant women is a strategic action. The aim of the study was to analyze the effect of conducting nutrition education using "Bumil-Kit" media as a comprehensive tools on knowledge, attitudes, and behavior of the cadres in performing ANC.

Method: The quasi-experimental research with one group pre and posttest design was used to analyze 40 cadres as subject working in the area of Lebdosari Community Health Center. Cadres were trained by the nutrition workers the procedures for using "Bumil-Kit/Pregnant Mother-kit" consisting of weight scales, mid-upper arm circumference (MUAC) ribbon, microtoise, ANC books, chart of pregnancy growth, and booklets as well as conducting ANC. Knowledge, attitudes, and behaviors were measured before and after a given intervention using a structured questionnaire and data gathered were analyzed using Wilcoxon Signed Rank Test.

Result: The results showed that most cadres (45%) had 6-20 years of working experience. There was an effect of nutritional education on knowledge ($p = 0.001$), attitudes ($p = 0.001$), and behavior ($p = 0.038$) regarding ANC. The increased score of knowledge, attitudes, and behaviors before and after intervention was 7.15%, 6.53%, and 6.43%.

Conclusion: Providing nutrition education using "Bumil-Kit" media as a comprehensive tool increases knowledge, attitudes, and behavior of health cadres regarding ANC.

Keywords: Knowledge, attitude, behavior, health cadres.

Introduction

Maternal mortality is one of the health problems having been considered a major concern by a country, as most of the maternal mortalities is caused by labor and other factors during pregnancy. According to a survey

conducted by Indonesian Basic Health Research, the maternal mortality rate (MMR) in Indonesia fell from 359 per 100,000 live births in 2012 to 305 per 100,000 live births in 2015. Despite the decline, the figure is still relatively high compared to that in other countries in Asia. Even when compared to one of the Sustainable Development Goals (SDG's) targets in 2030, reducing MMR to 70 per 100,000 live births, the gap is still high and therefore more comprehensive efforts are extremely in need. Compared to MDG's target in 2015, which failed to be accomplished, the current target, 102 per 100,000 live births, is still low.¹

Ante natal care (ANC) has been implemented as a strategy in reducing MMR in several countries, including

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Indonesia.² ANC service is an integrated program by which pregnant women will receive comprehensive services related to pregnancy care, prevention of babies' low birth weight (LBW), and high-risk prevention for pregnant women; thus, this program provide a positive impact on maternal and fetal health.³ To achieve these objectives, cooperation among stakeholders, one of which is health cadres, is required. However, the cadres have to have a certain competence to implement the program. Therefore, cadres' competence associated with ANC needs to be improved by providing them nutritional education related subject. In addition, to support the effectiveness of the education, a comprehensive media supporting training, such the "Bumil-Kit", is needed. The objective of this study was to analyze the effectiveness of nutritional education using "Bumil-Kit" media as a comprehensive tool on the knowledge, attitudes, and behavior of the health cadres regarding ANC of the pregnant women.

Method

The quasi-experimental research with one group pre and post test design was used to analyze 40 cadres as subject working under the administration of Lebdosari Community Health Center. The subjects were given an intervention in the form of nutritional education using "Bumil-Kit" media as a comprehensive tool in ante natal care (ANC). The "Bumil-Kit" consisted of weight scales, mid-upper arm circumference (MUAC) ribbon, microtoise, ANC books, growth chart of pregnancy, and booklets about how to use "Bumil-Kit", Pregnant Mothers Health and Prevention of Low Birth Weight (LBW), Exclusive Breastfeeding Management, and the Role of Husband in the Health of Pregnant Women and Prevention of LBW.

The concept of nutritional education was in the form of socialization and training provided by the Nutrition Workers conducted in Lebdosari Community Health Center for one day. The variables of knowledge, attitude, and behavior regarding ANC of the subjects were measured before and after intervention using a structured questionnaire. Data were analyzed using univariate and bivariate. Univariate is used to determine the characteristics of the subject, while bivariate is used to analyze the impact of providing nutrition education on the subject's knowledge, attitudes, and behaviors regarding ANC. Bivariate data analysis in this study was Wilcoxon Signed Rank-Test. Subjects' participation was voluntary proven by signing of informed consent;

in addition, all research data collected was confidential. This research has passed the ethical review from the Health Research Ethics Commission of the Faculty of Public Health, Diponegoro University with Ethical Clearance Number: 224/EA/KEPK-FKM/2018.

Results and Discussion

Subject Characteristics: Most of the subjects were cadres having long working experiences, possessing high school education (SMA), and belonging to productive age.

Table 1: Frequency Distribution of Age, Last Education, and Working Experience of Cadre

Variable	n	%
Age		
a. 20 years–35 years		
b. 36 years–50 th	1	3.5
c. More than 50 years	24	59.0
Last Education	15	37.5
a. Elementary School	0	0
b. Junior High School	9	22.5
c. Senior High School	20	50.0
d. Vocational High School	7	17.5
e. Diploma1	1	2.5
f. Diploma 3	2	5.0
g. Under graduate	1	2.5
Working Experience of Cadre	16	40.0
a. 1–5 years	18	45.0
b. 6–20 years	6	15.0
c. More than 20 years		

Table 1 shows that the subjects of the research belong to age ranging from 36-50 years (59%) are higher than those over 50 years (37.5%), and most of them completed senior high school and only a small percentage completed tertiary education either diploma 1 (2.5%), diploma 3 (5.0%), or undergraduate (2.5%). The working experience of the subjects as cadres is relatively long; 6-20 years (45%), 1-5 years (40%), and more than 20 years (15%).

Health cadres in *Posyandu* are a group of people who voluntarily participate in *Posyandu* activities and have a very important role, one of which is as a motivator of the community in achieving good health status. As *Posyandu* has become a pillar in improving public health through sociocultural approach, the active role of health cadres determines *Posyandu* activities and health programs within the region to be better. In *Posyandu*, the role of health cadres is not only taking

care of toddlers, but also assisting pregnant women in doing ANC compliance.⁴

The result of the analysis showed that as most of the subjects had relatively long work experiences, they had to have a good related competence, yet needed to be updated all the time including increasing knowledge related nutrition. Knowledge is the basic capital in health assisting activities in the community, so providing education is very important.⁵ A study in Sidoarjo showed that the activeness of cadres can be identified from their knowledge related competence under which status health programs in the community including *Posyandu* depend on.⁶ In this study, the intervention for cadres applied was nutrition education consisting of counseling and practice using media "*Bumil-Kit*" in order to increase cadres' knowledge and competence in ANC.

Effect of Nutrition Education on Knowledge, Attitudes, and Behavior: Cadres' knowledge was measured using a structured questionnaire containing questions regarding pregnancy care, LBW prevention, and high risk prevention for pregnant women. Questionnaires observing pregnancy care covered the number of pregnant women having checked during pregnancy, taking pills containing Fe, recommended and not recommended intake for pregnant women, immunization, smoking history and cigarette smoke exposure, and breast care during pregnancy. Meanwhile, LBW prevention, a component in the knowledge questionnaire, covered LBW definitions and cut-off points, age affecting the occurrence of LBW, factors influencing and preventing LBW. In addition to the two components, other components included in the questionnaire observing knowledge were of high-risk prevention for pregnant women consisting of marriage and pregnancy age, interval and number of pregnancies, signs and symptoms of high-risk pregnant women, and smoking habits as well as drug consumption.

Moreover, the attitude of the cadres in relation to ANC was measured using a structured questionnaire consisted of questions observing pregnancy care, LBW prevention, and high-risk prevention of pregnant women. The pregnancy care component contained questions asking cadres' perceptions about the number of examinations pregnant women had in the first trimester (<20 weeks), recommended and not recommended foods

for pregnant women, and activities that might or might not be carried out by pregnant women. In the LBW prevention component, the questionnaire contained questions asking cadres' perceptions about the efforts that should be taken in preventing LBW including examining toxoplasmosis, recommendations for family planning, monitoring the history of pregnant women, and intake and things or activities recommended for mothers during pregnancy. The component of high risk prevention for pregnant women contained questions about maternal perceptions related to encouragement or advice to have health checked when an abnormality occurred during pregnancy, advice to avoid pregnancy at a young age (less than 20 years) and to deliver at home, monitor maternal pregnant conditions during pregnancy, dan suggestions for joining pregnancy exercises.

Similar to knowledge and attitude variables, the behavioral variable also consisted of three question components, namely pregnancy care, LBW prevention, and high risk prevention for pregnant women. The pregnancy care component contained some questions about actions taken by cadres in providing advice to pregnant women to do consultation regarding pregnancy issues, helping organize classes of pregnant women, suggesting to do stimulation for the fetus in the womb, and suggesting what to be done during pregnancy, such as suggestions regarding food intake, lifestyle, and body position when resting.

The LBW prevention component contained several questions regarding recommendations for ANC treatment, attending counseling activities on pregnancy health conducted by health workers, and suggesting intake that may be consumed as well as activities that may be done by pregnant women. Meanwhile, the pregnancy risk prevention component contained several questions regarding cadre actions in giving advice to pregnant women to have health checked at least four times during pregnancy, Tetanus Toxoid (TT) immunization, regular exercise, as well as giving advice on intake and activities that should be consumed and carried out by pregnant women.

The results of the analysis of the effect of providing nutrition education regarding ANC care to health cadres can be seen in Table 2.

Table 2: Effect of Nutrition Education on Knowledge, Attitudes, and Behaviors of Health Cadres regarding ANC Care for Pregnant Women

Variable	Mean ± SD		p ^a
	Pre-test	Post-test	
Knowledge	38.74 ± 2,86	41.51 ± 2,05	0.001*
Attitude	38.26 ± 2,65	40,76 ± 1,64	0.001*
Behavior	38.85 ± 9,90	41.35 ± 5,28	0.038*

^aWilcoxon Signed Rank Test, *Intervention significantly influences the three variables (p <0.05)

The results of the analysis showed that nutrition education regarding ANC of pregnant women affected cadres' knowledge, attitudes, and behavior (p <0.05). The increased score of knowledge, attitudes, and behavior was 7.15%, 6.53%, and 6.43%, respectively. Meanwhile, the purpose of the intervention in the form of socialization and practice using “*Bumil-Kit*” media was to make the content of the material taught easy to understand and apply by cadres. This result of this study was in line with the one of a study in Egypt by providing health education for one month to patients with kidney failure and having hemodialysis treatment showed that health education succeeded in increasing knowledge and compliance in relation to fluids and limited sodium consumption.⁷

Other research results in several cities in Europe showed that providing nutrition education can reduce weight loss and improve cognitive function in Alzheimer's patients. The nutrition education conducted in nine sessions and consisted of socialization and practice was given to caregivers of Alzheimer's patients.⁸ However, a study in Iran showed that nutrition education for four weeks to patients with kidney failure with hemodialysis treatment increases the score of knowledge, but do not change the practice of food selection, as other factors may influence behavior; it takes a long time for nutritional education to affect the patient's food selection behavior.⁷

Furthermore, the results of the interview after being educated was that all cadres (100%) had a good understanding of the consumption of milk, Fe tablets, no smoking or exposure to cigarette smoke, and prevention of anemia and hypertension in pregnant women, while only a few cadres (62.5%) knew the definition of ANC. Cadres also had a good perception related to ANC examinations in the first trimester, monitoring case history of the pregnant women, pregnant women should

consume high protein, and assisting pregnant women when experiencing hyperemesis during pregnancy. Meanwhile, the majority (75%) of cadres did not have a good understanding of family planning and childbirth in health facilities. In this study, cadres did not only have knowledge and understanding related to ANC, but also had taken several actions in the context of giving advice to pregnant women regarding balanced nutrition intake, physical activity, and personal hygiene.

Conclusion

Ante natal care (ANC) is one of the strategies or efforts in overcoming maternal mortality that need intense support from related stakeholders one of which is health cadres. For this reason, nutrition education assisting ANC pregnant women using media “*Bumil-Kit*” as a comprehensive tool is very important for cadres, as this education has proven to have a significant effect on knowledge, attitudes, and behavior of the cadres.

Conflict of Interest: The authors hereby declare that they have no conflict of interest within this research.

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References

1. Kementerian Kesehatan RI. Profil Kesehatan Republik Indonesia Tahun 2017. 2018.
2. Simkhada B, Van Teijlingen ER, Porter M, et al. Factors affecting the utilization of antenatal care in developing countries: Systematic review of the literature. *J Adv Nurs* 2008; 61: 244–260.
3. Awusi VO, Anyanwu EB, Okeleke V. Determinants of antenatal care services utilization in Emevor Village, Nigeria. *Benin Journal of Postgraduate Medicine (Supplemental December)*. 1385; 21–26.

4. Soedirham O. Integrated Services Post (Posyandu) as Sociocultural Approach for Primary Health Care Issue. *Kesmas Natl Public Heal J* 2012; 7: 195.
5. Isaura ER, Probosuseno P, Rialihanto MP. Pemanfaatan internet untuk edukasi gizi bagi penyandang diabetes mellitus. *J Gizi Klin Indones* 2013; 10: 71.
6. Rhapsodia NA, Andari S, Sumarmi S. Hubungan Keaktifan Kader dan Partisipasi Ibu pada Kegiatan Posyandu dengan Cakupan ASI Eksklusif di Wilayah Kerja Puskesmas Waru Sidoarjo Relationship between Cadres Activity & Mother's Participation to Posyandu Activity with Exclusive Breastfeeding Cover. *Iagikmi* 2019; 94–99.
7. Sharaf AY. The impact of educational interventions on hemodialysis patients ' adherence to fluid and sodium restrictions . *IOSR J Nurs Heal Sci Ver II* 2016; 5: 50–60.
8. Riviere S, Gillette-Guyonnet S, Voisin T, et al. A nutritional education program could prevent weight loss and slow cognitive decline in Alzheimer's disease. *J Nutr Heal Aging* 2001; 5: 295–299.

The Effectiveness of Progressive Muscle Relaxation with Benson Relaxation on the Sleep Quality in Hemodialysis Patients

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Abstract

Objects: To identify effectiveness of progressive muscle with benson relaxations on the sleep quality in hemodialysis patients.

Method: The study used a quasi-experimental with comparison of pre and post-tests without control groups. The samples were selected by consecutive sampling technique based on criteria inclusion. The sample size was 48 patients. Sleep quality was measured by applying Pittsburgh Sleep Quality Index. Data analysis used Wilcoxon signed rank and Mann-Whitney U test.

Results: the result showed that there was effect of muscle relaxation with benson relaxation on the sleep quality in hemodialysis patients with p-value 0.00 ($p < 0.005$).

Conclusion: The intervention of progressive muscle relaxation and benson relaxation have same effectiveness to improve the sleep quality of the hemodialysis patients with sleep disorders so that nurse should apply this intervention to improve the sleep quality patients with hemodialysis.

Keywords: *Progressive Muscle Relaxation, Benson Relaxation, Sleep Quality, Hemodialysis.*

Introduction

Hemodialysis is one of the method of treatment of end-stage kidney failure that is considered to be able to save lives ⁽¹⁾. This therapy is also a stressor for patients because it requires some lifestyle restrictions and modifications that negatively impact physical and psychological well-being⁽²⁾. Hemodialysis patients are considered to be very vulnerable to psychological problems due to chronic stress associated with client dependence on hemodialysis machines, duration of dialysis therapy, restrictions on physical activity,

changes in body image, sexual dysfunction, as well as fluid and food restrictions ⁽³⁾.

Mollahadi, Tayyebi and Daneshmandi⁽⁴⁾ said psychological problems that often occur in hemodialysis patients, namely anxiety, depression, and stress. This study is in line with research conducted by Wang and Che⁽⁵⁾ stated that hemodialysis is a therapy that can affect a patient's psychological status. Psychological problems are a major factor contributing to sleep disorders in patients undergoing hemodialysis ⁽⁶⁾.

Sleep disturbance is the most frequently reported complication among hemodialysis patients with a prevalence of 80%⁽⁷⁾. Sleep disturbance is an abnormality in the normal sleep-wake cycle, causing distorted and fragmented sleep patterns ⁽⁸⁾.

Sleep disorders during long periods refer to poor sleep quality can result in physical and psychological complications in patients undergoing hemodialysis⁽⁹⁾.

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Physical complications related to sleep disorders such as daytime drowsiness, lack of energy, psychomotor dysfunction, and can lead to decreased patient appearance such as cognitive and memory dysfunction⁽¹⁰⁾. Sleep disorders can also result in impaired immune function, obesity, diabetes, hypertension, stroke and heart disease⁽¹¹⁾.

Non-pharmacological management that can be used to improve the sleep quality of hemodialysis patients is progressive muscle relaxation and benson relaxation. Progressive muscle relaxation is a therapy that aims to provide emotional balance and peace of mind by focusing on muscle activity by identifying tense muscles and then reducing tension by using relaxation techniques to achieve a relaxation response (relax)⁽¹²⁾.

The study by Rambod, Pourali-Mohammadi, Pasyar, Rafii and Sharif stated that Benson’s relaxation has a significant effect on daytime sleep disorders in hemodialysis patients⁽¹³⁾. Supporting related study by Masry, Aldoushy and Abd showed that Benson’s relaxation techniques have a positive effect in reducing postoperative pain and improving sleep quality among adults and elderly patients undergoing joint replacement surgery⁽¹⁴⁾.

Based on the description above, researchers are interested in conducting research on “The Effectiveness of Progressive Muscle Relaxation with Benson Relaxation on the Sleep Quality of Hemodialysis Patients in H. Adam Malik General Hospital Medan”.

Method

This research was a quasi-experimental research with a comparative approach. This research was carried

out in the hemodialysis unit in July-September 2018. Sampling using consecutive sampling. The sample size in this study was determined using the Power Analysis table with power $(1-\beta)=.90$, effect size $(\gamma)=.73$ and $\alpha=.05$. Anticipating the possibility of selected subjects or samples dropping out, it is necessary to increase the number of samples by 10% so that the sample size remains fulfilled so that the sample in each intervention becomes 48 people.

This research used The Pittsburgh Sleep Quality Index (PSQI) instrument. PSQI is the gold standard for the assessment of subjective sleep quality⁽¹⁵⁾. PSQI is a questionnaire that assesses sleep quality during a month interval. This instrument is to identify “good” and “bad” sleep quality by measuring sleep based on 7 sleep components including sleep duration, sleep disturbance, sleep latency, sleep dysfunction during the day, sleep efficiency, sleep quality, and use of sleeping pills. The score on the subjective sleep quality assessment is divided into 4 criteria: very good, good, bad, and very bad. The assessment is done by giving a score of 0-3 with a range of scores of 0 for very good and a score of 3 for very bad. Then the total score for the seventh. This component produces a global score which has a range of scores from 0 to 21. The overall PSQI score which shows ≤ 5 means that the respondent has good sleep quality and if it shows a number > 5 means poor sleep quality⁽¹⁶⁾.

The bivariate analysis used in this study was the Wilcoxon signed ranks test. This test was to see differences in sleep quality before and after relaxation interventions in each intervention group, while the Mann-Withney U test is used to see differences in sleep quality between progressive muscle relaxation groups and Benson relaxation.

Results

Table 1: Frequency distribution of demographic characteristics of hemodialysis patients

Variable	Progressive Muscle Relaxation (n=48)		Benson Relaxation(n=48)	
	f	%	F	%
Age				
18-34 years	18	37.50	14	29.20
35-54 years	23	47.90	32	66.70
≥55 years	7	14.60	2	4.20
Gender				
Male	37	77.10	31	64.60
Female	11	22.90	17	35.40

Variable	Progressive Muscle Relaxation (n=48)		Benson Relaxation(n=48)	
	f	%	F	%
Long of Hemodialysis				
< 1 year	20	41.70	18	37.50
1-2 years	18	37.50	19	39.60
> 2 years	10	20.80	11	22.90
Hemodialysis Session				
Morning	32	66.70	30	62.50
Afternoon	16	33.30	18	37.50

Based on table 1, respondents in both intervention groups were more male, age 35-54 years old, long of hemodialysis is in the range <1 year to 1-2 years and morning hemodialysis session schedule.

Table 2: Mean rank difference in sleep quality of hemodialysis patients before and after progressive muscle relaxation and benson relaxation (n = 48).

Variable	Mean rank		Z	p-value
	Pre-test	Post-test		
Progressive Muscle Relaxation Group				
Sleep quality	21.00	,00	-5.59	,00
Benson Relaxation Group				
Sleep quality	22.50	,00	-5.78	,00

Based on table 2, the results of data processing using the Wilcoxon Signed Rank Test showed that there were differences in the sleep quality of hemodialysis patients before and after the intervention of progressive muscle relaxation and benson relaxation as measured by PSQI.

Table 3: Differences in the quality of sleep of hemodialysis patients after the intervention between progressive muscle relaxation and benson relaxation groups (n = 48)

Variable	Median (Minimum-Maximum)	z	p-value
Progressive Muscle Relaxation Group			
Sleep quality	4.00 (3-14)	-1.85	.06
Benson Relaxation			
Sleep quality	4.00 (2-14)		

Based on table 3. the results of statistical tests using the Mann-Whitney U Test, obtained p=0.06 (p> 0.05), showed that there was no difference in the quality of sleep of hemodialysis patients after the intervention of progressive muscle relaxation and benson relaxation as measured by PSQI.

Discussions

The results of this study indicate that there was a significant difference between sleep quality before and after progressive muscle relaxation interventions (p=0.00). According to Seyedi Chegeni, Gholami, Azargoon, Hossein, Birjandi and Norollahi progressive muscle relaxation can improve sleep quality in

hemodialysis patients, where by contracting and relaxing muscles it can reduce the input and output of motor neurons, i.e. pre-synapse it will reduce proprioceptive reflex control and post-synapse will reduce the control of the ecstropective reflexes⁽¹⁷⁾. Proprioceptive and ecsteroseptive reduction will result in decreased motor evoked potential (MEP) which will further reduce the activity of the skeletal-motor system, autonomic nervous system (sympathetic and parasympathetic) and cortical pathways⁽¹⁸⁾.

Activation of the parasympathetic nervous system, also called trophotropic, will manipulate the hypothalamus by causing a feeling of relaxation and being more physiologically and emotionally comfortable,

and can cause feelings of wanting to rest, and physical repair of the body, whereas a decrease in the cortical and hypothalamus can cause a relaxed sensation and calm psychological⁽¹⁹⁾. This relaxed feeling will be transmitted to the hypothalamus so that the hypothalamus produces Corticotropin Releasing Factor (CRF). CRF will stimulate the pituitary gland so that the production of several hormones will increase, such as β -endorphin, enkephaline and serotonin. Physiologically, the need for sleep will be fulfilled because of the decreased activity of the Reticular Activating System (RAS) and norepinephrine as a result of decreased activity of the brain stem system. The relaxation response will occur because of the activity of the nuclear nucleus parasympathetic autonomic nervous system⁽²⁰⁾.

The results of this study indicate that there was a significant difference between sleep quality before and after the Benson relaxation intervention ($p=0.00$). Improving sleep quality can be done by using Benson relaxation. This technique is a combination of deep breath relaxation by involving the beliefs held, where by saying a word or sentence can be the name of God or a series of prayers repeatedly according to each religious beliefs accompanied by an attitude of resignation can produce an optimal relaxation response that is the condition of relaxation is not only physical but also mind. This relaxation response is needed to enter the alpha wave, which is a condition that someone needs to enter the initial sleep phase. The basis of this theory is that in the human nervous system there is a central and autonomic nervous system⁽¹³⁾. The function of the central nervous system is to control the desired movements, while the autonomic nervous system has two opposing functions, namely the sympathetic nerve function which stimulates the work of organs and the parasympathetic nervous system which dampens the work of organs. When humans are in tension or stress, the sympathetic nerves are stimulated so that the workings of the body's organs will increase, whereas when humans do Benson relaxation will produce a relaxation response, where the resulting relaxation response will cut off the activation pathway of the sympathetic nervous system and replace it by activating the parasympathetic nerve response resulting in a decrease in the workings of body organs. This condition will accelerate someone entering the alpha wave which is a condition needed by someone to enter the early sleep phase⁽²¹⁾. Physiologically when humans enter the relaxation phase, then they enter the alpha wave (7-14 Hz). When the brain enters this wave,

the brain will produce endorphin hormones which produce a sense of comfort and calm⁽²²⁾.

Mann-Whitney test results, obtained $p=0.06$ ($p>0.05$), so it can be concluded that there is no difference in sleep quality between the progressive muscle relaxation and Benson relaxation groups. This can be understood because based on the theory of both progressive muscle relaxation and Benson relaxation can produce trophotropic relaxation responses, where the resulting relaxation response will cut off the activation pathway of the sympathetic nervous system and replace it by activating the parasympathetic nerve response. Activation of the parasympathetic nervous system will manipulate the hypothalamus by causing feelings of wanting to rest and physical repair of the body⁽¹⁹⁾.

Conclusion

Based on the results of this study, it can be concluded that progressive muscle relaxation exercises and Benson relaxation performed twice a day for 4 weeks have the same effectiveness in improving the sleep quality of hemodialysis patients. Progressive muscle relaxation and Benson relaxation can be complementary therapies in hemodialysis patients who experience sleep disturbance problems.

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References

1. Shariati A. Crvhoef. 2019; (January 2012).
2. F. K, M.A.H. Z, M. S. The effect of Benson's relaxation method on hemodialysis patients' anxiety. Biomed Res [Internet]. 2017;28(3):1075–80. Available from: <http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L614479670%0Ahttp://iacs.c17.net/openurl?sid=EMBASE&issn=0970938X&id=doi:&atitle=The+effect+of+Benson's+relaxation+method+on+hemodialysis+patients'+anxiety&stitle=Biomed.+Res.&title=>
3. Gerogianni SK, Babatsikou FP. Psychological aspects in chronic renal failure. Heal Sci J. 2014;8(2):205–14.

4. Mollahadi M, Tayyebi A, Ebadi A, Daneshmandi M. Comparison of anxiety, depression and stress among hemodialysis and kidney transplantation patients. *Iran J Crit Care Nurs Winter*. 2010;2(4):153–6.
5. Wang L-J, Che C-K. The Psychological Impact of Hemodialysis on Patients with Chronic Renal Failure. *Ren Fail - Facts*. 2012;
6. Roumelioti ME, Argyropoulos C, Pankratz VS, Jhamb M, Bender FH, Buysse DJ, et al. Objective and subjective sleep disorders in automated peritoneal dialysis. *Can J Kidney Heal Dis [Internet]*. 2016;3(1):1–11. Available from: <http://dx.doi.org/10.1186/s40697-016-0093-x>
7. Sabry AA, Abo-zenah H, Wafa E, Mahmoud K, El-dahshan K. Brief Communication. 2010;21(2):300-5.
8. Novak M, Shapiro CM, Mendelssohn D, Mucsi I. Diagnosis and management of insomnia in dialysis patients. *Semin Dial*. 2006;19(1):25–31.
9. Augner C. Associations of subjective sleep quality with depression score, anxiety, physical symptoms and sleep onset latency in students. *Cent Eur J Public Health [Internet]*. 2011;19(2):115–7. Available from: <https://doi.org/10.21101/cejph.a3647>
10. ElGhoney S. Obstructive sleep apnea: Impact on daytime functioning and quality of life. *Sleep Med*. 2015;16:S213–4.
11. Watson NF, Badr MS, Belen G, Bliwise DL. Recommended amount of sleep for a healthy adult. *Am Acad Sleep Med Sleep Res Soc*. 2015;38(6):843–4.
12. Sundram BM, Dahlui M, Chinna K. *Indhealth-54-204*. 2016;204–14.
13. Rambod M, Pournali-Mohammadi N, Pasyar N, Rafii F, Sharif F. The effect of Benson's relaxation technique on the quality of sleep of Iranian hemodialysis patients: A randomized trial. *Complement Ther Med [Internet]*. 2013;21(6):577–84. Available from: <http://dx.doi.org/10.1016/j.ctim.2013.08.009>
14. Masry SE, Aldoushy EE, Abd N. Effect of Benson's Relaxation Technique on Night Pain and Sleep Quality among Adults and Elderly Patients Undergoing Joints Replacement Surgery. *Int J Nurs Didact*. 2017;7(4).
15. Sadeh A. III. Sleep assessment method. *Monogr Soc Res Child Dev*. 2015;80(1):33–48.
16. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res*. 1989;28:193–213. 1989;
17. Seyedi Chegeni P, Gholami M, Azargoon A, Hossein Pour AH, Birjandi M, Norollahi H. The effect of progressive muscle relaxation on the management of fatigue and quality of sleep in patients with chronic obstructive pulmonary disease: A randomized controlled clinical trial. *Complement Ther Clin Pract [Internet]*. 2018;31:64–70. Available from: <https://doi.org/10.1016/j.ctcp.2018.01.010>
18. Guissard N, Duchateau J, Hainaut K. Mechanisms of decreased motoneurone excitation during passive muscle stretching. *Exp Brain Res*. 2001;137(2):163–9.
19. Conrad A, Roth WT. Muscle relaxation therapy for anxiety disorders: It works but how? Vol. 21, *Journal of Anxiety Disorders*. 2007. 243–264 p.
20. Brunelli S, Morone G, Iosa M, Ciotti C, De Giorgi R, Foti C, et al. Efficacy of progressive muscle relaxation, mental imagery, and phantom exercise training on phantom limb: A randomized controlled trial. *Arch Phys Med Rehabil [Internet]*. 2015;96(2):181–7. Available from: <http://dx.doi.org/10.1016/j.apmr.2014.09.035>
21. Purwanto S. Mengatasi insomnia dengan terapi relaksasi. *J Kesehat*. 2008;1:141–8.
22. Hendriyanto B, Sriati A, Fitria N. Pengaruh Hipnoterapi Terhadap Tingkat Stres Mahasiswa Fakultas Ilmu Keperawatan Universitas Padjadjaran Angkatan 2011. *Students e-Journal [Internet]*. 2012;1(1):30. Available from: <http://jurnal.unpad.ac.id/ejournal/article/download/713/759>

Analysis of Factors Relating to Loyalty of Patients in Pertamina Bintang Amin Hospital Lampung in 2019

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Abstract

Background: Presentation of inpatient satisfaction of Pertamina Bintang Amin Hospital only reached 75%. The purpose of this study is to determine the factors associated with inpatient loyalty at Pertamina Bintang Amin Hospital Lampung in 2019.

Method: This is a quantitative study with a cross sectional approach. The population in this study were all patients who used inpatient services in 2019. Sampling using accidental sampling technique with a sample of 196 respondents. Univariate, bivariate, and multivariate data analysis used multiple logistic regression tests.

Results: Factors related to patient loyalty are gender, cost bearer, empathy, reliability, and hospital image with p-value (0.015; 0.000; 0.014; 0.007; 0.000). Factors not related to loyalty are age, job, and income. Reliability is the most dominant factor affecting the patients loyalty with OR 5.732.

Conclusions: Reliability is the most dominant factor influencing patient loyalty. It is recommended to the hospital for training to improve human resources through increasing knowledge, skills and abilities.

Keywords: *Patients loyalty, inpatients, hospital.*

Introduction

Hospitals are the spearhead of public health services. The number of hospitals in Indonesia encourage hospitals to compete to provide the best service in order to get patient loyalty.¹⁻³

In Indonesia, the number of hospitals from 2014-2018 increased by 16.92%. In 2014 the number of hospitals was 2,406, becoming 2,813 in 2018. The existence of hospitals in the city of Bandar Lampung had grown. The number of hospitals in Bandar Lampung City is 17 hospitals.⁴

There are 2 basic approaches to creating patient loyalty, namely the attitudes and behavior of health workers. The loyalty approach based on attitude is empathy. While the loyalty approach based on behavior is reliability. A number of other factors turned out to play a role in customer loyalty issues in addition to service quality factors, namely customer characteristics.⁵⁻⁹

Pertamina Bintang Amin Hospital (PBAH)

Lampung is a hospital that has been Paripurna accredited by the Hospital Accreditation Committee (KARS) in 2012. Based on the data obtained from the PBAH service section, it was found that the presentation of PBAH inpatient satisfaction was assessed to have reached 75% internally. This value is still below the standard inpatient service indicator (90%).

According to the initial survey conducted by researchers, data obtained in 2016 the number of inpatients 36.6% (13,323 patients), fell to 33.6% (12,258 patients) in 2017, and fell again to 29.6% (10,804 patient) in 2018. The data showed that there was still a lack of patient loyalty which is marked by a decrease in the number of inpatient visits for 3 years in a row. This study aimed to determine the factors associated with inpatient loyalty in PBAH Lampung in 2019.

Method

This is a quantitative study with cross-sectional design. The study was conducted at PBAH Lampung October-November 2019. The population in this study

were all inpatients. In this study the number of samples was 196 respondents obtained using lameshow formula. With inclusion criteria namely inpatients, aged ≥ 17 years, patients in a conscious condition and able to communicate well, patients are willing to be interviewed. The exclusion criteria are patients < 17 years, patients or families of patients who work in PBAH Lampung. The sampling technique in this study was accidental sampling. Primary data collection was carried out in the inpatient room using a questionnaire through interviews. Before being distributed, the questionnaire was tried out first in PBAH to respondents who were different from the research respondents. From the test of the validity and reliability of the questionnaire before the study, it was found that the questionnaire was valid and reliable with a significance of 5%, all regression coefficients r counted $> r$ table (0.361) and Cronbach alpha > 0.60 . Secondary data were obtained from literature studies, literature books, and other important documents such as

annual reports, profiles and PBAH Lampung Medical Records. Data analysis used univariate to determine the frequency distribution, bivariate chi-square test and then multivariate test using multiple logistic regression tests. This research was compiled from the Loyal Customer Behavior theory¹⁰; Individual Characteristics¹¹; Customer Satisfaction^{10,11}; Services Quality¹²; Company Images¹³.

Results

The results showed that of the 196 respondents most of them had good loyalty 105 respondents (53.6%). The Bandar Lampung community acknowledges that PBAH has complete facilities and adequate doctors so that many patients return to PBAH. Most respondents were adults (84.2%), didn't work (65.8%), low income (70.4%), had good empathy (93.9%), and had good reliability (93.4%) (Table 1).

Table 1: Patient Characteristics in Inpatient Unit PBAH Lampung in 2019

Variable	Category	Total (n=196)	%
Patients Loyalty	Good	105	53.6
	Not Good	91	46.4
Age	Adult (17-60 tahun)	165	84.2
	Elderly (>60 tahun)	31	15.8
Sex	Male	94	48.0
	Female	102	52.0
Occupation	Working	67	34.2
	Not Working	129	65.8
Income	High (IDR $\geq 2,445,141$)	58	29.6
	Low (IDR $< 2,445,141$)	138	70.4
Cost Bearer	Independent	46	23.5
	Institution (Insurance)	150	76.5
Empathy	Good	184	93.9
	Not Good	12	6.1
Reability	Good	183	93.4
	Not Good	13	6.6
Hospital Images	Good	106	54,1
	Not Good	90	45,9

Relationship age with patient loyalty: The older a person needs their health services will increase.¹⁴ The type of disease can affect patient loyalty because some diseases require health services in the hospital more often than other types of diseases.¹ Chi-square test results showed a p-value 0.696 (> 0.05), it can be concluded that there was no statistically significant relationship

between age and patient loyalty (Table 2). This result is in line with the study of Ulfa (2012) which states there was no significant relationship between age and patient loyalty.¹⁵ In research on the correlation between demographic factors and loyalty, the older a person is significantly more loyal than the younger age.^{11,16,17}

Relationship sex with patient loyalty: Most respondents were female (102.0%). The results of the chi-square test relationship of sex with patient loyalty in the inpatient ward of PBAH obtained p-value 0.015 <0.050, it can be concluded that there was a significant relationship between sex and patient loyalty (Table 2). Sex differences between women and men, for example in differences in needs, desires and expectations. Women’s group usually uses health services or products more than the male group. They also presented a national survey in the United States in 2006 which showed a conclusion that women have an important role as decision makers in health care, not only for themselves but also for their families.¹⁸

Relationship occupation with patient loyalty: The majority of respondents was not working 129 (65.8%). Chi-square test results of the relationship of occupation with patient loyalty obtained p-value 0.230 > 0.05, it can be concluded that occupation has no relationship with patient loyalty. Occupation also affects consumption patterns, someone who had a certain job would buy the needs that were in accordance with his job. In this case if the majority of workers who had relatively high risk of health problems, thus affecting the patient’s behavior in repurchasing because of his needs, which ultimately reflects his loyal behavior.¹¹

Relationship income with patient loyalty: Most respondents had low income 138 (70.4%). Consumer perceptions about the economic resources they have affect their willingness to use money .¹⁸ Chi-square test results obtained p-value 0.158 > 0.05 which means there was no significant relationship between income and patient loyalty (Table 2). The results of this study were in line with other studies that show income has no relationship with patient loyalty and there was no difference between the level of patient income to patient loyalty.^{15,19}

Relationship cost bearer with patient loyalty: Most respondents have agency expense insurers 150 (76.5%), where the dominant agency cost bearers with good loyalty are 92 (87%) and the dominant independent cost bearers with poor loyalty 33 (36.3%) (Table 2). Chi-square test results obtained p-value 0.007 <0.05, it can be concluded that there is a significant relationship between the cost insurer and patient loyalty. In addition, from the calculation, an OR 2.75 is obtained, which means that the independent cost insurer has a 2.75 times probability of generating good loyalty compared to the agency cost insurer. The results of this study are in line with previous research which states that cost bearers have a relationship with loyalty.¹⁵

Table 2: Factors Associated with Patient Loyalty in Inpatient Unit PBAH Lampung in 2019

Variable	Loyalty				Total		OR 95% CI	P-Value
	Good		Not Good		N	%		
	n=105	%	n=91	%				
Age								
Adult	87	52.7	78	42.3	165	100	0.80 (0.37-1.75)	0.696
Elderly	18	58.1	13	41.9	31	100		
Sex								
Male	59	62.8	35	37.2	94	100	2.05 (1.15-3.63)	0.015
Female	46	45.1	56	54.9	102	100		
Occupation								
Working	40	59.7	27	40.4	67	100	1.45 (0.80-2.85)	0.230
Not Working	65	50.4	64	49.6	129	100		
Income								
High (>IDR 2,445,141)	36	62.1	22	37.9	58	100	1.63 (0.87-3.06)	0.158
Low (<IDR 2,445,141)	69	50.0	69	50.0	138	100		
Cost Bearer								
Independent	13	28.3	33	71.3	46	100	2.75 (1.34-5.63)	0.007
Institution	92	61.4	58	38.6	150	100		

Variable	Loyalty				Total		OR 95% CI	P-Value
	Good		Not Good		N	%		
	n=105	%	n=91	%				
Empathy								
Good	103	56.0	81	44.0	184	100	6.35 (1.35-29.83)	0.014
Not Good	2	16.7	10	83.3	12	100		
Reliability								
Good	103	56.3	80	43.7	183	100	7.08 (1.52-32.85)	0.007
Not Good	2	15.4	11	84.6	13	100		
Hospital Images								
Good	76	71.7	30	28.3	106	100	5.32 (2.89-9.82)	<0.001
Not Good	29	32.2	61	67.8	90	100		

Relationship empathy with patient loyalty: Most respondents have good empathy 184 (93.9%). Chi-square test obtained p-value 0.014 <0.05, it can be concluded that there was a significant relationship between empathy and patient loyalty (Table 2). In addition, from the calculation, an OR 6.35 is obtained, which means that good empathy has a 6.35-fold chance of generating good loyalty compared to not good empathy. The results of this study were in line with Yasril’s study (2019) which states that there was a relationship between the dimensions of empathy and patient loyalty.²⁰

Empathy is the individual and personal care and attention given by service providers to customers by trying to understand the desires of consumers specifically.¹² Table 2 showed that out of 184 empathy both dominant loyalty was good as many as 103 (56.6%) and from 12 empathy was not good dominant loyalty was not good as many as 10(83.3%).

Relationship reliability with patient loyalty: Most respondents have good reliability 183 (93.4%). Chi-square test results obtained p-value 0.007 <0.05, it can be concluded that there was a significant relationship between the reliability of health personnel with patient loyalty, besides that the calculation obtained OR 7.08 which means that good reliability had a possibility of 7.08 times generate good loyalty compared to less good reliability. Reliability of services means the ability of health workers to provide services in accordance with what was promised accurately and reliably in the form of procedures for receiving patients served quickly,

readiness to serve patients at any time, providing drugs according to the procedure.^{21,22}

Relationship hospital image with patient loyalty: Most respondents have good hospital images 106 (54.1%). Chi-square test results obtained p-value 0,000 <0.05, it can be concluded that there was a significant relationship between the image of the hospital with patient loyalty, in addition to the calculation obtained OR 5.32, which means that a good hospital image has a 5.32 chance times generate good loyalty compared to not a good hospital image. Image is a set of beliefs, ideas, and messages that a person has towards an object. The image of the hospital is closely related to patient loyalty, there are still many people in this study choosing government hospitals as the first choice in the use of health services.^{13,23}

The Most Dominant Factors Associated with Patient Loyalty: Based on the results of multiple logistic regression tests of 5 variables that have the highest OR value is the reliability (OR = 5,732), it can be assumed that the reliability is the variable that most influences on patient loyalty. Based on the results of the multivariate analysis as a whole, the logistic regression equation is obtained in part below:

Patient loyalty = -6,787+(1,300*handling costs)+(1,746*reliability)+(1,687*hospital image). With the equation model above, it can be estimated the possibility of patient loyalty. The equation shows that with a constant - 6,787 the possibility of patient loyalty will turn out to be good at 1,746 if reliability is good.

Table 3. The Most Dominant Factor in Patient Loyalty

Variable	B	SE	P Wald	P-Value	OR	95% CI
Cost Bearer	1.300	0.421	9.521	0.002	3.670	1.607-8.381
Reliability	1.746	0.815	4.588	0.032	5.732	1.160-28.329
Hospital Images	1.687	0.331	26.013	0.000	5.405	2.826-10.337
Constant	-6.787	1.337	25.783	0.000	0.001	-

The results of the analysis showed that the determinant coefficient (R²) showed a value of 0.284 meaning that the regression model obtained can explain 28.4% of the reliability variable is able to explain the incidence of patient loyalty and the remaining 71.6% is explained by other variables. Reliability is the ability to provide the promised service immediately, accurately and satisfactorily.²⁴ Reliability relates to the ability of hospital medical staff to provide or deliver services as expected.³ The results of this study were in line with the Djohan study's (2015) which states that reliability has a positive and significant influence on the level of patient loyalty.²⁵

Based on the theory and results of the study, researchers argue that when health workers and hospital staff provide timely service time, listen to patient complaints gently, treat patients and families, explain the patient's condition, how to treat, how to take medication, do not differentiate- differentiate services based on social levels, complete facilities and comfortable rooms, these things will foster a high sense of satisfaction, comfort and trust so that good empathy and reliability arises.

Conclusions

Loyalty of patients in the PBAH inpatient unit in 2019 shows good loyalty. Factors that influence patient loyalty to be good were sex, female is a determinant of increased patient loyalty, cost bearer, agency cost bearer is a factor that can affect patient loyalty in the future, empathy is one of the factors that can affect patient loyalty, physician reliability and health workers is very influential on patient loyalty and the image of the hospital can increase patient loyalty, of the five variables, the reliability factor is the most dominant factor on patient loyalty.

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Conflict of Interest: Nil.

Reference

1. Setiawan S. Customer Service Loyalty: A Case Study of How Hospitals Manage Their Customers. First. Bogor: IPB Press, 2011.
2. Pratiwi M. The Effect of Health Service Quality toward Patients' Loyalty in Raden Mattaher Hosiptal Jambi 2016. Scientia Journal 2016;5(1):31-38.
3. Wati L. Relationship between Reliability and Responsiveness with Patient Loyalty in the Inpatient Room. Silampari Nursing Journal 2018, 2(1):252-269.
4. Ministry of Health RI. Indonesian Health Profile 2018. Jakarta, 2019.
5. Hidayat R. The influence of functional quality, technical quality and image on hospital customer satisfaction. Journal of Economics and Finance 2014;18(2):139-164.
6. Christasani PD. Study of Demographic Factors on National Health Insurance Patient Satisfaction in First Level Health Facilities. Journal of Pharmaceutical Sciences and Community 2016,13(1):28-34.
7. Setianto G. Effect of Physical Evidence and Empathy on Consumer Loyalty Through Consumer Satisfaction, 2017.
8. Chabibah AN. Functional Quality and Patient Satisfaction with Nurses and Dentists in Hospitals. Indonesian Health Administration Journal 2018,6(2):143.
9. Asnawi AA, et al. The influence of hospital image and service quality on patients' satisfaction

- and loyalty', *Management Science Letters* 2019;9(6):911-920.
10. Griffin J. *Customer Loyalty: Grow & Maintain Customer Loyalty*. Jakarta: Erlangga, 2016.
 11. Kotler P & Keller KL. *Marketing Management*. Edition 13. Jakarta: Erlangga, 2009.
 12. Wijono D. 2000. *Quality Management of Health Services: Theory, Strategy and Application*. Volume 2. Surabaya: Airlangga University Press, 2000.
 13. Mardalis A. *Achieve Customer Loyalty*. Vol. 9. Surakarta: Institute for Economic Research and Development Faculty of Economics University of Muhammadiyah Surakarta, 2005.
 14. Trisnantoro L. *Understanding the Use of Economics in Hospital Management*. First. Yogyakarta: Gadjah Mada University Press, 2004.
 15. Ulfa R. *Relationship of Patient Characteristics, Service Quality, and Transfer Barriers with Patient Loyalty in Outpatient Installation at Tugu Ibu Hospital, Depok in 2011*. University of Indonesia, 2012.
 16. Jannah M. *Range of Human Life (Life Span Development) in Islam*. 2017;3(1):97-114.
 17. Mudayana AA, et al. *The Relationship Of Patient Satisfaction With Loyalty Of Outpatients In PKU Muhammadiyah Hospital in DIY*, 2018;1(2):12-17.
 18. Dharmmesta BS. *Marketing Management Analysis of Consumer Behavior*. First. Yogyakarta:BPFE, 2018.
 19. Fitri A & Ainy A. *The Relationship between Service Quality and Patient Loyalty in the Outpatient Installation of Eye Hospital in South Sumatra Province*, 2016;7:22-31.
 20. Yasril T. *The Relationship of Service Quality of the Servqual Dimension with Patient Loyalty in the Arosuka Public Hospital Polyclinic in 2018*, 2019;19(3):694-705.
 21. Tjiptono F. *Marketing Strategy*. Edisi 4. Yogyakarta: CV. ANDI OFFSET, 2019..
 22. Ningrum ES. *Relationship of Service Quality to Loyalty of General Inpatients in Kendari City General Hospital in 2016*. *Scientific Journal of Unsyiah Public Health Students* 2016;1(3):1-7.
 23. Hasan S. *Government Hospital Patient Loyalty: Judging from the Perspective of Service Quality, Image, Value and Satisfaction*. *Indonesian Management Journal* 2019;18(3):184.
 24. Muninjaya AAG. *Quality Management of Health Services*. Jakarta: EGC Medical Book Publisher, 2011.
 25. Djohan A J. *Factors that Influence Satisfaction and Trust in Achieving Loyalty of Inpatients at Private Hospitals in the City of Banjarmasin*. *Journal of Management Applications* 2015;13(2):257-271.

Risk Factors Associated with the Incidence of Cervical Cancer in Dr. H. Abdul Moeloek Hospital Bandar Lampung in 2019

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Abstract

Cervical cancer is the most common cause of death in developing countries. The number of cervical cancers in Lampung was 385 cases in 2016. The prevalence of cancer morbidity in Lampung was 0.7 per 1000 population, many factors that cause cervical cancer were the age of first sexual intercourse, parity, multiple sexual partners, smoking, use of vaginal cleansers, use of hormonal contraception, history of sexually transmitted infections and family history. This is a quantitative study with a case control approach. The study population was all women who had cervical cancer and not cervical cancer, with a sample ratio of 1:2. Study respondents numbered 174, univariate data analysis, bivariate using chi-square and multivariate using multiple logistic regression. The results showed the most dominant factor associated with cervical cancer was a family history of p-value 0.009 OR 3.33 (95% CI 1.41-7.83). It is recommended that health workers can provide information about cervical cancer and prevent it by carrying out HPV immunization and pap smears regularly.

Keywords: Risk factors, cervical cancer, family history.

Introduction

Cervical cancer is one of the leading causes of death in women in developing countries. The main cause of cervical cancer is chronic infection by HPV (Human Papilloma Virus). The International Agency for Research on Cancer (IARC) notes that cervical cancer ranks first with an average incidence of 0.015% and a mortality rate of 7.8% per year of all female cancers in the world.¹ The number of cervical cancer sufferers in Lampung Province was 385 cases in 2015.²

Risk factors for cervical cancer include age > 35 years old, married age < 20 years, having > 1 sexual partner, smoking, low personal hygiene, poverty, giving birth to children at a young age, use of hormonal contraceptives, number of parities > 3 and the presence of materials mutagens were thought to genetically alter cells in uterine tissue such as HPV types 16 and 18.³⁻⁵

Women who had sex for the first time at the age of less than 20 years had a risk 3 times greater than women who had sex once at age more than 20 years.⁶⁻⁸ Sex partner changing habits was an important risk factor.

Women who were married were 2-4 more likely to get cervical cancer than those who were not married.⁹⁻¹¹

Having many children also triggers cervical cancer, when giving birth the fetus will pass through the cervix and cause injury to the cervix. If this happens repeatedly then the cervix will be more susceptible to infection and exposure to cervical cancer.^{12,13} Using long-term birth control pills for more than 5 years can increase cervical cancer exposure by 1.53 times.^{14,15}

Family history such as mother and sister also determine the high potential for cervical cancer. At least the risk increased 2-fold compared with those with no family history.¹⁶ Moreover, washing the vagina with antiseptics that have a high PH can increase the risk of cervical cancer.¹⁷

Method

This is a quantitative study with case-control design by selecting cervical cancer patients as cases and not cervical cancer patients as controls. The approach used is a retrospective approach, this research will be conducted

at Dr. H. Abdul Moelok Hospital in March-April 2019. The study sample consisted of 58 respondents in the case group and 116 respondents in the control group with a comparison between case groups and control groups of 1:2. Sampling for the case is taken by using purposive sampling technique by accidental sampling, data collection by interview in questionnaire format as well as primary and secondary data.

Data processing consists of several processes namely editing, entry, coding, and tabulating. Data were analyzed by finding the Odds Ratio (OR) of each variable for cervical cancer and to see the difference in risk between the exposed and unexposed groups. OR is the ratio between the risk of disease in the exposed group

and the risk of disease in the non-exposed group. If the value of the OR confidence interval includes a value of 1 then it means maybe OR = 1, so it cannot be concluded that the factor under study is a risk factor or protective factor.¹⁸

Results

Abdul Moelok Hospital has the main task of carrying out the preparation and implementation of regional policies in the field of hospital services, the task of deconcentration and assistance tasks given by the government to the governor and other tasks in accordance with the policies set by the governor based on applicable laws and regulations.

Table 1: Characteristics of Respondents at Dr. H. Abdul Moelok Hospital 2019

Characteristics	Group			
	Cases		Control	
	n=58	%	n=116	%
Umur (Years)				
<20	-	0	29	25
≥20	58	100	87	75
Education				
Low (Elementary/Middle)	14	24	30	26
Moderate (High School)	32	55	51	44
College	12	21	35	30
Occupation				
Civil servant	11	19	30	29
Entrepreneur	17	29	51	26
Farmer	10	17	25	22
Labor	20	23	27	23
Marital Status				
Married	38	83	81	70
Widow	20	17	35	30
Number of Children				
<2	31	53	81	70
≥2	27	47	35	30

Majority of respondents were ≥20 years old and in the case group were 58 people (100%). The majority of education in the case group was moderate (high school) as many as 32 people (55%). Occupation for the majority of case groups were 20 workers (34%).

In the marital status of the majority of the case group married 48 people (83%). For the number of children, the majority of case group respondents had <2 children 31 people (53.4%) (Table 1).

Table 2: Association of Risk Factors and Cervical Cancer at Dr. H. Abdul Moeloek Hospital 2019

Variable	Cases		Control		P-Value	OR95% CI
	n=58	%	n=116	%		
First Age Sex						
≥20 years	23	39.7	77	66.4	0.001	3.00 (1.56-5.76)
<20 years	35	60.3	39	33.6		
Parity						
<3	31	53.4	81	69.8	0.050	2.01 (1.05-3.86)
≥3	27	46.6	35	30.2		
Sexual Partner						
1 Partner	39	67.2	99	85.3	0.010	2.83 (1.33-6.01)
>1 Partner	19	32.8	17	14.7		
Smoking						
Yes	12	20.7	33	28.4	0.359	-
No	46	79.3	83	71.6		
Use of Vaginal Cleansers						
No	24	41.4	79	68.1	0.001	3.02 (1.57-5.81)
Yes	34	58.6	37	31.9		
Use of Hormonal Contraception						
No risk	36	62.1	91	78.4	0.035	2.22 (1.11-4.43)
Risky	22	37.9	25	21.6		
STI History						
No	21	36.2	74	63.8	0.001	3.10 (1.11-5.98)
Yes	37	63.8	42	36.2		
Family History						
No	43	74.1	105	90.5	0.009	3.33 (1.41-7.83)
Yes	15	25.9	11	9.5		

Noted: STI: Sexual Transmitted Infections; OR: Odds Ratio; CI: Confidence Interval

Based on table 2 shows that in the case group, the majority of respondents first had sexual intercourse <20 years as many as 35 people (60.3%). In the parity variable the majority of respondents had parity <3 children as many as 31 people (53.4%). In the variable sexual partner change the majority of respondents have the number of sexual partners 1 partner as many as 39 people (67.2%). Mayoritasrespondenmerokoksebanyak 46 orang (79,3%). The majority of respondents used vaginal cleansers as many as 34 people (67.2%). The majority of respondents not using hormonal contraception were at risk as many as 36 people (62.1%). The majority of respondents had a history of STIs of 37 people (63.8%). The majority of respondents did not have a family history of 43 people (74.1%).

Bivariate statistical test results showed a relationship between the age of first sexual intercourse (p=0.001; OR=3.004 95% CI 1.565-5.767), parity (p=0.050; OR=2.016 95% CI 1.052-3.864), alternating sexual partners (p=0.010; OR=2.837 95% CI 1.338-6.018), cleaning use (p=0.001; OR=3.025 95% CI 1.575-5.807), use of hormonal contraception (p=0.035; OR=2.224 95% CI 1.115-4.438), history of STI disease (p=0.001; OR=3.104 95% CI 1.611-5.981), family history (p=0.009; OR=3.330 95% CI 1.416-7.831) for cervical cancer. In addition there is no relationship between smoking and cervical cancer.

Table 3: Prediction Models of Risk Factors Affecting Cervical Cancer Occurrence in Dr. H. Abdul Moeloek Hospital Bandar Lampung in 2019

Variable	Sig	Exp(B)	95% CI for Exp (B)	
			Lower	Upper
First Age Sex	0.011	2.716	1.261	5.853
Parity	0.020	2.540	1.160	5.560
Sexual Partner	0.027	2.540	1.120	6.479
Use of Vaginal Cleansers	0.034	2.348	1.067	5.168
Use of Hormonal Contraception	0.033	2.473	1.075	5.693
STI History	0.033	2.246	1.067	4.728
Family History	0.036	2.842	1.073	7.523

Based on the OR values of the variables in the model it can be seen that, family history (OR = 2,848) is the most dominant variable as a risk factor influencing the incidence of cervical cancer in Dr. H. Abdul Moeloek Hospital Bandar Lampung in 2019, probability/chance of cervical cancer occurrence in women with a family history, age of first sexual intercourse <20 years, multiple sexual partners > 1 sexual partner, parity \geq 3 children, usage Hormonal contraception is risky, using female cleansers, and there is a history of STIs of 0.9720 (97.20%), as much as 3.80% is influenced by factors not examined.

Discussions

Before the age of 20, the female reproductive organs were immature.¹⁹ This will get worse if pregnant women under the age of 20 years have a risk that is twice as big as cervical cancer later in life.²⁰ The results of this study were in line with the results of Rhina's study (2017) which showed that in the case group, the majority of respondents who had first had sexual intercourse <20 years were 36 people (62.1%).²¹ The study conducted by Darmayanti (2015) also got the same results as the researchers did, namely there is a relationship between the first age of sexual intercourse with the incidence of cervical cancer ($p=0.001$).²² According to researchers the age of first sexual intercourse is recommended at age > 20 years because mucosal cells are no longer too vulnerable and sensitive to changes. Judging from the first age of sexual intercourse a woman who is sexually active since a young age will increase the risk of cervical cancer.

Having many children can trigger cervical cancer, because during delivery the fetus will pass through the cervix and will cause trauma to the cervix. if this

happens continuously the cervix will become infected and can cause cancer.¹² The results of this study were also compatible with research conducted by Aziyah (2017). Based on the results of statistical tests after the merger, the p-value of $0.000 < \alpha 0.05$ results shows that there is a relationship between parity status and cervical cancer in Dr. Kariadi Hospital Semarang in 2016.²³

According to researchers, respondents who had parity \geq 3 children were caused by respondents not suitable to use contraception and the lack of knowledge and information to choose suitable contraception, in addition this was worsened by husbands who did not want to participate in using contraception.

Women who frequently change sex partners, especially if the man does not use a condom, the greater the chance of suffering from cervical cancer. The injuries that arise will be a place for developing HPV viruses.⁹ This study is in line with research conducted by Indiani (2010), that the number of sexual partners associated with the incidence of cervical cancer lesions. In the bivariate analysis p value was 0,000 with OR 3,805 (95% CI 1,791-8,084).²⁴

In the opinion of researchers changing sexual partners is very risky to transmit sexual diseases, at the time of the study many women were found to have been married 2-3 times, but they did not know that getting married more than once was included in the category of changing partners.

In addition to active smokers, passive smokers were also at greater risk of cervical cancer attack three times more likely than active smokers.¹⁷ The results of this study were in line with Melva note that the largest proportion of cervical cancer cases from the

Chi-square test value of 0.572 $p > 0.005$ means that there is no significant difference between smoking and cervical cancer. According to researchers at the time of conducting research in addition to the presence of respondents who smoke actively there are respondents who said that many family members who smoke, such as parents, children's husbands and work environment.

Diananda (2007) stated that washing the vagina with antiseptic or deodorant drugs will cause irritation to the cervix that stimulates cancer. The results of this study were in line with the results of Rhina's (2017) study, the most dominant risk factor for cervical cancer incidence is the use of vaginal cleaning OR 8,428 (95% CI 2,991-23,744). The use of antiseptics is a risk for cervical cancer. According to researchers, respondents argued that after using antiseptic soap there was a rough and clean effect, making women continue to use the soap especially during vaginal discharge and after sexual intercourse, in addition many respondents who performed vaginal care in the salon to get a rough and tight effect on the area womanhood. This is not good because it can kill good bacteria that should remain in the vagina to maintain the PH balance and prevent the entry of bad bacteria.

Conclusions

Most age of first sexual intercourse <20 years (60.3%), parity <3 children (53.4%), changing sexual partners > 1 partner (67.2%), smoking (79.3%), using female cleansers (58.6%), using risky hormonal contraception (62.1%), there is a history of STIs (63.8%) and there is a family history (74.1%).

There was a relationship between age at first sexual intercourse (OR = 2.716 (95% CI 1,261-5,853), parity (OR = 2,540 95% CI 1,160-5,560), changing sexual partners (OR = 2,254 95% CI 1,120-6,479), vaginal cleaners (OR = 2,348 95% CI 1,067-5,168), use of hormonal contraception (OR = 2,473 95% CI 1,075-4,728), history of STI disease (OR = 2,246 95% CI 1,067-4,728), family history (OR = 2,842 95% CI 1,073-7,523) with cervical cancer incidence. There is no relationship between smoking and cervical cancer incidence. Family history is the dominant variable on cervical cancer events.

Health workers are expected to improve promotive services by providing information about cervical cancer especially to women who have a family history of cervical cancer, providing HPV immunization and pap

smears to prevent and detect cervical cancer.

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Conflict of Interest: Nil.

References

1. WHO.2010. Cancer Can be Prevented. Amerika Serikat: International Agency for Research on Cancer. Indonesian Cancer Foundation, 2016. Indonesian Cancer Patients Increasingly. Accessed December 20, 2016.
2. District Health Office of Lampung. Health Profile, 2015.
3. Ambarita RH. The relationship of knowledge, attitudes, and means of Pap Smear examination with Pap Smear examination behavior in married women in the Obstetrics and Gynecology Outpatient Polyclinic Dr. H. Abdul Moeloek Hospital Lampung Province, 2012.
4. Kartikawati E. Dangers of Breast Cancer and Cervical Cancer. Bandung: New Book, 2013
5. Jean D et al. Prevalence and risk factors for cervical cancer and pre-cancerous lesions in Rwanda. Pan African Medical Journal, 2015.
6. CaturiniY, R Rosmiati, A Wardiyah. Factors of Cervical Precancerous Lesions in Ryacudu Regional Hospital, Lampung Utara City. Jurnal Dunia Kesmas, 2015.
7. Setiati, E. Beware of 4 Cancerous Malignant Female Killers. Jakarta: PT Revika Aditama, 2009
8. Lasut et al. Characteristics of Cervical Cancer Patients in Dr. Kandou Hospital. Journal E-Clinik, 2015 Vol.3.
9. Diananda R. Know the ins and outs of Cancer. In Cervical Cancer: A Warning For Women. HPV Information Centre. (2017). Ghana Human Papilloma virus and Related Cancers, Fact Sheet. ICO/IARC Information Centre on HPV and Cancer, 2009.
10. Sukaca BE. The Smart Way to Face Cervical Cancer. Yogyakarta: Genius, 2009.

11. Pitriani. Risk Factors for Cervical Cancer Occurrence in Inpatients at Dr. Wahidin Sudirohusodo Hospital Makassar. Thesis. University of Hasanuddin, 2013.
12. Arum S. Stop Cervical Cancer. (Mufid, Ed.) (1st Ed.). Yogyakarta: Notebook, 2017.
13. Sjamsuddin S. Prevention and Early Detection of Cervical Cancer, *Mirror of Medical World* No. 133, p 9. Research and Development Center of PT Kalbe Farma, Jakarta, 2012.
14. Wuri. The Influence of Sociodemographic Factors on the Incidence of Pre-cancerous Lesions with Skining Visual Acetate Inspection (IVA) in Bendo Health Center, Pare District, Kediri Regency. *Jurnal FK UNAND* 2018.
15. Wanda. Factors Related to the Occurrence of Padang Cervical Cancer. *Journal of Health Sciences* 2018.
16. Cancer Study Info Center. Indonesian Cancer Patients Increasingly. Accessed December 20, 2016.
17. Savitri A, Syatriani S. Risk Factors for Cervical Cancer in Government General Hospital Dr. Wahidin Sudirohusodo Makassar, South Sulawesi. *National Journal of Public Health*, 2015;5(6): p.284
18. Akbar H. Introduction to Epidemiology. PT Refika Aditama. Bandung, 2018.
19. Aryawati W. Development of a Planned and Anticipatory Model of High Risk Prevention of Pregnancy and Childbirth. Public Health Science Study Program, Policy Interest and Management of Health Services, 2016.
20. Mega. Factors Related to the Occurrence of Cervical Cancer in Dr. M. Djamil Hospital Padang. *Journal of Health Sciences* 2017
21. Rhina. Effect of Age at First Sexual Relationship, Parity, Sexual Partner Changes, Smoking Against Cervical Cancer Occurrence in Dr. Pirngadi Hospital Medan. *Journal Muara Sains* 2017.
22. Damayanti. HPV Vaccination is a Primary Prevention of Cervical Cancer. *Indonesia Medicine Magazine* 2015.
23. Azyiah. Risk Factors Related to Cervical Cancer Occurrence; Case Study in Dr. Kariadi Hospital Semarang. *Journal of Health Research* 2017.
24. Indiani. Risk Factors for Cervical Cancer Occurrence in Inpatients at Dr. Wahidin Sudirohusodo Hospital Makassar. Tesis. Universitas Hasanuddin, 2010.

Building Healthy Open-minded Measure for the Fourth Stage Students in the Faculties of Physical Education and Sports Sciences in Iraq

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Abstract

The psychology from the sciences which is concerned with the psychological aspects of the individual and has an active role in building the human civilization, positive psychology is a modern branch of psychology that seeks to improve the psychological life through caring to the personal life of the individual. The Open-mindedness is one of the positive psychological concepts that make the student has a happy life, whether academic, social or professional through his mental and physical abilities to achieve success and make him an effective productive member of the society. Hence the importance of the current research in scarcity of scientific studies about the concepts of open-mindedness in Iraq, especially for fourth stage students in the faculties of physical education and sports sciences as well as the importance of university education of students as being one of the most important corners of the educational process, the problem of the research that there is no standardized measurement tool enables researchers to identify the concepts of open-mindedness of the fourth stage students in the faculties of physical education and sports sciences, so the researchers decided to build a measure of open-mindedness for the fourth stage because it is the vanguard of the society youth and elite and basis of the society renaissance.

Keywords: Physical education, open-minded measure.

Research Objective

Building open-mindedness measure of the fourth stage students in the faculties of physical education and sports sciences in Iraq. The students sample of the Faculty of Physical Education and Sports Science, the fourth stage of the year 2018-2019.

Introduction and Importance of the Research

The psychology of the sciences which cares about the psychological aspects of the individual and has an active role in building human civilization, and the positive⁽¹⁾. Psychology is a modern branch of psychology branches, which seeks to improve the psychological life through caring of the individual personal⁽²⁾. It is a science interested of study and analysis the self-experiences such as open-mindedness and the psychological life and satisfaction of the past, flow and happiness in the present, hope and optimism for the future, At the individual level⁽³⁾. It is concerned with studying and analyzing the positive features such as the ability to work, social relations with others, open mindedness and

looking forward to the future. At the community level, it revolves around the virtues that move the individual towards good citizenship, responsibility, dealing with others and caring them.

Research Problem: The social, economic and political changes witnessed of the present era and which have a change in some human values, and carried many psychological difficulties and stresses of different life, including pressures during the university study that led to a lot of unhappiness and negatively affected on the level of students' academic, athletic and professional ambition and appreciation Self, open-mindedness is a positive psychological characteristics that must students have to qualify them to perform their role in the future and accept the variables with innovative and creative abilities.

The Research Objectives: Building a measure of open mindedness for students of the fourth stage in the faculties of physical education and sports science in Iraq.

Research Fields Human field: Includes the

students of the fourth stage in the faculties of physical education and sports sciences for the preliminary study only morning, for the academic year 2018 - 2019.

The Time field: from 10/11/2018 to 7/2/2019

Spatial Field: Classrooms and playgrounds in the Faculties of Physical Education and Sports Science in Iraq.

Open-mindedness: It is a pattern of thinking characterized by a flexible, growing, developing and accepting change, where the individual interested in knowing the other ideas and thoughts and accept it, and has the ability to change his thoughts if proven that it is wrong⁽⁴⁾.

The procedural definition of the open mindedness concept: the degree that the students obtained of the fourth stage in the faculties of physical education and sports science through their responses to the open mindedness measure ⁽⁵⁾.

Research Methodology: One of the most important steps that will lead to the success of the research. It is to choose the appropriate approach for researching the problem and achieve the object, therefore the researchers used the descriptive approach in the survey method because it is more appropriate to the nature of the research problem and its objectives in building a measure of open mindedness, as descriptive research “aims to determine the nature and the characteristics of some phenomena to identify or depict the current situation and analyze it to try to draw conclusions and make predictions or projections on the evolution of these phenomena(1).

Research population and sample: The current research population is determined by the students of the faculties of education, physical and sports sciences/the fourth stage in the Iraqi universities for the morning study only and the academic year (2018-2019) the number of (1591) student distributed to (14) faculties, Kirkuk University excluded because most of its students do not speak the correct Arabic language and the researchers were unable to translate a measure with Arabic and to preserve the true meaning of the measure. The sample of building and technique was selected randomly for the measure of open mindedness, the sample of building (statistical analysis sample) reached (400) students from the total population with 25.14%.

Research tools: The researchers used in collecting research data of the following means:

3-3-1 Means of data collection

Note

Personal interviews

Questionnaire

Previous psychological measures

3-3-2 Means of information collection

- Scientific sources and references
- Previous studies and research
- Internet

3-3-3 Means of Data Analysis

- Calculator manual (1) made in china.
- Statistical means
- (laptop) brand: TOSHIBA

3-3-4 Assistant means:

- Assistant Working Group (*).
- Pens.
- HUAWEI mobile phone for Photography and timing.

Field research procedures:

Research tools: The researchers used in the current research pen mindedness measure that was built, the researchers care of the scientific measurement conditions such as honesty, consistency and the distinguish ability, and the following steps taken by the researchers

Steps of Building the open mindedness Measure:

To achieve the goal of the research, which is to build a measure of openmindedness, the researchers will follow the steps of⁽⁷⁾ who determines he aim of the measure is building open mindedness measure, as the researchers did not find a local measure to measure the open mindedness of the fourth stage students in the faculties of physical education and sports sciences (as far as the researchers know) suits with the nature and objectives of the current research, and its sample to make the measure accessible to specialists and researchers of⁽⁸⁾determines the phenomenon to be measured for the measure.

After determining the objective of the measure, determine some basic considerations and theoretical

premises for building the measure before starting of preparation because it is important step and necessary to forms the basis which the measure depend on and derived its scientific components are summarized as follows.

- (1) Determine the theoretical concept of the measure through informing the researchers on the literature, studies and theoretical frameworks that interested of this concept, and the researchers adopted ⁽⁹⁾ theory (2) in the formulation of paragraphs open minded measure.
- (2) Adopt the method of self - report in answering the paragraphs of the measure as the student's emotional experience is able to express what it feels, as evidenced by the verbal behavior of the respondent about his psychological state (3), especially the current measure is relevant to that situation.

1. Determine the measure Fields (open mindedness): Open mindedness measure does not determine any field, and the researchers developed a procedural definition

2. Develop the initial formula of (open mindedness measure)

To develop the initial formula of measure, the researchers conducted several steps:

- 4. Preparation of measure Paragraphs:** To prepare a special paragraph of the measure of open mindedness of students, the researchers followed two ways:
 - Review the theoretical framework and previous studies
 - Questionnaire exploratory
5. Determine the method and bases of formulating the measure paragraphs

After the researchers used the two method described to collect and prepare measure paragraphs, and obtained (53) paragraph,

Determine the validity of paragraphs and alternatives for answering the measure: After the collection and preparation of paragraphs in its initial formula of the measure and the identification of answering alternatives which contained (53) paragraph for the measure of open mindedness, the researchers presented the measure of the initial formula Annex (9), the experts and specialists in sports psychology, educational psychology, testing and measurement

annex (4), to judge on its validity, as well as making adjustments, calendars, rephrasing, merging, deleting and adding on the paragraphs

Main Experiment of measure (open mindedness)

(Statistical Analysis Sample): The main experiment through the application of the measure in its initial formula on the building sample of (400) students of the fourth stage students in the faculties of physical education and sports sciences to analyze their paragraphs statistically and choose the valid ones and exclude invalid ones based on the discriminatory strength and internal consistency as well as to extract the indicators of honesty and stability of the measure, which referred on Annex (11), on 18/10/2018 to 20/11/2018, and the measurement forms were distributed collectively and individually on students by the researchers and the assistant team.

Measure Correction: After collecting the answer forms of the sample, the total grades were extracted to them using the five-point correction key prepared for this purpose. In order to extract the total score of the measure, the grades obtained by each student in the answer on the measure paragraphs reached (30) paragraph as well as the highest score is (150) for being the highest score of the paragraph is (5 degrees and the lowest score is (30 degrees for being the lowest score for paragraph (1) degree, and the total grades of students ranged from (70-150) degree with an arithmetic mean of (33105)degree and standard deviation (6112) and the hypothetical mean of the measure in its initial formula reached (90), and (15) form was excluded for not fulfilling the general conditions, because some testers did not answer all the paragraphs, and some of them were answered some paragraphs, through this procedure the number of forms returned became (385) form, and also excluded some forms for not achieving the objective of the required answering.

Validity of the measure: Honesty is defined as “the degree which measured the test or measure something to be measured” ^[1], the concept of honesty is very important in the tests field and measurement as it is an indicator of whether the test measures the feature or phenomenon to be measured or not. The test is honest if it succeeds in measuring the achievement of the goals which set, In order to verify the validity of the measure; the researchers depend on the following:

First-the validity of the arbitrators (virtual honesty) of the measure: The researchers presented

the measure and its paragraphs on an experts group in sports psychology, general psychology, education and measurement to determine its validity to measure the researched problem, and to evaluate the appropriateness of each paragraph, and thus accepted the paragraphs that got the experts approval and deleted the not agreed paragraphs, and thus check of the content validity. And “this honesty is calculated after presenting on a number of specialists and experts in the field which the test is conducted, if the experts recognize that this test measures the behavior which set to measure it, so the researcher can rely on the judgment of experts.

Second, the validity of the building of the measure: Usually the measure is applied on building sample as an experimental sample, in order to try to avoid the difficulties and obstacles encountered the application way during the main test of the research, and “Building validity is one of the most appropriate types to building the measures, because it is based on experimental verification of the matching degree of paragraphs with the property or concept to be measured ^[1].

The researchers have verified the building validity in the measure through the following:

1. Method of the two terminal groups of the measure:

To reveal the discriminatory power of paragraphs of open mindedness, this method is used to identify the ability of paragraphs to distinguish between individuals with higher levels and individuals with lower levels of attribute measured by the paragraph and this is evidence of the building validity (2), as this method is one of the appropriate method to distinguish paragraphs, the researchers arranged the total degrees which obtained by students after the measure correction descending and then select the percentage (27%) for the top group from the total number of forms (380) and (27%) for the lower group to represent the two terminal groups. Accordingly, each group included (103) students.

2. Internal uniform ness coefficient of the measure:

“One of the most common measures of consistency, the idea of this method depends on how the paragraphs are related to each other within the measure and also how each paragraph is related to the measure as a whole. This method shows us how are homogeneous the paragraphs, There may be convergent paragraphs but it measure a different dimensions

In order to achieve this purpose it uses the coefficient of internal consistency, and many studies have used this method because it is characterized by the following:

1. Provides us a homogeneous measure in its paragraphs.
2. The discriminatory power of a paragraph is similar to the discriminatory measure power.
3. Ability to highlight the link of the measure paragraphs.

To find coefficient with the degrees of sample members on each paragraph and their degrees on measure (the degree of the paragraph and the total degree of the measure separately), the researchers used the correlation coefficient (Pearson), and therefore the correlation of the paragraph with the total degree of the measure means that the paragraph measures the same concept that it measures total degree (1).

The value of this indicator was extracted by using the Person correlation coefficient with the degree of each paragraph and the total degrees of the measure for all sample members of (380) students by Statistical Portfolio of Social Science s(SPSS).

- Correlation coefficient (Pearson) with measure paragraphs and the total degree of open mindedness measure

Conclusion

It is concluded that in the study the stability of the test means the test accuracy in the measurement and the consistency of its results when applied several times on the same individuals (2).

In order to verify the stability of the open mindedness measure, the researchers adopted the measure stability on their way:

1. Half reliability
- 2.- Alfa Kronbach coefficient.

First: Half reliability way of the measure:

Second: Alpha-Kronbach coefficient of the measure:

1. The relative importance law
2. Ca 2 Law
3. T test of independent samples
4. The simple coefficient of Pearson

5. The Fakronbach equation
6. Factor analysis
7. Arithmetic mean
8. Standard deviation

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References

- [1. Mohammed Hassan Allawi; Sports Psychology, edition 9, Cairo, Dar al-Maarif, 1994, p. 63
2. Rokeach Some Unsolved issues in Theories of Beliefs Attitudes and Values, University of Nebraskapress, 1980p 50.
3. Essam Abdel Khalek, Mathematical Training (Theory -applications 12(Cairo, The Origin of Knowledge, 2005.
4. Emad Eddin Fattah, Planning and scientific foundations for the construction and preparation of African Games, for his colleagues, 1 Alexandria, 2001.
5. Aravind, Rajasekaran, Advanced technological modality to explore ESL learners' vocabulary knowledge through social strategies, Journal of Advanced Research in Dynamical and Control Systems, 2018, 10, 10, 250-6.
7. Sharma N, Anu K, The occupational stress women teachers towards joint and nuclear society, International Research Journal of Management, IT and Social Sciences, 2014, 1, 1-5.
8. Mohamed Mahmoud Abdel-Dayem, The Impact of a Proposed Program for the Development of Basic Skills for Youngsters in Basketball, International Conference Research,2, Sport Heights, Cairo.
9. Suresh, Suman R, An Analysis of Psychological Aspects in Student-Centered Learning Activities and Different Method, Journal of International Pharmaceutical Research. 2019, 46, 1, 165-172.
10. Risan Khreiba Majid, Applications in Physiological Science and Sports Training, Nun for Preparation and Printing, 1995, Baghdad.
11. Ali Salloum Jawad al-Hakim, Tests, Measurement and Statistics in the field of sports, Al Tif for printing, 2004.

Value of Use Chest Ultrasound in Diagnosis of Pulmonary Embolism

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Abstract

Background: Pulmonary embolism (PE) is a serious cardiovascular disease. Its symptoms are vague and resemble many other diseases. So diagnosis carries a great challenge.

Aim: Aim of this study is to assess value of chest ultrasound in diagnosis of pulmonary embolism using computed tomography pulmonary angiography (CTPA) as a gold standard.

Material and Method: In this study seventy three patients of suspected pulmonary embolism were evaluated in the period between June 2018 to October 2019 at the emergence department of chest, cardiology and internal medicine departments at Minia University Hospital. The patients were included according to inclusion criteria listed later. The patients were evaluated clinically and assess risk factors and probability scores (modified wells criteria). Then, Thoracic Ultrasonography (TUS) was done. Multi-slice computed tomography (MSCT) was the reference gold standard method in this study. MSCT scans were interpreted by a radiologist who was unaware of the TUS results. Predictive value of chest ultrasound in diagnosis of pulmonary embolism was evaluated by measuring sensitivity, specificity, positive predictive value (PPV), and negative predictive values (NPVs) of thoracic ultrasonography.

Results: In this study, sensitivity, specificity, PPV, NPV, and accuracy of chest ultrasound (CUS) for PE diagnosis were 81.25%, 95%, 98.3%, 77.3% and 87% respectively.

Conclusion: TUS is bedside, safe, easily available, noninvasive method for early diagnosis of PE in emergency department and in situations where CTPE couldn't be used.

Keywords: Chest ultrasound, pulmonary embolism, CTPA.

Introduction

Pulmonary embolism considered to be the third most frequent acute cardiovascular event after acute myocardial infarction and stroke. PE may cause about 300 000 deaths per year in the US.⁽¹⁾

Pulmonary embolism (PE) has many risk factors predispose for its development. Major trauma, surgery, lower-limb fractures and joint replacements, and spinal cord injury are strong provoking factors for pulmonary embolism⁽²⁾

The most common sources of PE (up to 85% of cases) include DVT followed by thrombosis of iliac and renal veins, and the inferior vena cava. The upper limbs are not usually identified as a source of major PE. ⁽³⁾

Cancer is a well-recognized predisposing factor for PE. The risk of PE varies with different types of cancer; pancreatic cancer, hematological malignancies, lung

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cancer, gastric cancer, and brain cancer carry the highest risk. Moreover, cancer is a strong risk factor for all-cause mortality following an episode of VTE.⁽⁴⁾

Also, Pregnancy, peripartum, estrogen containing oral contraceptives and cesarean section all are predisposing factors for development of PE.⁽⁵⁾

The use of transthoracic ultrasound (TUS) as a diagnostic tool was previously considered unjustifiable on the grounds of conventional knowledge that the lungs are filled with air and that the TUS beam cannot normally pass through air-filled structures⁽⁶⁾.

TUS has become now an important diagnostic tool in modern chest medicine as it is a noninvasive, readily available, bedside imaging modality that can be used in association with physical examination and clinical evaluation⁽⁷⁾.

So, this study tried to clarify role of chest ultrasound in diagnosis of pulmonary embolism and assess its accuracy, sensitivity, specificity and also its positive & negative predictive values.

Material and Method

This prospective, randomized clinical study was carried out after obtaining the local ethics committee of El-Minia university hospital approval and written informed consent was taken from the patients.

It had been done from June 2018 to October 2019 at the emergence department of chest, cardiology and internal medicine departments at Minia University Hospital. In this study 73 patients aged between 21-90 years old were clinically suspected pulmonary embolism and enrolled in research according to inclusion and exclusion criteria.

Inclusion criteria:

- a. The main inclusion criteria will be clinical suspicion of PE under consideration of the presence of:
 1. Any age group and both sex
 2. Risk factors of pulmonary embolism as malignancy, lower extremity fracture, COPD, obesity, postpartum period, and history of venous thromboembolism, operation, and PE.
 3. The presence of unexplained dyspnea, tachypnea, pleuritic pain.

Exclusion criteria:

- (i) Other acute ischemic diseases newly diagnosed during the ED visit in question, as acute coronary syndrome, acute ischemic cerebrovascular disease, acute peripheral arterial occlusion, or acute mesenteric ischemia.
- (ii) An abnormal serum albumin level making the determination of IMA levels impossible (normal level 3,5–5,5 mg/dl);
- (iii) Advanced liver, kidney or heart failure;
- (iv) Troponin-I and ECG testing was performed for evidence of asymptomatic coronary ischemia;
- (v) Allergy to contrast material and
- (vi) Refusal to participate in the study.

Included patients will be subjected to:

1. Complete history taking
2. Clinical examination
3. Pretest clinical probability and simplified Wells score.
4. CXR.
5. Compression ultrasound (CUS) of both lower limb if needed.
6. Trans-thoracic ultrasonography (TUS)

There are number of criteria which can be applied in the diagnosis of PE. The most characteristic finding in PE is hypoechoic, pleural-based paranchymal alteration. Greater than 85% of these lesions are wedge-shaped. They may also have rounded or polygonal configuration. A single hyperechoic structure localized at the center of the lesion which indicates the presence of air-filled bronchiole may be detected in 20% of the patients. Pleural involvement in PE initially leads to localized fluid collection adjacent to the affected pulmonary region and may eventually develop into a basal pleura effusion. Exploration of lesions by color Doppler imaging may provide additional diagnostic information. In pulmonary infarction, pulmonary arterial flow cannot be detected by color Doppler ultrasound, referred to as “consolidation with little perfusion”. A congested thromboembolic vessel may be visible called “vascular sign”. These described TUS findings support the diagnosis of PE, but in the absence of them PE cannot be ruled out⁽⁸⁾.

7. Electrocardiography (ECG)

- 8. Echocardiography
 - Ischemia Modified Albumin (IMA)
- 9. Laboratory and Serological tests including:
 - CBP, ABGs
 - D-dimer
- 10. **Multislice Computed Tomography Pulmonary Angiography (CTPA)** was used as the reference method in diagnosis of PE.

Results

Table (1): Findings of Computed Tomography with Pulmonary Angiography in patients positive for pulmonary embolism

		N	(%)
CTPA thrombus location	Bilateral	27	(50.9%)
	Rt.	18	(34%)
	Lt.	8	(15.1%)
CTPA site of affected artery	Main pul. Art.	8	(17%)
	Lobar branch	6	(12.8%)
	Segmental	12	(25.5%)
	Subsegmental	20	(42.6%)
	All	1	(2.1%)

Table 1 showed location of thrombus in CTPA in PE positive patients. There were 27(50.9%) patients had bilateral PE and 26 patients with unilateral PE (18 patients “34%” at Right side and 8 patients “15.1%” at Left side. Also, the level of the occluded artery was

mainly at subsegmental branches (42.6%) followed by segmental branches (25.5%) then lobar branches (12.8%), main pulmonary artery in (17%) and only one patients had occlusion at all levels (2.1%).

Table (2): Comparison of the lesions detected by chest ultrasonography in both PE positive and PE negative groups

TUS		All cases	-Ve	+Ve	P value
		N=73	N=20	N=53	
Number of lesions	Range	(0-2)	(0-1)	(0-2)	
	Mean ± SD	0.8±0.7	0.1±0.2	1.1±0.5	
	Median	1	0	1	
Shape	Normal	8(11%)	4(20%)	4(7.5%)	<0.001*
	Wedge shape	18(24.7%)	0(0%)	18(34%)	
	wedge with pleural effusion	19(26%)	0(0%)	19(35.8%)	
	Rounded or oval shaped lesion	6(8.2%)	0(0%)	6(11.3%)	
	Polygonal shaped lesion	6(8.2%)	1(5%)	5(9.4%)	
	Compressive atelectasis	0(0%)	0(0%)	0(0%)	
	Consolidation	15(20.5%)	14(70%)	1(1.9%)	
Multiple B lines “suggestive pulmonary edema”	1(1.4%)	1(5%)	0(0%)		
Site	No	8(11%)	4(20%)	4(7.5%)	0.489
	Bilateral	11(15.1%)	3(15%)	8(15.1%)	
	Rt.	32(43.8%)	7(35%)	25(47.2%)	
	Lt.	22(30.1%)	6(30%)	16(30.2%)	

TUS		All cases	-Ve	+Ve	P value
		N=73	N=20	N=53	
Location	No	8(11%)	4(20%)	4(7.5%)	0.229
	Upper lobe	4(5.5%)	2(10%)	2(3.8%)	
	Middle lobe	8(11%)	1(5%)	7(13.2%)	
	Lower lobe	53(72.6%)	13(65%)	40(75.5%)	
Effusion loculation	No	43(58.9%)	12(60%)	31(58.5%)	0.907
	Free	30(41.1%)	8(40%)	22(41.5%)	
	Loculated	0(0%)	0(0%)	0(0%)	
Thinned or fragmented visceral pleural line		35(47.9%)	0(0%)	35(66%)	<0.001*

Table 2 describe characters of the lesions detected by chest ultrasound in both groups as regard number of lesions in PE positive group ranged from (0-2) lesion/patient with Mean ± SD 1.1±0.5.

Wedge shape lesion was significantly common in PE +VE group either alone(34%) or with effusion(35.8%)

followed by rounded shape (11.3%) and polygonal shape (9.4%).also table demonstrate distribution of lesions, affected lobes, condition of visceral pleural line that showed significant thinning and fragmentations among PE +VE patients.

Table (3): Demonstrate pattern of vascular flow signals and qualitative and quantitative colour Doppler ultrasound in all patients

		All cases	-Ve	+Ve	P value
		N=73	N=20	N=53	
Qualitative CDU					
Normal perfusion	N (%)	23(31.5%)	18(90%)	5(9.4%)	<0.001*
Decrease perfusion		4(5.5%)	0(0%)	4(7.5%)	
No vascularity		46(63%)	2(10%)	44(83%)	
Pattern of flow					
No perfusion	N (%)	46(63%)	2(10%)	44(83%)	<0.001*
Monophasic		4(5.5%)	0(0%)	4(7.5%)	
Triphasic		23(31.5%)	18(90%)	5(9.4%)	
Quantitative CDU					
RI	Range	(0-2.7)	(0-2.7)	(0-1)	<0.001*
	Mean ± SD	0.4±0.5	0.9±0.6	0.2±0.3	
	Median	0	0.9	0	
PI	Range	(0-19.5)	(0-13.2)	(0-19.5)	<0.001*
	Mean ± SD	2.5±4.2	5.5±4.2	1.4±3.7	
	Median	0	4.5	0	
PSV	Range	(0-81.5)	(0-81.5)	(0-49.5)	<0.001*
	Mean ± SD	10.5±18	27.9±20.6	3.9±11.5	
	Median	0	22.7	0	
EDV	Range	(0-19)	(0-19)	(0-11)	<0.001*
	Mean ± SD	1.6±3.9	4.5±5.8	0.5±2	
	Median	0	1.1	0	

Table 3 show the use of color Doppler ultrasound (CDU) in qualitative & quantitative assessment of vascular flow in lesions detected by gray scale ultrasound. It showed significantly absent perfusion in lesions in PE +Ve cases 44(83%) associated with no flow signals. quantitative measurements of Resistive Index (RI), Pulsatile Index (PI), Peak Systolic Velocity (PSV) and End Diastolic Velocity (EDV) showed significant changes in different lesions between two patient groups.

Table (4): Show sensitivity, specificity, positive predictive value, negative predictive value and accuracy of chest ultrasound in diagnosis of pulmonary embolism:

	TUS
AUC	0.831
95% CI	0.743-0.899
P value	<0.001*
Sensitivity	81.25
Specificity	95
PPV	98.3
NPV	77.2
Accuracy	87

Table 4 show sensitivity, specificity, positive predictive value, negative predictive value and accuracy 81.25%,95%,98.3%,77.2% and 87% respectively.

Discussion

Pulmonary embolism (PE) is a major health problem. It may be life-threatening if not early diagnosed and treated⁽⁹⁾.

Clinical picture of pulmonary embolism is vague and nonspecific, so there is a great need for protocol for early diagnosis & management of pulmonary embolism.

CTPA has brought a great improvement in the diagnostic approach to patients with suspected PE, allowing an adequate visualization of the pulmonary arteries and their level of obstruction up to at least the segmental level, and this make it the gold standard in diagnosis of pulmonary embolism⁽¹⁰⁾.

In the current study we assessed role of noninvasive bedside chest ultrasonography in diagnosis of pulmonary embolism.

In the current study the age of patients insignificantly different between PE +Ve & PE +Ve groups. The mean age in PE positive group (**47.1±16.1**) was younger than

negative group (**52.5±16**). These results are in agreement with⁽¹¹⁾ and also in agreement with⁽¹²⁾.

In contrast to **Stein et al.**,⁽¹³⁾ who found that pulmonary embolism is associated with advancing age due to the cumulative effect of risk factors that patients acquire with aging such as immobility, hypertension, obesity, trauma, and surgery.

In this study, we noticed that female patient were more among PE positive group proved by CTPA (60.4%).But it was statistically insignificant finding.

This in disagreement with **Nataliia et al.**,⁽¹⁴⁾ who noted that PE is more common among men than women and explained by the more exposure of men to smoking and trauma .

In this study, dyspnea was the most common symptom (95.9%) that was mainly grade IV (54.2%) followed by chest pain (63%) and lastly Hemoptysis (53.4%).

In this study the location of the lesions were detected mainly in the lowerlobe (40 lesions, 75.5%) followed by the middle lobe (7 lesions, 13.2%) and the upper lobe(2 lesions, 3.8%).

This is in agreement with **Comert SS et al.**,⁽¹⁵⁾

These results can be explained by that the lower lobes are easily viewed by chest ultrasound,while the upper lobes can only be inspected with difficulty because of masking by bones of chest wall.

In this study the majority of lesions were wedge-shaped. This finding was similar to that reported in **Pfeil A et al.**,⁽¹⁶⁾.The anatomy of the lung could explain the finding. Wedge-shaped opacities are representative of pulmonary ischemia which characterized, as areas of lung filled with red blood cells, with or without tissue necrosis.⁽¹⁷⁾

The blood flow and perfusion in pulmonary infarction can be easily demonstrated. Color Doppler ultrasound is the only imaging modality capable of assessing the vessels in peripheral pulmonary lesions.⁽¹⁸⁾

In the present study, the majority of PE positive patients (83%) show a predominantly no vascular flow. On the other hand, we noticed that a monophasic flow was found only in (7.5%) of cases in positive pulmonary embolism.the vascular sign with characteristic

circulation stop was found in any lesion which could be attributed to absence of blood flow in infarct area.

Also, in this study, quantitative CDS values revealed statistically significant differences in RI, PI, PSV and EDV values between PE positive and negative groups as the majority were absent flow.

This in contrast to **Yuan et al.** ⁽¹⁹⁾ and **Mathis et al.** ⁽²⁰⁾ stated that, in very few cases, the investigator was able to visualize, on Color Doppler ultrasound, a circulation stop caused by embolism.

The current study reported the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of chest ultrasound in the diagnosis of PE 81.25%, 95%, 98.3%, 77.2% and 87% respectively.

This is in agreement with **Ghanem, M. K et al.**, ⁽²¹⁾ who reported the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of TUS in clinically suspicious PE cases were presented as 82%, 90%, 94%, 72% and 85% respectively.

Conclusion

Chest ultrasound is noninvasive, safe, inexpensive, available, bedside diagnostic alternative to CTPA at emergency sitting and in critically ill patient or when CTPA is contraindicated.

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Conflicts of Interest: None of the authors have any proprietary interest in this work.

Ethical Clearance: Taken from local research ethical committee of faculty of Medicine, Minia University.

References

1. Keller K, Hobohm L, Ebner M, Kresoja KP, Munzel T, Konstantinides SV, Lankeit M. Trends in thrombolytic treatment and outcomes of acute pulmonary embolism in Germany. *Eur Heart J*; doi: 10.1093/eurheartj/ehz236. Published online ahead of print 18 May 2019.
2. Rogers MA, Levine DA, Blumberg N, Flanders SA, Chopra V, Langa KM. Triggers of hospitalization for venous thromboembolism. *Circulation* 2012;125:2092_2099.
3. J Bělohávek, V dytrych, a linhart. pulmonary embolism, part I. epidemiology, risk factors and risk stratification, pathophysiology, clinical presentation, diagnosis and nonthrombotic pulmonary embolism. *exp clin cardiol* 2013;18(2):129-138.
4. van Vlijmen EF, Wiewel-Verschueren S, Monster TB, Meijer K. Combined oral contraceptives, thrombophilia and the risk of venous thromboembolism: a systematic review and meta-analysis. *J Thromb Haemost* 2016;14:1393_1403.
5. de Bastos M, Stegeman BH, Rosendaal FR, Van Hylckama Vlieg A, Helmerhorst FM, Stijnen T, Dekkers OM. Combined oral contraceptives: venous thrombosis. *Cochrane Database Syst Rev* 2014;3:CD010813.
6. Yu CJ, Yang PC, Chang DB. Evaluation of ultrasound guided biopsies of mediastinal masses. *Chest* 1991; 100:399–405.
7. Volpicelli G, Melniker LA, Cardinale L. Lung ultrasound in diagnosing and monitoring pulmonary interstitial fluid. *Radiol Med* 2013; 118:196–205.
8. Nazerian P, Vanni S, Volpicelli G, et al. Accuracy of point-of-care multiorgan ultrasonography for the diagnosis of pulmonary embolism. *Chest* 2014; 145:950.
9. Konstantinides SV, Torbicki A, Agnelli G, Danchin N, Fitzmaurice D, Galiè N, Gibbs JS, Huisman MV, Humbert M, Kucher N, Lang I, Lankeit M, Lekakis J, Maack C, Mayer E, Meneveau N, Perrier A, Pruszczyk P, Rasmussen LH, Schindler TH, Svitil P, Vonk Noordegraaf A, Zamorano JL, Zompatori M (2014) ESC Guidelines on the diagnosis and management of acute pulmonary embolism: the Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC) Endorsed by the European Respiratory Society (ERS). *Eur Heart J* 35:3033–3073
10. Ghaye B, Szapiro D, Mastora I, Delannoy V, Duhamel A, Remy J, Remy-Jardin M (2001) Peripheral pulmonary arteries: how far in the lung does multidetector spiral CT allow analysis? *Radiology* 219:629–636
11. El-komy, H. M. A. (2018). VALUE OF TRANSTHORACIC ULTRASONOGRAPHY IN DIAGNOSIS OF PULMONARY EMBOLISM. *Zagazig University Medical Journal*, 23(6).
12. Nandita K and Rakesh V: Pulmonary Embolism in

- Medical Patients. *Clin Appl ThrombHemost.* 2008; 14-159.
13. Stein, P. D., Sostman, H. D., Dalen, J. E., Bailey, D. L., Bajc, M., Goldhaber, S. Z., ... & Pistolesi, M. (2011). Controversies in diagnosis of pulmonary embolism. *Clinical and Applied Thrombosis/Hemostasis*, 17(2), 140-149.
 14. Tsybamuk N, Mostovoy Y and Slepchenko N. study of pulmonary embolism prevalence depending on age and sex by autopsy data. *European Respiratory Journal.* 2012; 40:p 3985.
 15. Comert SS, Caglayan B, Akturk U, Fidan A, Kırıl N, Parmaksız E, Salepci B, Kurtulus BA. The role of thoracic ultrasonography in the diagnosis of pulmonary embolism. *Ann Thorac Med.* 2013; 8(2): 99-104.
 16. Pfeil A, Reissig A, Heyne JP, Wolf G, Kaiser WA, Kroegel C, et al. Transthoracic sonography in comparison to multislice computed tomography in detection of peripheral pulmonary embolism. *Lung.* 2010;188:43–50
 17. evdaSenerComert and others, “The Role of Thoracic Ultrasonography in the Diagnosis of Pulmonary Embolism.,” *Ann Thorac Med.* 2013;8:99–104.
 18. Hsu WH, Yu YH, Tu CY, et al. Color Doppler US pulmonary artery vessel signal: a sign for predicting the benign lesions. *Ultrasound Med Biol* 2007;33:379–88.
 19. Yuan A, Yang PC, Chang CB. Pulmonary infarction: use of color doppler sonography for diagnosis and assessment of reperfusion of the lung. *AJR Am J Roentgenol* 1993;160: 419–420.
 20. Mathis G, Blank W, Reissig A, Lechleitner P, Reuss J, Schuler A, Beckh S: Thoracic ultrasound for diagnosing pulmonary embolism. A prospective multicenter study of 352 patients. *Chest* 2005; 128:1531–1538.
 21. Ghanem, M. K., Makhlouf, H. A., Hasan, A. A. A., & Alkarn, A. A. (2018). Acute pulmonary thromboembolism in emergency room: gray-scale versus color doppler ultrasound evaluation. *The clinical respiratory journal*, 12(2), 474-482.

Assessment of the Knowledge Regarding HIV/AIDS among Nursing College Students in University of Basrah

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Abstract

Background: AIDS is a common infectious disease worldwide, so every health staff have to have a knowledge about it, specially nursing staff .

Aim: To evaluate the knowledge of nursing college students about HIV/AIDS.

Method: The study was carried out on 150 nursing students at University of Basrah College of nursing during the 2018-2019. Structured questionnaire was used for data collection, which was consisted of twenty multiple choice questions to assess knowledge of students about HIV. Data was analyzed by using SPSS statistics version 23.

Results: The current results reveal that (76%) of nursing students have poor knowledge toward HIV/AIDS, and there was a nonstatistically significant difference between the stages.

Conclusion: The study concluded that nursing students need to increase their knowledge regarding HIV/AIDS by for example developing the curriculum of nursing college.

Keywords: Assessment, nursing, knowledge, HIV/AIDS.

Introduction

World Health Organization (WHO) estimated that 75 million people have been infected with HIV while about 32 million people have died of it. Globally, 37.9 million people were living with HIV at the end of 2018¹.

In Iraq about 0.1% of the total population are living with HIV comparing to other parts of the world, it is considered low-prevalence HIV epidemic^{2,3}.

Nurses play an important role in prevention of HIV by providing care and treatment for people living with HIV/AIDS. Therefore, nurses should be competent in caring and solving health problems of them⁴.

Nurses have to deal with collecting various body fluid samples of patient for investigation, giving medication as per instructions, taking care of patients, and giving injections⁵.

Nurses and nursing students' attitude toward HIV/AIDS patient is determined by their knowledge of the same. It is important to assess the knowledge of nurses regarding the HIV/AIDS to evaluate the prevailing conditions and gap so that policy measures can be taken to improve the knowledge, if there is a gap. Since health care professionals including nurses have the responsibility of educating people about the ways of HIV contamination, their knowledge regarding HIV/AIDS patients play an important role in communicating with patients⁶.

The purpose of this study is to assess the knowledge of nursing students regarding HIV/AIDS.

Amongst the health care professionals, nurses and nursing students are an important component of the

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health care delivery system. Since they are the one who are responsible for the constant care of in-patients and thus, they come in close contact with blood and other body fluids of patients. Due to frequent and prolonged contact, they are being identified as a potential risk group for the HIV/AIDS spread. To reduce the transmission, adequate knowledge about the disease and practice of safety measures are of great importance. Generating awareness regarding HIV/AIDS in this group is crucial for AIDS management and the prevention of HIV spread⁷.

Methodology

Design of study: Descriptive cross-sectional study carried out to evaluate knowledge of students about HIV.

Setting of study: The study was conducted at university of Basrah college of nursing 2018-2019

Sample of study: Sample [150] from first, second, third and fourth stage of the college of nursing. Number of male [59] and female [91].

Study instruments: structured questionnaire was used for data collection, consisted of two part:

Part one: Included demographic data [age, sex, type of study (morning or evening), residency (rural or urban), marital status, stage, to identify effect of demographic variables on students' knowledge.

Part two: Questionnaire was consisted of twenty multiple choice questions to evaluate knowledge of

students about HIV. Right answer given 5 score and false answer given zero score. Data was analyzed by using SPSS statistics version 23.

Results

Table 1: Demographic characteristics of the study sample

Variables		Frequency	%
Sex	Male	59	39.3%
	Female	91	60.7%
Stage	First Stage	40	26.7%
	Second Stage	33	22%
	Third Stage	38	25.3%
	Fourth Stage	39	26%
Marital status	Single	140	93.3%
	Married	10	6.7%
Study type	Morning Study	91	60.7%
	Evening Study	59	39.3%
Residency	Urban	70	46.7%
	Rural	80	53.3%

The table (1) showed that the number of females were more than males (60.7%, 39.3% respectively). Majority of the samples was single (93.3%). Students from morning study were relatively more than students from evening study (60.7%, 39.3% respectively), rural and urban areas had a slight difference in number of students (53.3%, 46.7%). Only (24%) of students had good knowledge regarding AIDS (table 2).

Table (2): Students' knowledge regarding AIDS

Variable	F	%	Mean of score	Std. Deviation	p-value	Result
Good knowledge	36	24%	37.64	10.035	0.000	significant
Poor knowledge	114	76%	60.92	8.611		
Total sample = 150		Mean of score = 55.33		Std. Deviation = 13.395		

Table (3): Relation between variables and students' knowledge regarding AIDS

Variables		Mean of score	Std. Deviation	p-value	Result
Sex	Male	55.93	13.566	0.661	Insignificant
	Female	54.95	13.344		
Stage	First Stage	53.88	13.936	0.149	Insignificant
	Second Stage	54.55	13.132		
	Third Stage	59.61	13.968		
	Fourth Stage	53.33	11.994		

Variables		Mean of score	Std. Deviation	p-value	Result
Marital status	Single	55.39	13.345	0.839	Insignificant
	Married	54.50	14.804		
Study type	Morning Study	54.12	13.976	0.169	Insignificant
	Evening Study	57.20	12.327		
occupation	Urban	59.21	10.654	0.001	Significant
	Rural	51.94	14.637		

When comparing the variables under study with knowledge, the result showed that there was no statistical significant difference between sex, stage, marital status and type of study but there was a significant difference between students residency and knowledge (table 3). This difference may reflect the development in urban areas in terms of social and cultural communication, the Internet, the large number of schools, health centers, hospitals, and the multiplicity of occupations and businesses, as opposed to those in rural areas.

Table (4): Source of information regarding AIDS

Source of information	Frequency	Percent
Books and social media	83	55.3%
Schools & colleges	71	47.3%
Friends & family	42	28%
Heath care provider	20	13.3%

Books and social media were the major source of information for students about AIDS(55.3%)which can be used as a way to educate students about various diseases, where health care provider (13.3%) could not be consider as a good source of information for students (table 4).

Table (5): Students' answers regarding HIV

True and False Questions	Right Answer	Wrong answer
AIDS is considered viral diseases	143	7
AIDS Attacks Immune system	142	8
AIDS is transmitted by Sex with the infected person	132	18
HIV infection leads to joint pain	17	133
HIV infection leads to Swelling of the lymph nodes	18	132
HIV infection leads to Diarrhea	29	121

Table (5) showed that Most students knew that HIV/AIDS was viral, attacked the immune system and sexually

transmitted. On another hand most of them did not know the signs and symptoms of the patient, especially: pain joints, swollen lymph nodes, and diarrhea .

Discussion

This study was done to assess the knowledge regarding HIV/AIDS among students of nursing college at Basrah University. In this study, it was found that main source of information among nursing students was Books and social media, followed by Schools and colleges. They got very less information from Heath care provider. This result reflects the weak role of health care centers in educating the community about the seriousness of the disease and its transmission.

Large proportion of students had misconception regarding symptoms and complications of the disease. In Iraq there is a kind of silence on the cases of AIDS for religious and social reasons, because of the disease is association with forbidden sexual relations which makes people believe that there are no cases.

Iraq is considered a country with a low level epidemic of HIV/AIDS. The prevalence of HIV in Iraq is currently less than 0.1% of population, but associated risk factors may increase because of liberalized trade relations and increased drug use. As of December 2014, less than 100 people living with HIV were reported. They were nationals and foreigners. 57% were infected by blood transfusion and blood products (WHO). Iraq faces greater HIV risks as a result of poverty, low literacy and inadequate knowledge of modes of transmission².

Nursing students should have adequate information about the disease because in future they will play important role in educating peoples and saving the life of patients and save themselves from infection.

Low knowledge regarding HIV/AIDS among nursing college students need national awareness programs.

Ethical Clearance: Approval to conduct the study was obtained from the dean of college of Nursing, University of Basrah.

Source of Funding: Self

Conflict of Interest: Nil.

References

1. WHO. Global Health Observatory (GHO) data, HIV/AIDS. <https://www.who.int/gho/hiv/en>; 2018.
2. During OZS. Evidence Summary of Provision of Oral Zinc Supplementation During Acute Diarrhea For Iraq.
3. Global AIDS progress reporting. 2012.
4. Geethika N. Nanayakkara_1,2, Eun-Ok Choi. Effectiveness of AIDS education program on nursing students' AIDS knowledge and AIDS attitudes in Sri Lanka. *Journal of Nursing Education and Practice*. 2018; 8(6).
5. Taher E, Abdelhai RAA. Nurses' knowledge, perceptions, and attitudes towards HIV/AIDS: effects of a health education intervention on two nursing groups in Cairo University, Egypt. *J PublHealth Epidemiol*. 2011;3(4):144-54.
6. Foisy M., Hughes C. A., Kelly D., Chan S., Dayneka N., Giguère P., Higgins N., Hills-Niemenen C., Kaple J., la Porte C., Nickel P., Park-Wyllie L., Quiaia C., Robinson L., Sheehan N., Stone S., Sulz L., Yoong D. Role of the Pharmacist in Caring for Patients with HIV/AIDS: Clinical Practice Guidelines. *Can J Hosp Pharm*. 2012;65(2): 125-145.
7. Goel N. K., Bansal R., Pathak R., Sharma H.K., Aggarwal M., Luthra S.C. Knowledge and Awareness of Nursing Students about HIV/AIDS. *Health and Population: Perspectives and Issues*. 2010;33 (1): 55-60.

Levels and Differences of Leadership Practices by Eminent Coaches Amongst the Team Athlete's at Universiti Pendidikan Sultan Idris (UPSI)

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Abstract

This research is conducted to identify the level and differences of leadership practices between the popular coaches among team athletes at Universiti Pendidikan Sultan Idris (UPSI). A total of 50 respondents comprising 30 male athletes and 20 female athletes were selected from the team athletes at Universiti Pendidikan Sultan Idris (UPSI). The research instrument used is Leadership Scale for Sports (LSS) Questionnaire which was developed by Chelladurai and Saleh (1978; 1980) and has been translated into Malay language. This questionnaire has 5 dimensions of coaching style, ie a) Training and Instruction Dimension, b) Democratic Dimension, c) Autocratic Dimension, d) Social Support Dimension, e) Positive Feedback Dimension. An independent t-test inferential statistical analysis is used to analyze data. The findings show that there is no significant difference between male team athlete and female team athletes in all the favourite dimensions of coaching style amongst the athlete's team. The findings also showed that the dimension of leadership style using Training and Instruction is the most favourable among the athlete team at Universiti Pendidikan Sultan Idris (UPSI).

Keywords: Leadership style, Trainer's Behavior, Performance, Leadership.

Introduction

Leadership is a complex and dynamic behavioral process among group members, interpersonal communication and moving towards a defined goal^{1,2}. Leadership of coaches are important as it affects the attainment of athletes and the team's performance³. The effectiveness of a coach is influenced by several factors which are adequately important to ensure the athlete is in excellent guidance. Among the most important factors are coach leadership style, coach behavior, athlete character and situation⁴.

According to Chelladurai⁵, the coach's leadership style covers the dimensions of training and instruction,

democratic, positive feedback or rewards, social and autocratic support. The style of coaching is important to form outstanding athletes or team athletes to optimum performance level.

Coaching is classified as a leader who has been given authority and responsibility for forming followers in a team under his guidance in acquiring skills and confidence also competitiveness when competing⁹.

Literature Review: The coach should respect the uniqueness of each different athlete to ensure proper coaching style to improve the athlete's performance. According to Chelladurai and Saleh¹¹, the style of coaching is divided into three components namely the behavior of real leaders, the behavior of leaders chosen by the athlete and the expected behavioural from the leader. All components of this coaching style depend on the suitability of athletes to determine the satisfaction and improvement of the athlete's performance. In line with Ramalu⁷ research finding that coaches that design motivation program into their coaching lesson will enhance their performance in the actual game meet. The

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most important factor for a coach is to help improve the performance of athletes in terms of sports development and the more specialized basic and psychological skills. Chelladurai et al.¹³ states that the coach coaching style of leadership is effective in certain contexts due to changes in athletic characteristics and situations. The context of the sports situation and the behavior of the athlete itself determine the appropriate leadership style to achieve improved performance and control athlete discipline¹⁵.

Problem Statement: The purpose of this study was to provide information to the coaches at UPSI in relation to the leadership of the team athlete. Coaches can also identify the level and style of leadership that is the choice of team athletes. In addition, the difference between gender and leadership style of team athletes at UPSI will be answered through this study.

As the study relates to the style of coach leadership that is still limited and under-reported at UPSI level, the previous study focuses only on school athletes. A study at UPSI should be carried out to identify the coaching leadership that the athlete is interested in.

Research Objectives: Based on the current study, among the objectives of the study to find out different levels of coach leadership practices at UPSI are:

- a) Examining gender differences in leadership style dimensions of team athlete’s at UPSI.
- b) Identifying the level of the leadership style dimension which is the choice of team athletes at UPSI based on the level of leadership style difference.
- c) Identify the effectiveness of leadership-style practices on athlete’s current performance.

Research Findings:

Table 1: Raw Data of The Leadership Style which is favoured by Team Athletes at Sultan Idris Education University (UPSI) By Gender

		Variable Leadership Dimension				
Gender		Training and Instruction	Democratic	Authocratic	Social Support	Positive Feedback
Male	Min	2.58	2.376	2.052	2.388	2.364
	SP	0.368	0.419	0.570	0.507	0.444
	N	30	30	30	30	30
Female	Min	1.72	1.584	1.368	1.592	1.576
	SP	0.246	0.280	0.380	0.338	0.296
	N	20	20	20	20	20
Total	Min	4.3	3.96	3.42	3.98	3.94
	SP	0.614	0.699	0.950	0.845	0.740
	N	50	50	50	50	50

Research Methodology: This chapter contains the procedures and method used to obtain and analyze data and information on the level and differences in the practice of coach leadership amongst athletes in the UPSI. The results of the questionnaire were obtained and identified after the questionnaires were distributed to team athletes at UPSI.

Data Collection/Analysis: The data of this study was analyzed using the Statistical Packages for the Social Sciences (SPSS) version 23.0. The data analysis used in this study was an independent t-test analysis to find the mean, standard deviation and significance to analyze the dimensions and differences of leadership styles diminished by team athletes at UPSI. While the t-test is independent, it is used to examine the differences in the aspects of gender in the dimensions of leadership style of coach that interested by team athletes at UPSI.

Procedure: The design of this study is quantitative and uses the survey method. This survey method is suitable because the questionnaire can be given to the respondents ie team athlete at UPSI.

Study Participants: Participants for this study consist of 50 athletes that selected through a purposive sampling technique at UPSI, 30 are male team athletes and 20 are female team athletes. The selection of participants was chosen based on the participation of participants representing UPSI in team sports such as martial arts, football, netball, volleyball, tennis, badminton, table tennis, hockey, softball and sepak takraw. Selected candidates are from 19 to 25 years old and involved in university team sports.

The findings in demographic aspects are as in Table 1, overall, team athletes at UPSI are more interested in training and instruction dimensions (min = 4.3, SD = 0.614) and the leadership style most disliked by male and female athletes and not suitable for the team athlete leadership dimension is an autocratic dimension (min = 3.42, SD = 0.950).

The objectives of the study in table 1 are to identify the levels and dimensions of leadership style which are the preferences of team athletes at UPSI based on gender differences.

Table 2: Descriptive Analysis Based on Gender Differences and Based on Preferred Leadership Positions In The Dimensional Coaches Leadership Style

Leadership Style Dimension Gender						
	Male (N=30)			Female (N=20)		
	Min	SD	Position	Min	SD	Position
Training and Instruction	2.58	0.368	1	1.72	0.246	1
Social Support	2.388	0.507	2	1.592	0.338	2
Democratic	2.376	0.419	3	1.584	0.280	3
Positive Feedback	2.364	0.444	4	1.576	0.296	4
Autocratic	2.052	0.570	5	1.368	0.380	5

The findings of the descriptive statistics in Table 2 show the t-test on the gender differences in UPSI. The findings show that there is no significant difference between male athlete and female athletes of team athletes in all the preferred dimensions of coaching style amongst the athletes at UPSI. From the finding, that leadership style dimensions of instruction and training

is in the first place of the male and female athletes and the least liked by team athletes for both gender is an autocratic dimension.

The objective of this study is to examine the differences in gender aspects in leadership style dimension of team athlete at UPSI.

Table 3: Raw Data of Preferred Leadership Style by Team Athlete of Universiti Pendidikan Sultan Idris (UPSI) By Age

Age (Year)		Training and Instruction	Democratic	Authocratic	Social Support	Positive Feedback
19	Min	0.258	0.238	0.205	0.239	0.236
	SD	0.037	0.042	0.057	0.051	0.44
	N	3	3	3	3	3
20	Min	0.43	0.396	0.342	0.398	0.394
	SD	0.061	0.07	0.095	0.085	0.074
	N	5	5	5	5	5
21	Min	0.258	0.238	0.205	0.239	0.236
	SD	0.037	0.042	0.057	0.051	0.044
	N	3	3	3	3	3
22	Min	0.774	0.713	0.616	0.716	0.709
	SD	0.111	0.126	0.171	0.152	0.133
	N	15	15	15	15	15
23	Min	1.29	1.188	1.026	1.194	1.182
	SD	0.184	0.21	0.285	0.254	0.222
	N	15	15	15	15	15
24	Min	0.946	0.871	0.752	0.876	0.867

Age (Year)		Training and Instruction	Democratic	Authocratic	Social Support	Positive Feedback
	SD	0.135	0.154	0.209	0.186	0.163
	N	11	11	11	11	11
25	Min	0.344	0.317	0.274	0.318	0.315
	SD	0.049	0.056	0.076	0.068	0.059
	N	4	4	4	4	4
Total	Min	4.3	3.961	3.42	3.98	3.939
	SD	1.277	0.7	0.95	0.847	0.739
	N	50	50	50	50	50

The findings based on descriptive analysis as in Table 3 show leadership styles of team athletes in UPSI according to age and this study is divided into 7 age distribution starting from the age of 19 to 25 who are the team sports athlete. Based on the descriptive analysis the min and standard deviation from all the age distribution shows that autocratic dimension is the least favoured dimension that preferred by athletes at UPSI).

Discussion

Based on the findings of the analysis table 1, the level and the difference in practice of coach leadership amongst the team athletes at UPSI as a whole shows that the percentage and the difference in leadership practices reveal no significant difference in terms of the level and differences in popular leadership practices. Overall, team athletes at UPSI would go for the leadership-style dimension of training and instruction and would not favour the autocratic dimension.

The athlete age factor is very much influential on the results of the analysis that has been conducted as older athletes love the training and instruction dimensions because these dimensions are intended to improve behavior or to develop the right skills by emphasizing on some of the essential and earnest training elements¹⁶. In addition, training and instruction dimension focuses on game techniques and tactics as well as coordinate activities for athletes resulting in instructional and training dimensions that are well-liked amongst the team athletes at UPSI. Furthermore, the autocratic dimension of leadership style is very unpopular with team athletes at the UPSI because of coaching style that does not help to improve performance or conduct of free coaching skills and behaviors and to emphasize personal power without taking care of the athlete's welfare and not giving athlete the opportunity to make a decision and do something to improve their performance or skills¹⁰.

If referring to table 2 the findings show that there is no difference in terms of leadership dimensions of male and female athletes. Men and women's team athletes have similarities in choosing the most disadvantaged dimensions, which is the autocratic dimensions and this dimension should not be applied in the leadership style of team athlete at UPSI. The objective of this study is to examine the differences in gender aspects in leadership style dimension of team athlete at UPSI. Gender factors is seen to have strongly influence the style of coaching but being men and women have no significant difference in aspects of the dimension of the coaching style by interest^{10,16}.

In addition, based on the independent t-test analysis, there was no significant difference between male team athletes and female team athletes in all the favoured dimensions of coaching style the team athletes at UPSI.

The results of the study have shown similarities with the study conducted by Chelladurai et al.¹¹ and Serpa and Antunes¹⁷ who chose the leadership style of training and instruction as the researchers assumed that most of the chosen athlete which have represented state or country that causes athletes to prefer training and instruction dimensions. This is because it facilitates trainer's to train athletes and manage teams under their control besides being able to train effectively to improve performance and correct mistakes made by athletes immediately^{11,17}.

Choosing the right leadership style is crucial in ensuring the effectiveness in controlling and managing the team effectively to give positive impact to athletes and teams. Appropriate leadership style is also important to influence athlete's behavior to ensure athlete's ability to exercise and not to be exercised⁸. It is clear here that the leadership style or coach should choose a leadership style that is compatible with the team or its athlete's guidance to ensure that planned goals are achieved and able to improve athlete's performance.

Conclusion

Based on the studies conducted and certain constraints we can conclude that there is no significant difference between the level and differences in the practice of coaching leadership amongst athletes in the UPSI. This can be demonstrated by the results of the study conducted on the participants who have chosen the training and instruction dimensions as the ultimate choice for the dimensions of the most popular leadership style. The dimension of leadership style of training and instruction is the most appropriate dimension and is most favored by male and female team athletes. This style of leadership is more pragmatic as it helps coaches in facilitating the team or athlete while being able to correct the mistakes of the athletes and at the same time emphasizing the strategy of a game⁷.

Furthermore, there is no coaching style approach that can be determined by the appropriate suitability and effectiveness as each sport has a different coaching style approach. It is clear that the successful coach who practices a well-defined leadership style with the will of the player or team under his guidance^{10,15}. All these aspects can be fulfilled if the coach recognizes the athlete under his control and understands the importance and suitability of the team and athlete. Hence, the success of an athlete and team can be determined if the coach uses an appropriate and effective approach to achieving a defined goal^{6,14,15}.

An effective coach is a coach who understands the wishes of his followers in planning and making good decisions. A good coach will pay attention to what this is and focus on what to share with athletes and teams. The coach who cares and focuses on what he or she wants to achieve will give the athlete a sense of appreciation and this will further bond with the team and the coach^{5,11,12}.

Ethical Clearance: The study has been done in accordance with human research ethics as per required by the declaration of Helsinki¹⁷.

Source of Funding: Self

Conflict of Interest: Nil

References

1. Riemer HA. Multidimensional Model of Coach Leadership. In S. Jowette & D. Lavallee (Eds.), *Social Psychology in Sport*. 2007; 57-73.
2. Yukl G. *Leadership in Organizations* (6th ed.). Upper Saddle River, NJ: Pearson Education. 2006.
3. Patterson MM, Carron AV, & Loughhead TM. The influence of team norms on the cohesion-self-reported performance relationship: A multi-level analysis. *Psychology of sport and exercise*. 2005; Vol 6: 479-493.
4. Shaharudin AA. *Perkaitan di antara orientasi matlamat dan stail kepimpinan dengan pencapaian atlet SUKMA negeri Perak di Kejohanan SUKMA*. 2004; Available from. <http://www.ppp.upsi.edu.my/eWacana/Sukma.html>.
5. Chelladurai P. Leadership in sports. In G. Tenenbaum & R. C. Eklund (Eds.), *Handbook of sport psychology*. Hoboken, NJ, US: John Wiley & Sons Inc. 2007; 113-135.
6. Karim Z B A. *Development Characteristics of Football Coaches in Australia and Malaysia* (Published doctoral thesis). Victoria University of Technology, Melbourne. 2016.
7. Ramalu RR. *Keberkesanan Motivasi Terhadap Pencapaian Prestasi Atlet Sekolah Menengah* (Published Masters Thesis). University of Malaya, Malaysia. 2007.
8. Karim ZA, Nadzalan AM. Malaysia football coaches: Development characteristics. *International Journal of Academic Research in Business and Social Sciences*. 2017; Vol 7(9), 305-312.
9. Yukl G. *Effective Leadership Behaviour: What we know and What Questions need more Attention*. *Academy Management Executive*. 2016; 66-85.
10. Asiah M P, Rosli S. *Coaching Leadership Styles and Athlete Satisfaction Among Hockey Team*. Centre for Languages and Human Development. 2009; Vol 2(1). 76-87.
11. Chelladurai P, Saleh SD. Dimension of leadership behavior in sports Development of a leadership scale. *Journal of Sports Psychology*. 1980; Vol 2, 34-35.
12. Zhang J, Jensen BE, Mann L. Modification and revision of the leadership scale for sport. *Journal of sport behavior*, 1997; Vol 20(1), 105-122.
13. Chelladurai P, Riemer HA. A Classification of Facets of Athlete Satisfaction. *Journal of Management*. 1997; Vol 11(2), 133-159.
14. Mackenzie B. *Coaching. Successful Coaching Issue*. Dimensions of leader behavior in sports: development of a leadership scale. *Journal of sport psychology*, 2003; Vol 2, 34 - 45.

15. Karim ZBA, Razak N. Lesson Learned from Coaches of Malaysia National Football Development Program (NFDP): Preferred Career Development Pathway and Accredited Coaching Course. *International Journal of Academic Research in Business and Social Sciences*, 2018; Vol8(6), 1069–1082.
16. Nazarudin MN, Fauzee MSO, Jamalis M, Geok SK, Din A. Coaching Leadership Style as Athletes Satisfaction among Malaysian University Basketball Team. *Research Journal of International Studies*. 2014; Vol 9, 4-11.
17. Serpa SY Antunes I. Leadership styles in sports. Characterization of the women's volleyball coaches in Portugal. Comunicación presentada en el VI International Congress on Sport Psychology, Lathi. 1989.

Study of Implementation of the Early Breastfeeding Initiation Program at the Lepo-lepo Public Health Center in Kendari City

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Abstract

Early Initiation of Breastfeeding (EIB) apparently decreased infant mortality rate for 8.8% and increased exclusively breastfeeding success for 2 years. Less attention to EIB implementation and less counseling by health professional drove a low implementation of EIB. Objective of this study was to describe EIB implementation at Public Health Center of Lepo-Lepo Kendari in 2014. Type of the study was qualitative through phenomenological approach. Informants of the study were 5 within 1 key informant and the other 4 were common informants. The result of the study showed that midwives' knowledge regarding to EIB was good. Nevertheless, patient's knowledge about EIB was less. Patient didn't get information about EIB, either from birth assistance or socialization media. Attitude and support given by health professional was also less. EIB program was not realized and there was no socialization regarding to EIB given by midwives to the patient. Health resources were consisted of 14 midwives and none of those who ever received EIB training. There were no need special tools and infrastructures in implementing EIB. SOP of EIB announced on poster about it on the wall.

Keywords: *Implementation, Early Initiation of Breastfeeding.*

Introduction

The authorized capital for the formation of quality human resources starts from the baby in the womb and from an early age. One of the things that can be done in optimizing quality human resources is through breastfeeding, especially exclusive breastfeeding, namely breastfeeding for babies from birth to 6 months without other complementary foods¹.

World Health Organization in 2007 issued a new protocol about "*Asi Asap*" which must be known to every health worker. The protocol is to make mother's skin contact with the baby's skin immediately after birth for at least one hour and help the mother recognize when the baby is ready to breastfeed. The statement was confirmed by the government with the issuance of Government Regulation of the Republic of Indonesia Number 33 of 2012 in Chapter III article 7 which states that every mother giving birth must give exclusive breastfeeding to the baby she was born in, and article 9 which contains the implementation of Early Breastfeeding Initiation (EIB) by health workers².

Early initiation of breastfeeding or the beginning of early breastfeeding is the baby starts breastfeeding himself immediately after birth. Early breastfeeding initiation is by placing a newborn baby on the mother's stomach or mother's chest, in almost an hour the baby will crawl looking for her mother's nipples and start breastfeeding herself. The way the baby initiates breastfeeding early is called the breast crawl or crawl looking for breasts³. EBI will increase the success of exclusive breastfeeding for 6 months because early contact with the mother and baby will increase the duration of breastfeeding twice compared to slow contact. In Indonesia, early breastfeeding is 8 times more likely to give exclusive breastfeeding⁴. Based on the results of the Basic Health Research in 2010, the percentage of breastfeeding started in children from 0 to 23 months in Indonesia in less than one hour (<1 hour) after the baby was born was 29.3%, for Southeast Sulawesi was 27.6%⁵.

The success of the Early Breastfeeding Initiation program is also strongly influenced by the attitudes,

knowledge and motivation of the midwife/physician assisting childbirth itself. This is also supported by the statement of Siregar A, that the success of early breastfeeding is largely influenced by the attitudes and behavior of health workers (doctors, midwives, nurses) who first helped the mother during the birth process. In addition, the success of nursing mothers must also be supported by their husbands, families, health workers and the community⁶. The Lepo-lepo Health Center is one of the Health Centers in Kendari City that implements the EIB program. The number of mothers giving birth at the Lepo-lepo health center from 2011 to 2013 continues to increase. In 2011, the number of mothers giving birth was 127 people, in 2012 there were 148 people, and in 2013 there were 218 people. Of these 80% were assisted by midwives and the remaining 20% were assisted by doctors⁷.

The implementation of EIB activities at the Lepo-lepo Health Center has not been fully implemented. This is due to medical indications in infants that make it impossible to do EIB, lack of awareness of the importance of EIB, and the lack of counseling by health workers. Based on the description of the problem, the researcher is interested in conducting research on *“Study of Implementation of the Early Breastfeeding Initiation Program at the Lepo-lepo Health Center in Kendari City”*.

Method

This research is a qualitative research with a phenomenological approach, namely qualitative research conducted because researchers want to explore phenomena that cannot be quantified that are descriptive such as the process of a work step, notions of a diverse concept, characteristics of goods and services, etc.⁸. Then the data is used triangulate, through interviews, observation, and documentation.

Results

Knowledge Knowledge found Early Breastfeeding Initiation or EIB is the giving of newborn breast milk directly breastfed without waiting for an interval of, approximately 30 minutes. The where appropriate EIB management is done by means of the baby in his stomach or mother’s stomach, with the baby’s skin attached to the skin of the mother and left to look for her mother’s nipples.

The benefits of early breastfeeding initiation for

babies are to get exclusive breastfeeding as early as possible and increase the baby’s immunity. While the benefits of EIB for mothers are to stimulate the mother’s contractions and other benefits. In the provision of early breastfeeding initiation, there are several factors that hinder the implementation of EIB, among others, lack of maternal knowledge, factors of health workers, the condition of infants with problems such as Low Birth Weight or premature, and the condition of mothers who are still sick, the mother’s nipples do not come out, and the absence breast milk from mother.

Attitude: The mother’s attitude in the implementation of early breastfeeding initiation found that the implementation of the EIB program was very good to be carried out. Besides being very beneficial for babies, EIB is also beneficial for the mother. However, the results of observations made by researchers, there is no EIB implementation as proud of the health workers in the study location Puskesmas. Midwives immediately clean, measure, and weigh the baby, without doing an EIB first. The tthough it is expected to get as early as possible in order to get closer to the mother and baby, increase immunity to the wedge after getting the colossus from her mother’s milk.

Furthermore, it was also found that health workers strongly supported the existence of the EIB program. They always recommend and teach patients to immediately do EIB. The however, different statements made by patients. They never get an explanation about the EIB from the delivery assistant midwife. Even though it is highly expected that the support of health workers on the importance of mothers breastfeeding early.

Health Resources: Health resources in understanding the initiation of early breastfeeding which is a motivator found the availability of 14 health workers (midwives) in the delivery room, which is always recommended to do EIB in patients being treated. Midwives who assist with childbirth are always encouraged to do EIB on their patients. Found with work shift scheduling used is a division of three shifts. Work shift scheduling with this model is very suitable to be used in the Lepo-lepo Health Center in carrying out its duties as a service provider, including EIB. Shift division of the job is suitable, division of three shifts.

Furthermore, it was found that there were no midwives or doctors who had participated in EIB training, other than just other training, because to do

EIB no special facilities and infrastructure were needed, as long as the mother and baby were in good condition, EIB could be carried out with special facilities that were important and her mother understands and feels that it is enough, and the media for socializing CDs, and flip charts is still a problem because there are no trained personnel.

Standard Operating Procedure (SOP): The availability of SOPs regarding EIB at the Lepo-lepo Puskesmas is included in the midwifery care SOP. In addition, SOP on EIB is only limited to posters about EIB that are posted on the wall. Whereas the stages of implementing EIB contained in the SOP in a nutshell are appropriate, for newborns to be thrown on their mother's chest to make skin contact and look for their own nipples.

Discussion

Knowledge: Knowledge related to EIB is what is known, understood and able to be remembered by health workers or mothers giving birth about EIB in the Lepo-lepo health center. Health workers involved in care during pregnancy until the baby is born are the primary in this study are midwives. But the lack of explanation about breastfeeding makes mothers less knowledge about EIB. Midwives and delivery mothers have not been able to explain EIB properly.

The results of this study are in line with the results of research conducted by Rati⁹. The Which shows that post-partum mothers have not been able to explain about EIB like their understanding of exclusive breastfeeding so that the EIB does not seem as popular as Exclusive breastfeeding. Even though post-partum mothers do not know anything about EIB, EIB will still be implemented because this is a program from the Puskesmas.

Inappropriate early initiation will reduce the success rate of early initiation of suckling. Inadequate early initiation is like pushing a baby's mouth into his mother's nipples for breastfeeding. Then this can result in a lack of success rate for early breastfeeding initiation. For this reason, health workers

EIB is very beneficial for babies, which is able to calm the baby, prevent hypothermia, and prevent the death of newborns through breastfeeding as early as possible at one hour of birth. In normal newborns that are separated directly from the mother to be bathed, weighed, measured, and cleaned resulting in 50%

of babies unable to suckle on their own. EIB is also very beneficial for the mother, namely the presence of baby suction will stimulate the release of the hormone oxytocin which will stimulate uterine contractions so that bleeding does not occur, and will make the mother calm, relaxed and happy¹⁰.

There are a number of things that can interfere with or hinder a baby's natural ability to find and discover his own breast or EIB Among these chemicals are given when the mother gives birth and may get to the fetus through the placenta, making it difficult for the baby to suckle the mother's breast. Births with actions and drugs such as surgery, vacuum, forceps, even feeling tired and aching in the area of skin cut during an episiotomy can also interfere with the implementation of EIB¹¹.

The results of Wahyuningsih's research¹² show that the implementation of IMD requires a long time, if bleeding is not carried out, the discharge of the placenta is difficult, less patient to do because it wants to be finished quickly, people who are not ready to do it because they feel dirty (disgust) get hit blood, born in a Private Hospital and lack of understanding of the implementation of the EIB program.

Attitude: Attitude is a reaction or response of someone who is still closed to a stimulus or object. Attitude is how people's opinions or assessments are related to health risk factors¹³. The results of the study were also conducted, that EIB is very important because mothers feel its benefits directly. But there are also those who say that EIB is not so important in accordance with the experience that has been passed. This attitude is apparent from the results of the interview. So there should be an agreement from the mother to make a decision.

This is in line with the results of a study in Switzerland in 2005, which stated that babies born in hospitals with the support of high health workers were more likely to have EIB than those born in hospitals with the support of low health workers¹⁴.

Health Resources: Midwives are health workers who have the most roles in implementing EIB, because midwives are tasked with helping and motivating mothers to do EIB. Midwives become one of the factors that influence the success of the EIB program, both in terms of quantity and quality. Whether or not early breastfeeding is successful at a maternity service in a hospital is highly dependent on health workers, namely

nurses, midwives or doctors, because they are the first to help the mother with her EIB. No matter how limited the time possessed by a midwife, is expected to still be able to take the time to motivate and help mothers after giving birth to implement EIB and exclusive breastfeeding.

The readiness of health workers including midwives in the EIB program is the key to success. The role of midwives in the success of exclusive EIB and ASI cannot be separated from the authority of midwives in providing services to mothers and children in improving the maintenance and use of breast milk. In addition, midwives also inform the importance of breastfeeding to every pregnant woman and help mothers start breastfeeding in the first hour after the baby is born.

Health workers, in this case midwives, can be a motivating factor, but they can also be a barrier to the success of the EIB program. Therefore, midwives need to get training on EIB. Training is a short-term process that uses systematic and organized procedures, in which non-managerial employees learn technical knowledge and skills for specific purposes. The training is intended as a planned effort to improve and enhance the knowledge and attitudes of midwives towards the EIB program¹⁵.

Facilities and infrastructure in this study is the availability of everything needed to support the implementation of EIB program activities. The lack of socialization given about the EIB program was due to the lack of knowledge of the midwife itself because she had never attended EIB training. Therefore, efforts can be made to socialize the EIB program not only to mothers or patients, but also to midwives assisting childbirth.

Standard Operating Procedure: SOP or work procedure is a written statement that is compiled systematically and can be used as a guide by the implementers in decision making. SOP is a guide for employees to carry out a job with established standards¹⁶. SOP as a document contains the processes and procedures of an activity that is effective and efficient based on a standard that has been standardized. EIB SOP becomes a need to be carried out and run systematically in accordance with applicable regulations.

Conclusion

Knowledge about EIB midwives is good enough, but implementation is not optimal, while patients are still lacking and they have never gotten information about EIB, either through midwifery delivery assistance

or from socialization media. The EIB program is still lacking with program implementation and there is no attitude and support from midwives. Human resources, especially midwives, are adequate and have attended EIB training. Evidenced by work shift scheduling that is applied to the four shift group four model, and no special facilities and infrastructure are needed in implementing the EIB. The EIB Standard Operating Procedure includes a poster about the EIB attached to the wall and the stages of EIB implementation that are reflected in the SOP are briefly correct, newborn babies bend over their mother's breast to make skin contact and look for their own nipples.

Suggestions: It is expected to provide confirmation of the EIB implementation program and encourage midwives to socialize EIB to patients, support providing training to all midwives on EIB, and issue and determine EIB SOPs at the Lepo-lepo Puskesmas.

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Contribution

Conflict of Interest: Authors declares that there is no any conflict of interest within this research

References

1. Ministry of Health RI. General Guidelines for Balanced Nutrition. Directorate of Community Nutrition. Jakarta, 2002.
2. _____ Decree of the Minister of Health of the Republic of Indonesia concerning exclusive breastfeeding for Indonesian infants Number 450/MENKES/IV/2004. Jakarta, 2012
3. Roesli, U. Early Breastfeeding Initiation. Mother Library. Jakarta. 2008
4. Aprilia. Analysis of the Early Breastfeeding and Exclusive Breastfeeding Initiation Program to Midwives in Klaten Regency. Postgraduate Thesis. Diponegoro University. Semarang. 2009
5. Riskesdas. Early Breastfeeding Initiation Coverage is less than 1 Hour. Jakarta. 2010.
6. Siregar, A. Exclusive breastfeeding and the factors that influence it. Thesis Faculty of Public Health. University of North Sumatra. 2004

7. PuskesmasLepo-Lepo. Profile of Lepo-Lepo Health Center in 2013. Kendari. 2014.
8. Satori & Kamariah. Qualitative Research Method. Alfabeta. Bandung. 2009
9. Rati, S. Post-Partum Mother Behavior in the Implementation of Early Breastfeeding Initiation (IMD) in Batua City Health Center Makassar. Makassar Health Ministry Polytechnic. Makassar.2013
10. RI Ministry of Health. Normal Childcare Clinic Training. Jakarta. 2009.
11. Afifah. Early Breastfeeding Initiation and Exclusive Breastfeeding in Johan Pahlawan District, West Aceh Regency. Thesis. Faculty of Public Health, University of North Sumatra. Field. 2009
12. Wahyuningsih, E. Analysis of the Implementation of the Early Breastfeeding Initiation Program (IMD) by the Midwife of Inpatient Health Centers in Sukoharjo District 2011. Postgraduate Thesis Program. DiPonegoro University. Semarang. 2011
13. Nursalam. Concepts and Application of Nursing Science Research Methodologies. SalembaMedika. Jakarta Publisher. 2001
14. Ananda. Epidemiology Overview of Early Breastfeeding Initiation Implementation at the Mauk Health Center in Tangerang Regency January - March 2009. Thesis. Faculty of Public Health, University of Indonesia. Depok. 2009
15. Munandar. Industrial and Organizational Psychology. UI-Press. Jakarta. 2001
16. Wijono. Leadership Management and Health Organization. Translator. Air Langga University Press. Surabaya. 1997.

Psychosocial Factors to Increase Adherence Antiretroviral Treatment on New PLWH Infection

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Abstract

HIV become iceberg phenomenon. All HIV infected people have risk illness and die. Data of WHO 2018 were 37.9 million PLWH and 23.3 million on antiretroviral treatment. Every month about 8-15 new people got new HIV infection in Probolinggo district, Indonesia. HIV cumulative in Probolinggo at January 2018 were 1.140 people and only 60% ARV active and 15% lost to follow up. Many factors that influence adherence and many impact of it. The aim to analysis psychosocial factors to increase adherence antiretroviral treatment on New PLWH infection. This method use observational study. The population were 61 PLWH on ARV treatment in Clini VCT Waluyo Jati General Hospital at January-May 2018, and sample were 54 people, systematic random sampling, instrument questionnaire, observational sheet, medical record, independent variable were level of knowledge, age, sex, ethnics, level of education, employment, dependent variable was adherence to take ARV, analysis logistic regression with SPSS 16.0. α (0,05). The result that level of education ($p=0.999$; prevalence ratio (PR)=0.000), duration of ARV treatment ($p=0.210$; PR=2.988), level of knowledge ($p=0.001$; PR=4.450). It means only level of knowledge can increase 4.450 times of adherence to take ARV. The conclusion was respondent that have good level of knowledge about antiretroviral schedule, risk, side effect, benefit, and outcomes influence adherence to take ARV than they have low level of knowledge. Health worker in Clinic VCT should conduct to increase counselling quality by giving about risk of ARV treatment, side effect, and all about ARV treatment and need social support to make them adhere to take ARV as doctors instruction.

Keywords: *Psychosocial, Adherence, Antiretroviral, PLWH.*

Introduction

HIV become iceberg phenomenon and pandemic in the world.¹ All HIV infected people have risk illness and die. Antiretroviral (ARV) is an HIV-proven drug that can inhibit HIV replication so decrease the level of viral load in the blood infecting immune cells or CD4 increases, so immunity begins to recover or increase.¹

Data of World Health Organization (WHO) 2018 were 37.9 million People Living with HIV (PLWH) and 23.3 million on antiretroviral treatment (ART).² Since HIV AIDS was first discovered in Bali-Indonesia from 1987 to December 2016, about 80% of HIV AIDS has spread in 80.2% of regencies and cities.³ Based on this data that only 70.5% was getting ARV treatment in Indonesia.⁴ Every month about 8-15 new people got new

HIV infection in Probolinggo district, Indonesia. HIV cumulative in Probolinggo at January 2018 were 1.140 people and only 60% ARV active and 15% lost to follow up. From 60% that ARV active, they were on adherence I (<3 dose forget to take it on 30 days, CD4 increase), adherence II (3-12 dose forget to take it on 30 days, CD4 increase), adherence III (>12 dose forget to take it on 30 days, CD4 decrease).⁵

Many factors that caused non adherence to take ARV were lack of knowledge about ARV, perceived susceptibility, perceived severity about ARV.⁵ According to other researcher that belief, self efficacy, self concept, barriers about side effect, disclosure of their status, stigma and motivation.^{6,7,8} Whereas, according to Holstad that adherence can influence by

self management, self efficacy, external motivation.⁹The impact of not adhere to take ARV as doctor instruction were resistance, failure treatment, and might make them drug poisoning.¹⁰

The aim of this study isto analysis psychosocial factors to increase adherence antiretroviral treatment on New PLWH infection.

Materials and Method

Our study was used observational design and conducted as long as 2.5 months start on 6 November 2018– 8 January 2019. The population this study were 61 all PLWH on ARV in VCT Clinic Waluyoati General Hospital and sample were 54 respondent. The inclusion criteria, PLWH have age more than 15 years old, have low and midle economic status, stay on Probolinggo district, on treatment ARV between 2 weeks until 3 months, and willing to be respondent. The exclusion criteria, PLWH with TB positive and on treatment TB < 2 weeks;They ARV treatment were stopped by their doctors because of the drug’s side effects of systemic symptoms or organ dysfunction as well as hypersensitivity such as severe rash, impaired hepatic function. Data collection technique i.e respondentswho agreed to participate in our study signed a written informed consent after explaine the procedure and aim of this study.The instrument in this study were use quessionnaires to identify the characteristics of patient, observation sheets and medical records. Independent variable were age, sex, ethnics, level of education, employment, duration of ARV treatment (weeks), level of knowledge; dependent variable were adherence with indicators (schedule to follow up, dose and CD4 status). Data analysis was use logistic regression with SPSS 16.0 vertion.

Findings: Findings on this study conducted in the VCT Clinic of Waluyoati General HospitalProbolinggo District as long as for 2.5 months, and the result study can seeing on table 1-3. Base on the result study of the 54 samples that 79.6% respondents were age between 20-49 years old and mean 36 years old, 59.3% were female, 61.1% have ethnics madurese, 40.7% were level of education at junior high school and almost half of respondent were employment as house wife (33.3%), then most of respondent about duration of ARV medication between 2-8 weeks (64.9%), mean 6.61 weeks. Additionally, level of knowledge of respondent shows that 33.3% were good, mean 6.04. Base on CD4 status from 54 respondent that 9 respondent not check

CD4 because they don’t have Health Insurance and 45 respondent after checked CD4 status were 60% increase and 40% were decrease after drinking ARV (Table 1).

The increase in the number of CD4 patients can be caused by the initial CD4 count is not too low, so the respondent’s body ability to improve the immune system is easier than those who have early CD4 therapy. In addition, low CD4 patients will easy to suffer of opportunistic infections that can greatly reduce the patient’s condition. To start ARV treatment in patients who have health insurance based on CD4 values and in patients who have not checked CD4 because they do not have health insurance, initiation to start treatment ARV based on patient clinical stage and rapid test results obtained HIV positive results (Table2).

The result of logistic regressionshows that the education level has $p\ 0.999 > \alpha\ 0.05$ and the value of Prevalence Ratio (PR) = 0.000, while the duration of treatment ARV obtained $p\ 0.210 > \alpha\ 0.05$ and the value Prevalence Ratio (PR)= 2.988 as well as knowledge level obtained $p\ 0.001 < \alpha\ 0.05$ and the value of Prevalence Ratio (PR) = 4.450 so that it can be concluded that the level of education and duration of treatment of ARV does not affect the adherence of ARV medication while the level of knowledge of ARV affects compliance. The better the level of knowledge about ARV will increase compliance by 4.450 times (Table 3).

Table 1: Caracteristics of respondent and Candidate Selection

Caracteristics (n=54)	n (%)	p, mean*
Age (Years)		1.000
15-19	2 (3.7)	
20-49	43 (79.6)	
≥50	9 (16.7)	
Mean		36.15*
Sex		0.251
Male	22 (40.7)	
Female	32 (59.3)	
Ethnics		1.000
Javanese	20 (37.0)	
Madurese	33 (61.1)	
Others	1 (1.9)	
Level of education		0.180
Never/Elementary school	21 (38.9)	
Junior high school	22 (40.7)	
Senior high school	9 (16.7)	

Collage	2 (3.7)	
Employment		0.772
House wife	18 (33.3)	
Privat job	8 (14.8)	
Entrepreneur	13 (24.1)	
Labor	5 (9.3)	
Farmer	9 (16.7)	
Civil servants	1 (1.9)	
Duration of ARV treatment(weeks)		0.224
2-8	35 (64.9)	
9-12	19 (35.2)	
Mean		6.61*
Level of knowledge		0.001
1-2 (Very low)	1 (1.9)	
3-4 (Low)	17 (31.5)	
5-6 (Midle)	12 (22.2)	
7-8 (Good)	18 (33.3)	
9-10 (Very good)	6 (11.1)	
Mean		6.04*
CD4 Status **		0.000
Decrease	18 (40.0)	
Increase	27 (60.0)	
Adherence (dose and schedule)		-
Not Adhere	17 (31.5)	
Adhere	37 (68.5)	

** n=45

Table 2: Caracteristics adherence of respondent to take ARV treatment base on CD4 status

CD4 Status	n (%)		Total (n=45)
	Not adhere	Adhere	
Decrease	16 (88.9)	2 (11.1)	18 (100.0)
Increase	0 (0.0)	27 (100.0)	27 (100.0)

Table 3: Logistic Regression Influence of Level of Education, Duration of ARV treatment and Level of knowledge toward adherence

Variable	p	Prevalence Ratio (PR)
Level of education	0,999	0,000
Duration of ARV treatment	0,210	2,988
Level of knowledge	0,001	4,450

Discussion

The results of this study indicate the level of education and the duration of treatment of ARV has no

effect on the adherence of ARV treatment, whereas the level of knowledge about ARV affects adherence to ARV treatment. The highest level of education in this study is junior high school, duration of ARV treatment averages 6 weeks, the respondent’s level of knowledge was good about ARV and adherence about ARV in this study was measured through obedient dosages, schedule visits and the patient’s CD4 status although there are some patients who do not check CD4 when they start ARV treatment due to health insurance theirs status. CD4 status was use to check that any correlation about adherence by dosage and schedule visit status and CD4 count in their body.

Adherence is the extent which the patient can follow the instructions of health workers.³ Factors that affect the adherence of ARV treatment i.e. communication between patients with doctors, patient knowledge about an ARV treatment, health facilities and other factors including individual factors, beliefs, support social support and healthcare personnel support.⁷ Individual factors include the modification factor of age, gender, ethnicity, level of education, personality, socio-economic, knowledge, belief and trigger (cues to action).¹¹ The modification factor includes duraton of ARV treatment, religion, sex orientation, marital status.¹² and the supporting factors of compliance with ARV medications are internal factors including motivation, perception, level of knowledge, and external factors include service factors, social support factors of the family, support group or peer group, non-governmental organizations (NGOs), health worker and availability factors and the affordability of the drug.¹³

The level of respondents education and duration of ARV treatment does not necessarily affect of adherence. Whereas level of knowledge may affect of adherence to take ARV. Education in this study is a formal education pursued by individuals through a systematic process and gaining recognition from the government.¹⁴ Although knowledge can be correlated with education, but not all knowledge is gained through formal education. The duration of ARV treatment is the length or number of days the individual follows the ARV treatment to the present.¹² Whereas level of knowledge is the result of know after a person does sensing against a particular thing or object. Knowledge can be a direct and indirect factor that can make their behavior.¹⁵

The result in this study, similar with other researcher, that levels of education have no effect on ARV treatment adherence. The results showed the level of education

of the majority respondent not at the college level and the greatest factor affecting the study was depression, conflict with spouse or partner as well as the maladaptive coping.¹⁶ Additionally, education status does not affect the adherence of ARV treatment in both the intervention group and the control group. In their research socio economic or financial constraints were factors that affect adherence compared to the level of education. Financial constraints will cause respondents difficulty in accessing the transportation to go to the Clinic, so it impacts on the not adhere of respondents to take ARV.¹⁷

Duration of ARV treatment not affect of adherence. In this study, all respondent follow the ARV treatment between 2 weeks-3 months. At the beginning of ARV treatment between 2 weeks – 6 months, respondents tended to not be able to receive any side effects caused by ARV. Some types of ARV can cause side effects with different durations, such as the longer using the drug ARV of d4T (Stavudin), the more likely the effectiveness of the side effect.¹⁸ Duration of ARV treatment with a range of 0-1 years, 2-6 years and 7-23 years proved to have no effect on adherence. It is a major influence on adherence of ARV treatment in their study i.e. anxiety and depression to initiate ARV treatment. Anxiety occurred due to lack of knowledge about ARV and depression occurred because of the still existence of stigma and discrimination against the PLWH.¹²

The level of knowledge in this study has an effect on adherence. The result of other study about “Difference between patients who do and do not adhere to antiretroviral therapy” shows that there were a difference level of knowledge in both groups between the care group and the ARV relapse group. The process of behavioral adaptation involves a person beginning with the conscious need of treatment because it has gained a particular knowledge of ARV treatment, a sense of interest in following treatment, the stage of evaluating interest on treatment and attempted and performed or behaved following the treatment of ARV. It means the better one’s knowledge, the more positive it will be.¹⁹

Conclusions

In conclusions were level of education, duration of ARV treatment not influence toward adherence to take ARV, but level of knowledge about antiretroviral schedule, risk, side effect, benefit, and outcomes influence of adherence to take ARV than they have low level of knowledge. Health worker in Clinic VCT

include doctors, midwife and case manager should conduct to increase counselling quality by giving about risk of ARV treatment, side effect, and all about ARV treatment and need social support to make them adhere to take ARV as doctors instruction.

Conflict of Interest: This study didn’t have conflict of interest with General Hospital that become location of our study.

Source of Findings: This study have self findings by the authors.

Etichal Clearance: Prior to the research, an ethical approval was conducted by a reviewer of Health Science of Hafshawaty *Pesantren*(Islamic Boarding School) Zainul Hasan Probolinggo, East Java, Indonesia, with number: KEPK/318/STIKes-PZH/VIII/2018.

References

1. Directorate General of Disease Control and Environmental Health. Statistics of HIV AIDS in indonesia, Health Ministry 2017, <http://spiritia.or.id/Stats/detailstat.php?no.8>, Citation date 14 June 2017.
2. WHO. Antiretroviral therapy (ART) coverage among all age groups [Internet]. Vol. 2005. 2018. p. 2018. Available from: https://www.who.int/gho/hiv/epidemic_response/ART_text/en/
3. WHO. 10 Fact on HIV/AIDS, <http://www.who.int/features/factfiles/hiv/en/>, citation date 13 June 2017.2016.
4. Yuniar Y, M S, Isakh. Logistic Management of ARV Drugs in Indonesia. [Internet]. Health System Research Departement, 2014;17(29):1–10. Available from: <http://oaji.net/articles/2015/820-1432778621.pdf>
5. Clinic VCT of General Hospital Waluyoajati. Data of HIV AIDS Case 2012-2018 and Antiretroviral Treatment Terapi ARV in Clinic VCT General HospitalWaluyoajati, General Hospital. Probolinggo. 2018.
6. Ilmiah W S, Qommaruddin M B, Putri S.U, Iswardani N. Belief, Self Efficacy And Other Predictors Of Adherence To Art Among Women Live With Hiv. Proceeding 2nd Symp Public Health. 2017;2(1):610–5.
7. Gouse H, Henry M, Robbins RN, Lopez-Rios J, Mellins CA, Remien RH, et al. Psychosocial

- Aspects of ART Counseling: A Comparison of HIV Beliefs and Knowledge in PMTCT and ART-Naïve Women. *Journal Assoc Nurses AIDS Care* [Internet]. 2017;28(4):504–17. Available from: <http://dx.doi.org/10.1016/j.jana.2017.03.002>
8. Ware NC, Pisarski EE, Haberer JE, Wyatt MA, Tumwesigye E, Baeten JM, et al. Lay Social Resources for Support of Adherence to Antiretroviral Prophylaxis for HIV Prevention Among Serodiscordant Couples in sub-Saharan Africa: A Qualitative Study. *AIDS Behavior* [Internet]. 2015;19(5):811–20. Available from: <http://dx.doi.org/10.1007/s10461-014-0899-4>
 9. Holstad MMD, Spangler S, Higgins M, Dalmida SG, Sharma S. Psychosocial Characteristics Associated with Both Antiretroviral Therapy Adherence and Risk Behaviors in Women Living with HIV. *AIDS Behavior*. 2016;20(5):1084–96.
 10. Lestary H, Mujiati, Mulyana N. Concordance Model : An Alternative Model for Increasing Art Adherence In PLWHA In Bandung City, 2012. *Journal Health Reproduction*. 2013;(November).
 11. Glanz K, Rimer BK, Viswanath K. *Health Behavior and Health Education Theory, Research, and Practice* 5th Edition. C. Tracy Orleans, editor. San Fransisco: Jossey Bass; 2015. 553 p.
 12. Hanif H, Bastos FI, Malta M, Bertoni N, Surkan PJ, Winch PJ, et al. Individual and contextual factors of influence on adherence to antiretrovirals among people attending public clinics in Rio de Janeiro, Brazil. *BMC Public Health*. 2013;13(1).
 13. Yuniar Y, Handayani RS, Aryastami NK. Factors that facilities of adherence of People Living with HIV AIDS (PLWHA)IN Taking Antiretroviral drugs in Bandung Citiesand Center for Public Health Intervention Technology, Health Research and Development Agency of Humanities Center, Community empowerment and health policy, *BuletineHealth Research*. 2012;41(2):72–83.
 14. National Education System Legislation. About Collage System. Ministry of Law and Human rights. Jakarta. 2012
 15. Notoatmodjo, S. *Health behavior Sciences*. Nuhamedika. Yogyakarta. 2014.
 16. Malow R, Dévieux JG, Stein JA, Rosenberg R, Jean-Gilles M, Attonito J, et al. Depression, substance abuse and other contextual predictors of adherence to antiretroviral therapy (ART) among haitians. *AIDS Behavior*. 2013;17(4):1221–30.
 17. Zubaran C, Michelim L, Medeiros G, May W, Foresti K, Madi JM. A randomized controlled trial of a protocol of interviews designed to improve adherence to antiretroviral medications in Southern Brazil. *International Journal STD AIDS*. 2012;23(6):429–34.
 18. Health Ministry . *Antiretroviral treatment Guidelines*. Health Ministry. Jakarta. 2014.
 19. Lasti MH. *Antiretroviral Drug Compliance Analysis (ARV) In MSM Community (Men Sex With Men) PLWH In Pare Pare Town of South Sulawesi*. Antimicrobial Agents and Chemotherapy. 2017.

Reproductive Health Behavior of Street Youth Guided by Karya Putra Indonesia Mandiri Foundation in Central Jakarta Region

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Abstract

Background: Adolescents psychologically have a negative self-concept that is easily influenced and tends to behave freely. This study aims to determine whether there is a relationship between the role of parents and the role of friends with the reproductive health behavior of street adolescents. The problem with this research is the high rate of teenage pregnancy in Indonesia and adolescents account for 30% of unwanted pregnancies and unsafe abortions.

Material and Method: Cross sectional research design. The sample in this study was YPKIM fostered adolescents aged 15-19 years. Data processing and analysis using chi square test and multiple logistic regression.

Findings and Discussion: Poor reproductive health behaviors in YPKMI street adolescents by 33.3%. Based on the results of bivariate analysis found there is a relationship between the role of parents and the role of friends with reproductive health behavior. Multivariate analysis shows that knowledge is the most dominant risk factor associated with reproductive health behavior (OR = 6,610).

Conclusion: The results of this study prove the need to increase reproductive health knowledge in street adolescents to improve reproductive health behavior better by creating programs specifically for the coaching of adolescents, especially street adolescents.

Keywords: *Reproductive health, Sexual behavior, Street youth.*

Introduction

Adolescent relationships today tend to be free and experience a shift in values, where adolescence is a critical period where changes in emotions, thoughts, social environment and responsibilities are experienced¹. Sexual Behavior is any behavior carried out because of

sexual urges. In this concept no matter how and with whom or what that impulse is released. In adolescent sexual behavior, open communication with parents seems to be important.

Teenagers need sex education from older people to access contraception or refuse peer calls or partners to have sex before they are ready. In the US, public health activities to improve open communication between parents and adolescents to produce positive adolescent health. Not all sexual relations are voluntary, especially for girls, but also because of coercion among women aged 17 years, according to data from the National Survey of Children, there are 7% who are forced to have sexual relations².

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Sexually transmitted infections (STIs) and unwanted pregnancies are very important public health problems, although in the long term they are needed to prevent them. Because there are a number of risk factors for STIs, prevention includes the delays in the emergence of sexual relations between teenagers who are actively engaging in sexual relations³. In 2012, an estimated 2.1 million adolescents were living with HIV. Despite effective interventions to prevent and treat HIV, adolescents face difficulties in accessing it. As a result the emergence of new infections among adolescents infected with HIV is common. Programs designed specifically for HIV-positive adolescents must focus more on interventions that have proven to be more effective in overcoming fundamental factors that drive incidents and the lack of effective care and care in this age group.

In adolescent sexual behavior, open communication with parents seems to be important⁴, Because teenagers need sex education from older people to access contraception or refuse peer calls or partners to have sex before they are ready. In the US, public health activities to improve open communication between parents and adolescents to produce positive adolescent health. Not all sexual relations are voluntary, especially for girls, but also because of coercion among 17-year-old women in the National Survey of Children, 7% are forced to have sexual relations. Data from research from Katherine in 2003, parents who communicate with their daughters about sex will influence sexual behavior in a more positive direction. A family-based approach to improving communication can reduce the risk of risky sexual risk-related behaviors related to HIV⁵.

The halfway house is a temporary informal camp, where street children meet to get information and initial guidance before being referred to further development processes. The purpose of establishing a halfway house is to re-socialize to reshape children's attitudes and behaviors that are in accordance with the values and norms prevailing in society and provide early education to meet the needs of children and prepare their future so that they become productive societies. Of the dozens of Shelter Houses that carry out street youth development in the DKI Jakarta area and in the Central Jakarta area there are five Shelter Houses Foundation, two of which are still active to date and one of them is shelter Yayasan Karya Putra Indonesia Mandiri (YKPMI). Based on observations made by researchers together with interviews with the Chairperson and Staff of the YKPMI Shelter Foundation, the 2014 data of the YKPMI Shelter

Foundation has 215 street children assisted in 10 points in Central Jakarta and East Jakarta.

Material and Method

This type of research is a quantitative study using a cross-sectional approach, which is a study that studies the relationship between the role of parents and the role of friends on the reproductive health behaviors of YKPMI street adolescents by observation or data collection at the same time.

This research is a descriptive-analytic study using the quantitative cross-sectional method used to analyze the relationship between parental role variables and the role of friends on reproductive health behaviors in street children fostered by YKPMI in the Central Jakarta Region in 2015.

The sample in this study has the characteristics of inclusion, namely street children fostered by YKPMI in Central Jakarta and East Jakarta, aged 15-19 years and came to YKPMI at the time determined by the researcher. The exclusion characteristics in this study were adolescents aged <15 years and street adolescents who could not read and write.

Findings and Discussion

Univariate Analysis: Univariate analysis is used to look at quantitative data obtained from descriptive research, using tables, graphs and measures of central tendencies, such as the mean or average value of each variable.

The assessment results found that most of the street adolescents fostered by the Karya Putra Indonesia Mandiri foundation had good reproductive health behaviors as many as 40 people (66.7%) and only a small proportion were behaving less well, 20 people (33.3%).

Table 1: Frequency Distribution of Street Youth Assisted by Karya Putra Indonesia Mandiri Foundation according to Reproductive Health Behavior in Jakarta

Reproductive Health Behavior	Total (n)	Percentage (%)
Poorly	20	33,3
Well	40	66,7
Total	60	100

Based on the results of table 1 analysis, it is known that most of the street adolescents fostered by Karya Putra

Indonesia Mandiri Foundation have good reproductive health behaviors, as many as 40 people (66.7%) and only a small portion whose behavior is not good, namely 20 people (33.3%) . This study is consistent with Joseph’s research findings that the lack of knowledge about reproductive health will affect health behaviors in adolescents⁶.

Table 2: Frequency distribution of YKPIM-assisted street teenagers based on the role of parents and the role of friends in Jakarta

Variable	Total (n)	Percentage (%)
The role of parents		
Fewer roles	20	33,3
Most of the roles	40	66,7
The role of Friends		
Fewer roles	18	30,0
Most of the roles	42	70,0

Based on the results of table 2, it is known that the frequency distribution of the role of parents of YKPMI street teenagers is that most of the roles of parents are mostly 40 people (66.7%) and a small part has fewer roles, 20 people (33.3%). The distribution of the role of YKPMI street adolescent peers mostly played 42 people (70%) and a small part has fewer roles that 18 people (30%).

Bivariate Analysis: Bivariate analysis was performed to see the relationship between each independent variable with the dependent variable, namely reproductive health behavior using a statistical test, the Chi Square test. Bivariate analysis was used in this study as a method to see the relationship between the reproductive health predisposing variables of street children who are under the guidance of YKPIM Jakarta.

Table 3: Relationship between the role of parents and the role of friends with reproductive health behaviors

Variable	Reproductive Health Behavior				Total		OR (95% CI)	p-value
	poorly		Well		n	%		
	n	%	n	%				
The role of parents								
Fewer roles	12	60,0	8	40,0	20	100	6,000	0,005
Most of the roles	8	20,0	32	80,0	40	100	(1,837-19,594)	
The Role of Friends								
Fewer roles	12	66,7	6	33,3	18	100	8,500	0,001
Most of the roles	8	19,0	34	81,0	42	100	(2,444-29,562)	

Based on the results of the analysis in Table 3 shows that in YKPMI street adolescents, it is known that there are 60.0% of teenagers who lack the role of parents, the behavior is not good, while in the youth group who feel the role of parents there are only 20.0% of bad behavior. Statistical test results obtained p-value 0.005 meaning that there is a significant relationship between the role of parents with reproductive health behavior. The results of the analysis obtained OR 6,000 means that a group of adolescents who do not feel the role of parents has a 6 times greater chance to have bad behavior than adolescents who feel the role of parents.

The results of the analysis showed that in the street adolescents guided by YKPMI, it was found that in the group of teenagers who felt the lack of the role of

friends there were 66.7% whose behavior was not good whereas in the group of adolescents who felt the role of friends there were only 19.0% whose behavior was not good. statistics obtained P value 0.001 means that there is a significant relationship between the role of friends with reproductive health behavior. The analysis results obtained OR 8,500 means that the group of adolescents who do not feel the role of friends has a 8.5 times greater chance to have bad behavior than adolescents who feel the role of friends.

The results of this study are consistent with the results of Jennifer’s research that parent and teen communication about reproductive health has an important role in improving reproductive health in adolescents⁷.

Multivariate Analysis: Multivariate analysis used is multiple logistic regression test, the steps being carried out are as follows: selection of predictive model candidates. Multivariate analysis in this study was conducted to see the most dominant independent variables related to the dependent variable simultaneously, because the independent variables are categorical and the dependent variables are dichotomous categories, so the analysis conducted is multiple logistic regression. Variables that have been analyzed bivariately and have a p value <0.25 are used as candidate variables to be included in the next analysis multivariately, to determine the best model. The results can be seen in table 4 below.

Table 4: Results of variable analysis as a candidate model

Variable	p-value	Explanation
The role of parents*	0,003	Following the Multivariate
The Role of Friends*	0,001	Following the Multivariate

The results of bivariate tests that have been done previously, it is known that of the eight variables, there are four variables that can be included in multivariate analysis, namely knowledge, attitudes, the role of parents and the role of friends (p-value <0.25). Other variables (age, gender, education and media access) have p-values >0.25 so they are not included in the multivariate analysis.

Conclusions

Communication that occurs between adolescents and parents is very lacking so that there is a failure of family function, this triggers adolescents to behave freely and even violate the norms, because they feel no one cares or prevents it. Lack of appropriate sources of information from the mass media, health workers, religious leaders, religious leaders and peers causes adolescents to obtain information and choose the wrong actions so that they regret after pregnancy after having premarital sex. Although premarital sexual behavior is at risk of being influenced by individuals and the environment, sometimes parents are met who do not regret the pregnancy that occurs in their children.

Conflict of Interest: There is no conflict of interest to be declared.

Source of Funding-self or Other Source: The source of funding for this research came from private funds.

Ethical Clearance: This research was approved by Karya Putra Indonesia Mandiri Foundation (518/B.04.02/2015) and Postgraduate University Prof. Dr. Hamka (No. 103/SK/Mp-Mhs/YKPIM/X/2015).

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References

1. Herdiana I. Perilaku Seksual Anak Jalanan Ditinjau dengan Teori Health Belief Model (HBM). 2011;13(02):129–37.
2. Jones CL, Jensen JD, Scherr CL, Brown NR, Christy K, Weaver J. The Health Belief Model as an Explanatory Framework in Communication Research. Pmc. 2016;30(6):566–76.
3. Kiviat NB, Holmes KK, Koutsky LA. new england journal. N Engl J Med. 2006;354:2645–54.
4. Access O. Assessment of adolescents ’ communication on sexual and reproductive health matters with parents and associated factors among secondary and preparatory schools ’ students in. Reprod Health. 2014;1–10.
5. Hutchinson MK, Jemmott JB, Jemmott LS, Braverman P, Fong GT. The role of mother-daughter sexual risk communication in reducing sexual risk behaviors among urban adolescent females: a prospective study. J Adolesc Health. 2003;33(2):98–107.
6. Kyilleh JM, Tabong PT, Konlaan BB. Adolescents ’ reproductive health knowledge, choices and factors affecting reproductive health choices : a qualitative study in the West Gonja District in Northern region, Ghana. 2018;1–12.
7. Grossman JM, Jenkins LJ, Richer AM. Parents ’ Perspectives on Family Sexuality Communication from Middle School to High School. 2018;

Evaluation of the Antioxidant Levels and HbA1c of Type 2 Diabetes Patients

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Abstract

Type 2 Diabetes Mellitus is a chronic and inflammatory disease, characterized by chronic hyperglycemia associated with ROS generation, oxidative stress and lipid peroxidation.

A cross-sectional study was conducted with T2DM (n=60, male) aged over 40 years and nondiabetic control (n=30, male) with same age. All patients provided a written informed consent before the start of the study procedures. In the present study, we reported high differences ($p \leq 0.01$) in the antioxidants values (MDA, CAT, SOD, GPX and GSH) compared with control, value of HbA1c and duration of infection. High HbA1c is an indicator of high antioxidant enzymes activity. Serum MDA level was increased significantly in diabetes mellitus patients with a simultaneous decreased in SOD and CAT levels. Diabetes induces alteration in activity GPX and GSH. The hyperglycemia change the oxidative status which, in turn affects the endogenous antioxidant status in T2DM. They have high risk of experiencing micro and macrovascular complications. In addition to the combination of diet, exercise and medication can improve the level of HbA1c in T2DM. Further studies should be conducted to strengthen this evidence.

Keyword: HbA1c, T2DM, MDA, SOD, GPX.

Introduction

Diabetes mellitus (DM) is regarded by hyperglycemia due to disruption in the metabolism of fats, carbohydrates, and proteins which resulting from faults in insulin action, insulin action, or both¹⁻³. About 150 million diabetics, individuals were reported worldwide and the number is still increasing due to energy-rich diet consumption, sedentary lifestyle and obesity^{3,4}. The diagnosed diabetes person may not showed any notable symptoms for years or decades. The symptoms may be subtle. Polyuria, polyphagia and polydipsia are three first and noticeable signs of diabetes. They are mild at first and gradually worsen over weeks or months⁵. Individuals

may feel extremely fatigued, develop blurred vision, and may become dehydrated. However, early hypoglycemia was also reported in some cases^{5,6}. Rarely, the blood glucose levels above 1,000 mg/dL was also observed due to some superimposed stress, such as an infection or drug use. Now days, individuals with type 2 diabetes are diagnosed by routine blood glucose test before they develop such severely high blood glucose levels⁶.

The glycated haemoglobin can be diagnosed by the HbA1c (haemoglobin A1c or simply A1c) test. It develops when haemoglobin, the oxygen carrier protein within red blood cells, become glycated. An increase in the HbA1c levels is represented poorer glycemic control over a last period of weeks or months. The higher values of HbA1c, the risk of developing diabetes-related complications will be greater^{7,8}.

The free radicals such as O⁻, SO₄²⁻, PO₄²⁻, Cl⁻ etc. are recognized as a reactive radicle species short-lived, very unstable, and extremely reactive⁹. They are formed excessively in diabetes due to glucose oxidation and nonenzymatic protein glycation. Abnormally elevated

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free radical levels and the simultaneous decrease of antioxidant protective mechanisms can cause damage to cellular organelles and DNA, increased lipid peroxidation, and induction of insulin resistance¹⁰. Since, diabetes is considered as a consequence of increased in the radical formation, the autoimmune disorder is described during excessive and accumulation of free radicals, correlated with immune dysfunction and oxidative stress¹¹. The leading antioxidant enzymes that are engaged in the neutralization of both reactive nitrogen species (RNS) and reactive oxygen species (ROS) are superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), and glutathione reductase (GRx)¹². Studies have demonstrated that SOD can be used to prevent the destructive consequences of hyperglycemia-induced ROS production. In diabetes, a notable increase in CAT activity in lymphocytes was discovered in children with T2DM through all phases. Conversely, it has been reported that significant decreased CAT and significant increase in thiobarbituric acid reactive species concentration in T1DM patients with or without nephropathy compared with control¹³. Studies also indicated that the GPx activity was lower in children with diabetes compared with healthy children^{14,15}. It has been implied that lowered antioxidative defenses from the excessive production of lipid hydroperoxide and NOx overproduction are present in juvenile patients with T1DM¹⁶. With this background, we aim to analyze the antioxidant levels and HbA1c in the T2DM patients of Iraq.

Material and Method

Study design: A cross-sectional study was conducted on T2DM individuals (n=60) aged over 40 years who attended the Diabetic Consult Center (DCC), in Al-Yarmook hospital Baghdad, Iraq. In addition, a control group (n=30) composed of nondiabetic individuals with the same age range as the diabetes patients who were not administered any medications. A detailed medical history was taken, and a physical examination was performed upon all participants. All

patients provided a written informed consent before the start of the study procedures.

Blood samples: Blood samples (2ml) were collected into vacutainers after overnight fasting at the same standardized time to minimize any effect of diurnal variation for biochemical analysis. The serum, clear and nonhemolyzed supernatant, was separated by centrifugation and stored at -8°C for the analysis of lipid peroxidation (malondialdehyde) and antioxidant enzymes (GSH, GPx, SOD and CAT).

Oxidative stress parameters: Thiobarbituric acid-reacting substances content, a measure of lipid peroxidation was determined according to the method of Zhang et al¹⁷. The CAT activity was assayed based on the ability of hydrogen peroxide to form a stable stained complex with molybdenum salts¹⁸. GPx activity was determined according to the Hafeman et al¹⁹ method. The estimation of SOD activity was performed using a SOD Assay kit-WST (Sigma Aldrich, USA) according to the manufacturer's protocol (Dojindo, Gaithersburg MD, USA). Xanthine oxidase system was used to generate a superoxide flux, and nitroblue tetrazolium was used as an indicator of superoxide production. Reduced GSH was determined using Ellman's reagent according to manufactures protocol²⁰.

Statistical analysis: Results were expressed as a mean \pm standard deviation. The statistical significance was assessed using the analysis of variance. $P<0.05$ was considered statistically significant.

Results

Antioxidants levels of control and T2DM patients: The levels of antioxidants in the serum are depicted in the Figure 1. The the present study, in diabetics group, serum MDA, CAT, SOD, GPx and GSH were increased ($P\leq 0.01$) 0.149 ± 0.186 ; 2.82 ± 3.69 ; 2.82 ± 3.69 ; 0.529 ± 0.599 and 2.22 ± 13.52 as compared to control group, 0.0274 ± 0.0854 ; 0.429 ± 0.607 ; 0.539 ± 7.517 ; 0.0255 ± 1.1293 and 1.92 ± 11.11 , respectively.

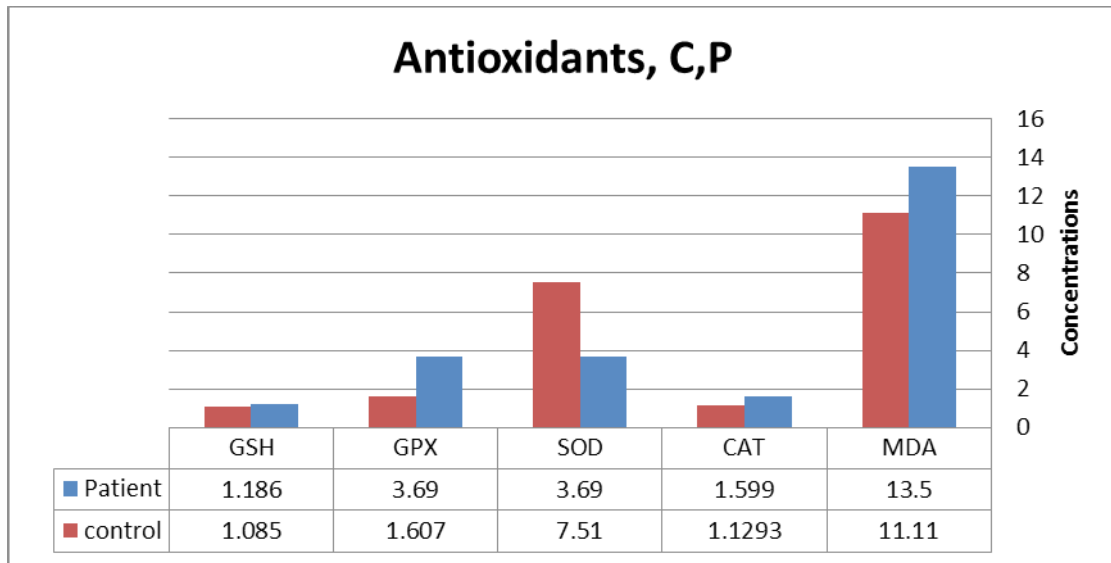


Fig. 1. Antioxidant levels of enrolled individual serum samples

Antioxidants levels of experimental group G1,G2: The results in the present study, as shown in Figure 2, showed high significantly differences ($P \leq 0.01$) between the experimental group with HbA1C less than 8(G1) and more than 8(G2) compared with the control group. The serum MDA concentration of G1 and G2 were 12.913 ± 2.467 and 14.130 ± 1.770 respectively as compared to the control group (11.105 ± 1.922). Serum CAT levels for G1 and G2 were 1.122 ± 0.02 and 0.076 ± 0.051 , respectively as compared to the control group (1.129 ± 0.025). The serum SOD concentration

for G1 and G2 were 6.325 ± 1.361 and 1.064 ± 0.042 , respectively as compared to the control group (7.517 ± 0.53).

The serum GPx for G1 and G2 were 0.341 ± 0.17 and 3.932 ± 1.3 , respectively, as compared to the control group (0.607 ± 0.42). The serum GSH in experimental group G1 and G2 were 0.0714 ± 0.042 and 0.301 ± 0.125 , respectively, as compared to the control group (0.085 ± 0.0274).

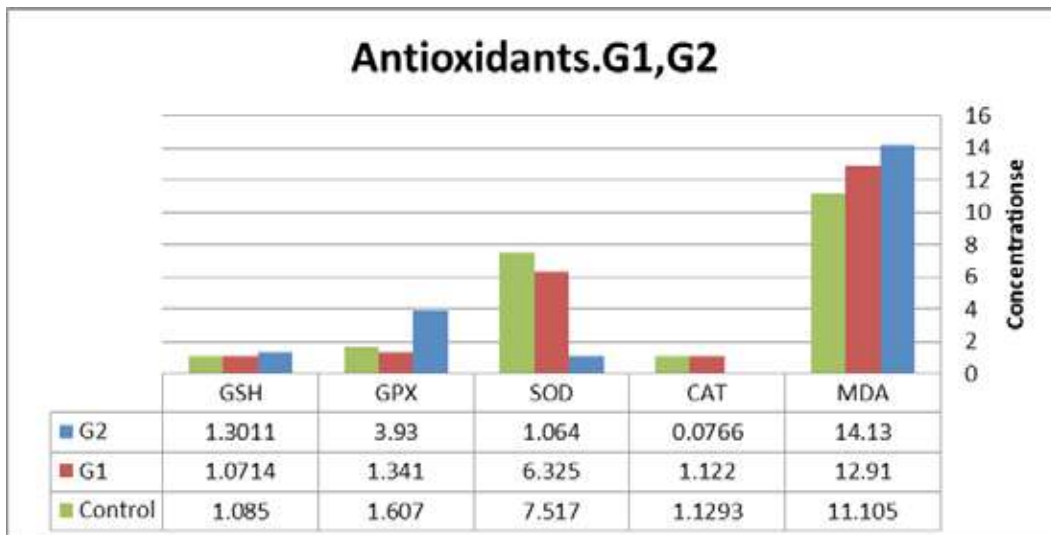


Fig. 2. Levels of antioxidants in experimental group G1 and G2

Antioxidants levels of experimental group G1P1,G2P1: The results in the present study, as shown in Figure 3 showed significant differences ($P \leq 0.01$) between the experimental group with HbA1C level less than 8(G1P1) and more than 8(G2P1) and the injury period P1 for groups G1 and G2(1-5) years compared to the control group of all antioxidants under study. The average concentration of MDA in the G1P1 and G2P1 groups was 10.32 ± 1.36 and 12.68 ± 1.734 respectively, compared to the control group which was MDA concentration 11.105 ± 1.105 .

The serum CAT levels for G1P1 and G2P1 groups were 1.123 ± 0.023 and 0.144 ± 0.017 , respectively, as compared to the control group (1.1293 ± 0.025). The SOD levels in G1P1 and G2P1 groups were 7.45 ± 0.77 and 1.106 ± 0.047 , respectively, while the SOD concentration in control group was 7.517 ± 0.53 . The average GPX concentration in G1P1 and G2P1 groups were 0.36 ± 0.10 and 5.08 ± 1.4 , respectively, while the average GPx concentration was in control group was 0.607 ± 0.429 . The GSH concentration in the G1P1 and G2P1 groups were 0.113 ± 0.038 and 0.35 ± 0.13 , while the GSH concentration in the control group was 0.085 ± 0.02 .

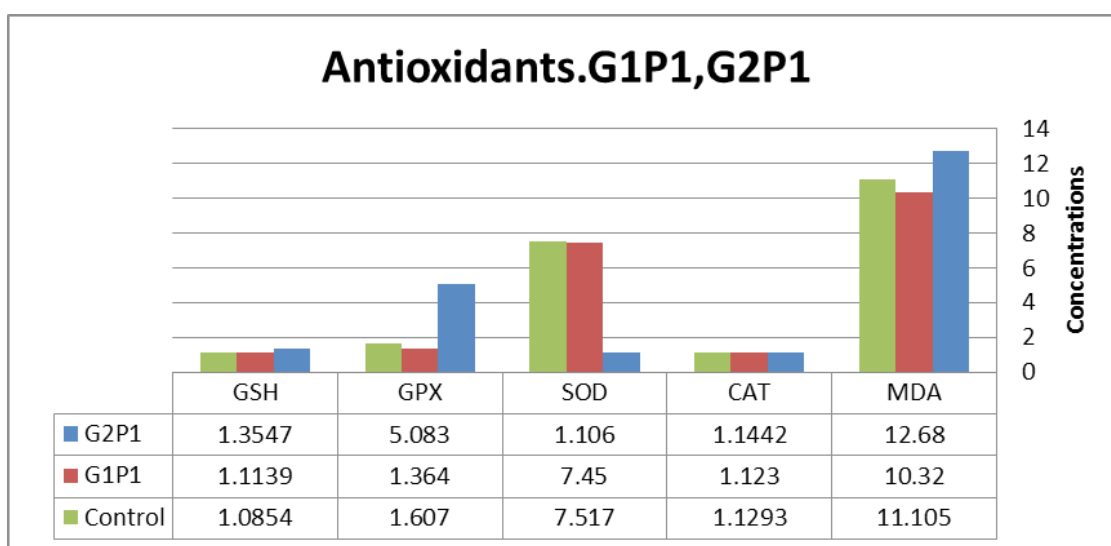


Fig. 3: Levels of antioxidants in experimental group G1P1 and G2P1.

Antioxidants levels of experimental group G1P2 and G2P2: The results in the present study, as shown in Figure 4, showed a high significantly differences ($P \leq 0.01$) between the experimental group with HbA1C less than 8 (G1P2) and more than 8 (G2P2) during last 6-10 years. The duration of P2 injury for groups G1 and G2 was between (6-10) years compared with the control group in terms of MDA, CAT, SOD, GPx and GSH.

The average concentration of MDA in the group G1P2 and G2P2 were 12.68 ± 0.69 and 14.08 ± 0.68 ,

respectively, a compared to control group was 11.105 ± 1.9 . The mean CAT concentration in G1P2 and G2P2 were 1.12630 ± 0.017 and 0.056 ± 0.015 , respectively. While, the CAT concentration in the control group 1.12 ± 0.02 . The SOD in the G1P2 and G2P2 are 6.89 ± 0.6 and 1.051 ± 0.01 , respectively, as compared to the control group (7.51 ± 0.53). The GPx in the G1P2 and G2P2 groups were 0.34 ± 0.22 and 3.75 ± 0.9 , respectively, as compared to control group (0.60 ± 0.4). The GSH levels in G1P2 and G2P2, 0.069 ± 0.01 and 0.33 ± 0.1 , respectively, while, in control group was 0.08 ± 0.02 .

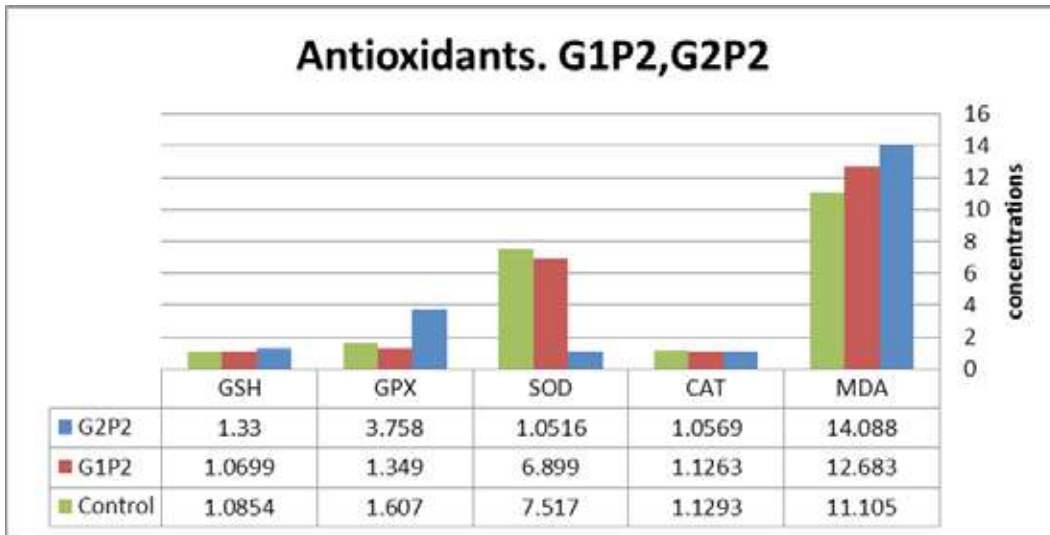


Fig. 4: Levels of antioxidants in experimental group G1P2 and G2P2.

Antioxidants levels of experimental group G1P3,G2P3: Figure 5 showed significant differences ($P \leq 0.01$) between the experimental group with HbA1C level less 8(G1P3) and more than 8(G2P3) and the injury period P3 for G1 and G2 groups 11 years and above compared with the control. The average MDA concentration in the group G1P3 and G2P3 15.736 ± 0.9 and 15.61 ± 1.3 , respectively. While, the average of mean concentration of CAT in control group was 11.10 ± 1.9 . The CAT levels of G1P3 and G2P3 were 1.11 ± 0.01 and 0.02 ± 0.009 , respectively. While, the average

concentration of CAT in the control group 1.12 ± 0.02 . The SOD concentration in G1P3 and G2P3 respectively were 4.62 ± 0.01 and 1.03 ± 0.01 , respectively. While, the mean SOD concentration in the control group was 7.51 ± 0.53 . The GPx concentration in G1P3 and G2P3 0.30 ± 0.18 and 2.95 ± 0.7 , respectively. The GPx in the control group 0.607 ± 0.4 . The GSH in G1P3 and G2P3 groups 0.03 ± 0.01 and 0.21 ± 0.08 , respectively. While, the mean concentration of GSH in the control group was 0.08 ± 0.02 .

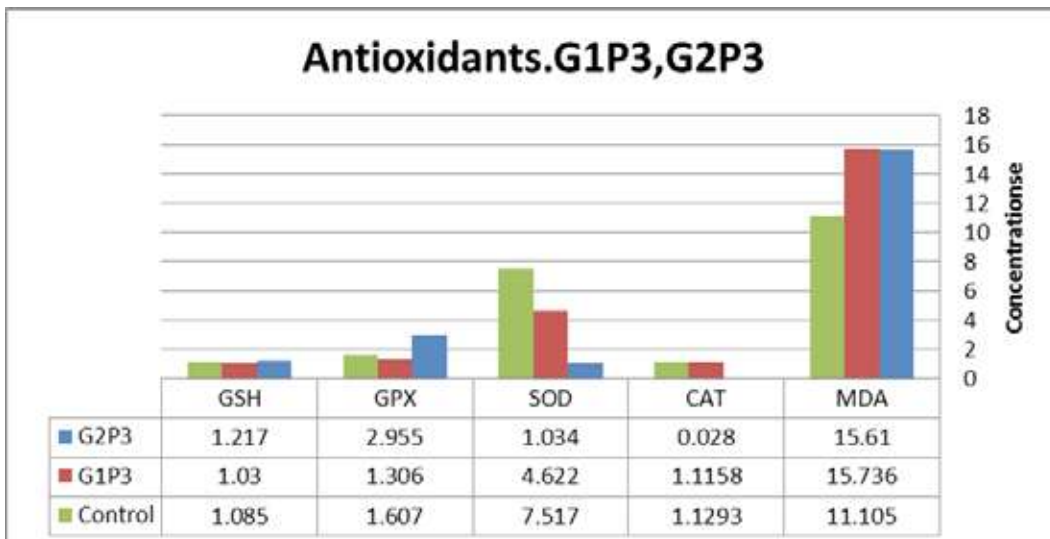


Fig. 5: Levels of antioxidants in experimental group G1P3, G2P3

Discussion

Diabetes Mellitus is a chronic and inflammatory disease, characterized by chronic hyperglycemia associated with ROS generation, oxidative stress and lipid peroxidation, and subsequent macro and microvascular complications²¹. The metabolic disorders such as hyperglycemia, altered lipid profile, carbohydrates and protein metabolisms and increased risk of cardiovascular disease complications are associated with diabetes mellitus. Our result in the present study showing high significant differences in the antioxidants values compared with control, value of HbA1c and duration of infection. We report the effects of the high value of HbA1c oxidative damage and its role in the significant changes in antioxidant enzymes activity in blood and liver or other organs such as muscle tissues and kidney^{22,23}.

The present study was aimed to investigate whether oxidative stress have any difference exists between diabetic male with HbA1c up of 8, and less than 8. Experimental studies suggest that oxidative stress plays a major role in the pathogenesis of type 2 diabetes mellitus. Free radicals are formed excessively in diabetes due to glucose oxidation and non-enzymatic protein glycation⁷.

Elevated free radicals levels and the decreased of antioxidant protective mechanism lead to increase the lipid peroxidation products in diabetic patients which have special interest because of their hyperlipidemia is considered to be significant risk factor for the development of vascular complications²².

MDA is an end marker of lipid oxidation processes²⁴. We found that MDA levels, which are the most important marker of oxidative stress were increased significantly in all patients with diabetes mellitus. Oxidative stress occurs in patients with diabetes mellitus due to the alteration of redox status, ROS overproduction, and dysfunction of main antioxidant enzymes. The first ROS generated is a superoxide anion which involves SOD to produce the hydrogen peroxide (H₂O₂), which in turn can act as an activator of the next antioxidant defense system CAT^{25,26}. Endogenous enzymatic antioxidants CAT and SOD act as reducing agents and detoxified highly reactive oxygen and nitrogen species, we found decreased in the activity and this result was agreed with Alghazeer et al (2018)²⁷. SOD catalyzes the superoxide to oxygen and hydrogen peroxide by reduction. Also SOD can be used to prevent the destruction consequences

of hyperglycemia –induced ROS production in patients of diabetes mellitus²³. CAT play important role in conversion of hydrogen peroxide to water and oxygen, therefore protect the cells from damage. Both of SOD and CAT decreased significantly in our study and this result was corresponding with many studies^{6,21}. GPX is the first antioxidant enzyme involved with preventing the aggregation of hydrogen peroxide in the cells, and play a role in converts hydrogen peroxide to water. GSH is oxidized by lipid peroxidase under the influence of GPX. GSH may serve a purpose in detoxifying lipid peroxides⁵. Diabetes induces alternation in activity of both enzymes GPX and GSH as we reports in our results which were parallel with^{6,8}.

HbA1c is the indicator of type2 diabetes mellitus and the main proved predictor of complications. The high glucose levels impair the free radicals metabolism and this confirms our result of the significant differences of antioxidant enzymes activity⁸.

Conclusion

The Diabetes mellitus change the oxidative status and it is clearly affected the endogenous antioxidant status in patients with T2DM. T2DM patients have a high risk of experiencing micro and macrovascular complications. In addition to the combination of diet, exercise and medication can improve the level of HbA1c for the patients with type2 DM.. Further studies should be conducted to strengthen this evidence.

Ethical Clearance: Ethical clearance taken from Iraqi University.

Funding Source: Self

Conflict of Interest: Nil

References

1. Georg P., Ludvik B. Lipids and diabetes. *J. Clin. Basic Cardiol.* 2000;3:159–162.
2. Nyholm B, Pørksen N, Juhl CB, Gravholt CH, Butler PC, Weeke J, Veldhuis JD, Pincus S, Schmitz O. Assessment of insulin secretion in relatives of patients with type 2 (non-insulin-dependent) diabetes mellitus: evidence of early beta-cell dysfunction. *Metabolism.* 2000;49(7):896-905.
3. Mandave P., Khadke S., Karandikar M., Pandit V., Ranjekar P., Kuvalekar A., Mantri N. Antidiabetic, Lipid Normalizing, and Nephroprotective Actions

- of the Strawberry: A Potent Supplementary Fruit. *Int J Mol Sci.* 2017;18(1):124.
4. Yajnik CS. The insulin resistance epidemic in India: fetal origins, later lifestyle, or both? *Nutr Rev.* 2001;59(1):1-9
 5. Badalzadeh R, Chodari L, Ghorbanzadeh V. Troxerutin, a bioflavonoid, improves oxidative stress in blood of streptozotocin-induced type-1 diabetic rats. *IJPS* 2017;13:75-86
 6. Maria E.B, Fernanda S.T, Antonio M.M, Helena H.B, Astrid.W, Ternando F-L, Roberto P. Antioxidant effect of vitamin in type 2 diabetes: a meta-analysis of randomized controlled trails. *Diabetol Metab Syndr*, 2018;10:18-30.
 7. Ighodaro OM, Akinloye OA. First line defence antioxidants-superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX): Their fundamental role in the entire antioxidant defence grid. *Alex J Med* 2017;53:1-7
 8. Dara.K, Skyarolla H, Maksymets T. Influence of HbA1c on nitric oxide level in patients with type 2 diabetes mellitus .*J. Global diabetes & clinical metabolism*, 2017;2(4):23-25.
 9. Bansal AK, Bilaspuri GS. Impacts of oxidative stress and antioxidants on semen functions. *Vet Med Int* 2011;2011:1-7.
 10. Khan AN, Khan RA, Ahmad M. Role of antioxidant in oxidative stress and diabetes mellitus. *J Pharmacogn Phytochem* 2015;3:217-20.
 11. Srivastava S, Singh D, Patel S, Singh MR. Role of enzymatic free radical scavengers in management of oxidative stress in autoimmune disorders. *Int J Biol Macromol* 2017;101:502-517.
 12. Halliwell B. The wanderings of a free radical. *Free Radic Biol Med* 2009;46:531-42.
 13. Dave GS, Kalia K. Hyperglycemia induced oxidative stress in type-1 and type-2 diabetic patients with and without nephropathy. *Cell Mol Biol (Noisy-le-grand)* 2007;53:68-78.
 14. Ngaski A. Correlation of antioxidants enzymes activity with fasting blood glucose in diabetic patients in Sokoto, Nigeria. *J Adv Med Med Res* 2018;25:1-6.
 15. Alghobashy AA, Alkholy UM, Talat MA, Abdalmonem N, Zaki A, Ahmed IA, Mohamed RH. Trace elements and oxidative stress in children with type 1 diabetes mellitus. *Diabetes Metab Syndr Obes* 2018;11:85-92.
 16. Mylona-Karayanni C, Gourgiotis D, Bossios A, Kamper EF. Oxidative stress and adhesion molecules in children with type 1 diabetes mellitus: A possible link. *Pediatr Diabetes* 2006;7:51-9.
 17. Zhang YT, Zheng QS, Pan J, Zheng RL. Oxidative damage of biomolecules in mouse liver induced by morphine and protected by antioxidants. *Basic Clin Pharmacol Toxicol* 2004;95:53-8.
 18. Sinha AK. Colorimetric assay of catalase. *Anal Biochem* 1972;47:389-94.
 19. Hafeman DG, Sunde RA, Hoekstra WG. Effect of dietary selenium on erythrocyte and liver glutathione peroxidase in the rat. *J Nutr* 1974;104:580-7.
 20. Ellman GL. Tissue sulfhydryl groups. *Arch Biochem Biophys* 1959;82:70-7.
 21. Araujo.A.J, Jesus-Lima J, Otoch J.P, and Pessoa A.F. Effect of ginger (*Zingiber officinale*) supplementation on diabetes: an update. *American J of Phytomedicine and clinical therapeutics*, 2018,6(3):13-33.
 22. Karam I, Ma N, Liu XW, Li SH, Kong XJ, Li JY, Yang YJ. Regulation effect of aspirin eugenol ester on blood lipids in Wistar rats with hyperlipidemia. *BMC Vet Res* 2015;11:217.
 23. Lubos E, Loscalzo J, Handy DE. Glutathione peroxidase-1 in health and disease: From molecular mechanisms to therapeutic opportunities. *Antioxid Redox Signal* 2011;15:1957-97.
 24. Khaled S, Mottar RR. Effect of traditional plant medicines (*cinammum zeylanicum* and *syzygium cumini*) on oxidative stress and insulin resistance in streptozotocin –induce diabetic rats. *J Basic Applied Zoology*, 2015,72:126-134.
 25. Ceriello A, Testa R, Genovese S. Clinical implications of oxidative stress and potential role of natural antioxidants in diabetic vascular complications. *Nutr Metab Cardiovasc Dis.* 2016;26(4):285–92.
 26. Natalia K, Alina.S, Sultana.K, Pawel J. WMelatonin restores white blood cell count diminishes glycated hemoglobin level and prevents liver, kidney, and muscle oxidative stress in mice exposed to acute ethanol intoxication. *J.Alcohol and Alcoholism* 2017,52(5):521-528.
 27. Alghazeer R, Nadia Alghazir, Nuri A, Obyda A, and Sana. Biomarkers of oxidative stress and antioxidants defense in patients with type1 diabetes mellitus, *IJMBS*,2018,10:198-204.

A Three-Years Survival Rates of Chronic Myeloid Leukemia Patients with Targeted Therapy

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Abstract

Background: Chronic myeloid leukemia (CML) is a hematopoietic stem cell cancer driven by the BCR-ABL fusion protein that arises from the translocation of chromosomes 9 and 22. Since the found of the Tyrosine Kinase Inhibitor (TKI) as a targeted therapy, the relative survival rate of 5 years has significantly increased compared to the era of the use of previous agents. As a successful leukemia treatment, it can be seen based on the survival rate. Several factors have been known to influence the survival and prognosis of CML patients, including the age of the patient at diagnosis, gender, and response to therapy and treatment. This study aims to determine how many a three-year survival rates for CML patients with targeted therapy in Makassar and the factors that affect survival.

Method: This study used a retrospective cohort using secondary data (medical records) of CML subjects who had been outpatient or inpatient followed in the same time period. The study was conducted in January 2015 to December 2017 at Dr. Wahidin Sudirohusodo Hospital, Makassar. The samples consisted of 108 subjects who met the inclusion criteria. Gender, age, BCR-ABL transcript, targeted therapy and status were taken from medical records. Data were analyzed with SPSS 22.0 version and survival analysis, Meier Kaplan curves, survival median, log-rank and test statistic

Results: There were 108 subjects of CML patients who received targeted therapy, 58 male (53.7%), 30-39 years old 32 subjects (29.6%), b3a2 transcript 67 subjects (73.6%), Imanitib 62 subjects (57.4%) and status for 36 months was followed during the targeted treatment of dead 19 subjects (17.6%) and alive 89 (82.4%). The survival rate of a three years CML subjects who received targeted therapy of 51%, found no significant relationship between gender, age, and targeted therapy

Conclusion: The survival rate of three years of CML patients at Wahidin Sudirohusodo Makassar Hospital is 51% and factors related to age, gender, and targeted therapy tend to influence even though statistically not significant

Keywords: *Three-year survival, CML, targeted therapy.*

Background

Chronic myeloid leukemia (CML) is a hematopoietic stem cell cancer driven by the BCR-ABL fusion protein that arises from the translocation of chromosomes 9 and 22. ⁽¹⁾ The conjugation of the breakpoint cluster region (Bcr) gene on chromosome 22 and the Abelson kinase (Abl) gene on chromosome 9 creates the Bcr-Abl oncogene, which encodes the deregulation of tyrosine

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kinase. Bcr-Abl activity will create uncontrolled cell proliferation and reduce apoptosis, thereby it will increase malignant expansion of pluripotent stem cells in the bone marrow.^(2,3)

Data on CML in Indonesia in 2018 obtained as many as 2,374 patients, most in Surabaya as many as 516, while at least, in Banda Aceh as many as 40, and in Makassar as many as 110. The median age for CML event is 45-55 years old and the event will increase with age.⁽⁴⁾

By recognizing the molecular basis of CML, a highly effective targeted therapy has been developed. This therapeutic agent will block the activity of the tyrosine kinase inhibitor (TKI) of Bcr-Abl in which will inhibit the course of the CML molecular process. Since the found of the Tyrosine Kinase Inhibitor (TKI), the relative survival rate of 5 years is much increased compared to the era of the use of the previous agent. The first generation of Tyrosine Kinase Inhibitor, Imatinib Mesylate was proven to provide excellent clinical outcomes. In Indonesia, the use of TKI has been applied to CML patients and has reached the use of the second generation namely Nilotinib (Tasigna). The comparison of the survival of the two target therapy was reported in the ENESTnd study (Evaluating Nilotinib Efficacy and Safety in Clinical Trial-Newly Diagnosed Patients) where from the 5-year follow-up of patients with nilotinib 300 mg of 93.7%; nilotinib 400 mg by 96.2% and Imatinib 400 mg by 91.7% did not show a significant difference between the two. However there were differences in death due to progression from CML, namely 16 Imatinib death 93.8% while 6 Nilotinib death 97.7%.⁽⁵⁾ The survival of CML patients with imatinib in 2006 reported by Drukker, et al. stated an overall survival of 89% after five years.⁽⁶⁾

As a successful leukemia treatment, it can be seen based on the survival rate.. In leukemia patients, using a five year survival rate. This was study carried out for three years as in the second or third year the patient level of compliance sometimes begins to decrease because they felt healed. Several factors that have been known to affect the survival and prognosis of CML patients include the patient's age at diagnosis, gender, and response to therapy and treatment. Nowadays there is no data of survival rates of CML with targeted therapy in Makassar, therefore we are conducting this research.

Method

This study used a retrospective cohort using secondary data (medical records) of CML subjects who had been outpatient or inpatient followed in the same time period. The study was conducted in January 2015 to December 2017 at Dr. Wahidin Sudirohusodo Hospital in Makassar. Samples were CML patients who met the inclusion criteria included (1) CML patients based on BMP (2) positive BCR-Abl (3) age ≥ 18 years (4) willing to join the study. Exclusion criteria (1) Patient cannot be contacted either by telephone (2) Incomplete data. The minimum number needed is 61 research subjects. Sampling was carried out consecutively during the study period until the desired number of samples was reached. Furthermore, Data were analyzed with SPSS 22.0 version and survival analysis, Meier Kaplan curves, survival median, log-rank and test statistic.

Results

From this research, subject studied was 108 CML patients with target therapy, consisted of 58 male (53.7%) and 50 female (46.3%). Age of the subjects were 30-39 years is 32 (29.6%). Bcr-abl transcripts of the subjects is b3a2 with 67 subjects (73.6%), 22 subjects (24.2%) b2a2, and 1 subject (1.1%) c3a2 and e1a3 respectively. Subjects receiving targeted therapy were imatinib 62 subjects (57.4%) and nilotinib 46 subjects (42.6%). The last status during the administration of target therapy is dead 19 subjects (17.6%) and alive 89 (82.4%). It can be seen in table 1.

Table 1: Distribution of Sample Characteristic (n=108)

Variable		n	%
Gender	Male	58	53,7
	Female	50	46,3
Age	<30 years	24	22,2
	30-39 years	32	29,6
	40-49 years	26	24,1
	50-59 years	16	14,8
	≥60 years	10	9,3
BCR-ABL Transcript	b2a2	22	24,2
	b3a2	67	73,6
	c3a2	1	1,1
	e1a3	1	1,1
Targeted therapy	Imatinib	62	57,4
	Nilotinib	46	42,6
Status	Dead	19	17,6
	Alive	89	82,4

Three-year survival rate for CML patients with targeted therapy, an analysis using the life table-Wilcoxon (Gehan) method was obtained, and a one-year survival rate (99%), a two-year survival rate (93%) and a three-year survival rate (51%) (table 2).

Table 2: A Three-Year Survival Analysis of CML Patients

Time Interval (Month)	n	Survival (%)
0	108	100
3	108	100
6	106	99
9	98	99
12	91	99
15	89	98
18	88	97
21	81	97
24	77	93
27	67	91
30	61	85
33	42	85
36	32	51

Figure 1 shows the probability of survival at each 3-month interval in the Kaplan-Meier curve. The duration of follow-up of all patients is from 5 to 102 months with a mean of 30.4±16.3 months.

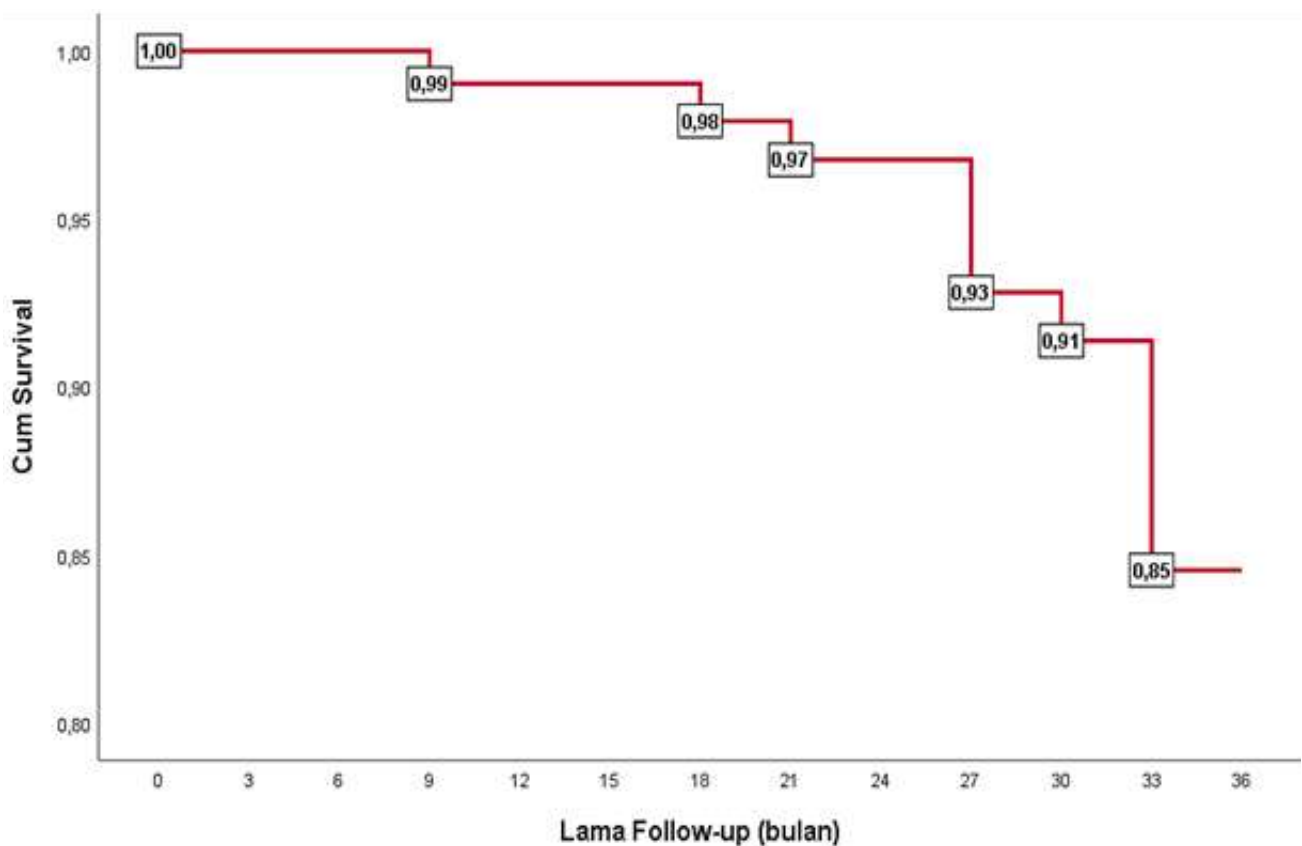


Figure 1: Kaplan-meier Curves of Three-year Survival Probability

Table 3. Three Years Survival of CML Patients by gender

Gender	n	Survival Estimation		p
		Mean (Month)	%	
Male	58	34,6	43	0,856
Female	50	34,2	57	

Table 3 shows that survival in female is higher than in male, which is 57% and 43% (34.2-34.6 month), but statistically not significant ($p > 0.05$).

Table 4. Three Years Survival of CML Patients by Age

Age (Years old)	n	Survival Estimation		p
		Mean (month)	%	
<30	24	34,5	73	0,631
30-39	32	34,9	64	
40-49	26	34,4	54	
50-59	16	34,1	37	
>=60	10	33,8	29	

Table 4 also shows a decrease with increasing age, but not statistically significant ($p > 0.05$). The highest survival occurred at age <30 years (73%) and the lowest was at age ≥ 60 years (29%).

In general, survival in the two treatment targets was not found to be statistically significant difference ($p > 0.05$) (table 5).

Table 5: Three Years Survival of CML Patients by Targeted Therapy

Targeted therapy	n	Survival Estimation		p
		Mean (Month)	%	
Imatinib	62	34,3	52	0,849
Nilotinib	46	34,7	47	

Table 5 also show imatinib gives the highest survival rate (52%) compared to nilotinib (47%). The mean survival rate is also not much different, namely 34.3-34.7 months.

Discussion

This study found that the subjects studied was 108 CML subjects. Most of the subjects were male: 58 (53.7%) and 50 female (46.3%). This result is in line with research conducted by Reksodiputro et. al. in 2011 in Jakarta, where 19 reported samples were studied, slightly dominant in males than females at 63.2%.⁽⁷⁾ Several overseas studies conducted by Hofmann in 2015 reported that CML patients were more frequent in male than female.⁽⁸⁾ Research was also supported by SEER (Surveillance, Epidemiology, and End Results) USA which stated that of all race, the ratio of male and female from CML is 2.2:1.3.⁽⁹⁾

Age range between 18-72 years old with an average of 39.8±13.1 years old. Research conducted by Reksodiputro et. al. in 2011 where the age of CML patients was in the age range of 13-62 years.⁽⁷⁾ It is different from American Cancer Society data that CML cases in the United States in 2019, the average age at diagnosis of CML is around 64 years. Nearly half of the cases are diagnosed in people aged 65 and older.⁽¹⁰⁾

The duration of follow-up of all patients is from 5 to 102 months with a mean of 30.4±16.3 months. In this study, a one-year survival rate of 99%, a two-year survival rate of 93% and a three-year survival rate of 51% (table 2 and figure 1). This study carried out for three years because, in the second and third years, the patient level of adherence in treatment slowly decreased, where patients sometimes seemed to have felt healed with the disease they experienced. In a study conducted

by Di Felice et. al. in 2018 in Italy, 357 subjects reported having CML after being given TKI, survivability for one year (from 83.3, 95% CI 76.2-88.5% to 91%, 95% CI 86.5-94.4%) and survival for three years (from 60.4, 95% CI 51.7- 68% to 84.5%, 95% CI 79-89%).⁽¹¹⁾

Survival rate for female was higher at 57% and for male 43%, with a mean survival rate at 34.2-34.6 months. But it did statistically not significant ($p > 0.05$) (table 3). Research by Berger et. al. in 2005 in Germany reported 856 subjects with Ph/BCR-ABL-positive CML in a randomized CML study, where the survival rate was average longer in female sufferers than in male with an average of 59-49 months and this also not significance.⁽¹²⁾

It is well known that age is a very important prognostic marker, and old age has several times been associated with poor survival. In this study, survival analysis according to age was found to be highest at age <30 years old (73%) and lowest at age ≥ 60 years old (29%). The decrease occurred with increasing age, but it was not statistically significant ($p > 0.05$) (table 4). Research by Castagnetti F et. al. in 2017 in Italy reported 337 CML patients, obtained OS was not affected by age in the interval between 18-69 years old (OS 5 years 92%, average from 89% to 95% in different decades), but the probability of OS 5 years for old age (≥ 80 years) was significantly lower (34%, $P < 0.0001$).⁽¹³⁾ Research by Di Felice et. al. in 2018 in Italy, reported survival by age was relatively decreased, age <65 years old (from 69%, 95% CI 55.3-79.5% to 94%, 95% CI 88.4-97.4%), age 65-74 years old (from 46%, 95% CI 30.8 -61.2% to 69%, 95% CI 52.5-80.4%) and age > 74 years old (from 8.05%, 95% CI 0.8-26.7% to 51, 2%, 95% CI 32.4-67.1%).⁽¹¹⁾ It can be assumed that relatively older ages have poor survival.

In general, the survival the Imatinib and Nilotinib, was not found to be statistically significant ($p > 0.05$). Imatinib highest survival rate (52%) compared to nilotinib (47%) with the mean survival rate also not much different, ie 34.3-34.7 months (table 5). The Food and Drug Administration (FDA) approved imatinib as the first-line treatment for newly diagnosed CML in December 2002 after the International Randomized Study (IRIS), which began in June 2000, the results of this study show the effectiveness of imatinib and its remarkable superiority with respect to complete haematological response rates (CHR), molekuler and complete cytogenetic responses (MCyR, CCyR) with an overall survival rate (OS) of 85% for patients receiving imatinib.⁽¹³⁾ This is different

from the ENESTnd study by Larson et. al. (2012) in the United States, which examined 868 subjects comparing nilotinib (300 mg and 400 mg doses respectively) with imatinib, estimated that the three-year survival rate was higher in nilotinib with imatinib is nilotinib 300 mg 95.1%, nilotinib 400 mg 97.0% and 94.0% for imatinib.⁽¹⁴⁾ While another study by Sanglio et. al. (2010) in Australia also found that nilotinib at a dose of 300 mg or 400 mg twice daily was better than imatinib in CML patients with newly diagnosed positive Philadelphia chromosomes.⁽¹⁵⁾ According to Au WY et. al. (2009), In general, Asian patients, the use of imatinib is still used as the first choice therapy for treating CML patients. Either from Asia, Europe or the United States for giving imatinib is generally giving a good response. Most health practitioners in Asia follow the guidelines found on ELN (European Leukemia Net) or NCCN (National Comprehensive Cancer Network). Based on the results of studies that have been collected regarding the response of CML patients to imatinib, in Europe and the United States shows a complete hematological response of more than 95%, while in Thailand, Philippines, India, China, Hong Kong and South Korea by 90-100%.⁽¹⁶⁾

This study carried out no dose distribution of nilotinib or imatinib and no further examination of the molecular response achieved which should be examined every year after administration of target therapy so that the results found were inadequate. Besides, various factors influencing the survival of the comparison between the two target therapy are not evaluated precisely such as adherence to take medication or how to take medication, cause of death and the presence or absence of a previous comorbid patient history.

Conclusion

Survival rate of three years of CML patients at Wahidin Sudirohusodo Hospital in Makassar was 51% and factors related to age, gender, and target therapy tended to influence even though it was not statistically significant.

Conflict of Interest: No Potential conflict of interest relevant to be declared

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Ethics Committee: It has been approved by the ethical committee of Hasanuddin University Faculty of Medicine with reference number: 429/UN4.6.4.5.31/PP36-KOMETIK/2019.

References

1. Faderl S, Talpaz M, Estrov Z, et al.. Chronic myelogenous leukemia : Biology and therapy. *Ann Intern Med.* 1999;131:207-219
2. Branford S, Rudzki Z, Hughes TP . A novel BCR-ABL transcript (e8a2) with the insertion of an inverted sequence of ABL intron 1b in a patient with Philadelphia-positive chronic myeloid leukaemia. *Br J Haematol.*2000; 109: 635-637.
3. Yuan H, Wang Z, Gao C, Chen W, Huang Q, et al. BCR-ABL gene expression is required for its mutations in a novel KCL-22 cell culture model for acquired resistance of chronic myelogenous leukemia. *J Biol Chem.*2010; 285: 5085-5096.
4. Reksodiputro, Arry Harryanto., Atmakusuma, et al. Chronic Myeloid Leukemia in Indonesia. 2018. Dharmais Hospital National Cancer Centre. DOI: 10.13140/RG.2.2.18070.24644
5. Hochhaus A, Saglio G, Hughes TP, et al. Long-term benefits and risks of frontline nilotinib vs imatinib for chronic myeloid leukemia in chronic phase: 5-year update of the randomized ENESTnd trial. *Leukemia.* 2016; 30(5):1044-1054
6. Druker BJ, Guihot F, O'Brien SG, et al. Five-Year Follow-up of Patients Receiving Imatinib for Chronic Myeloid Leukemia. *N Engl J Med.* 2006; 355:2408-2417
7. Reksodiputro A H, Tadjoeidin H, Rinaldi I.. Clinical Characteristic, Hematologic Response and Gene Mutation of Patients with Chronic Phase Chronic Myeloid Leukemia (CML) to Imatinib at Cipto Mangunkusumo National Hospital (RSUPN CM). *Depok: Indonesian Journal of Cancer.* 2011; 5(4): 419
8. Hofmann VS, Baccarani M, Hasford J, et al. THE EUTOS population-based registry: incidence and clinical characteristics of 2904 CML patients in 20 european countries. *Leukemia.* 2015; 29(6):1336-1343
9. Anonim. Surveillance, Epidemiology, and End Results Program Stat Fact Sheets: Leukemia. [Online] Tersedia di: <http://seer.cancer.gov/statfacts/html/leuks.html> diakses pada 18 September 2015
10. American Cancer Society. *Cancer Facts & Figures.* Atlanta. 2019
11. Di Felice enza, Francesca Roncaglia, Francesco Venturelli, et al.. The impact of introducing tyrosine kinase inhibitors on chronic myeloid leukemia survival: a population-based study. *BMC Cancer.* 2018;18:1069
12. Berger, O Maywald, M Pffirmann. Gender aspects in chronic myeloid leukemia: long-term results from randomized studies. *Leukemia.*2005;19; 984-989
13. Castagnetti F, Di Raimondo F, De Vivo A, et al. A population-based study of chronic myeloid leukemia patients treated with imatinib in first line. *Am J Hematol.* 2017; 92:82-87
14. Larson RA, Hochhaus A, Hughes TP,et al.. Nilotinib vs imatinib in patients with newly diagnosed Philadelphia chromosome-positive chronic myeloid leukemia in chronic phases : ENESTnd 3-year follow-up. *Leukemia.* 2012; 1-7
15. Sanglio G, DW kim, Issaragrisil S, et al. Nilotinib versus imatinib for newly diagnosed chronic myeloid leukemia. *N Engl J Med.*2010 Jun 17; 362(24):2251-2259
16. Au WY, Caguioa PB, Chuah C et al. Chronic Myeloid Leukemia in Asia. *Int J Hematol Springer.* 2009; 89:14-23

Gene Polymorphism of CSN1S1 and CSN3 Gene Associated with Casein Production Milk Trait in Iraqi Buffaloes (*Bubalus bubalis*)

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Abstract

Twenty-four blood samples of lactating Iraqi buffaloes were analyzed for the presence of CSN1S1 and CSN3 genes using two pair primers to amplify 314bp and 453bp DNA fragment, respectively. Most investigated samples showed the presence of the CSN1S1 gene. In contrast, all samples showed the presence of CSN3 gene. Sequence analysis of both CSN1S1 and CSN3 genes were analyzed using Blast algorithmic tool. The results showed that most of the investigated animals resemble those of the Middle East and Asian buffaloes at a percentage of 100%. Moreover, some of the investigated genes showed little differences than animals of the other countries by having polymorphism genes posing DNA mutations. Most mutations were either insertion or transition mutation and located between 10936-10938 region. In conclusion, the mutations occur in these genes, which play a role in milk productivity may face unflavored climate condition in the summer in the south of Iraq.

Keywords: Polymorphism, CSN1S1, CSN3, casein, milk, buffaloes.

Introduction

Domestic water buffalo (*Bubalus bubalis*) is an important milk source in many worldwide countries. About 185 million animals were found around the world⁽¹⁾. Buffalo is of great importance and superiority to domestic cattle due to its high capacity for climate changes, good nutritional benefits and disease resistance. Buffalo milk contains 7% fat, 16% solid not fat (lower phospholipids and cholesterol levels, and a higher saturated fatty acid ratio⁽²⁾). For best animal production, genotype selection of the animals must be used according to their productivity⁽³⁾. Animals have a high ability for genetic improvement in the production of milk and meat⁽⁴⁾. As in other bovines, buffalo milk is having four types of casein, α S1, α S2, β and π casein. They are under control of CSN1S1, CSN2, CSN1S2, and CSN3 genes. The most dominant one is β (53.45%), followed by α S1, α S2 and π at 20.61%, 14.28% and 11.66%, respectively⁽⁵⁾. Casein proteins are high in an essential amino acid such as lysine which is not found in many plant sources⁽⁶⁾. They also have a high concentration of phosphate that

compound which allows high amounts of calcium to bind to casein⁽⁷⁾. The purpose of this work was to characterize the genetic polymorphism of the CSN1S1 and CSN3 gene in the Iraqi buffaloes.

Materials and Method

Animals and sample collection: A total of 24 blood samples were collected from healthy lactating Iraqi buffaloes (*Bubalus bubalis*) from different farms of Basrah governorate.

DNA Extraction and Primers: Whole blood of buffalo was used for DNA extraction by ReliaPrep™ Blood gDNA Miniprep System. The primers used for CSN1S1 amplification were previously used (Chessa et al., 2007), with a fragment length of 314bp.

F: TGGATGCCTATCCATCTGG

R: CACTGCTCCACATGTTCTG.

The primers used for CSN3 amplification with 453bp fragment were described by⁽⁸⁾ and have been

used by ⁽⁹⁾. The 453bp fragment of CSN3 covers most of the exon IV coding region ⁽¹⁰⁾. They have the following nucleotide sequences:

F: 5'-3'TGTGCTGAGTAGGTATCCTAGTTATGG;

R: 5'-3'GCGTTGTCTTCTTTGATGTCTCCTT

Polymerase Chain Reaction: The PCR reaction contained (25µl) including 5 µl of DNA. The following conditions were used for CSN1S1 gene: initial denaturation for 5 min. at 94 °C; 35 cycles of denaturation for 1 min at 94 °C; annealing for 45 s at 60 °C; elongation for 80 s at 68–72 °C and a final extension for 7 min. at 72 °C. While the following cycling conditions were used for CSN3 gene: initial denaturation for 3 min. at 94 °C; 35 cycles of denaturation for 1 min at 94 °C; annealing for 45 s at 60 °C; elongation for 80 s at 72 °C and a final extension for 10 min at 72 °C.

The PCR reaction products were electrophoresed on 1.5% agarose gel stained with ethidium bromide to test the amplification success. Agarose gel was run at 75 V for 4 hrs. Gels were examined and photographed under

UV illumination (E - graph – ATTO -Japan). Fragment size of approximately 314bp and 453bp was verified as positive for CSN1S1 and CSN3 genes, respectively. A 100bp DNA ladder (Bioneer, Korea) was used as a molecular size standard.

DNA Sequencing: Purification of PCR products were done by using GeneJET™ PCR Purification Kit (Fermentas #K0701). The product then sequenced by Bioneer ABI 3730XL DNA analyzer. Blast analysis was done using Blast directory of the NCBI at (<https://blast.ncbi.nlm.nih.gov/Blast.cgi>).

Results

Twenty-four lactating Iraqi buffaloes were analyzed for the presence of CSN1S1 and CSN3 genes using two pairs of primers for the amplification of 314bp and 453bp DNA fragment, respectively.

PCR results of CSN1S1 gene: The fragment size of approximately ~314bp was verified as positive for CSN1S1 gene. Most investigated samples showed the presence of this gene (Fig. 1).

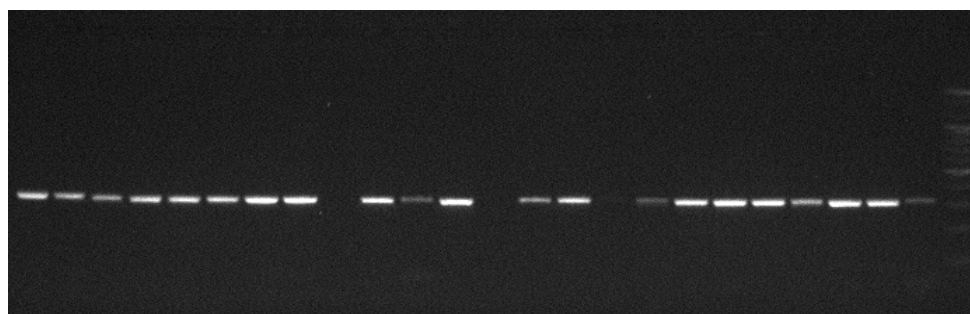


Figure 1: Agarose gel electrophoresis showing the presence of 314bp CSN1S1 gene in blood samples of Bubalus bubalis.

PCR results of CSN3 gene: Fragment size of approximately 453bp was verified as positive for CSN3 genes. All investigated samples showed the presence of this gene (Fig 2).

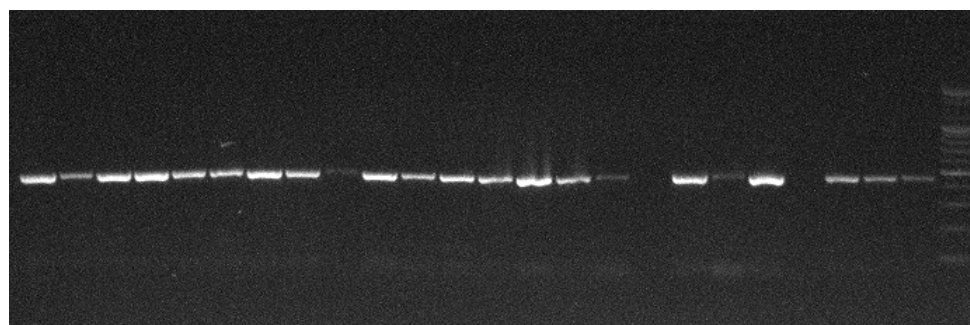


Figure 2: Agarose gel electrophoresis showing the presence of 453bp CSN3 gene in blood samples of Bubalus bubalis.

Sequencing Results: Sequence analysis of both CSN1S1 and CSN3 genes were analyzed using Blast algorithmic tool. The results showed that most of the investigated animals resembled those of the Middle East and Asian buffaloes at a percentage of 100%. Moreover, some of the investigated genes showed little differences than animals from other countries by having polymorphism genes posing DNA mutations.

Sequencing results of CSN1S1 gene: Results of sequencing of this gene showed 100% identity with Egyptian animal with accession numbers KC577235.1 and JQ670674.1. Only two strains showed insertion mutation at location 67 (Table 1).

Table 1: Results of sequencing of CSN1S1 gene

Source	Identities	GenBank	Nucleotide	Location	Mutation	Sample No.
B.bubalis Egypt	100%	KC577235.1	-	--	-	S2, S3, S6,S13, S15,S17-S23
B.bubalis Egypt	99%	JQ670674.1	- >G	67	Insertion	S4
B.bubalis Egypt	100%	JQ670674.1	-	-	-	S5
B. bubalis Egypt	99%	KC577235.1	- >C	67	Insertion	S7

Sequencing results of CSN3 gene: The results of sequencing of this gene were listed in table 2. The comparison was done with the most resembled Indonesian animals of Bubalus bubalis with accession number MF679163.1. Most investigated samples

showed 100% identity whereas five samples showed variable sequence having one or more mutations. Most mutations were either insertion or transition mutation and located between 10936-10938 regions.

Table 2: Results of sequencing of CSN3 gene

Source	Identities	GenBank	Nucleotide	Location	Type of mutation	No. of sample
B.bubalis Indonesia	100%	MF679163.1	-	--	-	N3,N5, N7,N10, N11,N14
B.bubalis Indonesia	99%	MF679163.1	T>C	11131	Transition	N12
B.bubalis Indonesia	99%	MF679163.1	- >C G>A	10936 10937	Insertion Transition	N13
B.bubalis Indonesia	99%	MF679163.1	- >A	10894	Insertion	N15
B. bubalis Indonesia	99%	MF679163.1	- >A - >A	10894 10938	Insertion Insertion	N17
B.bubalis Indonesia	100%	MF679163.1	-	--	-	N18,N20, N21,N22
B.bubalis Indonesia	99%	MF679163.1	- >C G>A	10937 10938	Insertion Transition	N19

Phylogenetic tree of the sequenced results showed that both genes (CSN3 and CSN1S1) of local animal are closely related to those previously registered in GenBank from Egypt, Brazil, India, China and Indonesia (Figure 3, A & B).

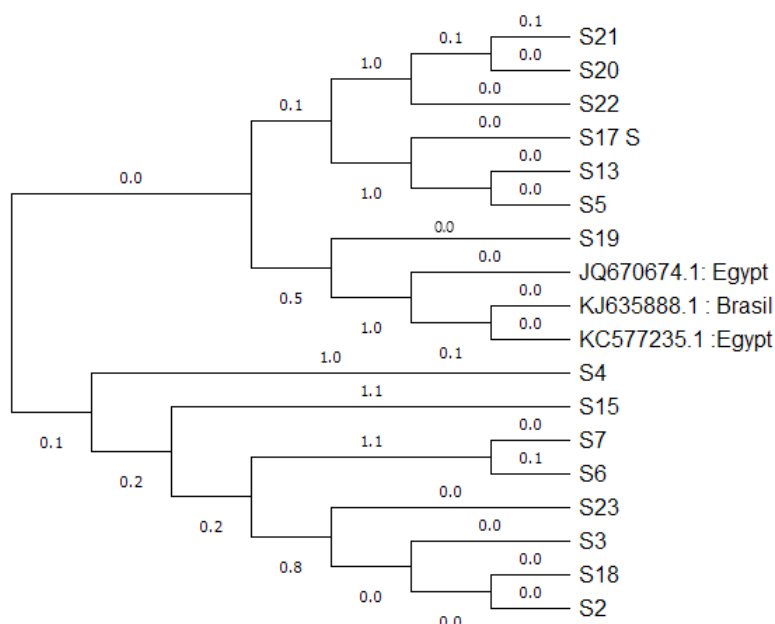


Figure 3: The neighboring phylogenetic tree of A= CSN3; B= CSN1S1 genes of local animal compared with that previously registered at GenBank from different countries.

Discussion

In order to select more efficient breeding of farm animals there is an interest in applying genetics technology of specific gene markers associated with productivity characteristics (Spelman et al., 1998). In order to improve animal characteristics and productivity, animals should be selected periodically based on the genotype that reflects their productivity and national economy⁽¹¹⁾. CSN1S1 Polymorphism and CSN3 exon IV have not been previously investigated in Iraqi buffaloes. In this study, for the first time we report here, sequence analysis in 24 unrelated Iraqi buffaloes lactating has characterized CSN1S1 Polymorphism and CSN3 exon IV.

Several genes, including casein genes, control the milk trait. CSN1S1, CSN1S2, CSN2, and CSN3 are closely linked to four casein genes. They code α (S1) and α (S2), β , and κ casein, respectively. Approximately 80% of the total milk protein is kappa casein⁽¹²⁾ CSN1S1 gene sequencing results showed 100% identity with Egyptian animals.⁽¹³⁾ confirmed the monomorphism at 178Ser by analyzing Indian buffalo's full CSN1S1 mRNA (accession number: DQ111783). However, a different variant was detected at 192Glu (GAA) versus 192Gly (GGA). Variation of Glu/Gly was detected in bovine animals as investigated by⁽¹⁴⁾. The Mediterranean type belongs to the Egyptian and Italian

buffalo. Mediterranean buffalo appeared as descendant of Indian Murrah buffalo. The long isolation lead to development of some unique characteristics⁽¹⁵⁾. In this study, location 67 strains showed only two additional mutations. It was noted that there were two variants of CSN1S1 in buffalo from Egypt. The variation occurred in the CSN1S1 (178Ser (TCA)/178Leu (TTA) 178 mature protein codon and have been reported in Italian buffalo and referred to HE573920 and HE573919 by⁽¹⁶⁾. CSN3 gene sequencing results have been analyzed and most of the samples showed 100% identity with Bubalus bubalis Indonesian animals. Between the locations 10936-10938, there was a change in insertion or transition. Exon IV was involved in most of the CSN3 polymorphism. Exon IV mutations are responsible for gene expression differences⁽¹⁷⁾. The samples of animal blood were collected from buffaloes known for their high production of milk and meat. High temperatures, drought and high water salinity, unflavored climate conditions during the summer in the south of Iraq may result in increasing the prevalence of mutations in genes coding for high productivity and higher resistance of animals. Using nucleotide sequence analysis, CSN3 polymorphism has been investigated in buffalo over the past decade. Two variants of nucleotides in codons 135 Thr (ACC)/Ile(ATC) and 136Thr (ACC/ACT) (silent mutation) were reported in Italian⁽¹⁸⁾, Bulgarian⁽¹⁹⁾, and genomic library of water buffalo⁽²⁰⁾. Buffalo

polymorphism was investigated using the method of PCR–RFLP. BB monomorphic were mentioned in Egyptian buffalo⁽²¹⁾, in Pakistani buffalo⁽²²⁾, and in⁽²³⁾.

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Conflict of Interest: None

References

1. Abo-Al-Ela H.G. El-Magd, M.A. El-Nahas, A.F. & A.A. Mansour, Association of a novel SNP in exon 10 of the IGF2 gene with growth traits in Egyptian water buffalo (*Bubalus bubalis*). *Trop Anim Health Prod*, 2014, 46: 947-952.
2. Ahmad S., Anjum F.M. Huma N., Sameen A. & T. Zahoor, Composition and physico-chemical characteristics of Buffalo milk with particular emphasis on lipids, proteins, minerals, enzymes and vitamins. *The Journal of Animal and Plant Sciences*, 2013, 23: 62-74.
3. Azevedo, A.L.S., Nascimento, C.S., Steinberg, R.S., Carvalho, M.R.S., Peixoto, M.G.C.D., Teodoro, R.L., Verneque, R.S., Guimarães, S.E.F. & M.A. Machado, Genetic polymorphism of the kappa-casein gene in Brazilian cattle. *Genetics and Molecular Research*, 2008, 7(3):623–630.
4. Barroso, A., Dunner, S. & J. Canon, Detection of bovine kappa-casein variants A, B, C, and E by means of polymerase chain reaction-single strand conformation polymorphism (PCR-SSCP). *Journal of animal science*, 1998, 76(6):1535-1538.
5. Beneduci, B., Krastanov, I., Maretto, F., Oblakov, N. & M. Cassandro. Molecular characterization of k-casein allelic variants in Bulgarian buffalo breed. *Acta Agraria Kaposvariensis*, 2010 14(2):169-172.
6. Bonfatti, V., Giantin, M., Gervaso, M., Coletta, A., Dacasto, M. & P. Carnier. Effect of CSN1S1-CSN3 (α S1- κ -casein) composite genotype on milk production traits and milk coagulation properties in Mediterranean water buffalo. *Journal of dairy science*, 2012, 95(6):3435-3443.
7. Chessa, S., Chiatti, F., Ceriotti, G., Caroli, A., Consolandi, C., Pagnacco, G. & B. Castiglioni. Development of a single nucleotide polymorphism genotyping microarray platform for the identification of bovine milk protein genetic polymorphisms. *Journal of dairy science*, 2007, 90(1):451-464.
8. Cosenza, G., Pauciuolo, A., Coletta, A., Di Francia, A., Feligini, M., Gallo, D., Di Bernardino, D. & L. Ramunno, Translational efficiency of casein transcripts in Mediterranean river buffalo. *Journal of dairy science*, 2011, 94(11):5691-5694.
9. Das, P., Jain, S., Tiwari, G. & L.C. Garg. Rapid communication: nucleotide sequence of the river buffalo kappa-casein cDNA. *Journal of Animal Sciences*, 2000, 78(5):1389-1389.
10. Dayem, A.A., Mahmoud, K.G.M., Nawito, M.F., Ayoub, M.M. & S.F. Darwish, Genotyping of kappa-casein gene in Egyptian buffalo bulls. *Livestock science*, 2009, 122(2-3):286-289.
11. De Hondt, H.A. & S.M. El Nahas, Genetics and genomics mapping of the water buffalo *Bubalus bubalis* L., *Egyptian Journal of Veterinary Sciences*, 2001, 35:1–26.
12. DiStasio, L. & P. Mariani. The role of protein polymorphism in the genetic improvement of milk production, *Zootecnica e Nutrizione animale*, 2000, 26: 69–90.
13. El Nahas, S.M., Bibars, M.A., Taha, D.A. & H.I. El-Sayyad, Detection of two CSN1S1 variants in Egyptian buffalo. *Journal of Genetic Engineering and Biotechnology*, 2013a, 11(1):75-77.
14. El Nahas, S.M., Bibars, M.A. & D.A. Taha. Genetic characterization of Egyptian buffalo CSN3 gene. *Journal of Genetic Engineering and Biotechnology*, 2013, 11(2):123-127.
15. El-Magd, M.A., Abbas, H.E., El-Kattawy, A.M. & A. Mokhbatly. Novel polymorphisms of the IGF1R gene and their association with average daily gain in Egyptian buffalo (*Bubalus bubalis*). *Domestic animal endocrinology*, 2013, 45(2), pp.105-110.
16. El-Magd, M.A., Abo-Al-Ela, H.G., El-Nahas, A., Saleh, A.A. and A.A. Mansour. Effects of a novel SNP of IGF2R gene on growth traits and expression rate of IGF2R and IGF2 genes in gluteus medius muscle of Egyptian buffalo. *Gene*, 2014, 540(2):133-139.
17. FAO. 2008. <http://www.fao.org/home/en/.FFTC> (Food & Fertilizer Technology Center) Publication Database. Artificial reproductive biotechnologies for buffaloes. 2007 <http://www.agnet.org/>.

18. Fox P.F. & P.L.H. McSweeney. Dairy Chemistry and Biochemistry, Blackie Academic and Professional, London. 1998.
19. Gangaraj, D.R., Shetty, S., Govindaiah, M.G., Nagaraja, C.S., Byregowda, S.M. & M.R. Jayashankar. Molecular characterization of kappa-casein gene in buffaloes. *Sci. Asia*, 34:435-439.
20. Farrell Jr, H.M., Jimenez-Flores, R., Bleck, G.T., Brown, E.M., Butler, J.E., Creamer, L.K., Hicks, C.L., Hollar, C.M., Ng-Kwai-Hang, K.F. & H.E. Swaisgood. Nomenclature of the proteins of cows' milk—Sixth revision. *Journal of dairy science*, 2004, 87(6):1641-1674.
21. Cosenza, G., Pauciullo, A., Macciotta, N.P.P., Apicella, E., Steri, R., La Battaglia, A., Jemma, L., Coletta, A., Di Berardino, D. & L. Ramunno. Mediterranean river buffalo CSN1S1 gene: search for polymorphisms and association studies. *Animal Production Science*, 2015, 55(5):654-660.
22. Mahmoud, K.G.M., Nawito, M.F. & A.M.H. Dayem. Sire selection for milk production traits with special emphasis on kappa casein (CSN3) gene. *Global J. Mol. Sci*, 2010, 5(2):68-73.
23. Masina, P., Rando, A., Di Gregorio, P., Cosenza, G. & A. Mancusi. Water buffalo kappa-casein gene sequence. *Italian Journal of Animal Science*, 2010, 6(2s):353-355.

In Vitro Evaluation of Antibacterial Effect of a New Bioactive Restorative Material (Activa)

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Abstract

Aim: Evaluation in vitro the antibacterial effect of new bioactive composite restorative material (Activa) in comparison to two different bioactive materials on *Streptococcus mutans*, and *Lactobacillus acidophilus*.

Materials and Method: Three types of bioactive restorative materials were used. The materials used in this study were Bioactive composite Activabioactive composite (A1), FUJI II LCCapsules (A2) and Fuji IX Extra Capsules (A3). Each restorative material were manipulated in accordance with manufacturer's guidelines and embedded in wells made-up in plates of trypticase soy agar seeded with *Streptococcus mutans* (B1) and Lactobacillus MRS agar seeded with *Lactobacillus acidophilus* (B2). The antibacterial activity was evaluated by using a caliper to measure the diameter of growth inhibition zones after 1 day, 1 week, 2 weeks and 3 weeks.

Results: The results of the tested materials were collected, statistically analyzed using the ANOVA test to determine the difference between the mean diameters of the inhibition zone produced. The results indicate that Fuji IX had higher antibacterial effects in comparison with the other Activa Bioactive materials and Fuji II LC.

Conclusion: All three different bioactive materials promoted growth inhibition of the cariogenic bacteria assayed. Fuji IX glass-ionomer showed the highest efficacy and durability against the tested strains.

Keywords: Bioactive restorative materials; Glass-ionomers; *Streptococcus mutans*; *Lactobacillus acidophilus*; Agar diffusion test; Inhibition zone.

Introduction

Dental caries is one of the most common diseases and public health problems that affect human beings negatively which started with infection by cariogenic bacteria, leading to acid production as a result of the bacterial carbohydrates metabolism within the oral biofilm. *Streptococcus mutans* is a Gram-positive bacterium that is the primary causative agent in the

formation of dental cavities in humans and animals. *Lactobacillus acidophilus* is the principal bacteria related to caries progression and is responsible for the formation of secondary caries. [1]

The treatment of dental cavities does not always eliminate all microorganisms from the caries focus by therapeutic procedures. The presence of bacteria in dental tissue left behind or bacterial invasion through a micro-leakage between the tooth and the filling lead to secondary caries. It is the most frequent indication for replacement of all types of restoration and the limited durability of dental restorations.

One of the ways of controlling cariogenic activity was to reduce the number of such microorganisms in

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dental biofilm through the use of antimicrobial agents that can alter its composition and to be resistant to secondary caries and to micro-leakage at the edges, properties they possess on account of their ability to release fluoride and to be bonded to the prepared tooth surface. [2,3]

Modern approach to control dental caries requires dental materials that possess both restorative and anticariogenic characteristics. Fluoride is well documented as an anticariogenic agent. Its role includes reduction of demineralization, enhancement of remineralization, interference of pellicle and plaque formation and inhibition of microbial growth and metabolism.

Glass-ionomers (GIC) are considered to be the conventional restorative materials that are bioactive with heaps of uses in all restorative techniques. But their sensitivity to moistness is one of their main drawbacks. Changes in their structures have been made to overcome this defect. The resin modified glass ionomer (RMGI) materials appear to have considerable benefits, keeping the benefits of fluoride release and adhesion. [4]

Bioactive product is the first dental resins with a bioactive ionic resin matrix, shock-absorbing rubberized resin component, and reactive ionomer glass fillers that mimic the physical and chemical properties of natural teeth. These bioactive materials actively participate in the cycles of ionic exchange that regulate the natural chemistry of teeth and saliva and contribute to the maintenance of tooth structure and oral health.

Activabioactive (Pulpdent MA, USA) restorative materials are ionic composite resins which combine the biocompatibility, chemical bond and the ability to release fluoride of GIC with the mechanical properties, aesthetic and durability of resin based composite. [1]

This study was conducted to evaluate the antibacterial effect of bioactive composite against *Streptococcus mutans* and *lacto-bacilli* in comparison to two different bioactive materials.

Aim of the study: The purpose of this study was to evaluate the antibacterial effect of active bioactive composite in comparison to two bioactive restorative materials; conventional glass-ionomer and resin-modified glass-ionomer after 1 day, 1 week, 2 weeks and 3 weeks.

Subject and method: Three types of bioactive restorative materials were used. The materials used in this

study were Bioactive composite (ACTIVA BioACTIVE restorative)(Pulpdent Corporation, Watertown, MA, USA) (A1), a restorative Resin modified glass- ionomer (FUJI II LC)(GC corporation, Tokyo, Japan) Capsules (A2) and Conventional glass- ionomer (Fuji IX Extra) GC corporation, Tokyo, Japan) Capsules (A3).

Thirty discs from each of restorative materials were made. Each group was further sub divided into to 2 sub group; 15 discs for streptococcus-mutans (B1) and 15 discs for lactobacillus (B2). Capsules (A2, A3) were activated and mixed mechanically for 10 seconds using a Silamat device (Vivadent, Schaan, Liechtenstein).

The material was then injected in a mold. Each specimen was prepared by packing each mix into a split Teflon ring with a central hole having dimensions (10mm in diameter X 2mm in thickness) to standardize the dimensions of each tested specimen. The split Teflon mold was encircled with a copper ring to stabilize the mold during specimen preparation.

Each mold was placed on the top of a microscope glass slide and a Mylar strip. Each mold was then filled with the each tested material and second Mylar strip was used to cover the top side of the mold and another microscope glass slide was applied over it. Hand pressure was applied to insure no air was trapped and an excess material was removed.

The self-cured glass- ionomers Fuji IX (A3) was allowed to set before their removal from the mold. While in the mold, the light-cured material; Fuji II LC (A2) was cured with a 40-second exposure of each flat surface to a visible light source by using a light-emitting diode (LED) light cure unit (Demi, Kerr).

Activa Bioactive Restorative (A1) samples were made by light-curing 2 mm thickness of the material for 20 seconds from both sides as the manufacturer instructed. Specimens were removed from their molds and then rechecked for their diameter and thickness using a digital caliper. [9,10]

Agar Diffusion Testing: The antibacterial activity was evaluated against *Streptococcus mutans* ATCC® 25175™ and *Lactobacillus acidophilus* ATCC® 314™ (Microbiologics®, Lyophilized microorganisms, USA) using the agar diffusion test.

Each bacterial strain from stock cultures were cultivated overnight in specific culture media: Trypticase-soy agar for *Strep. mutans* (Becton Dickinson

Microbiology systems, Cockeysville, MD21030, USA) and Lactobacillus MRS agar for *L.acidophilus* (Himedia laboratories PV, 23 Vadhani India, Est., LBS Marg., Mumbai, India) after incubation for 24h for *Strep. mutans* and 48h for *L. acidophilus* in incubator (Gallenkamp cooled incubator, IR211GAmode, Pinal way, Loughborough, England) at $37^{\circ}\text{c} \pm 1^{\circ}\text{c}$, Two or three discrete representative overnight colonies of each tested strain were inoculated into 2 ml sterile saline and diluted to obtain a turbidity equal to 107 CFU/ml equivalent to 0.5 McFarland turbidity standard solution (About 9.95 ml of solution A (1% (V/V) of sulfuric acid) was mixed with 0.05 ml of solution B (1.175% (W/V) aqueous solution of barium chloride dehydrate) slowly and with constant agitation in a clear glass test tube.

The tube was sealed and stored in the dark at room temperature)] Petri dishes (15 cm diameter) containing 30 ml agar to a thickness of 2 mm were seeded by 0.5 ml of microbial suspension using Automatic micropipette (Huawei Adjustable micropipette (H) series, Zhejiang, China Mainland). For each Petri dish, nine standardized wells with a diameter of 10mm were punched into the agar with the blunted end of a sterile Pasteur pipette. For each Petri dish 9 specimens (10mm in diameter x 2mm in thickness) were inserted in the wells onto agar with sterile forceps.

For monitoring the immediate antibacterial effect of the tested groups (day 0), the plates were incubated in incubator at $37^{\circ}\text{c} \pm 1^{\circ}\text{c}$ for 48h. Then the diameters of the circular inhibition zones produced around the specimens (specimens + inhibition zones) were measured in millimeters with a digital caliper (Owner's manual, IOS-USA) at three different points, and the mean was recorded as the (day 0) value.

The specimens were then left in the same plates for five more days in the incubator (total of 7 days) and transferred to freshly inoculated plates and incubated at 37°C for 24h for *Strep. mutans* and for 48h for *L.acidophilus* to obtain the inhibition zones for day 7. On that day, the respective culture media with fresh agar for the microorganisms were placed in new Petri dishes and microorganisms' suspensions were added and 9 wells were punched into the agar.

The glass ionomer specimens were taken out of their previous Petri dishes and placed in the new wells. The plates were then incubated with active microorganisms at $37^{\circ}\text{c} \pm 1^{\circ}\text{c}$ for 24h for *Strep. mutans* and for 48h for *L. acidophilus*, and the inhibition zones around the specimens were measured in millimeters with a digital caliper the day after. The same procedure was repeated every 7 day for 21 days (measurement at 7, 14 and 21 days).^[6,7,8]

Statistical Analysis: Statistical analysis was carried out using SPSS program, One way analysis of variance (SPSS, analysis, compare means, one way ANOVA) was used to test the effect of material on free bacterial area within each time. Duncan Post-Hoc Multiple comparisons at $p \leq 0.05$ was used for means comparison (SPSS Inc., Chicago, IL)

Results

I. Inhibitory zone (*S. mutans*):

A. Effect of tested materials: Figures (1) revealed significant difference among *Streptococcus mutans* inhibition zones of the three bioactive restorative materials at day 1, 1 week, 2 weeks and 3 weeks as Fuji IX A3B1 showed the highest inhibition zone followed by Fuji II LCA2B1 and Activa A1B1.

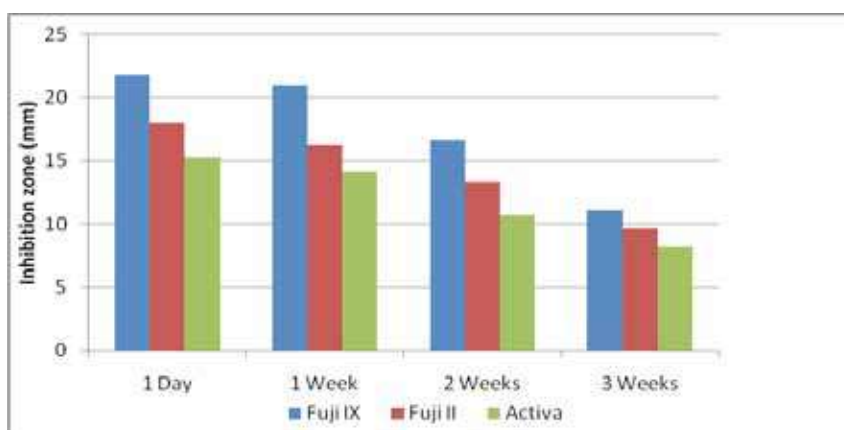


Figure 1: Bar chart showing mean Inhibitory zone (*S. mutans*).

B. Effect of time: Figure (2) revealed the effect of time on the Inhibitory zone (*S. mutans*) of each tested material. There was a statistical significant

difference $p < 0.001$ between the inhibition zones of 1 day, 1 week, 2 weeks and 3 weeks groups for Fuji IX, Fuji II LC and Activa.

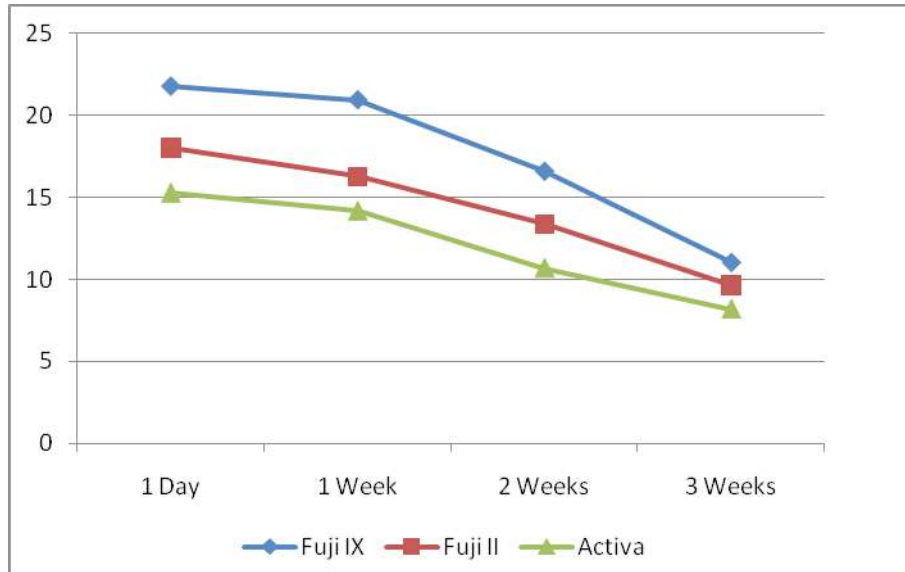


Figure (2): Line chart showing mean Inhibitory zone (*S. mutans*).

II. Inhibitory zone (*Lactobacillus*):

A. Effect of tested materials: Figure (3) revealed that; at day 1 there was a statistically significant difference $p < 0.001$ between the inhibition zone of the Fuji IX and the inhibition zones of Fuji II and Activa groups. At 1 week there was a statistical significant

difference $p < 0.001$ between the inhibition zone of the Fuji IX, Fuji and Activa groups. At 2 weeks and 3 weeks there was no statistical significant difference $p = 0.164$ between the inhibition zone of the three tested material Fuji IX, Fuji II and Activa groups.

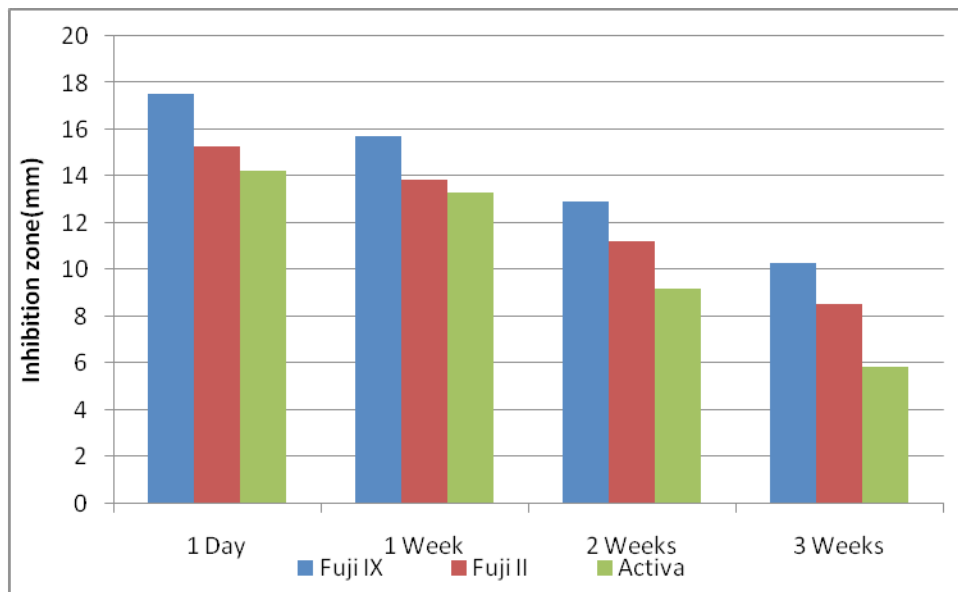


Figure (3): Line chart showing mean Inhibitory zone (*Lactobacillus*).

B. Effect of time: Figure(4) revealed that There was a statistical significant difference $p < 0.001$ between the inhibition zone of the 1day, 1week, 2weeks and 3 weeks of Fuji IX, FujiII LC and Activa

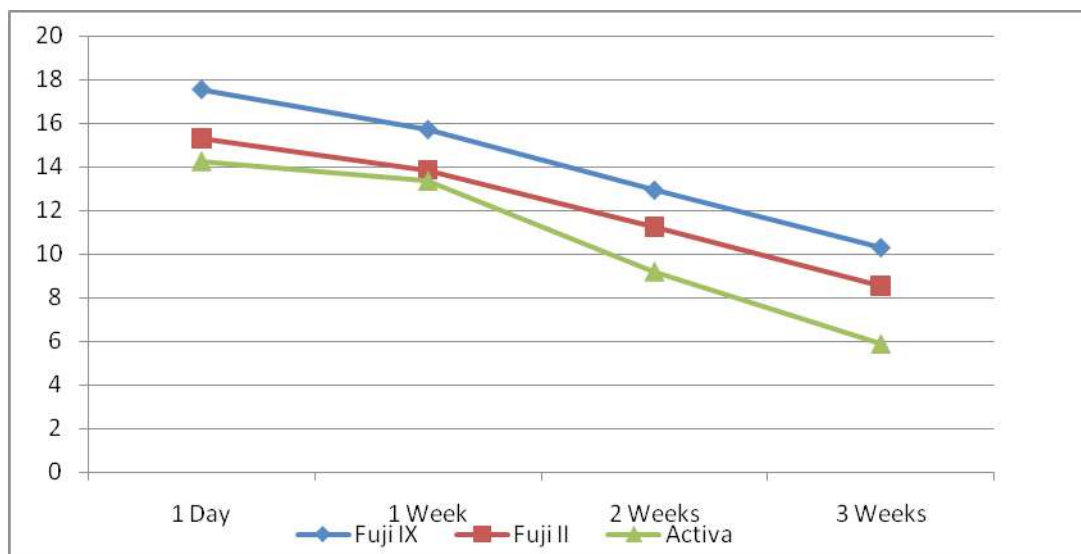


Figure (4): Line chart showing mean Inhibitory zone (Lactobacillus).

Discussion

Dental caries constitutes one of the most common infectious diseases. It is a multi-factorial disease related to the presence of cariogenic bacteria embedded in the dental plaque.

In this study *Streptococcus mutans* microorganisms were chosen because they are considered to be the most important group of bacteria initiating caries lesions. It was reported that the number of salivary S.M in the oral cavity is correlated to the formation of new caries lesions, and it is generally accepted that reducing the number of S.M also reduces caries activity. They are considered as the main bacteria responsible for caries formation. Also *Lactobacillus acidophilus* were chosen in the study because it is considered as the principle bacteria related to caries progression^[2,3] several experiments have been conducted to incorporate antibacterial agents into dental filling materials as resin composites and glass-ionomers, in order to inhibit bacterial attachment and thus plaque accumulation. However, the antibacterial activity is considered to depend upon release of the antibacterial agent^[1,2].

In this study, the antibacterial properties of three bioactive dental restorative materials were investigated using the agar diffusion test. The agar diffusion test was used to evaluate the antibacterial activity for each type of

tested material against the tested microorganisms. This method was chosen for this study because it is relatively inexpensive and can be performed rapidly and easily with a large number of specimens; also it had been widely accepted as a simple screening assay to assess the antibacterial properties of restorative materials. However, there are limitations associated with the agar diffusion test. One of the main limitations is the inability to distinguish between bacteriostatic and bactericidal effects, so the test does not provide any information about the viability of the test microorganisms within the inhibition zones and also this assay does not reflect the actual status in the oral cavity where the bacteria exist as a biofilm which exhibits an increased resistance to antibacterial agents^[1,2,3]

In contrast to other testing methods, direct contact test offers an advantage, in which the bacteria come in contact directly with the tested materials. In the present study, monitoring of the antibacterial effect of the tested groups carried out after 1 day, 7 days, 1 week, 2 weeks and 3 weeks. Digital caliper was used for measurement of the inhibition zones around the specimens^[7].

The results of this research suggest that Fuji IX extra had the highest antibacterial effect in comparison to Fuji II LC an active bioactive composite. The glass-ionomers results are in agreement with a study conducted by Klai

et al. where it was concluded that various products of GIC exhibited some degree of antimicrobial effect by reducing the number of colony forming unit of *S. mutans* and lactobacillus indicating limited bacteriostatic properties but not bactericidal properties.

The investigators suggested that the inhibitory effects were related to the ability of the material to release fluoride as has been indicated extensively. Fluoride has been reported to reduce the acidogenicity of *S. mutans* by influencing their metabolism and lactic acid production^[11,12]. The weak-to-moderate inhibitory effects of GIC in this study are in contrast to multiple studies which indicated that GIC had potent antibacterial effects against *S. mutans*^[13].

The bioactive materials Activa in this study also showed weak antibacterial activity. As it contains monomers such as urethane dimethacrylate (UDMA) in comparison to Fuji IX extra and FUJI II LC. Moreover, resin-based fluoride-releasing materials were reported to release a smaller quantity of fluoride in comparison with GIC. So the less fluoride release may contribute to less antibacterial effect. We believed that these variable results could be related to variations in making the dental samples such as polymerization of the materials. For example, the exact time of light-curing and how far the light-cure unit from the materials.

Conclusion

The highest antibacterial effect among the materials tested was obtained with Fuji IX. This could be related to the material ability to release fluoride as was reported in^[10,11]. The bioactive material Activa Bioactive Restorative showed weak antibacterial properties. Such a weak inhibition would not be effective in preventing secondary caries formation.

Recommendation: We suggest that future studies should investigate the antibacterial effect of the dental materials in vivo in order to evaluate the interaction between the bioactive dental restorative materials.

Ethical Clearance: Was taken from Faculty of Dentistry, Minia University.

Conflict of Interest: Nil

Source of Funding: Self-funding

References

1. Petersen, P.E., et al., The global burden of oral diseases and risks to oral health. Bull World Health Organ, 2005. 83(9): p. 661-9.
2. Marsh PD, N.B., The oral microflora and biofilms on teeth. In: Dental caries: the disease and its clinical management. Fejerskov O, Kidd EAM, editors. Oxford, UK: Blackwell Munksgaard, 2008: p. 163-187.
3. Marsh, P.D., Are dental diseases examples of ecological catastrophes? Microbiology, 2003. 149(Pt 2): p. 279-94.
4. Ferreira, G.e.a., Antibacterial Activity of Glass Ionomer Cements on Cariogenic Bacteria – An in vitro study. INTERNATIONAL JOURNAL OF DENTAL CLINICS, 2011.3(3): p. 1-3.
5. Chau NP, P.S., Cai JN, Lee MH, Jeon JG., Relationship between fluoride release rate and anti-cariogenic biofilm activity of glass ionomer cements. Dent Mater, 2015.31(4): p. e100–e108.
6. M.M. Zayed, R.E.H., M.I. Riad, Evaluation of the antibacterial efficacy of different bioactive lining and pulp capping agents. Tanta Dental Journal (2015), <http://dx.doi.org/10.1016/j.tdj.2015.04.003>, 2015.
7. Rehab Mahmoud Abd El-Baky and Sanya Maised Hussien. Comparative Antimicrobial Activity and Durability of Different Glass Ionomer Restorative Materials with and without Chlorohexidine. Journal of Advanced Biotechnology and Bioengineering, 2013, 1, 14-21.
8. Zero, D.T., et al., Dental caries and pulpal disease. Dent Clin North Am, 2011. 55(1): p. 29-46.
9. Krzysciak, W., et al., The virulence of *Streptococcus mutans* and the ability to form biofilms. Eur J Clin Microbiol Infect Dis, 2014. 33(4): p. 499-515.
10. Nakajo, K., et al., Fluoride released from glass-ionomer cement is responsible to inhibit the acid production of caries-related oral streptococci. Dental Materials, 2009.25(6): p. 703-708.
11. Loof, J., et al., A comparative study of the bioactivity of three materials for dental applications. Dent Mater, 2008. 24(5): p. 653-9.
12. Pulpdent, The Future of Dentistry Now in Your Hands. PULPDENT® publication XFVWPREV:

- 05/2014. Watertown, MA: Pulpdent Corporation. http://www.pulpdent.com/wordpress/wp-content/uploads/2015/02/ACTIVAWhitePaper_XF-VWP3_REV_11-2015.pdf, 2014.
13. Ngo, H.C., et al.. An in vitro model for the study of chemical exchange between glass ionomer restorations and partially demineralized dentin using a minimally invasive restorative technique. *Journal of Dentistry*, 2011. 39: p. S20-S26.

A Cross-sectional Study: Analysis Risk Factors Against Hypertension in Indonesia 2014

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Abstract

Background: Hypertension is one of the issues of global health problems. This is because hypertension can contribute greatly to the incidence of cardiovascular disease, stroke, kidney failure and early death. Moreover hypertension rarely causes symptoms at an early stage, so many cases are undiagnosed. The prevalence of hypertension based on measurements in Indonesia through Riset Kesehatan Dasar in 2007 was around 31.7%, this figure declined in 2013 to around 25.8%, and increased in 2018 to around 34.1%, which was the largest prevalence in last ten years. This study aimed to look at risk factors that can affect the incidence of hypertension in Indonesia.

Method: This study was a quantitative study with a cross-sectional design using Indonesian Family Life Survey-5 (IFLS-5) data in 2014. The sample of this study amounted to 36,405.

Results: The results of this study obtained the prevalence of hypertension by 21.8%. Some risk factors that are proven statistically and substantially can affect the occurrence of hypertension, including age > 57 years (PR= 1.18; 95% CI 1.12-1.24), <= junior high school education level (PR=1.52; 95% CI 1.46-1.58), with marriage status (PR = 1.36; 95% CI 1.30-1.18), have a diabetes mellitus history (PR= 2.28; 95% CI 2.11-2.46), have a high cholesterol history (PR= 2.16; 95% CI 2.03-2.29), and have a sleep disorders (PR= 1.08; 95% CI 1.03-1.13).

Suggestion: The results of the study suggest people especially those aged 15 years and over who have risk factors for hypertension in order to routinely maintain a healthy lifestyle; became input to the Ministry of Health of the Republic of Indonesia to improve the quality of the implementation of Posbindu PTM such as providing blood pressure measuring devices and equipping cadres' understanding of risk factors for hypertension.

Keywords: *Hypertension, Risk Factors, Indonesia.*

Introduction

Hypertension is one of the issues of global health problems because hypertension can contribute greatly to the incidence of heart disease, stroke, kidney failure and early death. Hypertension rarely shows symptoms at an early stage, so many cases are not diagnosed so

patients with early hypertension rarely get treatment. In connection with this, hypertension is also called Silent Killer disease.⁽¹⁾

The incidence of hypertension continues to grow along with the development of the epidemiological transition. Based on data from the World Health Organization (WHO) in 2008, there were around 1 billion people in the world who had been affected by hypertension. In 2015, that number increased to around 1.13 billion cases of hypertension. This shows that one in three people worldwide experiences hypertension. The prevalence of hypertension in the Southeast Asian region is around 36%, this figure is higher than the

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American region. This is due to the risk of hypertension in countries with low or moderate income which is about 40% greater than those with high income⁽¹⁾.

In the Southeast Asian region it is estimated that around 1.5 million people with hypertension each year. In Southeast Asia, Indonesia ranks the second highest with the highest incidence of hypertension after Myanmar⁽¹⁾. In Indonesia, the prevalence of hypertension based on measurements in Indonesia through Basic Health Research in 2007 was around 31.7%⁽²⁾, this figure declined in 2013 to around 25.8%⁽³⁾, and again increased in 2018 to around 34.1%⁽⁴⁾ which was the largest prevalence in last ten years. This is different from the hypertension survey rate based on doctor's diagnosis, in 2013, the prevalence of hypertension was based on doctor's diagnosis of 9.4% and in 2018, it dropped by around 8.4% .

Hypertension can occur due to several accompanying risk factors. These risk factors such as family history, unhealthy lifestyle, wrong dietary patterns, and poor sleep duration or quality⁽⁵⁾ According to the Ministry of Health of the Republic of Indonesia, the risk factors for hypertension are divided into 2 groups, namely: irreversible risk factors, namely risk factors inherent in hypertensive patients and cannot be changed, including: age, sex, and genetics. Risk factors that can be changed are risk factors caused by unhealthy behavior of people with hypertension including smoking, low fiber diet, excessive salt consumption, lack of physical activity, excessive body weight/obesity, alcohol consumption and stress.

This study aims to see an overview of hypertensive patients based on risk factors in the form of age, education level, marriage status, diabetes mellitus history, high cholesterol history, and sleep quality.

Materials and Method

Study Design and participants: The type of research used is descriptive research, namely research conducted on a set of objects that aims to see a picture of phenomena (including health) that occur in a particular

population and see some relationships between variables.⁽⁶⁾ This study used a Cross Sectional design. The data source comes from secondary data from the Indonesian Family Life Survey-5 (IFLS-5) survey in 2014/2015. The target population and study population in this study were all respondents of Indonesian Family Life Survey -5 in 2014-2015 totaling 50,148 respondents. There are 36,405 respondents whose data can be connected to all the variables studied.

This study used secondary data derived from the 2014/2015 Household Life Survey 5 (IFLS-5) in Indonesia 2014/2015. This survey provides extensive information on the socio-economic, health and other aspects of both the household and individual level. IFLS is considered as the most comprehensive survey ever conducted in Indonesia⁽⁷⁾. The IFLS-5 is a continuous health survey that began in 1993 with four subsequent rounds of data collection where the sample represented 83% of Indonesia's population (1997/1998; 2000; 2007/2008; 2014/2105)⁽⁸⁾. This survey activity was conducted in collaboration with the RAND Corp research organization (Santa Monica, California, USA) with the Population and Policy Center (Gajah Mada University and Survey METER research institute).

Measures: This study uses IFLS-5 data for 2014-2015, where before conducting research, researchers study the questionnaire first to find out the available variables that will be used in accordance with the research objectives. IFLS-5 has used the Computer-Assisted Personal Interview (CAPI) system so that it no longer uses paper questionnaires and there is no repeat data entry process. This CAPI system has been tested first. The variables assessed in this study were analyzed derived from several questionnaires.

Results

Proportion of Risk Factors against Hypertension:

The description of each risk factors variable from the the study: age, education level, marriage status, diabetes mellitus history, high cholesterol history, and sleep quality. The prevalence of hypertension in Indonesia was 21.8%.

Table 1: Frequency of Hypertension According to Individual Characteristics

Characteristics	Hypertension		Non Hypertension		Total
	n	%	n	%	
Age Category (Years)					
15-27	677	6.7	9456	93.3	10133
28-37	1168	12.2	8443	87.8	9611
38-47	1646	23.0	5510	77.0	7156
48-57	1859	39.6	2830	60.4	4689
>57	2598	53.9	2218	46.1	4816
Education Level					
<=Junior high school	4532	26.7	12419	73.3	16951
> Junior high school	3416	17.6	16038	82.4	19454
Marriage Status					
Single	654	9.2	6434	90.8	7088
Marriage	5772	22.2	20230	77.8	26002
Divorce	1522	45.9	1793	54.1	3315
Diabetes Mellitus History					
Exist	377	48.4	402	51.6	779
Not exist	7571	21.3	28055	78.7	35626
High Cholesterol History					
Exist	629	45.2	764	54.8	1393
Not exist	7319	20.9	27693	79.1	35012
Sleep Quality					
Sleep disorders	5729	22.3	19947	77.7	25676
Non sleep disorders	2219	20.7	8510	79.3	10729

Based on age category, the highest proportion of hypertension was ≥ 57 years group (53.9%) and the highest proportion of non hypertension was 15-27 years group (99.3%). The proportion of hypertension in education level <=Junior high school was 26.7% higher than > Junior high school 17.6% but non hypertension in education level <=Junior high school was 73.3%, and >Junior high school 82.4%. Based on marriage status, divorce status has the highest proportion of hypertension which is equal to 45.9%, at marriage was

22.2%, and single status was 9.2%. Respondents had diabetes mellitus history and suffered hypertension 48.4% but non hypertension 51.6%. Respondents had high cholesterol history and suffered hypertension 45.2% but non hypertension 54.8%. Based on sleep quality category, the highest proportion of hypertension was respondents who had sleep disorder group 22.3% and the highest proportion of non hypertension was non sleep disorder group 79.3%.

Table 2. Crude Association of risk factors against Hypertension

Characteristics	Hypertension	Non Hypertension	PR Crude
	n = 7.948	n = 28.457	95% CI
Age Category (Years)			
15-27	677	9456	1
28-37	1168	8443	1.25 (1.12-1.39)
38-47	1646	5510	1.45 (1.33-1.58)
48-57	1859	2830	1.25 (1.16-1.34)
>57	2598	2218	1.18 (1.12-1.24)

Characteristics	Hypertension	Non Hypertension	PR Crude
	n = 7.948	n = 28.457	95% CI
Education Level			
<=Junior high school	4532	12419	1.52 (1.46-1.58)
> Junior high school	3416	16038	1
Mariage Status			
Single	654	6434	1
Mariage	5772	20230	1.36 (1.30-1.42)
Divorce	1522	1793	1.18 (1.09-1.27)
Diabetes Mellitus History			
Exist	377	402	2.28 (2.11-2.46)
Not exist	7571	28055	1
High Cholesterol History			
Exist	629	764	2.16 (2.03-2.29)
Not exist	7319	27693	1
Sleep Quality			
Sleep disorders	5729	19947	1.08 (1.03-1.13)
Non sleep disorders	2219	8510	1

In table 2 could be seen, the risk of hypertension were 1.25 among 28-37 years category, 1.45 among 38-47 years category, 1.25 among 48-57 years category, and 1.18 among ≥ 57 years category. Education level especially \leq Junior high school has a significant risk of hypertension (PR=1.52: 95% CI 1.46-1.58). The size of the association based on Crude Prevalens Ratio (PR) found that the group with marriage marital status compared to the unmarried group made as referrals obtained 1.36 (95% CI 1.30-1.18) meaning marriage in the marital status category had 1.36 times the risk of the incidence of hypertension compared to single groups.

The proportion of groups with a history of diabetes mellitus (DM) in the incidence of hypertension was 48.4%, greater than the category that did not have DM history of 21.3%. PR was obtained at 2.28 (95% CI 2.11-2.46) meaning that the group with a DM history had a 2.3 times risk of the incidence of hypertension compared with those who did not have a DM history. The proportion of groups with a high cholesterol history in the incidence of hypertension was 45.2%, greater than the category that did not have high cholesterol history of 20.9%. PR was obtained at 2.16 (95% CI 2.03-2.29) meaning that the group with high cholesterol history had a 2.16 times risk of the incidence of hypertension compared with those who did not have high cholesterol history. The proportion of groups with a sleep disorders in the incidence of hypertension was 22.3%, greater than

the category that did not have sleep disorders of 20.7%. PR was obtained at 1.08 (95% CI 1.03-1.13) meaning that the group with sleep disorders had a 1.08 times risk of the incidence of hypertension compared with those who did not have sleep disorders.

Discussion

Based on the results of data analysis that has been done, it shows that most hypertensive patients in the age group > 57 years. Age is often associated with the incidence of hypertension. This is because with age, the elasticity of arterial blood will decrease. This is affected by the accumulation of collagen and hypertrophy of very thin, fragmented smooth muscle cells and fractures of elastin fibers. Hypertension Risk in Indonesia continues to increase as much as 11.5 times when a person is over 75 years old⁽⁹⁾. This is reinforced based on the results of Riskesdas (2013) that most of the elderly tend to experience hypertension, which is equal to 57.6%.

Based on research by Okpechi et al (2013)⁽¹⁰⁾ that there is a relationship between the level of education with hypertension. The relationship between education and the incidence of hypertension can be attributed to indirect relationships. Based on research conducted in Thailand, it was proved that respondents who received formal education 6.5 times were more aware of hypertension than those who had never received formal education⁽¹¹⁾. However, even a sufficient level of

knowledge does not necessarily guarantee that someone has the behavior to prevent hypertension. Information received outside the educational environment can also contribute to increasing one's knowledge⁽¹²⁾. Therefore the extension method needs to be considered in order to attract interest from the community.

Research by Tambunan⁽¹³⁾ found that people with not/unmarried status reduced the risk of hypertension, while widows/widowers were twice as likely to develop hypertension. This is caused by the stress of life because of the loss of loved ones and can be accompanied by the possibility of disease and death. Nevertheless the response of each individual is different, but losing someone who is loved decreases the body's immune system by about 50%⁽¹⁴⁾.

Diabetes mellitus is also one of the risk factors for hypertension. This is because people with diabetes can suffer from insulin resistance. This insulin resistance will increase blood pressure due to loss of normal vasodilator activity from insulin or long-term effects⁽¹⁵⁾. Some studies suggest that there is a relationship between the history of diabetes and the incidence of hypertension. In Brazil a history of diabetes increases the risk of hypertension by 4.43 times in urban areas and 4.61 in rural areas⁽¹⁶⁾.

Cholesterol is one of the risk factors that can be changed from hypertension. The higher the total cholesterol level, the higher the possibility of hypertension⁽¹⁷⁾. Increased blood cholesterol levels are experienced by many people with hypertension, this statement is reinforced by various supporting studies. In America, Framingham's heart research states there is a relationship between cholesterol levels and blood pressure.

In Javaheri's research, S et al⁽¹⁸⁾ showed that there was a relationship between poor sleep quality and the incidence of hypertension in adolescents. This proves that sleep disturbances continuously will affect the physiological changes of the body that interfere with the balance between the regulation of the sympathetic and parasympathetic nervous system. Sympathetic nerves play a role in increasing blood pressure while the parasympathetic nerves play a role in decreasing blood pressure.

Conclusion

Based on the results of the 2014/2015 IFLS-5 data analysis, the prevalence of hypertension was 21.8%.

Some risk factors that are proven statistically and substantially can affect the occurrence of hypertension, including age > 57 years, ≤ junior high school education level, with marriage status, have a diabetes mellitus history, have a high cholesterol history, and have sleep disorders.

Hypertension is a very dangerous disease. To control it, the government implemented a Healthy Indonesia Program with a Family Approach (PIS-PK) and the Healthy Living Society Movement (Germas). The hope is that all components of the nation consciously want to cultivate healthy living behaviors starting from the family (Ministry of Health, 2018). Communities, especially those aged 15 years and over, especially those who have risk factors related to hypertension, should routinely maintain a healthy lifestyle such as eating nutritious and balanced foods, maintaining sleep patterns and doing enough physical activity.

Ethical Considerations: The data used in this study collected from interviews directly with respondents using questionnaires and direct health measurements. IFLS data is data that is open to the public and its use has been approved by Institutional Review Boards (IRBs) in the United States (RAND) and Gajah Mada University in Indonesia. All IFLS-5 respondents before being interviewed and examined were asked to fill out the Informed Consent sheet. The confidentiality of the respondent's identity is very much considered and is only used for research purposes.

Conflict of Interest: Both author declared that no competing interest exist.

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Limitations: This study uses a cross sectional design, where the exposure and outcome are measured at the same time. The use of this design in this study has a weakness because of the temporal ambiguity, so that between the incidence of hypertension and the exposure variable can overtake each other which results in unclear aspects of causality.

References

1. WHO. A Global Brief on Hypertension. Geneva: WHO; 2013.

2. Indonesia Ministry of Health. Indonesian Basic Research of Health. Jakarta; 2007
3. Indonesia Ministry of Health. Indonesian Basic Research of Health. Jakarta; 2013
4. Indonesia Ministry of Health. Indonesian Basic Research of Health. Jakarta; 2018
5. Lu Kai, et al. Association Between Self Reported Global Sleep and Prevalence of Hypertension in Chinese Adults. *International Journal of Environment Research and Public Health*;2015. 12: 488-503.
6. Notoatmodjo. *Metodologi Penelitian Kesehatan*. Jakarta: EGC; 2010
7. Strauss J, Witoelar F, Sikoki B. The fifth wave of the Indonesian Family Life Survey (IFLS5): overview and field report. Doi: WR-1143/1-NIA/NICHD; 2016
8. RAND. Indonesian Family Life Survey (IFLS). Available: HYPERLINK “<https://www.rand.org/labor/FLS/IFLS/ifls5.html>. Accessed 20 January 2018” <https://www.rand.org/labor/FLS/IFLS/ifls5.html>. Accessed 20 January 2018.
9. Rahajeg, E dan Tumaninah. Prevalensi Hipertensi dan Determinannya di Indonesia. *Majalah Kedokteran Indonesia*; 2009
10. Okpechi, I, G dkk. Blood Pressure Gradients and Cardiovascular Risk Factor in Urban and Rural Populations in Arabia State South Eastern Nigeria Using the WHO STEPwise Approach. *PloS One* September; 2014.
11. Aung, M, N dkk. Assesing Awarness and Knowledge of Hypertension in an Atrisk Population in the Karen Ethnik Rural Community, Thensongayang, Thailand. *Internasional Journal Gen med*; 2012.
12. Suhardi et al. Asuman Lemak dan Ekspresi Gen pada Penderita Hipertensi Etnik Minangkabau. *Media Medika Indonesia*. Vol. 45, No 1; 2011
13. Tambunan, HP. Hubungan Aktivitas Fisik dengan Risiko Kejadian Hipertensi Tidak Terkontrol Pada Lima Wilayah di Di Jakarta;2006
14. Swarth, Judith. *Stres dan Nutrisi*, Bumi Akasara, Jakarta; 2004
15. Holt, R.I.G. *Textbook of Diabetes*. John Wiley & Sons; 2011
16. Moreira JP, dkk. Prevalence of self Reported Systematic Arterial Hypertension in Urban and Rural Environments in Brazil : A Population-Based Study; 2013
17. Fujikawa, S., Iguchi, R., Noguchi, T., & Sasaki, M. [Cholesterol crystal embolization following urinary diversion: a case report]. *Hinyokika Kyo. Acta Urologica Japonica*, 61(3); 2015. 99-102 p.
18. Javaheri S, et al. Sleep Apnea: Types, Mechanisms, and Clinical Cardiovascular Consequences. *Pub Med.gov*; 2017.

The Relationship between Obesity and Dyslipidemia in Adolescents

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Abstract

Background: Obesity is a condition of chronic accumulation of body fat and a factor for the onset of serious diseases such as dyslipidemia. Obesity and dyslipidemia are emerging as significant public health challenges in South Asian countries

Aim: This study aimed to assess the association of obesity with dyslipidemia by measuring LDL and HDL in adolescents

Method: This study is an observational analytic study with a cross-sectional design. Sixty-two adolescents aged 17 – 19 years were randomly using systematic random sampling. LDL and HDL, anthropometric (weight, height, and BMI). Analysis data was performed using an independent t-test, chi-square test, and Fisher test

Results: The results showed that the samples with a high risk for the measurement of LDL and HDL.

Conclusions: It was concluded that obese adolescents have close links with dyslipidemia and have low HDL level. Obesity in adolescents is essential as early as possible so that it does become a significant health problem.

Keywords: *Obesity, Dyslipidemia, LDL, and HDL.*

Introductions

Obesity is a chronic disease that can cause various other degenerative diseases. The development of the problem of obesity has been widespread throughout the country, and its occurrence has increased every year for the past 40 years. The increase in the incidence of obesity also increases the increase in the incidence of

degenerative diseases. Such as dyslipidemia which even increased in adolescence.

The Problem of Body Weight Proportion has experienced a very remarkable development, from 1975 to 2014, with changes in the average value of BMI of the world's population, ranging from 21.7 kg/m² in 1975 to 24.2 kg/m² in 2014, where in males from 22.1 kg/m² in 1975 to 24.4 kg/m² in 2014. These data indicate that an increase in BMI of the world population supports a positive shift towards obesity BMI. And finally in 2014 the face of the world changes increasingly concentrated due to obesity problems with the prevalence of morbidity due to obesity globally of 0, 64% of male sex and 1.4% of women¹. Thus, the change in BMI of the world's population for four decades supports the spread of obesity to high mortality rates.

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Likewise, the development of the problem of obesity in Indonesia is clearly illustrated in the 2007 Riskesdas data with the national prevalence of obesity in people aged > 18 years by 13.9% and becoming 19.7% in 2013 ². The picture of the population above the age of 18 shows that for the Indonesian population the coverage of adults and the elderly has a problem of obesity which is quite alarming and requires special attention in their snacks.

The incidence of obesity for South Sulawesi has experienced a very large increase. The prevalence of obesity in the Selayar Archipelago District is 32.49% greater than the prevalence of obesity at the provincial level in South Sulawesi which amounted to 23.67% in 2016.

Where in adolescence, obesity, drugs cannot be done because they are still in growth period. While on the other hand the condition of obesity experienced by adolescents raises new problems namely dyslipidemia.

LDL and HDL changes that occur in adolescents can cause dyslipidemia problems more quickly at a younger age. This change is a very big dynamic from very high LDL and very low HDL in adolescents. Or a standard LDL level but a very low HDL level.

This study aimed to assess the association of obesity with dyslipidemia by measuring LDL and HDL in adolescents. The purpose of this study is to prove that there are changes in LDL and HDL in adolescents due to their obesity. This is important to be the reason for the importance of promoting obesity treatment in adolescents. To prevent dyslipidemia.

Method

In our respondents we measured LDL, HDL, and anthropometric measurements including abdominal circumference using measuring tape, body weight with weight scales, height with microtoa, and BMI (Body Mass Index).

BMI measurement by calculating body weight in Kg divided by height in meters squared. Like the following formula:

$$BMI = \frac{weight(Kg)}{(height(m))^2}$$

Measurements of LDL and HDL were carried out as a result of venous blood tests taken from adolescents and measured in Lab. Prodia Makassar, Indonesia.

The data of this study were analyzed by independent t-test, chi-square test, and Fisher test to see the relationship of several measured variables.

Results

The results of this study:

Table 1: Characteristics of Adolescent Respondents

Variabel	N	%
Gender		
Men	27	43.5
Women	35	56.5
Age		
17	5	8.1
18	45	72.6
19	12	19.4
Central Obesity		
Normal	21	33.8
Obesity	41	66.2
BMI		
Normal	22	35.5
Obesity	40	64.5

Based on table 1 above shows the majority of respondents are female adolescents with a percentage of 56.5%. and dominated by 18 years old with 72.6%. Respondents who had central obesity based on measurements of abdominal circumference were 66.2%, and for respondents who were obese based on the results of BMI measurements were 64.5%.

Table 2: Lipid Profile and Obesity According to Central Obesity of Adolescent

Variable	Central Obesity		P
	Normal Mean ± SD (n=21)	Obesity Mean ± SD (n=41)	
HDL	51.9 ± 10	43.9 ± 7	0.001
LDL	98 ± 18	115 ± 33	0.01
LDL/HDL	2.2 ± 0.58	2.6 ± 1	0.063

From table 2 above shows that HDL levels in adolescents with central obesity conditions are much lower than in adolescents with normal abdominal circumference which is a mean of 43.9 ± 7 with a value of P < 0.005.

Table 3: Lipid Profile and Obesity According to Body Mass Index of Adolescent

Body Mass Indeks			
Variable	Normal Mean ± SD (n=22)	Obesity Mean ± SD (n=40)	P
HDL	51.4 ± 10.4	44 ± 7.6	0.002
LDL	98.2 ± 17	116.3 ± 32.8	0.007
LDL/HDL	2.2 ± 0.6	2.6 ± 1.05	0.057

In table 3 above shows that adolescents with obese conditions have very low HDL levels compared to normal adolescents. This obesity measurement was based on the Adolescent Body Mass Index adjusted for BMI chart percentile tables for children and adolescents based on CDC 2000.

Table 4. Obesity Based by Waist Circumferences According to Lipid Profile of Adolescent

Variabel		LDL				P	HDL				P	LDL/HDL				P
		Hight Risk		Low Risk			Low Risk		Hight Risk			Low Risk		Hight Risk		
		N	%	N	%		N	%	N	%		N	%	N	%	
Central Obesity	Obesity	29	70.7	12	29.3	0.153 *	14	34.1	27	65.9	0.036*	11	26.8	30	73.2	0.046**
	Normal	11	52.4	10	47.6		2	9.5	19	90.5		1	4.8	20	95.2	

*Chi-square test, **Fisher test

Based on table 4 above shows that central obesity has a close relationship with HDL levels and LDL/HDL ratio which shows a close relationship with the risk of

heart disease. This is seen as a significant value from the Chi-squer and Fisher test analysis results as attached in table 4 above.

Table 5: Obesity Based by Body Mass Index According to Lipid Profile of Adolescent

Variabel		LDL				P	HDL				P	LDL/HDL				P
		Hight Risk		Low Risk			Low Risk		Hight Risk			Low Risk		Hight Risk		
		N	%	N	%		n	%	N	%		N	%	N	%	
Obesity by BMI	Obesity	29	72.5	11	27.5	0.076*	13	32.5	27	67.5	0.104*	11	27.5	29	72.5	0.042**
	Normal	11	50	11	50		3	13.6	19	86.4		1	4.5	21	95.5	

*Chi-square test, **Fisher test

Based on table 5, the relationship of obesity based on BMI in adolescents shows a very close relationship with the LDL/HDL ratio for those who are at high risk of heart disease.

conditions experienced by adolescents putting the burden of other health problems. And giving the weight of obesity management treatments is important given to adolescents to prevent the occurrence of diseases due to weight gain.

Discussion

This study provides an overview of the relationship of Obesity in adolescents both based on BMI and Abdominal Circumference have very low HDL levels and this poses a severe risk for heart disease in the future. This research provides evidence of the obesity

The high prevalence of dyslipidemia problems in children is higher in the community of children with obesity so that the examination of lipid profiles in children with obesity is needed for prevention³. Conditions like this have a bad impact on their health status in adulthood⁴.

One important determinant that can cause early atherosclerosis problems at a younger age is adiponectin⁵. Low adiponectin is associated with atherogenic lipid profiles⁶. Likewise, the problem of cardio vascular disease in adulthood is suspected of having begun since childhood⁷. This is the main key to the importance of examining the lipid profile in the condition of observation both in children and adolescents.

Because further research is still needed to answer and provide a big picture of this in younger age groups and the involvement of more respondents.

Conclusions

Based on the results of this study it can be concluded that obesity experienced by adolescents can reduce HDL levels in lipid metabolism in adolescents' bodies and has a high risk of the appearance of heart disease.

Conflict of Interest: None.

Source of Funding: Source of personal funding

Ethical Clearance: From Faculty of Public Health, Hasanuddin University.

References

1. Di Cesare M, Bentham J, Stevens GA, Zhou B, Danaei G, Lu Y, et al. Trends in adult body-mass index in 200 countries from 1975 to 2014: A pooled analysis of 1698 population-based measurement studies with 19.2 million participants. *Lancet* [Internet]. 2016;387(10026):1377–96. Available from: [http://dx.doi.org/10.1016/S0140-6736\(16\)30054-X](http://dx.doi.org/10.1016/S0140-6736(16)30054-X)
2. Balitbangkes. Riset KESEHATAN DASAR TAHUN 2013. 2013.
3. Boyd GS, Koenigsberg J, Falkner B, Gidding S, Hassink S. Effect of Obesity and High Blood Pressure on Plasma Lipid Levels in Children and Adolescents. 2019;116(2).
4. Mijailović V, Micić D, Mijailović M. Effects of childhood and adolescent obesity on morbidity in adult life. *J Pediatr Endocrinol Metab* [Internet]. 2001;14 Suppl 5:1339–44; discussion 1365. Available from: <http://europepmc.org/abstract/MED/11964032>
5. Zech F, Tran H, Mong T, Clapuyt P, Maes M, Brichard SM. Determinants of Early Atherosclerosis in Obese Children. 2007;92(8):3025–32.
6. Marso SP, Mehta SK, Frutkin A, House JA, McCrary JR, Kulkarni KR. Low Adiponectin Levels Are Associated With Atherogenic Dyslipidemia and Lipid-Rich Plaque in Nondiabetic Coronary Arteries. *Diabetes Care* [Internet]. 2008;31(5):989–94. Available from: <https://care.diabetesjournals.org/content/31/5/989>
7. Cook S, Kavey REW. Dyslipidemia and Pediatric Obesity. *Pediatr Clin* [Internet]. 2011 Dec 1;58(6):1363–73. Available from: <https://doi.org/10.1016/j.pcl.2011.09.003>

Analysis of the Expression Toll-Like Receptor 4 (TLR4) in Chronic Suppurative Otitis Media with and without Cholesteatoma

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Abstract

In recent years, the increasing incidence of chronic suppurative otitis media (CSOM) diseases worldwide is often associated with the role of TLR4 as a component of innate immunity. This study aimed to analyze the TLR4 levels in patients with chronic suppurative otitis media with and without cholesteatoma. This study was conducted using the cross-sectional technique on 30 patients divided into two groups. The first group is CSOM with cholesteatoma that consisted of 10 patients and the second group is CSOM without cholesteatoma that consisted of 20 patients. Each sample was examined for TLR4 levels and bacterial identification cultures in secretions and several samples were also examined for TLR4 levels in the middle ear mucosa. TLR4 levels were examined by the ELISA method.

The results showed that TLR4 levels in middle ear secretions and mucosa of CSOM patients with cholesteatoma were higher than chronic suppurative otitis media without cholesteatoma but there were no significant differences. TLR4 levels in mucosal samples are higher than secret samples but there are no significant differences. There were no significant differences in TLR4 levels in both secret and mucosal samples between groups of CSOM with cholesteatoma and CSOM without cholesteatoma. There were no significant differences in TLR4 levels between the secret and mucosal sample in both CSOM with and without cholesteatoma.

Keywords: *Chronic Suppurative Otitis Media, Cholesteatoma, TLR4, Innate Immunity.*

Introduction

Otitis media (OM) is a middle ear infection associated with inflammation. This disease frequently afflicts humans and is the major cause of hearing loss worldwide. Substantial morbidity associated with OM is further exacerbated by the high frequency of recurrent infections leading to chronic suppurative otitis media

(CSOM).¹ Chronic suppurative otitis media (CSOM) is a serious health care concern worldwide due to its substantial financial and non-financial burden.² Otitis media is the most common disease in children in the United States, with about 5 billion spent each year in direct and indirect costs.³ The World Health Organization (WHO) estimates that about 65-330 million people suffer from CSOM and that as many as 50% of these have some form of significant associated hearing loss and this disease results in reduced quality of life for patients.^{1,4}

Chronic suppurative otitis media is divided into chronic suppurative otitis media without cholesteatoma and with cholesteatoma. Both are distinguished by looking at the inflammatory process, the presence or absence of cholesteatoma and the location of the tympanic membrane perforation, and different

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management.⁵ The pathogenesis of otitis media is considered multifactorial, however, a bacterial infection is a major cause of acute and chronic otitis media.^{6,7} In a study conducted by Pancawati in 2016 in Makassar, it was found that the overall pattern of the pathogen that caused CSOM was gram-negative aerobic bacteria.⁸ The body's immune response to microorganisms, including bacteria, consists of innate immunity and adaptive immunity. The innate immunity response acts as a non-specific first-line barrier to defense.^{4,9}

Toll-like receptor (TLR) is a homologous protein in the cell membrane Antigen Presenting Cell (APC) that functions as a functional receptor that activates leukocytes to trigger innate immune responses or inflammatory responses to fight pathogens.¹⁰ TLR is an important mediator and the best innate immune receptor of the innate immune response.^{6,11,12} There are 11 types of TLRs have been identified from mammals and each response to a different class of pathogenic infections and is named TLR1-11.¹⁰ TLR4 mainly recognizes a large number of pathogens associated with PAMP that are specific to LPS (lipopolysaccharide) in gram-negative bacteria.^{13,14}

Studies in humans have been carried out regarding the role of TLR in CSOM.^{15,16,17,18,19} Studies in animals have added in vivo evidence regarding the importance of TLR as innate immunity in OM resistance.^{16,18} The involvement of the innate immune system and TLRs in OM, as well on their relevance for new vaccination strategies and immunotherapies.²⁰

Materials and Method

Patient Selection: The research subjects were selected from two patient groups of CSOM: Group I consist of 10 patients CSOM with cholesteatoma and Group II consist of 20 patients CSOM without cholesteatoma. Each sample was examined for TLR4 levels and bacterial identification cultures in secretions. 5 of 10 patients from Group I and 10 of 20 patients from Group II was examined for TLR4 levels in middle ear mucosa. All patients are diagnosed based on history, physical examination and CT-Scan of temporal bone examination. Patients with acute suppurative otitis media, inactive chronic suppurative otitis media, congenital and primary acquired cholesteatoma, and patients with a history of other acute and chronic infectious diseases were not included as subjects in this study.

Middle Ear Secretion Swab Culture: Middle-ear swab culture was performed for both sample groups. The external auditory canal was cleaned, and the middle ear discharge was collected using sterile cotton swabs than placed in a sterile tube and subjected to bacteriological examination.

Middle Ear Secretion Collection: The external auditory canal was cleaned, and the middle ear discharge was collected using sterile cotton swabs than placed in an Eppendorf tube contains 1 ml phosphate buffer saline (PBS). The samples were stored in a freezer with a temperature of -20°C for further use in ELISA.

Middle Ear Mucosa Collection: During each operation, the middle ear mucosa was exposed via tympanostomy anterior or posterior. The mucosae were collected using a microcurette and forceps than placed in an Eppendorf tube contains 1 ml phosphate buffer saline (PBS) than stored in a freezer with a temperature of -20°C for further use in ELISA.

Elisa: TLR4 protein levels were selectively tested by ELISA kits. The standard curve range of the ELISA kit is 0,05 ng/ml – 15 ng/ml and sensitivity are 0,027ng/ml. Middle ear secretion and mucosae from the two groups were recollected. Middle ear secretion and mucosae homogenized in 0.5 ml of PBS. All samples were centrifuged for 5min at 13,000 g and the supernatant was tested in duplicate for TLR4 according to the manufacturer's instruction.

Statistical Analysis: Data were analyzed using SPSS (Statistical Package for Social Sciences) version 24.0 for Windows. Samples were analyzed using independent T-test.

Results

Types and proportions of cultured pathogens: All of the samples were positive for bacteria. The most pathogen in CSOM without cholesteatoma are gram-negative bacteria, species *Pseudomonas aeruginosa* with 8 samples (40%), followed by gram-positive species *Staphylococcus haemolyticus* with 3 samples (15%). The most pathogen in CSOM with cholesteatoma are gram-negative bacteria, species *Pseudomonas aeruginosa* (Table 1).

Table 1: Organisms are cultured from middle ear swabs.

No	Bacteria	Gram (+)/(-)	Cholesteatoma (-)		Cholesteatoma (+)	
			n	%	n	%
1	Pseudomonas aeruginosa	Gram (-)	8	40	2	20
2	Acinetobacter baumannii	Gram (-)	1	5	1	10
3	Serratia marcescens	Gram (-)	1	5	0	0.0
4	Serratia rubidaea	Gram (-)	1	5	0	0.0
5	Enterobacter cloacae	Gram (-)	0	0.0	1	10
6	Providentia stuartii	Gram (-)	1	5	0	0.0
7	Proteus mirabilis	Gram (-)	1	5	1	10
8	Pantoea spp	Gram (-)	1	5	0	0.0
9	Achromobacter xylosoxidans	Gram (-)	1	5	0	0.0
10	Acinetobacter wolffii	Gram (-)	0	0.0	1	10
11	Staphylococcus haemolyticus	Gram (+)	3	15	1	10
12	Staphylococcus aureus	Gram (+)	0	0.0	1	10
13	Staphylococcus warneri	Gram (+)	1	5	0	0.0
14	Kocuria kryptinae	Gram (+)	1	5	1	10
15	Kocuria varians	Gram (+)	0	0.0	1	10
	Total		20	100.0	10	100.0

TLR4 Levels: In the secret samples with the independent T-test obtained p-value 0.460 ($p > 0.05$) that showed no significant difference. In the mucosal samples with the independent T-test obtained p value 0.114 ($p > 0.05$) that showed no significant difference (Table 2).

Table 2: TLR4 levels between groups of CSOM with cholesteatoma and CSOM without cholesteatoma based on secretions and mucosal samples.

CSOM		N	Mean	Std. Deviation	p-Value
Secret	With Cholesteatoma	10	3.7244	0.583	0.460
	Without Cholesteatoma	20	3.4615	1.024	
Mucosa	With Cholesteatoma	5	4.1660	0.610	0.114
	Without Cholesteatoma	10	3.7595	0.332	

*Independent T-Test

TLR4 levels were also examined to compare TLR4 levels in secretions with TLR4 levels in the mucosa in each study group. In the group of CSOM with cholesteatoma with the independent T-test obtained p-value 0.196 ($p > 0.05$) that showed no significant difference. In the group of CSOM without cholesteatoma with the independent T-test obtained p-value 0.381 ($p > 0.05$) that showed no significant difference (Table 3).

Table 3: TLR4 levels between secret samples with mucosal samples in CSOM with cholesteatoma and CSOM without cholesteatoma

Sample		n	Mean	Std. Deviation	p-Value
With Cholesteatoma	Secret	10	3.7244	.58336	0.196
	Mucosa	5	4.1666	.60976	
Without Cholesteatoma	Secret	20	3.4615	1.02485	0.381
	Mucosa	10	3.7595	.33240	

* Independent T-Test

Discussion

In this study, the most pathogen in CSOM with and without cholesteatoma are gram-negative bacteria, species *Pseudomonas aeruginosa*. Pancawati⁸ in Makassar also received the most pathogen in CSOM without cholesteatoma are gram-negative bacteria but species *Proteus mirabilis* in CSOM with cholesteatoma. Harshika²¹ in India also obtained the dominant microbiological pathogen in CSOM is *Pseudomonas aeruginosa*.

P. aeruginosa is the main cause of CSOM disease in the tropics.²² *Pseudomonas* is more able to survive than other pathogens because it only requires minimal food and produces pyocyanin and bacteriocin which is its ability to carry out local infections in the form of necrotic activity by extracellular enzymes, which have characteristics such as epithelium damage, circulatory breakdown, and loss of tissue protection devitalizing organisms from normal defense mechanisms.²³

Toll-like Receptors (TLR) 1-10 plays a very crucial role in inducing and activating the natural immune system during an infection. Recent data have shown an important role for TLR in the inflammatory response to bacteria in the ear, and these receptors are particularly important during recovery from otitis media in mice.^{24,25}

Si (2014) on examining TLR4 levels using Real-Time - PCR and Western blot found low TLR4 mRNA levels and TLR4 protein levels in the middle ear mucosa of CSOM compared to normal middle ear mucosa. This is one proof of the involvement of TLR4 in the pathogenesis and recovery of CSOM.²⁵

Usually, TLR is expressed in immune cells, epithelial cells, and endothelium. The ligand is called Pathogen Associated Molecular Patterns (PAMP). The TLR bond and its ligand will cause signal transduction to release proinflammatory cytokines such as IL-1 and TNF- α . The most important histopathological features of cholesteatoma are the cholesteatoma matrix, immune cells, and stroma (stroma). The pathogenesis of cholesteatoma is still controversial. Excessive production of several cytokines such as IL-1 α and IL-1 β is found in the cholesteatoma epithelium and stroma. IL-6 is found in the stroma and intestines of cholesteatoma. These cytokines affect epithelial proliferation and bone resorption that occur in cholesteatoma. The discovery of these inflammatory mediators and the intercellular connecting molecule explain the immunologic aspects of the growth of cholesteatoma.²⁴

The results of this study generally obtained levels of TLR4 secret samples and mucosal samples in the CSOM group with cholesteatoma higher than TLR4 levels in CSOM without cholesteatoma but did not show a significant difference. Jesic et al.¹⁷ also found no significant difference in TLR4 expression between the granulation tissue of CSOM with cholesteatoma and CSOM patients without cholesteatoma on TLR4 examination with histopathological and immunohistochemical examination techniques. Whereas Hirai et al.²⁶ found higher TLR4 expression in middle ear mucosa CSOM with cholesteatoma than middle ear mucosa CSOM without cholesteatoma by immunohistochemical examination.

Higher TLR4 levels in CSOM with cholesteatoma caused by an infection process that occurs in CSOM with cholesteatoma is more severe than in CSOM without cholesteatoma. Cholesteatoma is a good medium for bacterial growth so that infection occurs. Infection can trigger a local immune response which results in the production of various inflammatory mediators and various cytokines. Inflammatory mediators and cytokines can stimulate keratinocytes of the cholesteatoma matrix to be hyperproliferative, destructive.²⁷ In this study, TLR4 levels did not show a significant difference probably due to the lack of samples in this study.

The results of this study generally obtained levels of TLR4 in mucosal samples higher than TLR4 levels in middle ear secret samples both on group CSOM with cholesteatoma and CSOM without cholesteatoma but did not show a significant difference. TLR4 levels in the secretions and mucosa which are almost the same and statistically do not show a significant difference in each sample group show that TLR4 levels can be measured using secret samples and mucosal samples.

Bacterial infections are the dominant factor in most cases of otitis media. The natural immune system of the mucosa (epithelial cells and other mucous cells) functions as a barrier and anti-infection. The natural immune system of the mucosa plays an anti-infectious role by recognizing Pathogen Associated Molecular Patterns (PAMP) through Pattern Recognition Receptors (PRR), such as Toll-like receptors (TLR). TLR activation mobilizes the innate immune response, including infiltration of inflammatory cells, production of inflammatory cytokines, and defense against bacterial infections.²⁵

Conclusion

TLR4 levels in secret and mucosal samples are higher in CSOM with cholesteatoma than in CSOM without cholesteatoma but there were no significant differences. TLR4 levels in mucosal samples are higher than secret samples but there were no significant differences in both group CSOM with and without cholesteatoma.

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Ethical Clearance: Taken from Biomedical Research Ethics Committee on Human Faculty of Medicine Hasanuddin University Makassar Indonesia (Register number :1122/H4.8.4.5.31/PP36-KOMETIK/2018).

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References

- Mittal, R., et al. Immunity Genes and Susceptibility to Otitis Media : A Comprehensive Review. *Journal of Genetics and Genomics*. 2014a;41:567-581.
- Afolabi, O. A., et al. Socioeconomic Challenges of Chronic Suppurative Otitis Media Management in State Tertiary Health Facility in Nigeria. *Egyptian Journal Society of Ear, Nose, Throat and Allied Sciences*. 2014;15:17-22.
- Allen, E. K., Manichaikul, A., and Sale, M. M. Genetic Contributors to Otitis Media : Agnostic Discovery Approaches Topical Collection on Otitis. *Current Allergy and Asthma Report*. 2014;14:411.
- Mittal, R., et al. Role of Innate Immunity in The Pathogenesis of Otitis Media. *International Journal of Infectious Diseases*. 2014b;29:259-267.
- Acuin, J. Chronic Suppurative Otitis Media (Clinical Review). *BMJ*. 325 : 1159-1169.
- Leichtle, A., et al. 2011. The Rule of DNA Sensing and Innate Immune Receptor TLR9 in Otitis Media. *Innate Immunity*. 2007;18(1):3-13.
- Edward, Y. and Novianti, D. Biofilm on Chronic Suppurative Otitis Media. Department of Ear Nose Throat-Head and Neck Surgery Medical Faculty Andalas University Padang: Indonesia. 2015.
- Pancawati, A. The Analysis of Germ Pattern and the Test of Antimicrobial Sensitivity in Chronic Suppurative Otitis Media With and Without Cholesteatoma in Makassar in 2016. Department of Ear Nose Throat-Head and Neck Surgery Medical Faculty Hasanuddin University Makassar: Indonesia. 2016.
- Ahsani, D. N. Immune Response in Fungal Infection. *JKKI*. 2014;6:55-66.
- Abbas, A. K., Lichtman, A., H., and Pillai, S. *Basic Immunology : Function and Disorders of The Immune System*. 4th Edition. Elsevier : China. 2014.p.23-44.
- Thomason, P. C., et al. Recent Advances in Anatomy, Pathology, and Cell Biology in Relation to Otitis Media Pathogenesis. *Otolaryngology Head and Neck Surgery*. 2013;148(4S) E37-E51.
- Abbas, A. K., Lichtman, A., H., and Pillai, S. *Cellular and Molecular Immunology*. 6th Edition (Updated Edition). Elsevier : China. 2010.p.19-44.
- Bratawidjaja, K. G. dan Rengganis, I. *Basic Immunology*. 11th Edition. Issuing Agency Department of Ear Nose Throat-Head and Neck Surgery Medical Faculty Indonesian University Jakarta: Indonesia : Jakarta. 2014.p.57-90.
- Wahid, S., dan Miskad, U. A. *Immunology is easier to understand*. Brilian Internasional : Surabaya. 2016.p.9-28.
- [15] Jotic, A., et al. Polymorphisms in Toll-like receptors 2 and 4 genes and their expression in chronic suppurative otitis media. *Auris Nasus Larynx*. 2015;42:431-437.
- Li, J. D., et al.. Recent Advances in Otitis Media in Molecular Biology, Biochemistry, Genetics, and Animal. *Otolaryngology Head and Neck Surger*. 2013;148(4S)E52-E63.
- Jesic, S., et al. Expression of Toll-Like Receptors 2, 4 and Nuclear Factor Kappa B in Mucosal Lesions of Human Otitis: Pattern and Relationship in a Clinical Immunohistochemical Study. *Annals of Otolaryngology, Rhinology & Laryngology*. 2014;123(6):434-441.
- Preciado, D., et al. Report on Recent Advances in Molecular and Cellular Biochemistry. *Otolaryngology Head and Neck Surgery*. 2017;156(4S) S106-S113.

19. Lin, J., et al. Genetics and Precision Medicine of Otitis Media. *Otolaryngology Head and Neck Surgery*.2017;156(4S) S41-S50.
20. [20] Wigand, M, et al.The role of innate immunity in otitis media. *HNO*.2018;66:464-471.
21. Harshika, Y. K., Sangeetha, S., and Prakash, R. Microbiological Profile of CSOM and Their Antibiotic Sensitivity Pattern in a Tertiary care Hospital. *Int.J.Curr.Microbiol.App.Sci*. 2015;4(12):735-743.
22. Sulabh, B., Ojha,T., Kumar, S., Singhal, A., and Pratibha, V. Y. Changing Microbiological trends in cases of CSOM. *Int J Cur Rev*. 2013;5(15):76-81.
23. Govind, U. Aerobic Bacteriological Study of Chronic Suppurative Otitis Media and their AntibioGram at Vims Bellay. Dissertation. Bangalor: Rajiv Gandhi University of Health Sciencis Karnataka. 2012.
24. Pelealu, O. C. Immune Mechanism of The Cholesteatoma. 2012;4(2):96-103.
25. Si, Y., et al. Attenuated TLRs in Middle Ear Mucosa Contributes to Susceptibility of Chronic Suppurative Otitis Media. *Human Immunology*. 2014;75:771-776.
26. Hirai, H., et al. Expression of Toll-like Receptors in Chronic Otitis Media and Cholesteatoma. *International Journal of Pediatric Otorhinolaryngology*. 2013;77:674-676.
27. Samosir, I., Suprihati, Naftali, Z. The Relationship of Cholesteatoma with the Type and Degree of Hearing Loss in Chronic Suppurative Otitis Media Patients. *Jurnal Kedokteran Diponegoro*. 2018;7(2):562-573.

Effect of Different Levels of *Coriandrum Sativum* and *Piper Nigrum* and their Interaction on Production, Biochemical Parameter, Liver Enzymes, TSH and Growth Hormone for Broiler Chickens

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Abstract

This study was conducted in Agri. Faculty field, University of Sumer De-Qar province for period from 10th of April 2019 to 14th of May 2019, they had fed 35 days. The objective of this study was to evaluate the effective of watery extraction of Coriander and Black pepper to (80) chickens, one day old, Strain Rose 308, unsexed birds and breed in four cages of batteries. This experiment was divided into four groups, three treatments with different levels and the fourth as a control. The results showed a significant increase of weekly body weight (BW), as well the treatments were improving feed consumption $P < 0.05$, furthermore there is increase in feed conversion ratio with significant result $P < 0.05$. The study reported about biochemical parameters, It showed that a significant decrease in cholesterol and triglyceride (T.G.) $P < 0.05$ incompared with the control and no significant difference with total protein. Liver enzymes activity after use medicinal herbs and spice for broiler chicks were recorded a significant reduction in GOT and GPT and no Significant effect on ALP, $P < 0.05$. As well as the herbs and spice gave increase in growth hormone maybe that herbs contain mineral and vitamins which increased growth hormones $P < 0.05$ the efficient of growth hormone (somatotrophin) was increase protein retention and glycogen deposited in the muscles, as well increase in TSH hormone that gave significant result $P < 0.05$. Increased of TSH hormone secrete from pituitary gland and causes elevated in T_3, T_4 and increased the metabolism. The result indicated that there is significant differences between treatments for Immunological test of N.D. $P < 0.05$ when compared with a control and no significant differences for I.B. test. It is concluded the extraction enhanced the performance and health situation with improvement antibody titer against N.D. but the medicinal herbs did not effect on infection bronchitis (IB) disease as well all the chickens were vaccinated with N.D. and No vaccine with IB.

Keywords: *Coriander seed, spices, Liver enzymes, Growth hormone and chickens Rose 308.*

Introduction

Coriander is an annual, short, fast – growing and prefer dry climates and thrives in well-drained soils [8]. The plant grow up to 1-3 Feet high, the leaves are light green in color. The flowers are white or pink, the stem is green, erect Sympodial, which grow up to the height of 75cm, the plant blooms during late Summer. The plant yield a seed as a fruit. The brownish seed are round $\frac{1}{4}$ inch long and 6mm as a diameter. The seed possess sweet and orange flavor. Herbs and spices have recently emerged as alternatives to antibiotics in animal production. They are known to exert antimicrobial actions in vitro against important Pathogens including fungi [6]. It has also been reported that plant extracts and

spices as single compound or as mixed preparations can play a role in supporting both performance and health status of the animal [17]. About 20 gram of Coriander leaves contains 5 calories 0.73 gram of carbohydrate, 0.19. of Fat, 0.43g of protein, 3% daily value of Vit. B₉ and daily value of Vit. C. It possesses antioxidants such as selenium, Ascorbic acid, Vit. A., Beta-Carotene and Vit. E [8].

Functions of *Coriandrum Sativum*:

1. Reduce cholesterol. Its possesses oleic acid, Linoleic acid, Stearic acid and ascorbic acid which lower the level of cholesterol and bad cholesterol in the inner walls of veins and arteries.

2. Prevents anemia: Coriander contains good amount of iron which is helpful for the anemia patients.
3. Anti-allergic activity: Anti-histamine properties in coriander helps to lower the uncomfortable condition caused by hay fever and seasonal allergies.

Black Pepper: Piper Nigrum is a flowering vine extracted from the core of a pepper plant and belongs to the family Piperaceae, genus Piper and species Piper Nigrum. Black Pepper has been shown to be rich in glutathione peroxidase and glucose-6-phosphate dehydrogenase^[13].

The antioxidant and radical scavenging properties of black pepper Seed have been well documented^[9].

[12]: Showed that piperine Can increase the absorption of Selenium, Vit B Complex, beta Carotene and Curcumin as well.

The pepper is a Creeper and normally grown on tall trees and grows up to 4 meter. The pepper we use at home is the dried pepper Fruit, when ripe the pepper fruit is red in color and when dried it becomes black. A tea spoon of pepper which makes about four grams gives as low as (10) Calories and contributes to daily value requirement of about 10% Mn, 5.4% Vit.k, 14.4% Iron 4.9% copper and about 2.8% of dietary fiber, its Promotes production of hydrochloric acid in stomach and improves digestion. Black pepper antioxidant benefits as well established and known to promote good intestinal health. It is help food to stay no longer than required there by reducing stomach gas and irritations. The piperine seems to increase metabolic reactions to keep the fat levels under control. Black pepper also a good antiseptic, it prevents or reduce temperatures during fever.

Chickens Rose 308: is recognized globally as a broiler that will give consistent performance in broiler house.

Integrated and independent producers value the growth rate, Feed efficiency and robust performance.

Rose 308 is a robust, fast growing, Feed efficient broiler with good meat yield.

It is designed to satisfy the demands of customers who require consistency of performance and the versatility to meat a broad range of end product requirements.

Features of Broilers Rose 308:

1. Rapid growth, the possibility of early Slaughtering.
2. More muscle mass.
3. Bright skin.
4. High performance

Advantages of cross broiler Rose 308:

1. Excellent Live weight gain.
2. Large and long legs.
3. Excellent Feed Conversion.
4. White and large breasts.

Materials and Method

The experiment started from 10th of April 2019 to 14th of May 2019 the chickens Fed ad-libitum for 35 days. Its was done in Agri. Faculty Field, Univ. of Sumer, De- Qar/Raifae.

The project divided into four groups, three treatments with different levels and the fourth as a control.

The chickens Rose (308) were distributed randomly for (3) treatments and the fourth as control.

T₁ = Control : just water drank.

T₂ = Coriandrum sativum only 4 mL Ext. COR./Lit. Water.

T₃ = Coriander + Black Pepper 3 mL Ext. COR. + 1 ml Ext. B.P./Lit. water.

T₄ = Coriander + Black Pepper 2.5 mL Ext. COR. + 1.5 ml Ext. B.P./Lit. water.

The procedure of extraction: The medicinal herbs plant was brought from popular Market and Mill the seeds by electrical Machine to get Powder, after that it was dissolved with distilled water and left for 24 hours.

The percentage recorded 1g. Powder dissolved with 2ml of distilled water then the solution was kept in water bath on 60°C until boiling then left it to cool and filtered by sterile gauze after that the solution was ready for use.

Statistical analysis: The statistical computations were done by using SAS Software program (SAS, 2012). Duncan's multiple range test (1955) to comparison between means. (21 and 22).

Results

The study deal with different treatments of herbs on many differ Biological Parameters. It contain (6) tables.

Table 1: Effect of Extraction for medicinal herbs and spices on feed consumption of broiler chickens

C.F.C.	Weekly age					Treat
	5	4	3	2	1	
18.28±3247.40 d	12.35±1560.47 c	5.66±813.33 b	3.49±534.57c	1.67±217.95	1.13±121.08	T1
16.11±3369.93 c	10.29±1655.58b	6.14±817.05 b	2.95±553.26 b	1.33±223.20	0.96±120.84	T2
17.83±3460.83 a	11.33±1709.72 a	6.11±838.47 ab	2.77±569.73 ab	1.58±223.79	1.11±119.12	T3
18.83±3501.07 a	1.33±1717.30a	5.83±855.71 a	3.18±582.96a	1.38±223.94	1.11±121.16	T4
*	*	*	*	*	N.S	L.s.ig

There is significant decrease in cumulative feed consumption $P < 0.05$ and as well between the treatments, started from third week of the experiment.

Table 2: Effect of extraction for medicinal herbs and spice on feed conversion ratio to broiler chickens.

F.C.R.	Weekly age					Treat
	5	4	3	2	1	
0.012±1.77c	0.022±1.94c	0.016±1.75c	0.013±1.64c	0.011±1.49b	0.008±1.12	T1
0.011±1.68b	0.017±1.86b	0.014±1.66b	0.011±1.57b	0.010±1.44ab	0.010±1.13	T2
0.010±1.66ab	0.019±1.84ab	0.017±1.63ab	0.015±1.54ab	0.010±1.43a	0.006±1.12	T3
0.012±1.63a	0.017±1.80a	0.016±1.61a	0.013±1.50a	0.009±1.40a	0.008±1.13	T4
*	*	*	*	*	N.S	L.s.ig

This results indicated there is significant $P < 0.05$ on feed conversion ration started from third week of treatments.

Table 3: Shows the comparison between different treatments in Biochemistry.

Treatment	Mean ± SE		
	Cholesterol (mg/dl)	Triglyceride (mg/dl)	Total protein (g/dl)
T1:Control	140.00±8.31 a	55.00±2.58 b	3.30±0.09 a
T2:4 ml/L Coriander	90.00±4.58 b	56.00±2.75 b	3.00±0.06 a
T3: 3ml/L Coriander + 1 ml/L Black pepper	120.00±7.08 a	62.00±3.23 ab	3.20 ±0.11 a
T4: 2.5ml/L Coriander + 1.5 ml/L Black pepper	135.00±7.43 a	75.00±5.07 a	3.40 ±0.15 a
Level of sig.	*	*	NS

There is significant reduction $p < 0.05$ for cholesterol and $P 0.05 >$ for T.G and No. Sig. for total protein.

Table 4: Effect of medicinal herbs and spice on Liver enzymes.

Treatment	Mean ± SE		
	GOT	GPT	ALP
T1:Control	52.00±2.51 a	14.00±0.55 a	690.00±24.53 a
T2:4 ml/L Coriander	40.00±1.63 b	10.00±0.37 b	695.00±27.74 a
T3: 3ml/L Coriander + 1 ml/L Black pepper	47.0±2.06 a	9.00±0.41 b	680.00±19.47 a
T4: 2.5ml/L Coriander + 1.5 ml/L Black pepper	49.00±2.37 a	12.00±0.68 ab	680.00±25.04 a
Level of sig.	*	*	NS

The Results showed a significant $p < 0.05$ decrease in GOT and GPT but there is no significant in ALP.

Table 5: Effect of coriander and black pepper on growth and TSH hormones in broiler chickens.

Treatment	Mean ± SE	
	GH-Growth hormone	TSH
T1:Control	0.10±0.02b	0.20±0.03 a
T2:4 ml/L Coriander	0.10±0.02 b	0.21±0.05 a
T3: 3ml/L Coriander + 1 ml/L Black pepper	0.14±0.05 a	0.11±0.01 b
T4: 2.5ml/L Coriander + 1.5 ml/L Black pepper	0.12±0.02 ab	0.23±0.05 a
Level of sig.	*	*

The result showed a significant increase $p < 0.05$ for growth and TSH hormones.

Table 6: Effect of herbs and spice for Immunity in Broiler chickens.

Treatment	Mean ± SE	
	N.D.	I.B.
T1:Control	1504.00±62.48 b	0.00±0.00 a
T2:4 ml/L Coriander	2281.00±94.53 b	0.00±0.00 a
T3: 3ml/L Coriander + 1 ml/L Black pepper	5825.00±135.09 a	0.00±0.00 a
T4: 2.5ml/L Coriander + 1.5 ml/L Black pepper	6715.00±164.74 a	0.00±0.00 a
Level of sig.	*	NS

There is significant $p < 0.05$ for N.D. with different treatments compare with control and No. Sig. with infection bronchitis (IB).

Note: All broiler chickens vaccinated against N.D. only .

Discussion

The study was conducted to assessment the effect of watery extraction of medicinal herbs and spices on weekly Body weight gain (B.W.G.), Feed Consumption (FC.) and Feed conversion ratio (FCR).

Body weight gain (B.W.G.), Feed Consumption (FC.) and Feed conversion ratio (FCR). All treatments significant differences $p < 0.05$ compared with control, that study Carried out through Table [1 and 2] These results agreed with author^[20] who observed that COR. Supplementation improved BW., BWG, and FCR. As well author^[10] who started that COR. Supplementation at a level of 2% improved B.W. and FCR in Japanese quails.

Author^[4] observed that BWG, of male broiler during different weeks was no influenced by (BP) Black Pepper (TUR) Turmeric or their Combination.

From this study we observed improved with Biochemical parameters, the result showed a reduction in cholesterol $P < 0.05$ and increase with T.G. $P > 0.05$ but no significant with total protein, maybe due to active Fatty acid such as oleic acid palmitic acid and essential

oils such as Linalool that Lowered cholesterol by hepatocytes. Table 3.

The study showed that a significant reduction for two enzymes of the liver GOT and GPT $P < 0.05$ Compare with the control and no significant with ALP enzyme. Table 4. that medicinal herbs and spice maybe contribute to decrease liver damage.

The result unagreed with author^[18] who observed that TUR supplementation alone was not significant with total cholesterol.

Present study indicated that growth and TSH hormones had significant increased $p < 0.05$ compare with the control.

Growth hormone are protein and contribute to grow the bird to quickly. It is responsible for growth of the body including bones and help for increase metabolic process, as well as TSH hormone are principal hormone responsible for attainment the growth. Table 5.

Result of Table 6 deal with immunity test for chickens treated with different medicinal herbs and spice, and all chickens were vaccinated with N.D. only, and we found

a significant differences and increased antibody value against N.D. compare with the control, $P < 0.05$ and no significant antibody against IB. Author^[15] observed the chickens immunized with Eimeriaprofilin protein and fed diets supplemented with carvacrolcinamaldehyde and capsicum oleoresin or turmeric oleoresin and capsicum oleoresin had increased body weights and antibody levels compared with unimmunized and infected chickens Fed a non Supplemented diet.

Conclusions

From this project, it is concluded that supplementation of medicinal herbs and spice as watery extraction for Broiler chicken improving Body weight, Body weight gain, Feed Consumption, Feed Conversion ratio and reduction of Biochemical such as cholesterol and as well reduction of liver enzymes with enhanced the immunity of the birds.

Recommendation: Added medicinal herbs and spice for Broiler chickens enhanced flavor of the Feed and stimulate the digestive enzymes activity that improved B.W., B.W.G., F.C., F.C.R. and reduction the cholesterol, enzymes GOT, GPT.

The Author suggested that used the medicinal herbs and spices contribute for enhance daily body weight gain, gave reduction for liver enzymes and cholesterol as well Author suggest that herbs improving growth and TSH hormones to boost the metabolism and enhance the immunity of the birds .

Conflict of Interest: None of the authors have any conflicts of interest to declare.

Source of Funding: The research was performed independently, there is no funding, influence over study design, analyses, manuscript preparation, or scientific publication.

Ethical Clearance: The project was approved by the local ethical committee (College of Agriculture, University of Sumer).

References

1. Anilakumar KR.etal,: Effect of Coriander seeds on hexachlorocyclohexane induced Lipid Peroxidation in rat Liver. NURES. 2001; 21:1455-1462.
2. Arunak., etal,: Role of cumin and cuminon ethanol and preheated sunflower oil induced Lipid Peroxidation .J. herbs spice med. plants. 2006, 11:103-114.
3. Abou-Elkhair R. etal,: Effect of Black Pepper, Turmeric Powder and Coriander seeds and their combinations as Feed Additives on growth performance Carcass traits, Some blood Parameters and humoral immune response of Broiler chickens. Asian Australas J. Anim. Sci. 2014 VOL. 27, NO. 6:847-854.
4. Abarian A., etal,: Influence of turmeric rhizome and Black Pepper on blood constituents and Performance of Broiler chickens. African J. Biotechnol-2012, 11:8606-8611. [Google Scholar]
5. Benzie IFF, Wachtel-Galors. Herbal Medicine: Biomolecular and clinical Aspects. 28ed. CRC Press, 2011.
6. Dorman H. J. D. etal,: Antimicrobial agents from plants, antimicrobial activity of plant, volatile oils. Journal of applied microbiology VOL. 88 No. 2, PP 308-316, 2000.
7. Emamghoreishi M., etal,: Coriandrum sativum: evaluation of its anxiolytic effect in the elevated plus-maze. J. ethnopharmacol 2005, 96:365-370.
8. Firas R.J.,: Effect of using Levels of coriander seed and Leaves Rosemary and their interaction in performance, Some Quality and blood parameters to Broiler Carcass. Thesis 2014 Agri. College, Baghdad Univ.
9. Glucin I.: The antioxidant and radical scavenging activities of black pepper (Piper nigrum) seed. Int. J. Food Science Nat. 2005, 56: 491-499.
10. Güler T., etal,: Effect of COR. (Coriandrum sativum) as a diet ingredient on the performance of Japanese quail. S. Afr. J. Anim-Sci. 2005, 35: 261-267. [Google Scholar]
11. Jang T.P.,: Effect of different level of coriander oil on Performance and blood parameters of broiler chickens. Annals of Bio. Res., 2011, 2(5): 578-583.
12. Khalaf An., etal,: Antioxidant activity of some common plants. Turkish Biol., 2008, 32:51-55.
13. Karthikeyan J., Rani P.,: Enzymatic and non-enzymatic antioxidants in Selected piper species. Indian J. Exp. Biol. 2003, 41:135-140
14. Kim Dk., etal,: Dietary curcuma longa enhances resistance against Eimeria maxima and Eimeria tenella infections in chickens. Poult. Sci., 2013, 92:2635-2643.

15. Lee. Sh., etal,: Effect of dietary supplementation with phytonutrients on vaccine-stimulated immunity against infection with *Eimeriatenella*. *vet. Parasitol.* 2011,181.97-105.
16. Mohsen N., etal.: Effect of hydroalcoholic extract of *Coriandrum Sativum* on appetite. *Avicenna Journal of Phytomedicine*, 2013,[3]1:91-97.
17. Manzanilla E.G., etal,: Effect of plant extracts and Formic acid on the intestinal equilibrium of early weaned pigs. *Journal of animal science*, 2004, VOL. 82, No.11, PP: 3210-3218.
18. Mehala C., Moorthy M., : Production performance of broilersFed with Aloe vera and *Curcuma Longa* (Turmeric). *Int. J.Poult. Sci.*, 2008, 7: 852-856.
19. Rajeshwariu., Andallu B.: Medicinal benefits of Coriander (*Coriandrum Sativum*) spatula D.D., 2011, 1:51-58.
20. Saeid JM., AlNasry As.,; Effect of dietary Coriander Seeds Supplementation on growth performance Carcass triats and some blood Parameter of broiler chickens. *Int. J. Poult. Sci.*, 2010, 9:867-870.
21. SAS. 212. Statistical Analysis System, Users Guide. Statistical. Version 9.1th ed. SAS. Inst. Inc. Cary. N. C. USA.
22. Duncan, D. B. 1955. Multiple Rang and Multiple F- test. *Biometrics.* 11:

Diagnostic Study and Some Pathological Aspects of Parasites Associated with Appendicitis in Al-Najaf Al-Ashraf Governorate

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Abstract

The study is intended to investigate the parasites that exist and accompany appendicitis after its removal in the surgical department at al-Sadr Educational hospital and Al-Hakim General Hospital in Al-Najaf Al-Ashraf Governorate for the period from October 2017 to April 2018. The results of the current study of the appendectomy samples showed that 45 parasite samples were infected with 128 parasites (35.15%), the highest percentage of *Enterobius vermicularis* (28.8%), and *Ascaris lumbricoides* (22.2%). *Entamoeba histolytica* (17.7%), *Entamoeba coli* (13.5%), *Giardia lamblia* (11.3%), *Cryptosporidium* (6.5%), and male infection. The parasite appendicitis was 55.6%, while the female infection rate was 44.4%. 6 years had the highest incidence of parasitic appendicitis (33.3%), and the lowest rate of infection was in the 65-56 age group (4.4%).

Keywords: Parasites, inflammation, appendicitis, Al-Najaf Al-Ashraf, worms.

Introduction

Acute appendicitis is one of the most common cases of invasive surgical surgeries worldwide¹. The appendix is known. It is a tubular structure or a small, irregular cavity. There is a lot of lymph nodes in the wall, which is like a large intestine. Of four primary serological layers (serosa) Outside and then the muscle layer (muscularis) And under mucous (submucosa) And to the mucous layer inside (mucosa), The Appendix differs from the large intestine by containing fewer and fewer glands and the hollow walls of the coliform strips, as well as the internal tissue content of the appendix is not as new as the other histological content of the digestive tract. In addition to being a closed cavity, it is a suitable place for the growth and multiplication of different types of pathogens including parasites, and for these and other reasons they are often susceptible to inflammation

that may develop to a degree leading to inflammation of the abdominal cavity²³. Considered a protozoa. And worms are a cause of many symptoms and disorders such as vomiting, abdominal pain, diarrhea, intestinal obstruction, rectal inflammation, appendicitis and intestinal ulcers⁴⁵. The presence of intestinal parasites in the appendicitis cavity and subsequent activity may cause in some cases symptoms of appendicitis without infection by⁶, I pointed out a lot of studies have shown a close relationship between appendicitis and the presence of types of parasites in them such as *Ascaris lumbricoides* and *Enterobius vermicularis* and *Schistosoma spp* and *Taenia spp*⁷

Materials and Method

Collection of Samples: Was collected 128 Of appendectomy samples after resection in the surgical section of Al Sadr Teaching Hospital and Al Hakim General Hospital In the province of Al-Najaf Al-Ashraf Governorate for the period of October 2017 Until April 2018, And the samples were placed in special containers containing NaCl 0.9% Until diagnosis.

Examination of Samples: The appendectomy was performed longitudinally and was visually examined

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using a magnifying hand lens to diagnose and observe mature worms in the appendage cavity. The samples were then examined in several ways to identify the types of parasites present and their stages. precipitation And Direct smear method And the method of Floatation According to [9,10] Data on the sex and age of patients were recorded .

Results

Numbers and percentage of parasites that cause appendicitis: The results of the current study of the appendectomy samples showed that 45 parasite samples of 128 samples were infected with 35.15%. The highest incidence of *Ebterobius vermicularis* was 28.8%, while *Ascaris lumbricoidis* was 22.2%, *Entamoeba histolytica* was 17.7%, *Entamoeba coli* was 13.5%, *Giardia lamblia* was 11.3%, *Cryptosporidium* was 6.5%, as shown in Table (1).

Table No (1): Numbers and proportions of parasites that cause appendicitis.

Type of parasite	Number of injured	Percentage
<i>Enterobius vermicularis</i>	13	28.8
<i>Ascaris lumbricoidis</i>	10	22.2
<i>Entamoeba histolytica</i>	8	17.7
<i>Entamoeba coli</i>	6	13.5
<i>Giardia lamblia</i>	5	11.3
<i>Cryptosporidium</i>	3	6.5
Total	45	100%

Relationship of appendicitis with parasites by age and sex: The results of the current study showed that the incidence of male appendicitis was parasitic 55.6%, While the percentage of infection in females 44.4%, And recorded age group 45-36 The highest incidence of parasitic appendicitis was 33.3% The lowest incidence was in the age group 65-56 year it was 4.4%, as shown in table (2).

Table (2): Relationship between parasitic appendicitis, age and sex .

Age Categories	Sex	Samples Infected		Total Infected Samples	Percentage
		The Number	%		
15-10	Female	1	2.2	4	8.8%
	Male	3	6.6		
25-16	Female	4	8.8	7	15.4%
	Male	3	6.6		
35-26	Female	5	11.1	10	22.2%
	Male	5	11.1		
45-36	Female	6	13.3	15	33.3%
	Male	9	20		
55-46	Female	4	8.8	7	15.4%
	Male	3	6.6		
65-56	Female	0	0	2	4.4%
	Male	2	4.4		
Total	Female	20	44.4%	45	100%
	Male	25	55.5%		

Discussion

Results of the current study showed that the ratio of 35.15% Of appendicitis is caused by a parasite, and this result is consistent with some studies, where he noted ⁸ That the percentage of renal parasites in cases of appendicitis reached 64%, As consistent with the results a study ⁹ Which showed rates of injury of 39.7% Samples

of excised, recorded ¹⁰ Proportion of its approach to infection with parasites to study samples reaching 34.8%, While the results of the current study did not agree with other studies such as the study¹¹ As it recorded a lower percentage 16.2%, As well as record¹² Percentage of total injury hit 8%, While recording¹³ The highest injury rate reached 79% .Although parasites are present in the

tapeworm tissue, this does not mean that the cause of the appendicitis is always due to the effect of parasites. It is common knowledge that people with appendicitis may show symptoms only after parasites enter the waste into the appendix.¹⁴ However, to discharge the role of parasites in the incidence of infection, however, should be treated with parasites in excess of injuries appendicitis confirmed the parasite after surgery, in addition to a diagnosis of parasites of the family and those around the grave who are directly with him in contact, and should pay attention to personal hygiene and health care For people working in food factories and restaurants to reduce the spread of parasites as well as attention to water sanitation plants and the provision of safe drinking water, these factors help to reduce rates of appendicitis caused by parasites.¹⁴ Poor economic and social conditions such as poverty, low drinking water supply, environmental and climatic conditions such as high temperatures and population density, as well as the biological and mechanical resistance to phylogenetic growth are all factors contributing to the transition and survival of protozoa And intestinal worms in the environment, and spread in different age groups and in both sexes¹⁵ The record in the twentieth century atheist and high injury rates for appendicitis in industrialized countries in Asia, South America and the Middle East, compared with Western countries because of different environmental factors and exposure to injury ¹⁶ .

The current study showed that the incidence of the most common parasitic worm was *E.vermicularis* this result is in agreement with other studies.¹⁷ Bowel injury *E. The most common vermicularis* in all parts of the world between the parasitic worms injuries¹⁸, it should be noted that the eradication of APPENDICITIS does not necessarily mean appendicitis syndrome, because there is ambiguity and symptoms associated with some of the situations that could lead to an error in the diagnosis. Therefore, there must be increased vigilance in identifying possible cases of APPENDICITIS, especially the very young patients and adults because they have a high rate of complications which overlap with symptoms of APPENDICITIS¹⁹.

It may be due to the difference in the rates of infection between males and females to the nature of community life where the presence of males outside the home and thus exposure to various types of microbes, including parasites, as well as eating fast food, which are often the cause of various types of injuries.

The results of the present study showed that the age group with the highest incidence is 36-45 Year where it reached 33.3% Of the total infection rate, while the age group 56-65 Year is the least injury where it reached 4.4%, And this result corresponds to its findings ², In his clinical, clinical and pathological study of acute appendicitis cases in Babel governorate where the incidence rate was in the age group 40-31 Year 34.3% The highest rate of infection among the total infection rates for the other age groups, and is not consistent with the results of the study reached ¹⁴ Where the age group most affected in their studies are 20-35 Year.

Conclusion

It is concluded to Diagnosis of parasitic infections in appendix samples and their relationship with appendicitis surgically removed in Al-Najaf Al-Ashraf Governorate As well as to study of some pathological variables related to infection rates such as age and sex of the infected .

Ethical Clearance: Taken from Kufa Technical Institute committee

Source of Funding: My Self

Conflict of Interest: Nil

References

1. Armentrout JK. The Effects of Environmental Cross-Over on Inflammation-Induced Nociception. 2014.
2. Lanza R, Langer R, Vacanti JP. Principles of Tissue Engineering. Academic press; 2011.
3. Flum DR, Koepsell T. The clinical and economic correlates of misdiagnosed appendicitis: nationwide analysis. Arch Surg. 2002;137(7):799-804.
4. Sharma BC, Bhasin DK, Bhatti HS, Das G, Singh K. Gastrointestinal bleeding due to worm infestation, with negative upper gastrointestinal endoscopy findings: impact of enteroscopy. Endoscopy. 2000;32(04):314-316.
5. Aydin Ö. Incidental parasitic infestations in surgically removed appendices: a retrospective analysis. Diagn Pathol. 2007;2(1):16.
6. Levinson W, Jawetz E. Medical Microbiology and Immunology: Examination and Board Review. Appleton & Lange; 1996.

7. Sah SP, Bhadani PP. *Enterobius vermicularis* causing symptoms of appendicitis in Nepal. *Trop Doct.* 2006;36(3):160-162.
8. Olaifa F, Ayo JO, Ambali SF, Rekwot PI. Haemato-biochemical responses to packing in donkeys administered with ascorbic acid during the harmattan season. *J Vet Med Sci.* 2012:12-38.
9. Mahdi N, Mousa A, Noura M. Parasitic appendicitis: a prospective clinical and histopathological study of 665 cases of acute appendicitis. *J Dam Univ Sci Hlth.* 2009;5(1):87-99.
10. Al-Sammarai ASM. Diagnosis study of the parasites that cause appendicitis and histological changes accompanying her in Samarra city. *Al-Anbar J Vet Sci.* 2015;8(2):46-53.
11. da Silva DF, da Silva RJ, da Silva MG, Sartorelli AC, Rodrigues MAM. Parasitic infection of the appendix as a cause of acute appendicitis. *Parasitol Res.* 2007;102(1):99-102.
12. Huwart L, El MK, Lesavre A, et al. Is appendicolith a reliable sign for acute appendicitis at MDCT? *J Radiol.* 2006;87(4 Pt 1):383-387.
13. Okolie BI, Okonko IO, Ogun AA, et al. Incidence and detection of parasite ova in appendix from patients with appendicitis in south-eastern Nigeria. *World J Agric Sci.* 2008;4:795-802.
14. Dieng Y, Tandia AA, Wane AT, Gaye O, Diallo S. Intestinal parasites in the inhabitants of a suburban zone in which the groundwater is polluted by nitrates of fecal origin (Yeumbeul, Senegal). *Cah d'études Rech Francoph.* 2000;9(6):351-356.
15. Bredesen J, Falensteen AL, Kristiansen VB, Sørensen C, Kjersgaard P. Appendicitis and enterobiasis in children. *Acta Chir Scand.* 1988;154(10):585-587.
16. Hamad SM. Effect of histological parameters of appendicitis and related with age and sex. *J Univ Anbar Pure Sci.* 2011;5(1):13-16.
17. Ramezani MA, Dehghani MR. Relationship between *Enterobius vermicularis* and incidence of acute appendicitis. *Southeast Asian J Trop Med Public Health.* 2007;38(1):20.
18. Ferris M, Quan S, Kaplan BS, et al. The global incidence of appendicitis: a systematic review of population-based studies. *Ann Surg.* 2017;266(2):237-241.
19. Budd JS, Armstrong C. Role of *Enterobius vermicularis* in the aetiology of appendicitis. *Br J Surg.* 1987;74(8):748-749.

Chemical and Histological Study of Hexane Extract of Plant *Capsella Bursa-pastori* in Western Iraq

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Abstract

The study was carried out by extracting the aerial parts of the *Capsella bursa-pastoris* plant and performing quantitative and qualitative detection of seven types of active compounds that exist in it because of its importance, its therapeutic ability and its effect as active antioxidants on the male reproductive system. The results of the qualitative and quantitative detection of hexane extract of the *Capsella bursa-pastoris* plant showed the presence of polyphenols in high quantity (43.8) compared to other active compounds, soaps (11%), glycosides (0.55%), flavonoids (6%), tannins (0.88%) and alkaloids. (13.6%). The results of the analysis of hexane extract of the shepherd ki plant in mass chromatography gas mass - GC in that it contains many fatty acids where the highest percentage of fatty acid linolenic acid (31.38), while the lowest percentage of fatty acid palmitoleic acid (0.08) compared with other types of acids Fatty acids in the extract, and we arranged the fatty acids according to the retention period starting from the minimum duration of palmitoleic acid (14.36) to the highest duration of Eicosanoic acid (Arachidic acid) (22.41). The results of the study showed a significant increase of $p \leq 0.05$ for the second, third and fourth treatment compared with the control animals and the first treatment acetylcarnitin in the first and second duration of the testicular tubule diameters. The results indicated a significant increase of $p \leq 0.05$ height in the testicular epithelial lining epithelial cells. For the second, third and fourth treatment compared to the control and the first treatment for all durations, the results of the study showed a significant decrease $p \leq 0.05$ for the first treatment acetylcarnitine compared to the rest of the treatments in all durations in the rate of elevation epithelial cells lining Testicular tubules.

Keywords: Hexane, *Capsella bursa-pastori*, Western Iraq.

Introduction

Medicinal plants are considered as alternative drugs in the manufacture of medicinal drugs because they have a wide range of effective chemical compounds as a treatment and have an effect on biological functions and metabolic processes without any adverse side effects compared to medicinal chemical treatments that have harmful side effects⁽¹⁾; confirmed that there are numerous studies indicating the use of medicinal plants to cause certain physiological changes in different organs of the body. The chemical drugs manufactured to treat and strengthen fertility and reproductive performance in males have a lot of side effects⁽²⁾, the use of plants as a drug to the early years of human development as medicinal plants and extracts work as therapeutic alternatives and a safer option and effective treatment

alone or complementary Herbal medicine has attracted various social strata and has become a strong competitor for chemotherapy⁽³⁾, Many medicinal plants require discovery to be used to treat cases of infertility, ED or infertility⁽⁴⁾. *Capsella bursa-pastoris* is a medicinal plant that uses the herb to lower the temperature, prevent bleeding and increase urination rate for Japan and China for many centuries. It is also used as a whole plant to treat nephritis resulting in kidney swelling. For eating fresh or after cooking in a section of countries and the whole vegetarian part is used as a tea in the narrowing of the vessels and stimulant and antidepressant and a major treatment against bleeding of all kinds for the uterus, lungs, stomach and kidneys as well as classified within the plants stimulating fertility⁽⁵⁾ the continuous development in the extraction techniques of medicinal plants and

method of detection of their compounds according to the extraction method which was an incentive to conduct the study. Current use of hexane alcohol in the extraction of aerobic fractions of the capsella bursa-pastoris plant and investigation of its efficacy and quantitative and qualitative evaluation of hexane extract on histological changes of testis and cellular testicular activity by the production and composition of Tef and chemotherapy compared to male Swiss mice eggs.

Materials and Method

Plant collection, preparation and classification:

The shepherd bag plant was obtained from the western part of Anbar and was classified in the grassland Desert Studies Center. University of Anbar Common name Shepherd Bag (capsule Pasteur) *Capsella bursa-pastoris* L.Medic.

The plant was dried by distributing it as a thin layer permeated by air in a strayed area without exposure to direct sunlight to protect the chemical properties by stirring twice daily.

Preparation of *Capsella bursa-pastoris* Plant

Extract: The shepherd bag plant was obtained from the western part of Anbar and was classified in the grassland desert studies center. The common name is the shepherd bag (capsule Pasteur) *Capsella bursa-pastoris* L.Medic. The plant is exposed to direct sunlight to protect the chemical properties, stirring twice daily.

Preparation of *Capsella bursa-pastoris* Plant Extract.

The extract of hexane alcohol was prepared according to the method⁽⁶⁾. The qualitative and quantitative detection of the active compounds of the capsella bursa-pastoris plant of Glycosides according to Evans (1999) and the extraction and estimation of Glycoside extract Alkaloids⁽⁷⁾ and Alkaloids extract⁽⁸⁾ and Tannins⁽⁹⁾ and Tannins extract were carried out⁽¹⁰⁾. Flavonoids are also detected⁽¹¹⁾ Flavonoids were extracted and evaluated by⁽¹²⁾ and saponin⁽¹³⁾.⁽¹⁴⁾ The detection, extraction and estimation of polyphenols^(15,16). The quantitative and qualitative determination of fatty acids using GC-MS gas chromatography was done in a method⁽¹⁷⁾.

Laboratory animals: In this study, Swiss egg mice brought from the National Center for Drug Control in Baghdad were placed in plastic cages for breeding of these laboratory animals and sawdust. The cages were cleaned and brush replaced twice a week. All crate.

The mice were subjected to suitable ventilation conditions at a temperature of 21-24 ° C and a light cycle of 14 hours of light and 10 hours of darkness.

Special dietary food consisting of (flour, wheat, corn, barley, bran, lime, salt, iodine, calvostonicmulti.v.) Was given to these mice and water was available continuously free to the mice throughout the experiment.

The animals were left for a week before the experiment began to cope with new conditions.

Preparing the required dosages for the shepherd's sachet: In this study, three different doses of shepherd's sachet were 0.02 mg/day, 0.04 mg/day and 0.06 mg/day based on the British Pharmacopoeia herbal dosage. A weight-sensitive scales weighing 0.2 mg, 0.4 mg and 0.6 mg in 10 ml of distilled water were used to dissolve these weights to reach the required concentrations of 0.02 mg/day, 0.04 mg/day and 0.06 mg/day. Oral dosage method.

Experiment design: This study was conducted on 150 Swiss white variants and the average weight (14-21) g at an average of 18 g and the age of (4-6) weeks. The study was divided into three test groups according to the duration of oral dosage two weeks - four weeks - six weeks. Oral dosage method was used using the rat dosage tool and each treatment contains 10 male mice. The ear loan method was used to teach the mice and then weights were measured before starting the dosage. Each test group consists of five parameters as follows

1. Mice orally dosed with distilled water
2. Acetyl-carnitine T1 10 mice with a concentration of 0.02% mg/day
3. T2 *Capsella bursa-pastoris* extract (10 mice) at a concentration of 0.02% mg/day
4. T3 *Capsella bursa-pastoris* extract (10 mice) at a concentration of 0.04% mg/day
5. T4 *Capsella bursa-pastoris* extract (10 mice) at 0.06% mg/day

Histological preparations Conducted by⁽¹⁸⁾

Results and Discussion

***Capsella bursa-pastoris* extract:** The results of quantitative and qualitative detection of *Capsella bursa-pastoris* extract as shown showed the presence of polyphenols in high quantity (43.8%) compared to other active compounds, saponins (11%), glycosides (0.55%)

and flavonoids (6%). Tannins (0.88%) and alkaloids (13.6%).

Fatty acids in hexane extract geranium cyst germination: The results of the analysis of hexane extract of the shepherd ki plant in the gas chromatography device - GC in Table (1) and Figure (1) showed that it contains many fatty acids where the highest percentage of fatty acid was linolenic acid (31.38), while the lowest was for palmitoleic acid fatty acid (In comparison with the rest of the fatty acids found in the extract, we arranged the fatty acids according to the retention period starting from the lowest duration of palmitoleic acid (14.36) to

the highest duration of Eicosanoic acid (Arachidis acid) (22.41) Table (2).

Dietary fat type and feeding period rather than fat level significantly affected testosterone production and testosterone absorption by male rats since a rapeseed diet rich in unsaturated fatty acids stimulated testicular function in mice ⁽¹⁹⁾. Dietary fats may affect testicular function as omega-3 fatty acids are positively associated with testicular function ⁽²⁰⁾. Nigellasative seeds contain nutrients such as carbohydrates, vitamins, minerals and proteins including eight essential amino acids as well as a lot of unsaturated fats such as linoleic acid and oleic acid.

Capsella bursa pastori sample by GC-MS:

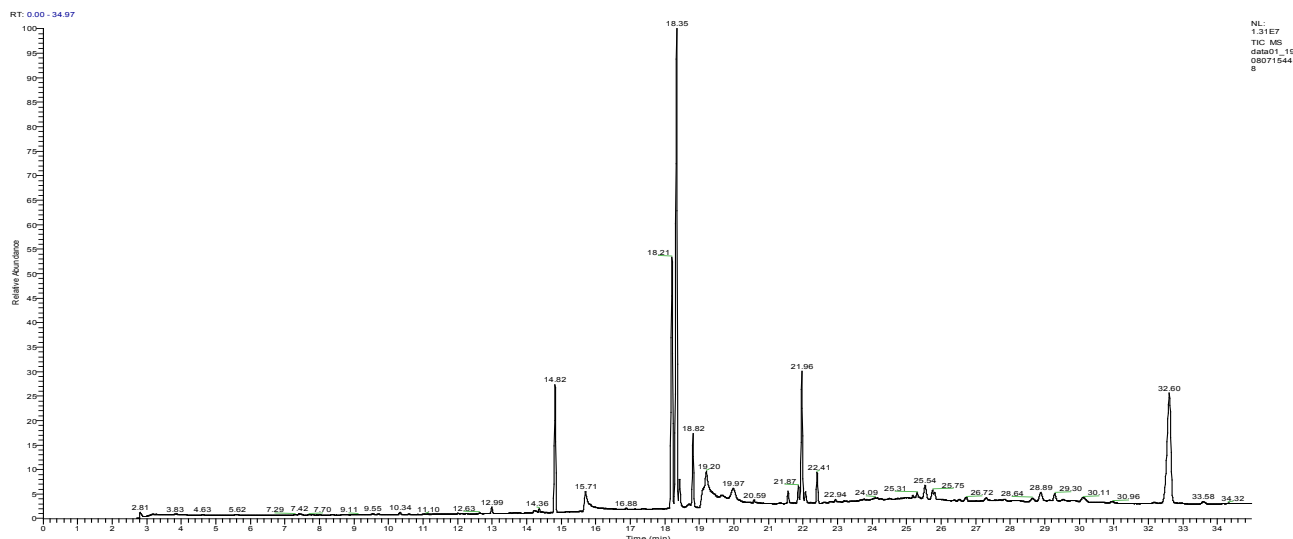


Figure 1: Illustrates the fatty acids present in the capsella bursa-pastoris extract by GC- (mass)

Table (1): Shows the fatty acids present in the capsella bursa-pastoris extract by GC- (mass)

Retention time	Compounds name	Content (%)
14.36	Palmitoleic acid	0.08
14.82	Palmitic acid	9.2
18.21	Linoleic acid	17.85
18.35	Linolenic acid	31.38
18.82	Oleic acid	4.07
19.2	Stearic acid	6.67
21.96	11-Eicosenoic acid	7.82
22.41	Eicosanoic acid (Arachidic acid)	1.56
	Other compounds	21.3

Testicle: The results of the study showed a significant increase of $p \leq 0.05$ height for the second, third and fourth treatment compared to the control animals and the first treatment of acetylcarnitin in the first and second period of the testicular tubule diameters and the highest increase in the third treatment in the first period (38.0) and the second duration (37.4) (1).

The results indicated a significant increase in $p \leq 0.05$ height in the testicular tubule lining epithelial cells for the second, third and fourth treatment compared with the control and the first treatment for all durations, if the highest increase was recorded for the second treatment 11.8 and the third 12.40 and the fourth 15.9 for the three durations respectively.

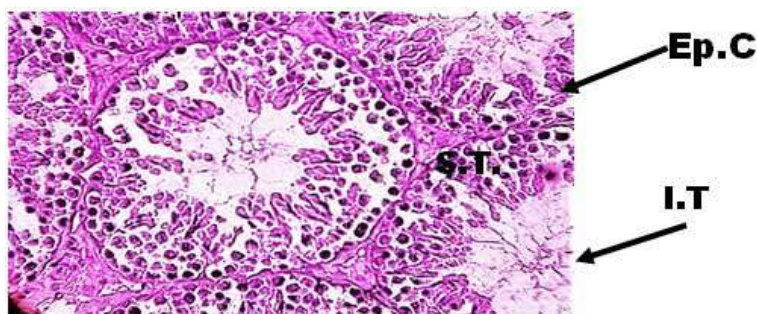
The results showed a significant decrease ($p \leq 0.05$) reduction for the first treatment acetylcarnitine compared to the rest of the treatments in all periods was the highest decrease in the first period (7.43) and the second (8.03) and the third (12.2) in the rate of elevation of epithelial cells lining the testicular tubules, As for the germ cells lining the testicular tubule appeared in all types, especially the completed sperm, which contacted the upper apical part of the supporting cells as well as inside the middle cavity of the tubule of the sperm carrier pictures (1) for the first two weeks, The second period of four weeks showed that the germ cells that line the sperm transporting tubule in Sur⁽²⁾ consist of layers that show various stages of the development of sperm sulfate and sperm cells of both primary and secondary types as well as spermatids. In the third six-week period, there was an increase in the diameter of the tubule transporting semen in the fourth treatment, where it exceeded the rest of the treatments and the control treatment $p \leq 0.05$. The Germ cells appeared in the form of layers showing all the stages of development and their numbers are many

starting from sperm sulphate and primary and secondary sperm cells as well as vanguard sperm, while sperm appeared densely within the cavity of the spermatid tubule⁽³⁾. It also agrees with⁽²²⁾ that containing sage powder is similar to the content of the shepherd's satchet of phenolic compounds, flavonoids, saponins and vitamins, which are antioxidants that help regulate cell metabolism and increase the effectiveness of enzymes and affect the secretion of testosterone, which has a role in The formation and transformation of sperm cells and also the hormone gonadotropin CSH, which stimulates the cells of your hand to secrete. It is also consistent with⁽²³⁾ that sesame seeds are rich in oils and protein and the most important fatty acid found is oleic acid, which is characterized by the highest percentage and linoleic acid, which used in diabetic mice to improve the thickness of the epithelium and tubular diameter of the seminal after six weeks treatment where It has been shown to have a protective effect against oxidative stress induced testicular function in diabetic mice.

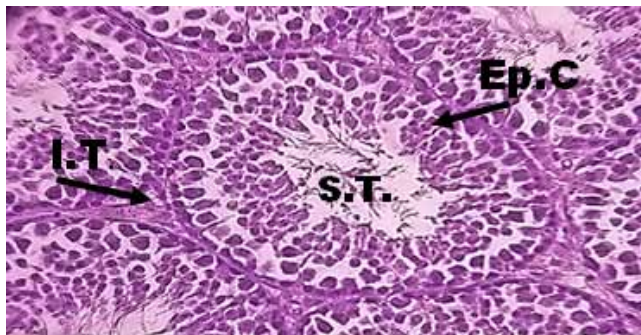
Table (2): Effect of Capsella bursa-pastoris Extract in Different Concentrations on Sperm Diameter and Height of Epithelial Lining Cells ($P \leq 0.05$).

Treatments						
T4	T3	T2	T1	C		
0.658 ± 36.7	0.653 ± 38.0	0.696 ± 36.2	0.776 ± 30.1	0.478 ± 33.1	Seminiferous tubules diameter	First Duration
0.100 ± 10.1	0.337 ± 10.2	0.252 ± 11.8	0.331 ± 7.43	0.141 ± 7.43	Height of Seminiferous epithelial cell	2 Week
0.641 ± 36.9	0.678 ± 37.0	0.593 ± 37.4	0.518 ± 31.9	0.678 ± 34.5	Seminiferous tubules diameter	Second Duration
0.344 ± 12.4	0.075 ± 9.96	0.170 ± 11.6	0.200 ± 8.03	0.136 ± 9.30	Height of Seminiferous epithelial cell	4 Week
0.986 ± 41.1	1.00 ± 38.8	0.894 ± 40.3	0.894 ± 40.3	0.678 ± 37.9	Seminiferous tubules diameter	Third Duration
0.347 ± 15.9	0.495 ± 14.7	0.478 ± 14.5	0.421 ± 12.2	0.315 ± 10.9	Height of Seminiferous epithelial cell	6 Week

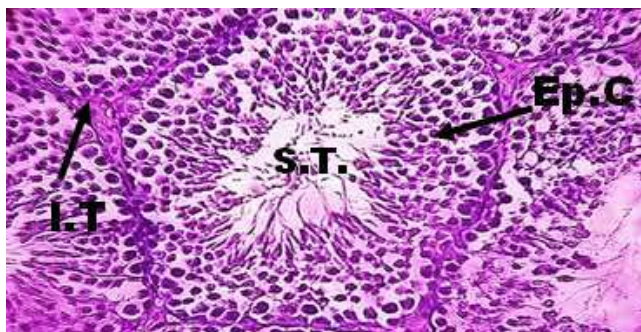
C Control T1 Treatment of Acetyl L-carnitine at 0.02 T2 Capsella bursa-pastoris extract 0.02 T3 Capsella bursa-pastoris extract 0.04 T4 Capsella bursa-pastoris extract 0.06



Picture (1) of testicle of a dosed animal with a capsella bursa-pastoris extract 0.6 mg/day for the first two weeks showing the height of the seminiferous tubules (ST) sperm diameter and the complete maturation of the bacterial wall Height of epithelial cell (Ep.C.) Advanced Interstitial tissue (I.T0) Haematoxyli and Eosin X1230



Picture(2) of testicle of a dosed animal with a capsella bursa-pastoris extract 0.6 mg/day for the second four weeks showing the height of the seminiferous tubules (ST)the maturation of the germ wall is completeHeight of epithelial cell (Ep.C.)and also the presence of mature sperm and sophisticated Interstitial tissue (I.T0) Haematoxyli and EosinX1230



Picture (16) of the testicle of an animal with the extract of the capsella bursa-pastoris plant for a period of six weeks showing the heightSeminiferous tubules (S.T) show the complete maturation of the germ wall Height of epithelial ce The sperm carrier diameter (Ep.C.) and also the presence of mature sperm and sophisticated interstitial tissue (I.T) Haematoxyli dye and Eosin 1230.X.

Conclusions

The hexane extract of the capsella bursa-pastoris plant has an effective effect on raising reproductive efficiency by stimulating teticular development with less duration.

Conflict of Interest: None

Funding: Self

Ethical Clearance: Not required.

Reference

1. SharmaM, Arya D, Bhagour K, Gupta RS. Natural aphrodisiac an0d fertility enhancement measures in males: A review. Current Medicine Research and Practice, 2017. 7(2), 51-58.
2. Alwan HD, Hasan HF, Fakhirdin MBM. A comparative study between the effect s of Arctiumlappa L. leaves extract and Pentoxifylline on DNA of sperms rats treated with Gentamicin. Iraqi Journal of Science, 2016. 57(3B), 1898-1905
3. Marbat MM, Abid Ali M, Hadi AM. The use of Nigella sativa as a single agent in treatment of male infertility. Tikret Journal of Pharmaceutical Sciences, 2013. 9(1), 19-29.
4. Al-Humaidawi Hussein Abbas Salman Al-Humaidawi. Study of the Effect of Alcohol Extract of Anise Fruits on Some Fertility Criteria in Male Rats. 2010.
5. Al-Snafi AE. Traditional uses of Iraqi medicinal plants. IOSR Journal of Pharmacy, 2018. 8(8), 32-96.
6. Vajira P,Bulugahapitiya P. Plants Based natural productsxtraction, Isolation and phyto chemical screening method. 2013.
7. Fahmy IR. Constituents of Plants Crude Drugs 1st ed., paulCario. Barbeg. 1980.51-58.
8. Harborne JB. "Phytochemical Method". A guide to Modern Techniques of Plant Analysis. 2nd. ed. Chapman and Hall. Press, London. 1984.
9. Dally Basil full, Wise Sadiq Hassan. Loading food. Mosul University Press. 1987. P. 273.
10. Al-Shaker Nadia Mohammed Mahdi. Biochemical Interactions of RotundusCyperus with Some Crops and Microorganisms. 2007.
11. Giesman TA.Chemistry of Flavonoid Componds. Malcmillan co. New York. USA. 1962
12. Harborne JB. "Phytochemical Method". A guide to Modern Techniques of Plant Analysis. 2nd. ed. Chapman and Hall. Press, London. 1984.
13. Shihata IM. "A pharma-cological study of AnagllisArrensis" M. D. vet, MSC. Thesis. Cario University. 1951.
14. ChemliR. Arvensoside A andB, triterpenoid saponin

- from *Calendula officinalis* L. *Phytochemistry*, 1987. 26 (6):1785–1788.
15. Gayon P. *Plant phenolics*, 1th (edn), Oliver and Boye, Edinburge. 1972. p.254
 16. Singleton VLR, Orthofer RM. *Lamuela-Raventos: Analysis Of Total*. 1999.
 17. Ribeiro B, Guedes de Pinho P, Andrade PB, Baptista P, Valentão P. Fatty acid composition of wild edible mushrooms species: A comparative study. *Microchem J*. 2009. 93: 29-35.
 18. Mukhtar, the planets of Abdul Qadir and the narrator, Abdul Hakim Ahmed. *Microscopic Preparations*. Ministry of Higher Education and Scientific Research. Books House for Printing and Publishing, University of Baghdad. 1982.
 19. Gromadzka-Ostrowska J, Przepiórka M, Romanowicz K. Influence of dietary fatty acids composition, level of dietary fat and feeding period on some parameters of androgen metabolism in male rats. *Reprod. Biol*, 2002. 2(3), 277-293.
 20. Mínguez-Alarcón L, Chavarro JE, Mendiola J, Roca M, Tanrikut C, Vioque J, Torres-Cantero AM. Fatty acid intake in relation to reproductive hormones and testicular volume among young healthy men. *Asian journal of andrology*, 2017. 19(2), 184.
 21. Ismail BH, Hammed SM. Effect of *Salvia Officinalis* on the Histological Parameters and physiological creteria of Male Reproductive System in Mice. *Al-Anbar Journal of Veterinary Sciences*, 2013. 6(1), 157-162
 22. Abbas YI, Yadigar MA. The Effect of L-carnitine supplement on seminal fluid parameters in males with infertility. *Tikret Journal of Pharmaceutical Sciences*, 2018. 13(1), 23-29

Formulation and Nutritional Appraisal of Renal Specific Formula

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Abstract

Enteral diet formula has shown to be beneficial in hemodialysis patients, where otherwise the gut is efficacious in digestion and absorption of food but oral intake is not possible due to anorexia, and side effects of treatments. Long term enteral feeding programmed with extreme use of commercially available expensive enteral formula all pose a requirement of development of an low cost diet Formula. The objective of this study was to appraisal of formulation and analyze its nutritional composition in comparison to other commercial formula available in market. Material and Method: The renal specific formula was developed by undergoing to different procedures. Samples of two different enteral formula (one renal specific formula and one commercial) were collected from each hospital on three separate occasions and evaluated for nutritional value and cost. Results: The results were compared with the nutritional requirements proposed by the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (K/DOQI) and the European Society for Clinical Nutrition and Metabolism (ESPEN) to enteral renal specific formula. This study demonstrates that hospital prepared enteral renal specific formula render unpredictable levels of micronutrients and macronutrients and appear likely to deliver less than the desired amounts of nutrients. The analysis showed diets with a normal distribution of carbohydrates. The total amount of dietary fiber in the renal specific formula was between 12 g and 15 g. In commercial formula dietary fiber was 3.40 g. Concerning minerals, all formulations were appropriate in iron and most of them in calcium, phosphorus, and sodium. No formulation evaluated presented appropriate values of potassium and magnesium. Additionally, the viscosity of renal specific formulas may be unsuitable for infusion through feeding tubes. The cost of the enteral renal specific formulas ranges from 60 – 88 baht/feed Conclusion: Enteral renal specific formula offers an efficacious, nutrient dense alternative, with known specifications, to assist medical professionals optimize nutritional strategies and improve clinical outcomes within the complex etiology in renal disease patient.

Keywords: *Formulation, Nutritional appraisal, Renal, Specific formula.*

Introduction

Malnutrition is common in patients with chronic kidney disease (CKD), with prevalence ranging from 9% to 72% in dialysis patients.^{1,2} Oral supplementation of malnourished patients undergoing hemodialysis³⁻⁵ and peritoneal dialysis⁶ may improve nutritional parameters. While the patient is being treated in the hospital, use of commercial formula makes it easier for the provision of energy, protein and all essential micronutrients. As many patients are from low socio-economic group, it may not be possible for all the patients to use ready to use, disease specific, and expensive nutrition products especially after obtaining discharge from the hospital.

Enteral tube feedings are commonly used in hospitals to provide nutritional support. While commercial, ready-to-use formulas have been available for over 20 years, many institutions prefer the use of Blenderized Tube Feedings (BTF). This preference may result from believing them to be more “natural” (physiologic) or more economical. BTFs typically contain common foodstuffs such as milk, eggs, meat, soft fruits, and vegetables that are pureed in a food blender or mixer. Other BTFs are made from a base of a commercial nutritional powder, which is reconstituted with water or other liquid. To this base, other foods may be added to modify the consistency or nutritional composition.

While BTFs appear to permit flexibility with regard to the selection of ingredients, and therefore nutritional content, problems with their use have been reported. Gallagher-Allred analyzed prepared BTFs for nutritional content, osmolality, and bacterial contamination¹. An institutionally prepared “high calorie” formula expected to deliver 1.5 kcal/mL yielded only 1.0 kcal/mL on analysis. In addition, this “high calorie” formula did not meet the US Recommended Dietary Allowances (US RDA) for vitamin B₁₂, biotin, iron, and copper in 3,000 kcal. By contrast, commercial feedings designated to provide 1.0 kcal/mL and 1.5 kcal/mL met all nutrient standards and provided the expected caloric density.

The purpose of this study was to appraisal of formulation and analyze its nutritional composition in comparison to other commercial formula available in market.

Materials and Method

4 hospitals in Khon Kaen Province, Thailand were selected for participation in the study. The participating hospitals all used BTFs as a standard of practice for their enteral tube fed patients. Each hospital submitted two different enteral formula (one renal specific formula and one commercial). The providers of the recipes believed them to be nutritionally complete, providing all essential nutrients. Supplies used for the collection of the tube feeding samples (sterile containers, dry ice, cooler) were provided by Nutrition Division, Queen Sirikit Heart Center (QSHC) in the Northeast of Thailand (Khon Kaen Province) . Each hospital prepared at least one liter of BTF recipes. The recipes was analyzed using nutritional analysis software (Inmucal Version 2.0). Recipes for all feedings are shown in Table 1.

Cost Calculations: The cost of the feeds was calculated by using the market price of every ingredient in the feeds.

Table 1: Recipes for Renal Specific formulas

Hospital A	
Cooked rice	34.1 g.
Egg white	32.0 g.
Chicken Breast	32.0 g.
Gourd	162.0 g.
White cabbage	149.0 g.
Sugar cane	21.3 g.
Soybean oil	21.3 g.
Total 237 ml.	
1.8 kcal/1ml.	

Hospital B	
Mung bean noodle	72.52 g.
Egg white	127.98 g.
Chicken Breast	85.32 g.
Banana	106.65 g.
Pumpkin	127.98 g.
Sugar cane	29.86 g.
Rice bran oil	53.32 g.
Total 237 ml.	
1.8 kcal/1ml.	
Hospital C	
Maltodextrin	42.66 g.
Job’s tear	106.65 g.
Egg white	85.32 g.
Nile Tilapia (Fish)	106.65 g.
White cabbage	100.25 g.
Rice bran oil	31.99 g.
Total 237 ml.	
1.8 kcal/1ml.	
Hospital D	
Maltodextrin	49.06 g.
Boiled rice	85.32 g.
Chicken Breast	127.98 g.
Egg white	170.64 g.
Apple	132.25 g.
White cabbage	127.98 g.
Sugar cane	10.67 g.
Soybean oil	29.86 g.
Total 237 ml.	
1.8 kcal/1ml.	

Results

The results were compared with the nutritional requirements proposed by the National Kidney Foundation’s Kidney Disease Outcomes Quality Initiative (K/DOQI)⁷, the European Society for Clinical Nutrition and Metabolism (ESPEN)⁸, and the European Best Practice Guidelines (EBPG)⁹ to enteral renal specific formula (Table 2 and Table 3) . This study demonstrates that hospital prepared enteral renal specific formula render unpredictable levels of micronutrients and macronutrients and appear likely to deliver less than the desired amounts of nutrients. The analysis showed diets with a normal distribution of carbohydrates. The total amount of dietary fiber in the renal specific formula was between 12 g and 15 g. In commercial formula dietary fiber was 3.40 g. Concerning minerals, all formulations were appropriate in iron and most of them

in calcium, phosphorus, and sodium. No formulation evaluated presented appropriate values of potassium and magnesium. Additionally, the viscosity of renal specific formulas may be unsuitable for infusion through feeding tubes. The cost of the enteral renal specific formulas ranges from 60 – 88 baht/feed

Table 2. Nutritional recommendations for Stage 5 CKD patients on dialysis

K/DOQI		ESPEN	EBPG
Energy	< 60 years: 35 kcal/kg/d ≥ 60 years: 30-35 kcal/kg/d	35 kcal/kg/d	30 - 40 kcal/kg/d
Protein	1.2 g/kg/d 50% high biological value	1.2 - 1.4 g/kg IBW/d	1.1 g/kg/d
Sodium	-	1.8 - 2.5 g/d	2,000 - 3,000 mg/d
Fluid	-	1,000 ml. + urine volume	-
Potassium	-	2,000 – 2,500 mg/d	1,950 – 2,730 mg/d
Phosphorous	800 – 1,000 mg/d or < 17 mg/kg IBW or SBW	800 – 1,000 mg/d	800 – 1,000 mg/d
Calcium	≤ 2,000 mg/d	-	2,000 mg/d

Table 3. Comparison of the costs and nutritional value of commercial formula with Renal specific formula.

	Commercial	Hospital A	Hospital B	Hospital C	Hospital D
Energy (kcal)	427	428.03	426.97	427.02	427.37
Energy Distribution					
Carbohydrate (%)	31.80	33.02	36.18	47.40	48.38
Protein (%)	18.00	16.29	19.21	18.71	18.57
Fat (%)	48.80	51.35	51.13	33.30	35.58
Fiber (g/100 ml.)	3.40	2.37	2.38	0.80	1.43
Modified mineral levels					
Calcium (mg./100 ml.)	106.00	26.50	17.89	64.18	55.12
Phosphorous (mg./100 ml.)	72.00	58.50	102.74	159.75	140.78
Iron (mg./100 ml.)	4.50	0.54	1.45	3.00	1.45
Sodium (mg./100 ml.)	70.00	80.40	144.27	124.49	258.01
Potassium (mg./100 ml.)	106.00	201.00	429.84	317.05	465.70
Magnesium (mg./100 ml.)	50.00	0.04	0.10	0.03	0.08
Zinc (mg./100 ml.)	6.40	0.20	0.51	0.23	0.50
Modified Vitamin levels					
Vitamin A (µg/100 ml.)	95.00	1.73	36.99	16.56	9.31
Vitamin C (µg/100 ml.)	25.00	15.70	10.80	19.07	15.70
Price/feed	120.00	60.00	65.00	88.00	85.00

The nutrient requirements for CKD patients are well known. Energy and protein requirements are well established, as are the requirements for phosphorus, potassium and sodium, although questions regarding quantities of other macronutrients and micronutrients have yet to be answered. Three major renal nutrition expert groups exist;. Each group has its own set of guidelines, however there is considerable agreement

amongst them, which is a major advantage; Table 2 shows the recommendations for dialyzed CKD Stage 5, also known as End Stage Renal Disease (ESRD).

Because of the nutrient requirements and especially because of the mineral restrictions, the renal diet is infamous for its limitations on what foods can be consumed. Furthermore, dialysis patients (ESRD)

are recommended to restrict fluids (water, coffee, tea, etc.) which is intricately linked with salt/sodium restrictions¹⁰. Many CKD patients also have diabetes, and other comorbidities, so diet confusion is elevated as the renal diet can contradict diabetes dietary guidelines as well as general healthy diet guidelines. Therefore, the first criterion for a renal specific formula would be to adhere to expert guidelines.

Viscosity was uniformly much lower and more consistent for feedings prepared from powdered formulas and water (usually <10 cps) than for feedings prepared from blenderized whole food ingredients (19,090 – 38,175 cps).

Conclusion

Enteral renal specific formula offers an efficacious, nutrient dense alternative, with known specifications, to assist medical professionals optimize nutritional strategies and improve clinical outcomes within the complex etiology in renal disease patient.

Protein is possibly the single most important nutrient in relation to CKD. As noted by all three expert groups⁷⁻⁹, at least 50% of the protein in a renal specific formula should be of high biological value. Using the latest protein scoring system recognized by the World Health Organization, the Protein Digestibility Corrected Amino Acid Score (PDCAAS), milk, soy and egg proteins are recognized as having the highest score¹¹. In addition, there should be two protein level options/products for CKD patients; a higher level for dialysis patients and a lower level of protein for those not on dialysis. Furthermore, K/DOQI recommends a phosphorus to protein ratio for

dialysis patients of < 10 mg/g¹². This recommendation is difficult as many high biological value proteins are high in phosphorus. Phosphorus is essential for life; it is a component of genetic material, phospholipids in cell membranes, and breaking phosphorus bonds is how humans make energy. Phosphorus is also required for protein function and regulation, bone structure and blood acid-base balance. The importance of phosphorus is recognized by the expert groups⁷⁻⁹, thus an intake of 800-1,000 mg/d is recommended. Casein, a milk protein contains 0.7-0.9% phosphorus¹³, whey protein, another milk protein, contains 0.1-0.6% phosphorus¹⁴, and soy contains approximately 0.8% phosphorus¹⁵. Currently no CKD specific guidelines for either the total lipid intake or the types of lipids exist; therefore, following current dietary guidelines for healthy people is the default option. Globally, healthy guidelines for lipid intake suggest saturated fat should be < 7% of total calories, unsaturated fat should substitute for saturated fat, increase n-3 (omega-3) fatty acid intake and aim for zero trans fatty acids^{16,17}. Therefore, the criteria for the lipid blend used in renal specific formula should follow healthy guidelines and include the n-6 and n-3 essential fatty acids (linoleic acid and alpha-linolenic acid respectively), and have a lower n-6/n-3 ratio, contain monounsaturated fatty acids, be low in saturated fats and have zero trans fatty acids.

Choosing a renal specific product over a standard or other disease specific nutritional supplement is a better choice for the patient as it follows expert guidelines and opinion. The following table summarizes the key differences between a standard oral nutritional supplement (ONS) and a renal specific ONS. (Table 4).

Table 4. Key differences between a standard oral nutritional supplement (ONS) and a renal specific ONS for development of new product.

Component	Standard ONS	Renal Specific ONS
Protein	Not optimized for CKD stages	Higher protein for dialysis Lower protein for nondialyzed
Glycemic index	Higher	Lower for diabetes
Monounsaturated fatty acids	Lower	Higher
Phosphorous, Potassium, Sodium and Calcium	Higher	Lower
Fluid volume	Higher	Lower
Caloric density	Lower	Higher
Fiber	Lower	Higher

Ethical Clearance: Taken from KKUEC (Khon Kaen University Ethics Committee in human research), this research to be exemption research as per the KKU's Announcement 1877/2559.

Source of Funding: Agricultural Research Development Agency (Public Organization), government organization.

Conflict of Interest: We have no conflicts of interest to disclose.

References

- Gallagher-Allred CR. Comparison of institutionally and commercially prepared formulas.
- Nutritional Support Services 1983; 3: 32-34.2. Tanchoco CC, Florentino RF, Flores EG, Castro Ma CA, Portugal TR. Survey of blenderized diets prepared by some hospitals in Metro Manila: Phase II. Nutrient composition of blenderized diets. Hospital Journal 1990; 22: 17-26.
- Sullivan MM, Sorreda-Esguerra P, Santos EE, Platon BG, Castro CG, Idrisalmann ER, Chen NR, Shott S, Comer GM. Bacterial contamination of blenderized whole food and commercial enteral tube feedings in the Philippines. J Hosp Infect 2001; 49: 268-273.
- Food and Nutrition Board, Institute of Medicine: Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride. Washington, DC: National Academies Press; 1997.
- Levenson DI, Bockman RS. A review of calcium preparations. Nutr Rev 1994; 52: 221-232.
- Coben RM, Weintraub A, DiMarino AJ Jr, Cohen S. Gastroesophageal reflux during gastrostomy feeding. Gastroenterology 1994; 106: 13-18.
- Clinical practice guidelines for nutrition in chronic renal failure. K/DOQI, National Kidney Foundation. Am J Kidney Dis. Jun 2000;35(6 Suppl 2):S1-140.
- Cano N, Fiaccadori E, Tesinsky P, et al. ESPEN Guidelines on Enteral Nutrition: Adult renal failure. Clin Nutr. Apr 2006;25(2):295-310.
- Fouque D, Vennegoor M, ter Wee P, et al. EBPG guideline on nutrition. Nephrol Dial Transplant. May 2007;22 Suppl 2:ii45-87.
- Tomson CR. Advising dialysis patients to restrict fluid intake without restricting sodium intake is not based on evidence and is a waste of time. Nephrol Dial Transplant. Aug 2001;16(8):1538-1542.
- Hoffman JR, Falvo MJ. Protein - Which is Best? J Sports Sci Med. Sep 2004;3(3):118-130.
- K/DOQI clinical practice guidelines for bone metabolism and disease in chronic kidney disease. Am J Kidney Dis. Oct 2003;42(4 Suppl 3):S1-201.
- Bosworth AW, Van Slyke LL. The Phosphorus Content of Casein. Journal of Biological Chemistry. September 1, 1914 1914;19(1):67-71.
- Kim BG, Lee JW, Stein HH. Energy concentration and phosphorus digestibility in whey powder, whey permeate, and low-ash whey permeate fed to weanling pigs. J Anim Sci. Jan 2012;90(1):289-295.
- USDA. Release 27 of the USDA National Nutrient Database for Standard Reference. <http://ndb.nal.usda.gov/ndb/foods/show/4834>. Accessed 01-Dec2014, 2014.
- Friedman A, Moe S. Review of the effects of omega-3 supplementation in dialysis patients. Clin J Am Soc Nephrol. Mar 2006;1(2):182-192.
- Kris-Etherton PM, Harris WS, Appel LJ. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. Circulation. Nov 19 2002;106(21):2747-2757.

The Effect of Using Healthy Programmed Education on Learning the Basic Skills of Futsal in the Republic of Iraq

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Abstract

We have noticed in the recent years that there is a clear improvement in the practice level of football in general and Futsal in particular, Which consider the product of the scientific development of modern multi-purpose training method, which all world countries seek to prepare their trainers in a scientific way to aim of improving their athletes to reach the international levels,Scientific research is the best method which to check of the various scientific theories in the sports field and benefit from them to serve and develop sport.

In view of the development of science and knowledge in many sports fields, including football, the game has received a large share of the attention researchers, which reflected on the development of play styles, plans and laws that contributed to give aesthetic in the players performance and increase the enthusiasm of the public, and from among those method is Futsal, which is one of the game method being a basic pillar for its development, as well as its skills, plans, events and unexpected positions in the game works to excite everyone and excitement towards practice and viewing because of the ease of law and small stadium space, the small of players number and similar of the basic skills with the football skills (Soccer), which led to practice by a large number of players.

Keywords: *Healthy programs, basic skills, performance.*

Introduction

According to Taha Ismail⁽¹⁾, physical preparation has become one of the essential pillars of the annual training plan through its various stages and periods, It has been scientifically and practically emphasized the importance of the physical and technical skill side which cannot be separated at any stage of preparation as well as during the competitions.

In addition, we find that⁽²⁾ explains that physical preparation is the most important element of the general preparation or one of the parts of the general preparation geared towards the development of fitness elements and raising the efficiency of the organs and the functional bodyorgans. Its generally goal is to acquire the physical and functional bases of the general and special type of sports activity to build high levels and achieve adaptation to the requirements of competitions through the exercises of quantity and quality that are fit with the player level and his age as well as the special activity

type, and continue these exercises throughout the entire sports season⁽³⁾.

Moreover, we can see that Mohammed⁽⁴⁾ agrees that skill preparation is also one of the basic aspects of the training process in football. The proficiency level of skill performance is one of the indicators of the general skill ability (skill achievement) of the player, especially if similar this performance with the requirements of play positions during the matches, the skill performance of football represents a group of motor performance integrated with the ball and without a ball, which requires the implementation of the player's physical, cognitive and psychological capabilities integrated together to output this performance in the form and appropriate form of competitive position in the game, The skill performance is consider a crucial and important element with the availability of other preparation elements and constitutes an important basis for football players in controlling the playing during the match⁽⁵⁾.

On the other hand, we notice that⁽⁶⁾ ensure that it is necessary to upgrade some aspects of the player, such as physical side and development till upgrade many things and get the required technical level which performed from the player and there is always a difference in the players abilities, which makes one distinct from the other in the performance.

Also, we see that⁽⁷⁾ explains that the skill performances in the football game means all the necessary and purposeful movements that lead to a specific purpose within the framework of the football law, whether those movements with ball or without the ball, and the player's proficiency is determined by the level of his handling of the ball and how to run and control The mastery of basic skills and the players ability to control and use the ball efficiently is the first basis to implement the plans, whether offensive or defensive, whenever the proficiency level of the player higher for the skill performance whenever high his value in the team, football is a collective educational sport requires that each player's performance complement the performance of the rest of his teammates, and this also applies on the basic skills till became each team fully diversified in the performance level of its players and thus become a good level of team⁽⁸⁾. There is a clear and abbreviated division of the skill performances with the ball are:

1. Individual (single) performances
2. Composite performance (integrated)

The only skill performances: are performed individually and have a definite beginning and end, the effect and the introductory movement role in accomplishing the main duty of the skill are evident, These skills appear in the player's performance of the control skill on the ball (suck, mute, receipt), the side glide, throw ball out of bounds, passes, free kicks and corner and penalty. Composite skill performances: They represent models of different forms of a set of individual skill performances that merged with each other and overlap their end stages to form the beginning of the next skill performed by the player in a particular game position to achieve a specific goal according to his requirement. The motor activity of the football player is not only a single skill, but a set of individual skills that merged to become a multi-skill performance that is connected and interdependent among them, where the distinguished players direct to integrate process and melting individual skills inside the only integrate skill

such as control the ball and running then pass where this includes integrated skills, i.e., abbreviated in terms of total time and the total area to perform thus become more connected performance⁽⁹⁾.

There are some skill performances that depend mainly on the technique and technical style of performances and some other skills depend on the player's ability to respond to external stimulants related to others in actual competition situations and this is what happens in football as we note the emergence of some players are highly skilled in training but fail to show the same superior level during matches because they are unable to respond properly to different playing situations⁽¹⁰⁾.

After conducting an analytical study to identify the most important of these composite skill performances (integrated) number of (10) composite skill performances are through direct pass from the movement (running). Receiving and passing (receiving and passing from movement). Receiving then run the ball and then pass. Receiving then dribbling and passing. Receiving with dribbling and passing. Receiving with dribbling then running the ball and passing. Receiving then running the ball then dribbling then passing. Receiving then dribbling then running the ball then passing. Receiving then running the ball then dribbling then run and pass. The same previous skill sentences but ending with the correction⁽¹¹⁾.

It is clear from the above that the physical preparation is an important pillar and an essential duty in Futsaland the modern football requires high capacity, where the players movementon the playground requires a great deal of physical abilities, in addition to the ability of accomplishing and control the ball throughout the periods of dealing with the ball, and to achieve the futsal's player the highest level of performance during the matches the player must be considered a completely physical preparation in the light of playing the game because the good preparation of physical players has a closely related to his mastery of the basic skills of the game and makes him perform competitions in a distinctive way because the skill and planning performance depends largely on the Physical competence of the player due to many factors, including the game nature, the game time, the size of the stadium space and the large duties lies on the player.

The studying process of any problem requires extensive knowledge and especial realization of the

problem type and basing on scientific grounds aimed at reaching the player to the highest levels, and in order to reach the player to high levels of sports in the performance of sports activities in general and futsal in particular, it requires a high level of skill performance and physical abilities, Through the researchers experience in the futsal training field have noticed that there is a very obvious weakness in physical and skills abilities of the players, and may be the reason is not to rely on scientific training programs to develop the physical qualities and skills and using the correct scientific evaluation for address these problems, therefore, the researchers see the need to develop effective training programs with using training means (Pleomorphic) and circular and cross training in order to develop some of the physical and skills abilities of futsal players for the deaf and mute.

The importance of the research is to identify the impact of the various training method (Pleomorphic, circular, cross) in the development of some physical abilities and integrated skills of futsal players, and through the reference research and access to Arabic and foreign studies within the researchers' knowledge limits, it was found that there are no studies have the various training method to develop some physical abilities and integrated skills of the players of the Paralympic Committee in Maysan province of futsal, this prompted the researchers to try to identify the impact of these method on the futsal players in Maysan and the relation of physical and developing the skill side of the players, which are clearly affecting the level of their performance while playing in the league.

The research aims to develop some of the physical abilities and skills performance of futsal players through; identify the impact of using the different training method to develop the physical abilities of the futsal players. In addition, though identify the impact of using the various training method to develop the skills performance of the futsal players.

Research Methodology: The researcher used the experimental method to design two experimental groups and the other controlled by using pre and post measurements to suit the type and nature of the research.

Research fields:

The human field:

1. **Research population:** The research population is represented by (44) players of the Paralympic Committee in Maysan governorate of futsal for the

season 2017-2018

2. **Research sample:** The research sample was selected by deliberate random method from the players of the Paralympic Committee in the Maysan province of futsal for the season 2017-2018 and the number (30) were divided into two groups (control group, experimental group) The number of each group (15) players were taken into account in the selection of the sample in accordance with the following conditions.

Sample selection conditions:

1. Age between 15 and 17 years.
2. The player's height and weight shall be Proportional with the stage of the age under study.
3. Hearing degree should be 91 decibels (deep loss).
4. Free from diseases that effect of performance.
5. To be committed and continuing in training without interruption.
6. Paralympic Committee officials agree to conduct the experiment on the players.

Spatial field: The application of scientific transactions to calculate the validity and reliability of the test and the proposed program of the basic research sample on the stadium of the closed hall in the Technical Institute of Technology in Maysan

Time domain:

1. Scientific transactions were applied to calculate the validity and reliability of the test on Saturday, 4/11/2017
2. The test was repeated on Tuesday 14/11/2017
3. Pre- tests were applied on Thursday 23/11/2017
4. The basic study of the proposed program was conducted on Sunday 26/11/2017 until Wednesday 24/1/2018
5. The tests were conducted on Thursday 25/1/2018.

Discussion

There are statistically significant differences between the pre-measurement and post-measurement of the members of the experimental group in favor of post-measurement in the development of special physical abilities of the futsal players.

There are statistically significant differences between the pre - measurement and post-measurement of the members of the experimental group in favor of post-measurement in the development of the skill performance of the futsal players.

It is a training method through which a sudden lengthening (ie, decentralized contraction) which precedes the maximum central contraction where the muscle is lengthened and shortened and helps to develop and improve the explosive capacity, and this type depends on the muscle rubber to give them great kinetic energy, and plyometric exercises are divided into (exercises related to the limb) Lower body and upper limb) and may be performed by using or without tools and include (partridge, jump, leap) and other free exercises, which is a sudden lengthening of the muscle and then followed by shortening them.

It means doing different things for a lot of people. For some, it may mean the effect of training one side of the body on the other, for others it is an activity used to give active rest from an organized training program, for some, it means using things related to the main activity to avoid the negative results in organized training.

It is a regulation of physical effort to achieve a state of adaptation, where it operates through a predetermined path, with a group of activities and performances of the momentary stop at each training station to perform a specified number of repetitions of exercises, free activities, tools or weights according to a specific system.

It is the term used internationally for the game, which is derived from the Spanish and Portuguese language and is an abbreviation word of (football) which means football in Spanish and the word (sala) its internal meaning to be the term is football for the halls, and this term is an alternative to the previous term, which is called five-way football.

Conflict of Interest: Nil

Source of Funding: Self

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References

1. Abdullatif A Aljuboury. Introduction of fibrin adhesive system (tissucol) in periodontal surgery; part ii: clinical pocket reduction and attachment regeneration. *Mustansiria DJ* 2005; 1(2):108-119
2. Prato GP, De paoli S, Clauser C, Bartolucci E. On the use of a Biologic Sealing system (tissucol) in periodontal surgery. *Int J periodontrestorat Dent* 1983;3(4):48-60
3. Abdullatif A Aljuboury. Periodontitis its prevalence among chronic periodontitis patients with cohort incentive condition. *Must DG* 2006;3(1):45-60
4. Abdullatif A Aljuboury, Hadeel M. Experimental gingivitis in overweight subjects, clinical and microbiological study. *J Bagh Coll Dent* 2011;23(1):51-54
5. Tomas I. M, Melisa S. G, Flavio C.E, et.al. Culture and Characterization of Mesenchymal Stem Cells from Human Gingival Tissue. *Periodontol*, 2010;81:917-925.
6. Sudo K, Kanno M, Miharada K, et al. Mesenchymal progenitors able to differentiate into osteogenic, chondrogenic, and/or adipogenic cells in-vitro are present in most primary fibroblast-like cell populations. *Stem Cells* 2007;25:1610-1617.
7. Fang W, Meijiao Y, Xinlong Y, et.al. Gingiva-Derived Mesenchymal Stem Cell-Mediated Therapeutic Approach for Bone Tissue Regeneration. *Stem Cells and Development*. December 2011, 20(12): 2093-2102.
8. Gronthos S, Akintoye SO, Wang CY. et.al. Bone marrow stromal stem cells for tissue engineering. *Periodontol* 2000, 2006;41:188-195.
9. Stephens P, Genever P. Non-epithelial oral mucosal progenitor cell populations. *Oral Dis* 2007;13:1-10.
10. Kolf CM, Cho E, Tuan RS. Mesenchymal stromal cells. *Biology of adult mesenchymal stem cells: Regulation of niche, self-renewal and differentiation*. *Arthritis Res Ther* 2007;9:204-214.
11. Cesselli D, Beltrami AP, Rigo S, et al. Multipotent progenitor cells are present in human peripheral blood. *Circ Res* 2009;104:1225-1234.

Assessment of Exam-related Anxiety among the Students of the High Healthy Vocations Institute at Medical City

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Abstract

The purpose of this study was to assess levels of anxiety among the Students of the High Healthy Vocations Institute, to find out relationship between students' anxiety levels and some socio-demographic characteristics such as (age, residency, marital status and department) of the Students of the High Healthy Vocations Institute. The period of the study was from April 2nd, 2019 to June 2nd, 2019). To meet the study objectives a questionnaire was constructed. This questionnaire consisted of two parts: the first part includes four demographic characteristics: age, residency, marital status, and department; the second part concerning with the test anxiety scale. The scale measures the most important symptoms that characterize the test anxiety. Data were analyzed by applying: descriptive statistical analysis: frequencies and percentages and distribution; and inferential analysis: Correlation Coefficient, Chi-square. The findings of the study revealed that assessment of exam-related anxiety among the Students of the High Healthy Vocations Institute is moderately to severe level of anxiety. There was a significant relationship between severity of anxiety and age of the students. The present study recommends encouraging the students to learn some coping strategies and stress managements by attending training and relaxation sessions. Advice to regular recreational programs that include trips to reduce stress and to help them to prevent and lessen the stress associated with every-day life events stress.

Keywords: Exam-Related Anxiety; High Healthy Students; Contributing Factors.

Introduction

Anxiety is an unpleasant state characterized by feelings of tension and apprehension, worrisome thoughts and the activation of the autonomic nervous system when an individual faces evaluative achievement demanding situations⁽¹⁾. Fear of exams and test situations is widespread and appears to become more prevalent and test anxiety has a negative detrimental effect on test performance⁽²⁾. If an examination particularly affects the person's carrier selection and future opportunities, it may be stressful. Exam anxiety prevalence has been

reported as 10-41% in school aged children. Researchers have estimated test anxiety prevalence rates of between 15-20% for college students⁽³⁾. Exam anxiety is primarily a concern over negative evaluation, so defined as a subtype of social phobia in DSM diagnostic system. Many studies have reported an association between exam anxiety and anxiety disorders⁽⁴⁻⁵⁾. Psychological factors which contribute significantly to exam anxiety are negative and irrational thinking about exams, outcomes of exams and feelings of no control over exam situation (e.g., going blank during exam) are reported by many authors⁽⁶⁾. Higher anxiety levels in the student community are considered as important indicators for poor mental health⁽⁷⁾. The potential negative effects of emotional distress on students include impairment of functioning in classroom performance and clinical practice, stress-induced disorders and deteriorating performance⁽⁸⁾. Students in extreme stress need serious attention, otherwise inability to cope successfully with

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the enormous stress of education may lead to a cascade of consequences at both personal and professional⁽⁹⁾. Moreover, studies suggest that test anxiety comprises of many negative effects such as low enthusiasm, poor performance, negative self-evaluation viewpoints and low concentration⁽¹⁰⁻¹¹⁾. Researches on examination anxiety have the notion that examination anxiety prepares threats for higher institution students. Anxiety symptoms are distributed along a continuum and different symptom levels of anxiety and predict outcomes. Responses consisted of increase heart rate, stress hormone secretion, restlessness, vigilance and fear of potential dangerous environments. Anxiety prepares the body for physical, cognitive and behavioral instincts to detect and deal with threats to students examination survival and then result to students, beginning to be hyperventilate to allow more oxygen to enter into the blood-stream, divert blood to muscles and sweat to cool the skin⁽¹²⁾. Posited that the difference between generalized anxiety disorders and examination anxiety. He explained that general anxiety disorders are characterized by trait anxiety that results to students experiencing higher levels of stresses across a wide range of situations. Contrarily, students that are prone to examination anxiety have a state of anxiety that results to higher levels of nervousness that are specific to examinations. The symptoms of examination anxiety range from moderate to severe anxiety. Students who exhibit moderate symptoms are able to perform relatively well on examinations. On the other hand, students with severe anxiety experience panic⁽¹³⁾; the common physical symptoms include: headache, upset stomach, feeling of fear, feeling of dread, shortness of breath, sweating, pacing or fidgeting, crying, racing thoughts and blanking out. Lyness explained that during the state of excitement or stress, the body releases adrenaline⁽¹⁴⁾. Adrenaline is known to cause physical symptoms that accompany examination anxiety such as increased heart beat-rate, sweating and rapid-breathing. In many cases, adrenaline is good; it is helpful when dealing with stressful situations, ensuring alertness and preparation. But to some students, the symptoms are difficult or impossible to handle, making them impossible to focus on examinations. The topic of test anxiety has prospered, in part, due to the increasing personal importance of test situations for people in modern society, making tests and their long-term consequences significant educational, social, and clinical problems for many. Since test results in most academic and occupational settings have important practical implications for a person's goals and future career, test anxiety is frequently reported

to be a meaningful factor impacting upon test scores. This study aims to (1) assess levels of anxiety among the students of the High Healthy Vocations Institute; (2) find out relationship between students' anxiety levels and some sociodemographic characteristics such as (age, residency, marital status and department) of these students.

Method

A descriptive analytical design study is applied to assess the anxiety among the students of the high healthy vocation institute at Medical City. The period of the study was from April 2nd, 2019 to June 2nd, 2019. The study included a probability (Stratified random) sample of 70 students. To meet the study objectives a questionnaire was constructed. This questionnaire consisted of two parts: the first part includes the demographic characteristics of age, residency, marital status, and department; the second part concerning the Sarason test anxiety Scale ⁽¹⁶⁾ of 38 item self-report scale that assesses all symptoms of test anxiety. The scale encompasses four domains, each item of scale was rated (1= never, 2= rarely, 3= sometimes, 4= always). By applying the descriptive data analysis of Quartiles which determine the cut-off-points for the levels of anxiety which are Mild (38-103), moderate (104-115), (severe (116-148). Reliability of the questionnaire was determined through pilot study and validity determined through a panel of experts consists of (11) experts. Data were analyzed by applying descriptive statistical (frequencies, percentages) and inferential statistical (Correlation Coefficient and Chi-square) through the SPSS (Statistical package for Social Sciences) version 21.0.

Results

Table 1: Participants' sociodemographic characteristics

Year	Age	
	Frequency	Percent
≤ 9	19	12.2%
20-24	37	23.7%
25-29	7	4.5%
30-34	2	1.3%
35-39	2	1.3%
≥40	3	1.9%
Total	70	100.0%

Residency		
Residency		
Baghdad	60	38.5%
Outside Baghdad	10	6.4%
Total	70	100.0%
Marital Status		
Marital Status		
Unmarried	60	38.5%
Married	10	6.4%
Total	70	100.0%

Department		
Department		
Nursing	40	25.6%
Midwifery	15	9.6%
Anesthesiology	10	6.4%
Emergency	5	3.2%
Total	70	100.0%

Most of the study sample 23.7% are of age 20-24-years, the highest percentage (38.5%) live in Baghdad, more than half (38.5%) are single, and the highest percentage (25.6%) are from the nursing students.

Table 2. Participants' levels of anxiety

Total No.	Levels of Anxiety							
	Mild		Moderate		Severe		Total	
	F	%	F	%	f	%	F	%
	35	22.4%	16	10.3%	19	12.2%	70	100.0%

There is different severity of Anxiety the students inflicted with; 22.4% have mild level; 10.3% have moderate level and 12.2% with severe level of Anxiety.

Table 3. Distribution of the sample according to the levels of Anxiety

			Levels of Anxiety			Total	
			Mild	Moderate	Severe		
Age	≤ 19	F	11	4	4	19	
		%	15.7%	5.7%	5.7%	27.1%	
	20-24	F	18	6	13	37	
		%	25.7%	8.6%	18.6%	52.9%	
	25-29	F	3	3	1	7	
		%	4.3%	4.3%	1.4%	10.0%	
	30-34	F	2	0	0	2	
		%	2.9%	0.0%	0.0%	2.9%	
	35-39	F	1	1	0	2	
		%	1.4%	1.4%	0.0%	2.9%	
	≥ 40	F	0	2	1	3	
		%	0.0%	2.9%	1.4%	4.3%	
	Total		F	35	16	19	70
			%	50.0%	22.9%	27.1%	100.0%

Less than a fifth (18.6%) of the age group 20-24 have severe level of Anxiety while just 1.4% of age groups 35-39 have mild level of Anxiety.

Table 4. Levels of Anxiety according to residency of the students participated

			Levels of Anxiety			Total
			Mild	Moderate	Severe	
Residency	Baghdad	F	32	14	14	60
		%	45.7%	20.0%	20.0%	85.7%
	Out Baghdad	F	3	2	5	10
		%	4.3%	2.9%	7.1%	14.3%
Total		F	35	16	19	70
		%	50.0%	22.9%	27.1%	100.0%

A fifth(20.0%) of the students who live in Baghdad have severe level of Anxiety while just 4.3% of students are living outside Baghdad have mild level of Anxiety.

Table 5. Participants’ levels of Anxiety according to the marital status

			Levels of Anxiety			Total
			Mild	Moderate	Severe	
Marital Status	Unmarried	F	32	14	14	60
		%	45.7%	20.0%	20.0%	85.7%
	Married	F	3	2	5	10
		%	4.3%	2.9%	7.1%	14.3%
Total		F	35	16	19	70
		%	50.0%	22.9%	27.1%	100.0%

A fifth(20.0%) of the students group unmarried has severe level of Anxiety while just 4.3% of the married students have mild level of Anxiety.

Discussion

The most important consequence of this study is that the results of table (2) show that the students have different levels of anxiety. This result is supported by Clark and her colleagues (2000) found that the majority of subjects had high levels of test anxiety, as can be inferred from the results of the present study, the high and moderate levels of anxiety are higher than those of studies cited above. This difference may be due to several factors that have an impact on anxiety, such as different course contents, educational environment, test conditions, types of test questions and other factors⁽¹⁷⁾.

The results show that the students are young and being around eighteen years old and of mid- aged and being around forty years old and have different levels of anxiety table (3). In addition, the age groups of (20-24) have more levels of anxiety (52.9%). This result is supported by McDonald (2001); Showed that fear of failing a test increased with age in American and Australian students, in studies that use specific test

anxiety scales, anxiety levels typically increase with age, found that test anxiety levels increase through in younger and middle-aged students⁽¹⁸⁾.

The study indicates that the students living in the City of Baghdad have more levels of anxiety 85.7% than the students living in the outside Baghdad table (4). This might be due to the long way those students need to reach to the institute everyday, but the other students live in places around the institute.

Regarding the marital status, this study shows that 85.7% of unmarried female students have more levels of anxiety Table (5). This is supported by Amuda and colleagues investigated the relationship between marital status and test anxiety, academic performance of undergraduate students in the USA, the result showed that the single students more anxiety than married students. This means that marital status influences students’ academic achievement and those that are married tend to do better than the single students⁽¹⁹⁾.

Conclusion

The results of present study indicated that most of the students jointed in the study are of age twentieth and twenty-four; about half of them live in Baghdad; more than half are unmarried; and most of them are of the nursing department students. The study indicates that high percentage of those students have anxiety in different levels; about a quarter of them are with mild level, less than the quarter are with moderate level, and a twelve of the sample have severe level of anxiety. The study describes statistically significant association between age and severity of anxiety.

Recommendations: The researchers recommend the following:

1. The teachers should acknowledge the existence of test anxiety on the part of students and should take initiatives for its effective reduction. They should identify individuals with signs of stress and anxiety and should apply appropriate strategies to help them counteract these feelings.
2. Teachers should initiate discussions in the class about the feelings of anxiety and should take measures to reduce the sense of competition among them.
3. There should be some specific teachers training courses on managing test anxiety in order to make teachers aware of this complex issue and, hence, alleviate it.
4. Students should seek counselling before doing tests so as to increase their confidence.
5. Building on 2 above, group counselling sessions may be more beneficial. Such sessions enable students to share their personal experiences and copes strategies with others so that they know that they are not alone.

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Ethical Clearance: A permission to conduct this study was obtained from the ethical committee in the College of Nursing, University of Tikrit.

References

1. Keogh E, French CC. Test anxiety, evaluative stress, and susceptibility to distraction from threat. *European Journal of Personality* [Internet]. 2001 Mar [cited 2019 Jul 27];15(2):123–41.
2. Bateson M, Brilot B, Nettle D. Anxiety: An evolutionary approach. *The Canadian Journal of Psychiatry*, [Internet]. 2011 Dec [cited 2019 Jul 27];56(12):707–15.
3. Driscoll R. Westside test anxiety scale. 2004; Retrieved January, 20, 2008.
4. Schlenger WE, Caddell JM, Ebert L, Jordan BK, Rourke KM, Wilson D, et al. Psychological reactions to terrorist attacks: Findings from the national study of Americans' reactions to September 11. *JAMA (Journal of the American Medical Association)* [Internet]. 2002 Aug 7 [cited 2019 Jul 27];288(5):581–8.
5. Harris HL, Coy DR. Helping students cope with test anxiety. 202; ERIC Counseling and Student Services Clearing House.
6. Hill KT, Wigfield A. Test anxiety: A major educational problem and what can be done about it. *Elementary School Journal* [Internet]. 1984 Sep [cited 2019 Jul 27];85(1):105–26.
7. Acharya S. Factors affecting stress among Indian dental students. *Journal of Dental Education* [Internet]. 2003 Oct [cited 2019 Jul 27];67(10):1140–8.
8. Aktekin M, Karaman T, Senol YY, Erdem S, Erengin H, Akaydin M. Anxiety, depression and stressful life events among medical students: a prospective study in Antalya, Turkey. *Medical Education* [Internet]. 2001 Jan [cited 2019 Jul 27];35(1):12–7.
9. Fuad MD, Nasir Al-Zurfi BM, Qader MA, Abu Bakar MF, Elnajeh M, Abdullah MR. Prevalence and Risk Factors of Stress, Anxiety and Depression among Medical Students of a Private Medical University in Malaysia. *Education in Medicine Journal* [Internet]. 2015 Jun [cited 2019 Jul 27];7(2):e52–9.
10. Fuad MD, Nasir Al-Zurfi BM, Qader MA, Abu Bakar MF, Elnajeh M, Abdullah MR. Prevalence and Risk Factors of Stress, Anxiety and Depression among Medical Students of a Private Medical University in Malaysia. *Education in Medicine Journal* [Internet]. 2015 Jun [cited 2019 Jul

- 27];7(2):e52–9.
11. Freling TH, Forbes LP. An examination of brand personality through methodological triangulation. *Journal of Brand Management* [Internet]. 2005 Nov [cited 2019 Jul 27];13(2):148–62.
 12. Cassady JC. Test anxiety: Contemporary theories and implications for learning. In Cassady J C (Ed.), *Anxiety in schools: The causes, consequences, and solutions for academic anxieties* (pp. 7-26). New York, NY: Peter Lang
 13. Cassady JC, Johnson RE. Cognitive test anxiety and academic performance. *Contemporary Educational Psychology* [Internet]. 2002 Apr [cited 2019 Jul 27];27(2):270–95.
 14. Cherry K. Causes of test anxiety, 2012; causes.htm – Retrieved 21st November 2018.
 15. Lyness D. Test Anxiety. 2012; The Nemours Foundation: Retrieved 4 April 2018.
 16. Marks AD, Sobanski DJ, Hine DW. Do dispositional rumination and/or mindfulness moderate the relationship between life hassles and psychological dysfunction in adolescents? *Australian & New Zealand Journal of Psychiatry* [Internet]. 2010 Sep [cited 2019 Jul 27];44(9):831–8.
 17. Sarason IG. The test anxiety scale: Concept and research. 1978; In C. D. Spielberger, & I. G. Sarason (Eds.), *Stress and Anxiety* (Vol. 5, 193-216).
 18. Clark JM, Fox PA, Sheneider HG. Test anxiety and performance in a college course. *Psychol Red*, 2000; 82, 203-8.
 19. Silver RSE, Alison EA, McIntosh DN, Poulin M, Rivas G. Nationwide longitudinal study of psychological responses to September 11. *JAMA (Journal of the American Medical Association)* [Internet]. 2002 Sep 11 [cited 2019 Jul 27];288(10):1235–44.
 20. McDonald AS. The Prevalence and Effects of Test Anxiety in School Children. *Educational Psychology* [Internet]. 2001 Mar [cited 2019 Jul 27];21(1):89–101.
 21. Amuda B, Bulus A, Joseph H. Marital status and age as predictors of academic performance of students of Colleges of Education in the North-Eastern Nigeria. *American Journal of Educational Research*, 2016; 4(12): 896-902. doi: 10.12691/education-4-12-7.

Botox Effect on Sex Hormones and Lipid Profile of Females Rats

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Abstract

The present study aimed to investigate the effect of Botox on sex hormones level which including follicle-stimulating hormone (FSH), luteinizing hormone (LH) and progesterone in female rats and measurement of serum lipid profile. Two doses 0.1/ml/animal and 0.2 ml/animal from Botox were used and the animals were injected intramuscular of botulinum toxin for 1 day as two doses only. The results showed a significant decrease ($P < 0.05$) in the level of FSH and LH, with a significant increase the level of progesterone of the female treated with 0.1 ml and 0.2 ml of Botox compared with the control group. The results showed a significant increase in the level of cholesterol, TG, HDL, LDL and VLDL of the female treated with Botox at dose 0.2 ml when compared with the control group. While, the female treated with Botox at dose 0.1 ml there was no significant in level of cholesterol compared with control group. Also, there was a significant decrease of HDL of female rats treated with Botox compared with control group. Injections of female rats with botulinum toxin are generally well tolerated and side effects are few. A precise knowledge and understanding of the functional anatomy of the mimetic muscles is absolutely necessary to correctly use botulinum toxins in clinical practice.

Keywords: BOTOX; FSH; LH; Progesterone; Lipid profile.

Introduction

Botulinum is a neurotoxin produced by the bacterium *Clostridium botulinum*, an anaerobic, gram-positive, spore-forming rod commonly found on plants, in soil, water and the intestinal tracts of animals¹. There are seven recognized serotype (BoNT/A to/G) with the recent addition of another serotype, BoNT/X^{2,3}.

All serotypes interfere with neural transmission by blocking the release of acetylcholine, the principal neurotransmitter at the neuromuscular junction, causing muscle paralysis².

BoNT-A is the most commonly used serotype for medical application and was the first to be licensed for

medical use. There are several commercially available forms; Botox (Allergan Pharmaceuticals, Parsippany, NJ, USA) is the most widely used and has the most medical applications. Each formulation varies slightly in structure, efficacy, duration, and safety profile⁴. The effect of BoNT is site specific; it is administered by local injection (subcutaneous or intramuscular) into the targeted area. It can be administered using endoscopic procedure and by injection directly through the skin. Given the high affinity of BoNT to cholinergic neurons, its effects are consistent and, given at a low dose, have limited systemic adverse effects⁵. Botulinum toxin was first used clinically in the late 1970s in ophthalmology to treat strabismus¹ and over the last 20 years has gained widespread use in conditions requiring inhibition of excessive muscle spasm.

The broad range of medical indications for botulinum toxin include treatment of movement disorders (e.g. spasticity, cervical dystonia), urological disorders (e.g. overactive bladder), dermatological conditions (e.g. axillary hyperhidrosis), as well as cosmetic applications. Botulinum toxin A inhibits the release of substance P

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from the dorsal root ganglia of the rat⁶ and iris sphincter of the rabbit⁷. Substance P is believed to sensitize primary afferents and promote local release of histamine and bradykinin, both known to excite nociceptors⁸. Also, BoNT-A was used in medicine in 1977 for the treatment of strabismus in children. Since then, it has been widely used for different conditions and by different specialties. It is best known for its use in the cosmetic industries⁹. In 2002, the FDA approved the use of Botox (Botulinum toxin-A) for the cosmetic purpose of temporarily reducing glabellar forehead frown lines. The present paper aimed to investigate the effect of local injection of botulinum toxin on the level of reproductive hormones and lipid profile of female rat.

Materials and Method

Experimental design: The study was carried out on 24 mature female rats (*Rattus norvegicus*), aged as 10-12 weeks and weighing between 180 - 200 gm were obtained from Department of Biology, College of Science, University of Thi-Qar, Iraq. The animals were housed in a well ventilated 12 hrs light and 12 hrs dark cycles. The animals were divided into three equal groups, each group consist of (8) rats:

1. The first group (control group) injected with 0.9% NaCl.
2. The second group was injected with (0.1ml/animal/day) of BOTOX.
3. The third group was injected with (0.2ml/animal/day) of BOTOX.

Blood collection: After 30 days of treatment, the animals were sacrificed. Blood samples were collected by cardiac puncture, 5mL of blood were drawn from each animal of experimental groups, and put in tubes without EDTA, centrifuged at 3000 rpm for 15 minutes, and then serum was separated and kept in the refrigerator at -20°C until the time of assay.

Hormone assay: Serum samples were analyzed for

FSH and LH level, through solid phase ELISA based on the principle of competitive binding, using commercial kits from VEDALAB (France), while for measurement of progesterone using kit from Bio Meraux (France).

Measurement of serum lipid profile: The used reagents were supplied by Biolabo (France), and serum total cholesterol was measured according to¹⁰, and serum TG was measured according to¹¹. While, serum HDL was measured according to¹² and measurement of LDL and VLDL according to¹³, LDL and VLDL concentration was measured as follows:

$$\text{LDL} = \text{total cholesterol} - (\text{HDL} + \text{VLDL});$$

$$\text{VLDL} = \text{serum TG}/5;$$

Statistical analysis: Standard analysis of the data of different studied groups was performed using the computerized statistical program: The SPSS program (Statistical Program for Social Sciences). The results were expressed as mean ± S.E. Analysis of variance (ANOVA) was used to compare the results of different groups. The differences are considered to be significant at the level ($P \leq 0.05$)¹⁴.

Results

The results showed a significant decrease ($p < 0.05$) in the level of FSH and LH of the female treated with BOTOX at dose 0.1 and 0.2 ml when compared with the control group. While the results showed a significant increase ($p < 0.05$) in the level of progesterone of the female treated with BOTOX at dose 0.1 and 0.2 ml when compared with the control group (table 1). The results showed a significant increase ($p < 0.05$) in the level of TG, LDL and VLDL of the female treated with Botox when compared with the control group, while, the female treated with Botox at dose 0.1 ml there was no a significant in level of cholesterol compared with control group. Also, there was a significant decrease of HDL of female rats treated with Botox compared with control group. (Table 2).

Table 1: Effect of BOTOX on sex hormones levels of female rats

Progesterone (mg/dL)	LH(mg/dL)	FSH (mg/dL)	Animal Groups
22.59 ± 0.17 ^c	4.06 ± 0.19 ^a	3.33 ± 0.14 ^a	First group
34.56 ± 0.64 ^a	1.45 ± 0.12 ^c	1.32 ± 0.33 ^c	Second group
31.11 ± 0.51 ^b	3.45 ± 0.02 ^b	2.34 ± 0.49 ^b	Third group
3.0	0.6	1.0	LSD

Values are means ± S.E., Different letters refer to a significant difference at ($p < 0.05$), Same letters refer to no significant differences at ($p < 0.05$).

Table 2: Effect of BOTOX on lipid profile of female rats

VLDL Mg/dl	LDL Mg/dl	HDL Mg/dl	T.G. Mg/dl	Cholesterol Mg/dl	Animal Groups
15.34±0.34 ^c	27.34±0.23 ^b	52.23±0.12 ^b	63.00±0.34 ^b	97.45±0.56 ^b	First group
20.34±0.56 ^b	48.45±0.87 ^a	43.34±1.12 ^a	77.00±0.65 ^a	110.66±1.77 ^b	Second group
28.45±0.43 ^a	51.16±0.34 ^a	41.23±0.34 ^a	80.56±0.55 ^a	140.78±2.78 ^a	Third group
4.0	5.0	3.0	8.0	21.0	LSD

Values are means ± S.E., Different letters refer to a significant difference at ($p < 0.05$), Same letters refer to no significant differences at ($p < 0.05$).

Discussion

The present study indicated the effect of Botox on sex hormones female rats by decreasing level of FSH and LH and increasing level of progesterone level compared with the control group. The indications for Botox have evolved beyond cosmetic use to urinary incontinence and muscle spasms. With this popularity come more potential adverse effects, which are known to be short-lived and involve general or extremity weakness and pain. Researcher findings present the first reported case of a potential severe adverse side effect affecting the pituitary gland and persisting over a year after the injection.

These results are in line with the findings of other studies which found that (Botox), Botulinum toxin inhibits neurotransmitter release by cleaving SNAP-25 and SNARE proteins¹⁵. These proteins are necessary for vesicular exocytosis and have been implicated in the release of hormones from the anterior pituitary. Similarly, Botox could have caused inhibition of ACTH release resulting in central adrenal insufficiency for patient. Central adrenal insufficiency is a severe but treatable condition. Being aware of this potential adverse event and further researching its mechanism can help diagnose and treat affected patients promptly. This mechanism for GH and prolactin release has made Botox a targeted secretion inhibitor to treat prolactinomas and acromegaly. In our results showed a significant decrease in the level of FSH and LH and a significant increase in the level of progesterone of the female treated with BOTOX when compared with control group, as this side effect was documented when used difference of doses. While the side effect profile of long-term botulinum toxin injections has been well documented, especially in individuals with dystonia and spasticity^{16;17}.

Although commercially available preparations of BoNT have an excellent safety profile, especially for

cosmetic purposes. Also, in our result we showed higher significant in lipid profile in animals groups injection with Botox, but, no significant in level of cholesterol in rats treated with 0.1 ml of Botox compared with control group and there was a significant decrease of HDL of female rats treated with Botox compared with control group. This result accept with several studies have reported that following multiple and higher doses of BoNT injections, there is evidence of intermuscular lipid accumulation as a pathological response^{18;19}. Although the mechanisms are not known, several factors such as activation of satellite cells or alteration of muscle ultrastructure could promote this lipid accumulation. Dysferlin^{18;19}, an important muscle membrane protein, is deficient in limb girdle muscular dystrophies which leads to intramuscular lipid accumulation^{20;21}. Additionally, treatment with acetylcholinesterase inhibitors such as pyridostigmine can restore synaptic function and aid in muscle strength recovery. As discussed above, after BoNT injections muscles have the propensity to accumulate lipid which may lead to underestimation of atrophy in these muscles²². In present study the lipid accumulation leads to increased cholesterol and lipid profile in the blood, the reason back to Dysferlin, an important muscle membrane protein, is deficient in limb girdle muscular dystrophies which leads to intramuscular lipid accumulation^{20;21}, this side effect was not documented. Some animal studies have focused on the atrophy-inducing effects of BoNTs; however, in this study showed when injection with high doses from Botox induced side effect on level sex hormones and lipid profile.

Conflict of Interest: There is no conflict of interest.

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Ethical Clearance: The study is part of regular Thi-Qar university observation.

References

1. Scott A. B. Botulinum toxin injection of eye muscles to correct strabismus. *Trans Am Ophthalmol Soc.* (1981); 79:734–70.
2. Nigam P. K. and Anjana N. *Indian J Dermatol*(2010); Jan-Mar; 55(1): 8–14.
3. Zhang S.; Masuyer G.; Zhang J.; Shen Y.; Henriksson L.; Miyashita S.I.; Martinez-Carranza M.; Dong M.; Stenmark P. Identification and characterization of a novel botulinum neurotoxin. (2017), *Nat. Commun.*, 8.
4. Mangera A.; Andersson K.E.; Apostolidis A. Contemporary management of lower urinary tract disease with botulinum toxin A: a systematic review of Botox (onabotulinumtoxin A) and Dysport (abotulinumtoxin A). (2011), *Eur Urol*;60:784-795.
5. Aoki K. R. A comparison of the safety margins of botulinum neurotoxin serotypes A, B, and F in mice. (2001), *Toxicon*39:1815–1820.
6. Welch M.J., Purkiss J.R, Foster K.A. Sensitivity of embryonic rat dorsal root ganglia neurons to Clostridium botulinum neurotoxins. (2000), *Toxicon*; 38:245–58.
7. Ishikawa H.; Mitsui Y.; Yoshitomi T. Presynaptic effects of botulinum toxin type A on the neuronally evoked response of albino and pigmented rabbit iris sphincter and dilator muscles. (2000), *Japn J Ophthalmol*;44:106–9. 8. Basbaum A.I and Jessell T.M. The perception of pain. In: Kandel ER, Schwartz JH, Jessell TH, Editors. *Principles of neuronal science*. New York, (2000), McGraw Hill Publishers;480–1.
9. Bhatia K.P. and Munchau A. Uses of Botulinum toxin injection in medicine today.(2000), *BMJ*;320:161-165.
10. Allan C., Deacon Peter J.G. Dawson, *Clin.Chem.* (1997) 25/, p.97-984
11. Tietz N.; Burtis C.; Ashwood E. and Saunderson W. *Text book of clinical chemistry*, 2nd Ed.: 1030-1058. (1994), 1073-1080.
12. Lopes-Virella, M. Cholesterol determination in high-density lipoproteins separated by three different methods. *Clin. Chem.*(1977); 23(25): 882-884.
13. Fried Wald W.; Levy, R. and Fredrickson, D. Estimation of concentration of LDL-C in plasma without the use of preparative ultracentrifuge. *Clinical Chemistry* (1972), Chapter 18: 499-502.
14. Steel, R. G.; Torrie, J.H. and Dickie, D.A. *Principles and Procedures of Statistics-A Biometric Approach*. 3rd Ed. (1997), McGraw-Hill Publishing Company: Toronto.
15. Pratima, N. and Benjamin O. Central Adrenal Insufficiency Post Botox Injection. *Endocrine Society's 98th Annual Meeting and Expo*,(2016), April 1–4, 2016 – Boston.
16. Ramirez-Castaneda, J. and Jankovic, J. Long-term efficacy and safety of botulinum toxin injections in dystonia. (2013), *Toxins*, 5, 249–266.
17. Hayek S.; Gershon A.; Weintraub S.; Yizhar, Z. The effect of injections of botulinum toxin type A combined with casting on the equinus gait of children with cerebral palsy. *J. Bone Jt. Surg.* (2010), Br. Vol. 92, 1152–1159.
18. Minamoto V.B.; Suzuki K.P.; Bremner S.N.; Lieber R.L.; Ward S.R. Dramatic Changes in Muscle Contractile and Structural Properties after Two Botulinum Toxin Injections. *Muscle Nerve*, (2015), 52, 649–657.
19. Yada E.; Yamanouchi K.; Nishihara M. Adipogenic potential of satellite cells from distinct skeletal muscle origins in the rat. (2006), *J. Vet. Med. Sci*, 68, 479–486.
20. Grounds M.D.; Terrill J.R.; Radley-Crabb H.G.; Robertson T.; Papadimitriou J.; Spuler S.; Shavlakadze T. Lipid accumulation in Dysferlin-deficient muscles. *Am. J. Pathol.*, 184, 1668–1676.
21. Coddling S.J.; Marty N.; Abdullah N.; Johnson C.P. (2016). Dysferlin binds SNAREs (soluble N-ethylmaleimide -sensitive factor (NSF) attachment protein receptors) and stimulates membrane fusion in a calcium-sensitive manner. (2014), *J. Biol. Chem.*, 291, 14575–14584.
22. Krajacic P.; Pistilli E.E.; Tanis J.E.; Khurana T.S.; Lamitina S. TFER-1/Dysferlin promotes cholinergic signaling at the neuromuscular junction in *C. elegans* and mice. (2013), *Biol. Open*, 2, 1245–1252.

Regional Health Care: Does Give Benefits for Poor Communities?

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Abstract

This research to observe implementation of the regional health care program of Banyuwangi Regency, especially in the implementation of pro poor budgeting in poverty alleviation and the benefits received by the poor. The method used in this research is descriptive qualitative with respondents and the informants are beneficiaries of regional health care, health offices and technical support officers at the village/urban village office. The results of this study indicate that the implementation of public health care in Banyuwangi has been going well. The poor health care program in Banyuwangi is more commonly called the Declaration of Poor Letter (SPM). Problems rise from the implementation of the SPM are convenience for some people who have access to village officials, so that they can have SPM. In addition to the single parent, the difficult rule which states that only family members in a Family Card that can take care of SPM. We suggest for regional governments to increase human resources at the village level in SPM services. Most of the respondents, 95 percent stated that the regional health care program provides considerable benefits for the community, especially the poor.

Keywords: *Regional health care, Declaration of Poor Letter (SPM), poor community.*

Introduction

Regional autonomy system expects full participation of the community and regional government to be able to realize regional welfare and independence in development. The main problem of development is that poverty and the main goal of the central government and regional governments to reduce it. Poverty is an integrated problem with various other sectors such as health, education, infrastructure and community income. Decresing poverty is expected to improve the quality of development, therefore regional government look for the potential regional to reduce poverty and improve the quality of human development.

Poverty are factor of lack of capital, productivity in poor households so that they reduce spending in

the education and health. Low-income people have relatively low spending in the health sector, adequate access to education that informs about health, nutrition and disease prevention.^(1,2)Some research states that the health sector has an impact on human resources that has an effect on economic growth and has a positive impact in developed countries. This shows that the role of government in developed countries is greater in the health sector than in developing countries ⁽³⁻⁵⁾.

Public expenditure is intended for management to public needs creating public welfare. Welfare is determined by the source of income or adequate income by having jobs according to ability and talent. Besides that, the services needed by the people of his country not only the availability of public needs (water, electricity, health, education, security) but also other public rights to be eligible for life ⁽⁶⁾.

Pro poor budgeting are (1) a budget that directs the importance of development policies of the poor, (2) the practice budgeting policies that are design aimed at making policies, programs and projects that are pro-poor community, (3) budget policies whose impact can

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improve welfare and basic needs of the poor people. Pro-poor budget requires support through pro-poor policies which commitment from the government to prioritize poverty alleviation. In general, pro poor policy is a political action carried out with the aim of providing the allocation of rights and resources to individuals, organizations and territories that are marginalized by the market and the state. This can be interpreted that the policies taken by the government must emphasize the improvement that affect the problem of poverty. The realization of the allocation and distribution is to provide basic services in the form of education, health, housing and others^(7,8). Health capital can increase the return on investment devoted to education, because health is an important factor so that someone can attend school for learning. Longer life expectancy can increase returns on investment in education, while better health will lead to lower levels of education depreciation⁽⁹⁾.

The human development index in Indonesia is quite low. One of the provinces with low human development index is East Java. East Java from 2010 to 2015 experienced an increase in the human development index even though it only ranged from 0.5 to 0.8. This shows that the efforts of each city/regency are very strong to realize a better community life. As one of the regencys in East Java, Banyuwangi Regency is one that committed to reducing poverty by improving the quality of human development. The commitment of the government can improve the quality of public health, especially the poor. Although indirectly the population's health will improve quickly but government intervention in providing health services or health subsidies will have a good impact both the access of the poor to health services^(3,10-12).

Increasing human development index of Banyuwangi Regency shows the commitment of the local government to improve the quality of education, health and community income as three factors making up the human development index. One form of this commitment is an increase in local government expenditure in the education and health sector. One of the policies set out in Banyuwangi Regent Regulation No. 28 of 2016 concerning Guidelines for the Implementation of the Regional Health Care program and Health Services through a Poor Declaration Letter. The regulation stated that the Banyuwangi Regency Government provided the Regional Health Care program (Jamkesda) for participants who were not included as Contribution Beneficiaries (PBI) participants and the National Health Care Program (JKN). With the support

of local government programs, it is expected that access to health for the community, especially the poor, will be easy, because the facilities provided are not only for outpatient but also inpatient facilities. It is hoped that the community, especially the poor who need it, will be able to receive benefits from this local government program. For this reason, this study will examine the benefits received by the community, especially people with incomes below the average decent income in utilizing the Regional Community Health Care program, especially in Banyuwangi Regency.

Based on the situation analysis presented, this study looks for the implementation of the Banyuwangi Regency Health Care and its impact on the poor. Several studies on health programs from the government have been carried out such as the results of Wagstaff's (2011) research using the Benefit Incidence Analysis (BIA) in Vietnamese society found that health social care in Vietnam is more enjoyed by the rich than the program's goal to reduce poverty. While the Afghanistan Ministry of Health's research (2013) shows that public spending on health is still concentrated in Afghanistan Central Hospital, so there is still a need for grouping for government programs related to health. In China, Zhao (2019) found that since the adoption of NCMS the rural poor did not delay treatment to the hospital, so that they could receive treatment in a timely manner^(10,13,14).

Material and Method

This type of research used in this research is descriptive qualitative research, which is research that emphasizes the quality of the process rather than just the final result. The approach used in this research is a descriptive approach that emphasizes the individual in understanding and creating his daily life. A descriptive qualitative research approach is more likely to explore information from sources and respondents directly and written narrative so that it is easily understood by other communities. The focus of research in qualitative research is useful in providing direction during the research process, especially at the time of data collection, namely to distinguish data relevant to our research goals. The focus of this research is the community receiving health care for the poor in Banyuwangi Regency in 2016. The limitations of the study year are due to the existence of a data system in the Banyuwangi Regency Health Office.

This research was carried out in Banyuwangi Regency within a period of one year with a sample

selection in the form of Regencys resulting from random purposive sampling based on Regencys with the largest recipients of health care for the poor. Subjects and sources of information in this study are the Banyuwangi Regency Health Office, Sub-District Officers and Village Heads, Officers at the village/urban level who are in charge of taking care of the Poor Statement and Recipients of Regional Health Care using the method of observation (observation) and in-depth interviews. In 2016 Jamkesmin recipients in Banyuwangi were 506 people, so researchers took samples to conduct in-depth interviews as 84 beneficiary program.

Findings: The health care program for the poor is a national program that is integrated with the regions. There are three criteria for the Jamkesmin program in Banyuwangi Regency, namely financing from the Central Government, funding from the East Java Provincial Government and from the Banyuwangi Regional Government. The Health Care Program for the Poor has been legally through Banyuwangi Regent Regulation No. 8 of 2017 concerning Guidelines for Implementing Health Services for the Poor in Banyuwangi Regency. This regent's regulation states that the health of the poor who are not included in the Contribution Beneficiary Participants (PBI) of the National Health Care Program (JKN) will be provided by the Banyuwangi Regency Government. The *Jamkesmin* Program in Banyuwangi is also called the SPM Program. The SPM program (Declaration of Poor Letter) is a letter or identity given to the community outside JKN membership that meets the criteria of being poor. The first process of issuing this letter was a recommendation from a local Household Head (RT/RW) which was strengthened at the Village/Urban Head and known to the Sub-district Head. The second process is the issuance of SPM by authorized officials in this case the Social Office which has been legalized by the Health Office.

The financing of this health program includes funding for outpatient and inpatient care at health service centers and hospitals in collaboration with the Banyuwangi Regency Government, including Health Center, Blambangan Regional Hospital, Genteng Regional Hospital and East Java Provincial Hospital. Financing of this SPM program is fully charged to the Regional Development Budget of Banyuwangi Regency on condition that there is no duplication from other sources. For people who get a Declaration of Poor Letter (SPM) can receive services free of charge valid for three months and when they have expired can be extended.

The SPM can be issued manually or electronically. SPM issuance is manually issued if the electronic publishing process cannot be carried out. The status of patient participation must be ensured from the beginning of entry to the Advanced Referral Health Facility (FKRTL) and given the opportunity to administer the SPM no later than 3 (three) working days after the patient is admitted to the hospital, if until the specified time the patient cannot show the SPM, the financing is stated as general patient. If the patient is in an emergency condition and has been hospitalized, the Health Center will issue a referral based on the Certificate of Hospitalization from the Hospital. This SPM is only valid for 3 (three) months from the date set. If the SPM is used when it expires, an extension must be made by carrying out all procedures from the beginning. The average time needed for the issuance of the SPM is around 1-2 days. This is in accordance with existing regulations that the opportunity to take care of SPM no later than 3(three) working days after the patient is hospitalized. However, based on the results of interviews with SPM user respondents, the SPM issuance process before 2017 is still done manually.

In accordance with the results of interviews with village officials, that the SPM submission by the applicant is required to bring a referral letter from the Health Center/Hospital after which the applicant completes administration and submits SPM requests to service officers at the village/urbanoffice. The village/urban official will input data on the online SPM system so that the SPM can be issued.

Discussion

The problem that occurs when interviewing beneficiaries and health providers is that some people who submitted SPM have been treated at the regional hospital so that the village/urban is late in issuing SPM so that patients are not accommodated for financing health services. To anticipate this, some respondents stated that they made SPM without any health problems just in case. Another problem is the incomplete requirements submitted by the SPM applicant. The SPM can be issued even in the absence of a referral letter from the Health Center or Hospital due to the close relationship factor between the applicant and village officials. One of the reasons respondents use SPM as a precaution is because the person who can apply for SPM is the person concerned or family on a family card, it is quite difficult for respondents, especially single female parents and have children who are still not old enough. Although

according to the Health Department this method can reduce brokering practices but for single parents especially women it is quite difficult because besides they have to take care of sick family members, they also have to take care of SPM.

In addition, some respondents felt that not all SPM recipients were poor people. Some beneficiaries are believed to be capable communities, only because of the proximity to village officials, they have easy access to SPM. The lack of socialization in the community about the criteria of the poor and the criteria of SPM recipients also makes the community not fully understand the categories of the poor. On the other hand, the regional government through the Health Service seeks to provide health services to the poor evenly and on target, not to cause double funding in the community. In addition to the SPM beneficiary criteria that have not yet been socialized, one of the obstacles is the area of Banyuwangi Regency. From the 2016 SPM beneficiary data of 506 beneficiaries, 60 percent of beneficiaries are located in areas close to the city, with a radius between 30-40 km. this reinforces the statement from the public that there is a lack of socialization about SPM.

From the positive side of SPM, the implementation of comparisons between the handling of SPM manually and online is very different. Managing SPM online in accordance with the statement of the village head and the health office only requires a maximum of one day. Meanwhile, according to the results of interviews with respondents, online SPM maintenance can take up to three working days, faster than the time needed for manual handling because it takes approximately one week. The differences in SPM maintenance need to be minimized so that all people are able to reach them. Besides SPM service officers at the village level also need to be added so that the task runs optimally. Most of the respondents, 95 percent stated that the regional health care program provides considerable benefits for the community, especially the poor.

Conclusion

From the results of this research it can be concluded that the Poor Public Health Care Program in Banyuwangi Regency from the Local Government Budget is called the Declaration of Poor Letter (SPM). Namely the health care program for the poor with beneficiaries who do not receive health care from the central government and others source. The implementation of the SPM program

in Banyuwangi has several constraints, namely the SPM recipients who are not on target because of the tendency of alignments of village/urban officials, lack of human resources in carrying out online issuance of SPM and targets who are able families.

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Ethical Clearance: At the Faculty of Economics and Business we don't make ethical clearance

References

1. Sweeney JM, Zielinska P, Deeb-sossa N, Tu B. Clinical one health : A novel healthcare solution for underserved communities. *One Heal* [Internet]. 2018;6(July):34–6. Available from: <https://doi.org/10.1016/j.onehlt.2018.10.003>
2. Sarti S, Terraneo M, Tognetti M. Poverty and private health expenditures in Italian households during the recent crisis. *Health Policy (New York)* [Internet]. 2017;121(3):307–14. Available from: <http://dx.doi.org/10.1016/j.healthpol.2016.12.008>
3. Azeez A, Abdul O, Kefeli Z. Projecting a Long Term Expenditure Growth in Healthcare Service : A Literature Review. *Procedia Econ Financ* [Internet]. 2016;37(16):152–7. Available from: [http://dx.doi.org/10.1016/S2212-5671\(16\)30106-X](http://dx.doi.org/10.1016/S2212-5671(16)30106-X)
4. Chaudhuri S, Dwibedi JK, Biswas A. Subsidizing healthcare in the presence of market distortions □. *Econ Model* [Internet]. 2017;64(April):539–52. Available from: <http://dx.doi.org/10.1016/j.econmod.2017.04.011>
5. Bhattacharjee A, Kook J, Subramanian C. Healthcare investment and income inequality. *J Health Econ* [Internet]. 2017;56:163–77. Available from: <https://doi.org/10.1016/j.jhealeco.2017.08.007>
6. Noor HF. *Ekonomi Publik (Ekonomi untuk Kesejahteraan Rakyat)*. 1st ed. Padang: Akademia Permata; 2013.
7. Institute for Research and Empowerment (IRE). *Mempertemukan Dua Hulu (Pelajaran Desentralisasi Fiskal dan Penanggulangan Kemiskinan dari Gunungkidul)*. 1st ed. Eko, Sutoro dan Zamroni S, editor. Yogyakarta: IRE Yogyakarta; 2011.

8. Hogantara SA. Evaluasi Bantuan Sekolah di Kota Semarang (Benefit Incidence Analysis). Skripsi. Semarang: Undip; 2011.
9. Todaro, P. Michael dan Smith SC. Pembangunan Ekonomi Dunia Ketiga. 2nd ed. Jakarta: Erlangga; 2006.
10. Zhao W. China Economic Review Does health care promote people ' s consumption? New evidence from China. *China Econ Rev* [Internet]. 2019;53(August 2018):65–86. Available from: <https://doi.org/10.1016/j.chieco.2018.08.007>
11. Tran LD, Zimmerman FJ, Fielding JE. SSM – Population Health Public health and the economy could be served by reallocating medical expenditures to social programs. *SSM - Popul Heal* [Internet]. 2017;3(December 2016):185–91. Available from: <https://doi.org/10.1016/j.ssmph.2017.01.004>
12. Bairoliya N, Canning D, Miller R, Saxena A. The Journal of the Economics of Ageing The macroeconomic and welfare implications of rural health care and pension reforms in China q. *J Econ Ageing* [Internet]. 2018;11:71–92. Available from: <https://doi.org/10.1016/j.jeoa.2017.01.004>
13. Wagstaffa A. Benefit Incidence Analysis Are Government Health Expenditures : More Pro-Rich Than We Think? *Health Econ.* 2011;4(April,2012):351–66.
14. Afghanistan IR of, Health M of P. A benefit incidence analysis. 2013.

The Effect of Olanzapine on the Improvement of the Clinical Symptom of Schizophrenia

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Abstract

Administration of atypical anti psychotics (risperidone, olanzapine and clozapine) can improve cognitive dysfunction which occurs in schizophrenia patients. This study was aimed at analyzing the effect of olanzapine on the improvement of clinical symptom (the positive and negative symptoms) in schizophrenia patients. The study was observational with analytic approach on inpatient and outpatient schizophrenia patients in Wahidin Sudirohusodo Hospital and its networking. Subjects comprised of 30 samples who were divided into two groups: the risperidone group which consisted of 15 subjects and the olanzapine group which consisted of 15 subjects. The positive and the negative Symptom Scale (PANSS) was used to evaluate the psychopathological symptoms. The results showed that improvement of clinical symptom based on the decrease of the positive symptom of the PANSS was significant ($p < 0.05$) since the 2nd week in both groups. However, comparison of the changes of the positive symptom of the PANSS after medical treatment showed that the decrease of the positive symptom of the PANSS was greater in the risperidone group compared to the olanzapine group ($p < 0,05$). As for negative symptom of the PANSS between the two treatment groups showed that the decrease of negative symptom of the PANSS was significant ($p < 0.05$) since the 2nd week.

Keywords: Risperidone, olanzapine, clozapine, positive and negative symptoms, Schizophrenia.

Introduction

The course of schizophrenia consists of three phases. The first phase is the acute phase, characterized by the emergence of positive and negative symptoms, then followed by a stabilization phase, characterized by the relief of a symptom, and then a stable phase, characterized by reduced symptom severity.¹ Schizophrenia is a chronic, severe, pervasive mental disorder, which is characterized by hallucinations, delusions, and impairments in reality assessment. This disorder has a profound and influential impact on many lives and ultimately affects the quality of life of patients.^{5,2} Several

studies have been conducted to compare the advantages of atypical antipsychotics, since atypical antipsychotics have a brood effect in reducing psychotic symptoms with lower extrapyramidal side effects, leading to a better quality of life than typical antipsychotics.³ Until now, schizophrenia was known as chronic disease. At the beginning, the goal of therapy is to control positive and negative symptoms in schizophrenia. A data published in 2013 showed that the prevalence of severe mental disorders in Indonesia such as schizophrenia reached around 400,000 people or 1.7 per 1,000 population, overall there was 1% of the population in the world who suffered from schizophrenia.⁷

Oral atypical antipsychotics are considered as the first line treatment, especially for people with newly diagnosed schizophrenia.⁹ Atypical antipsychotics are also referred to as second generation antipsychotic (SGA). Included in this class of drugs are risperidone, olanzapine, quetiapine, clozapine and ziprasidone. SGA can suppress positive symptoms, improve cognitive dysfunction, improvesymptom which are refractory to typical antipsychotic treatment by blocking more 5HT2A

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receptor than dopamine in mesocortical pathway. SGA also blocks D2 receptors, resulting in more dopamine being released in the mesocortical pathway and causing an improvement in negative symptoms of schizophrenia. However, the affinity of each drug varies with various types of neurotransmitter receptors which in turn give different therapeutic profiles.^{10,11,12}

Risperidone can improve schizophrenia, improve mood in schizophrenia and bipolar disorder. Serotonin has an important role in influencing dopamine but has different effects on each dopamine pathway. Serotonin inhibition occurs in the mesocortex pathway resulting in the release of dopamine in the body cells and axon terminal at post-synapse. This is why risperidone could improve negative symptom.¹⁰ Lately, the use of atypical antipsychotic drugs was more often, with minimal side effect and could improve the positive and negative symptoms of schizophrenia patients.

Previous research^{6,8} compared the administration of risperidone and olanzapine therapy in schizophrenic patients. The results showed improvement for clinical symptoms of schizophrenia patients, especially the negative symptoms of patients who received olanzapine therapy compared to those who received risperidone therapy, meanwhile the administration of risperidone showed improvement in positive symptoms of schizophrenia compare to those who received olanzapine therapy. Since it is importance to determine the right antipsychotic from the beginning of therapy to ensure a good response for the improvement of symptoms of schizophrenic patients, researchers were interested in comparing the effectiveness of the two types of atypical antipsychotics most commonly used in Makassar, which are risperidone and olanzapine. So far, there had never been any research on the comparison of these two types of drugs based on the positive and negative symptoms of general psychopathology of schizophrenia.

Materials and Method

Location and Time of Research: The study was conducted at Wahidin Sudirohusodo Hospital and its network and from June to August 2018. This study was

an analytic observational study. Subjects of the study were schizophrenia patients who were inpatient and outpatient whomet the inclusion and exclusion criterias.

Method of data collection: Every schizophrenia patients who met the inclusion criteria was included in the study and data was taken including name, gender, age, last education, occupation, history of the objects previous diseases. The subjects were divided into two groups, risperidone group treatment (group A), and olanzapine group (treatment group B). Each objects from both groups were assessed for PANSS scores before being given therapy with olanzapine or risperidone. The positive symptom of the PANSS and the negative symptom of the PANSS scores were assessed for both groups in the 4th and 8th week.

All data was processed and analyzed by statistic program

Results

Thirty subjects joined the study, consist of fifteen subjects who were given risperidone and fifteen subjects who were given olanzapine. The risperidone group was given 2 mg each 12 hours orally and the olanzapine was given 10 mg each 24 hours orally. Measurement of PANSS scores for each subject was carried out at baseline, on the 2nd week, on the 4th week and on the 8th week of therapy.

The change of the positive symptom of the PANSS score in risperidone group (A) and olanzapine group (B) by the Independent T-test showed that the positive symptom of the PANSS was greater in group A than in group B significantly ($p < 0.05$), which was respectively 14.6% vs 8.5% on the 2nd week, 26.1% vs 19.1% on the 4th week and 40.1 vs 31.0 on the 8th week. Result of the paired T-test for each group showed a significant decrease of the negative symptom of the PANSS ($p < 0.05$) since the 2nd week, in both groups. The longer the treatment, the greater the changes of the positive symptom of the PANSS which were 14.3% vs 11.5% on the 2nd week, 32.8% vs 24.3% on the 4th week and 48.1% vs 36.1% on the 8th week respectively.

Table 1: Comparison of Positive Symptom of The PANSS and Negative Symptom of The PANSS at Various Lengths of Treatment

Variable	Length of Treatment	Group		P*
		A	B	
		Mean (SD)% Changes	Mean (SD)% Changes	
Positive PANSS	the 2 nd week	14.6(8.6)%	8.5(5.7)%	0.029
	the 4 th week	26.1(8.4)%	19.1(9.1)%	0.036
	the 8 th week	40.1(11.7)%	31.0(8.9)%	0.024
Negative PANSS	the 2 nd week	14.3(8.4)%	11.5(7.1)%	0.318
	the 4 th week	32.8(9.3)%	24.3(5.6)%	0.008
	the 8 th week	48.1(11.1)%	36.1(6.9)%	0.001

* Paired T-test. A: risperidone group, B: olanzapine group. Source: Primary Data, 2018.

Paired T test was used to see change of the positivesymptom of the PANSS in the two groups because the data was distributed normally. There was a significant decreased of the positivesymptom of the PANSS (p <0.05) since the 2nd week in both groups.

The longer the treatment, the greater the changes of the positivesymptom of the PANSS, which were 14.6% vs 8,5% on the 2nd week, 26.1% vs 19.1% on the 4th week and 40.1% vs 31.0% on the 8th week respectively.

Table 2. The Effects of Both Treatment Groups on Positive Symptom of the PANSS Changes in Various Lengths of Treatment

Group	Length of Treatment	Decreases of positive PANSS			P*
		PANSS Value	Changes	% Changes	
A	the 2 nd week	24.33(8.36)	3.73(3.6)	14.6(8.6)%	0.001
		20.60(6.87)			
	the 4 th week	24.33(8.36)	6.67(3.96)	26.1(8.4)%	
		17.67(5.51)			
	the 8 th week	24.33(8.36)	10.07(4.71)	40.1(11.7)%	
		14.27(4.96)			
B	the 2 nd week	21.20(7.89)	2.13(1.51)	8.5(5.7)%	<0.001
		20.87(6.42)			
	the 4 th week	21.20(7.89)	4.47(2.48)	19.1(9.1)%	
		18.53(6.19)			
	the 8 th week	21.20(7.89)	7.27(2.99)	31.0(8.9)	

* Paired T-test. A: Risperidone group, B: Olanzapine group. Source: Primary Data, 2018.

Result of the paired T-test for each group showed a significant changes of the negative symptom of the PANSS (p <0.05) since the 2nd week. In both groups the longer the study, the greater the change of the

positivesymptom of the PANSS which were 14.3% vs 11.5% on the 2nd week, 32.8% vs 24.3% on the 4th week and 48.1% vs 36.1% on the 8th week respectively.

Table 3. Effects of Both Treatment Groups on Negative Symptom of The PANSS Changes in Various Lengths of Treatment

Group	Observation	Decrease of Negative PANSS			P*
		Values	Changes	% Changes	
A	the 2 nd week	20.27(6.27)	2.80(2.40)	14.3(8.4)%	<0.001
		17.47(5.95)			
	the 4 th week	20.27(6.27)	6.53(2.80)	32.8(9.3)%	
		13.73(5.04)			
	the 8 th week	20.27(6.27)	9.93(4.71)	48.1(11.1)%	
		10.33(3.58)			
B	the 2 nd week	21.20(7.89)	2.40(1.40)	11.5(7.1)%	<0.001
		18.80(7.19)			
	the 4 th week	21.20(7.89)	4.93(1.58)	24.3(5.6)%	
		16.27(6.64)			
	the 8 th week	21.20(7.89)	7.60(3.02)	36.1(6.9)%	

* Paired T-test. A: Risperidone group, B: Olanzapine group. Source: Primary Data, 2018

The difference in total PANSS score between the two groups was consistent ($p < 0.05$). Comparison of the changes in the total PANSS score in groups A and B by the Independent T-test showed a reduction of total PANSS in both groups ($p > 0.05$).

Table 4. Effects of Both Treatment Groups on Total PANSS at Various Lengths of Treatment

Group	Observation	Decrease in Negative PANSS			P*
		Value	Change	% Change	
A	the 2 nd week	105.4(18.8)	12.8(6.3)	11.8(5.0)%	<0.001
		92.6(15.7)			
	the 4 th week	105.4(18.8)	23.6(7.6)	21.5(4.9)%	
		82.3(14.0)			
	the 8 th week	105.4(18.8)	32.1(9.0)	30.0(4.3)%	
		73.2(11.5)			
B	the 2 nd week	74.2(21.3)	11.7(8.0)	62.5(17.9)%	<0.001
		62.3(17.9)			
	the 4 th week	74.2(21.3)	20.5(9.4)	53.7(15.7)%	
		53.7(15.7)			
	the 8 th week	74.2(21.3)	28.4(2.5)	45.8(14.4)%	
		45.8(14.4)			

Discussion

This study showed that risperidone and olanzapine were both effective for the positive symptoms and the negative symptoms, but risperidone was superior in dealing with both positive and negative symptoms. Olanzapine, a thienobenzodiazepine derivative is an atypical antipsychotic drug which shows affinity for D1-D5 receptors, serotonergic receptor (5HT₂, 3, 6), muscarinic receptors (subtypes 1-5), adrenergic

receptors (alpha 1-2), and histaminergic receptor (H₁). Structurally, this drug resembles clozapine but has little difference in terms of its affinity. This drug is weaker than clozapine as alpha 1 and alpha 2 adrenergic agonists, and is slightly different as D₂, D₄, or 5HT_{2A} receptor antagonists.⁴

Paired T-test was used to see the changes in the positive PANSS for both groups, and each group showed a significant decrease in positive PANSS ($p < 0.05$) on

the 2nd week of therapy in both groups. The longer the treatment, the greater the changes in the positive symptom of the PANSS score, which were 14.6% vs 8.5% on the 2nd week, 26.1% vs 19.1% on the 4th week and 40.1% vs 31.0% on the 8th week of study. Risperidone and olanzapine improved of the positive symptoms in both groups (risperidone group and olanzapine group) starting from the 2nd week to the 8th week ($p = 0.001$).

When the Independent T-test was used to see the difference of the positive symptom of the PANSS score between the group given risperidone and the group given olanzapine, different results were obtained. The decrease of the positive PANSS was greater in group A (given risperidone) than in group B (given olanzapine) significantly ($p < 0.05$) which were 14.6% vs 8.5% on the 2nd week, 26.1% vs 19.1% on the 4th week and 40.1% vs 31.0%.

The changes in the positive symptom of the PANSS score was higher in the risperidone group since the 2nd week ($p = 0.029$) and there were more clinical changes in the positive symptoms in the risperidone group compared to the olanzapine group on the 8th week. This finding was consistent with previous study,⁵ where risperidone have a greater affinity for D2 than olanzapine.

The paired T-test results for each group along the study showed a significant decrease in the total PANSS scores ($p < 0.05$), seen from the 2nd week for both groups. This suggests that risperidone and olanzapine were equally effective for the negative symptoms. It was seen that the longer the therapy was given, the greater the changes in the negative symptom of the PANSS, which were 14.3% vs 11.5% on the 2nd week, 32.8% vs 24.3% on the 4th weeks and 48.1% vs 36.1% on the 8th weeks.

This finding was not consistent with the publication results,⁶ on which those who received olanzapine was better for the negative symptoms compared to risperidone since the first 3 months of treatment. This might be caused by different sampling method, different subtypes of schizophrenic, where in this study most of the subjects were paranoid schizophrenia with positive symptoms dominated over negative symptoms and simplex schizophrenia with negative symptoms dominated over the positive symptoms thus affecting the assessment results. Another thing that might affect this outcome was the sampling which combined inpatients and outpatients, in where hospitalized patients were more often in acute phase and predominated with positive

symptoms compared to the outpatients. In addition, the outpatients had more family attention and support than those who were hospitalized, thus affecting the results of the assessment of the negative symptoms. Due to the limitations of the study, were the author's ability, time of study and costs. There were several weaknesses in this study, the PANSS score was not measured regularly every week due to clinical symptoms of schizophrenia, and this study did not examine the side effects of medication and drug effects that was used to minimize the side effects.

Conclusions and Recommendations

This study showed that risperidone and olanzapine were effective for both the positive and the negative symptoms, but risperidone was better for both positive and negative symptoms. Subject who received risperidone experienced more positive and negative symptoms improvement compared to olanzapine. The researchers suggested that further studies should be carried out with bigger samples size and longer observation times. It was necessary to differentiate the treatment status of patients taken as a subjects whether they were outpatients or inpatients.

Ethical Clearance: Taken from Wahidin Sudirohusodo Hospital and Hasanuddin University committee.

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Conflict of Interest: The authors declare that there are no conflict of interests.

References

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. BMC Med. 2013;17:133-7.
2. Awad AG, Voruganti LN, Heslegrave RJ. Measuring quality of life in patients with schizophrenia. Pharmacoeconomics. 1997 Jan 1;11(1):32-47.
3. Dilbaz N, Continuum Treatment Group. New targets for the management of schizophrenia. Klinik Psikofarmakoloji Bülteni-Bulletin of Clinical Psychopharmacology. 2015 Dec 1;25(4):407-28..
4. Jayaram MB, Hosalli P, Stroup TS. Risperidone versus olanzapine for schizophrenia. Cochrane Database of Systematic Reviews. 2006(2).
5. Kaplan HI, Sadock BJ. Synopsis of psychiatry:

- Behavioral sciences clinical psychiatry. Williams & Wilkins Co; 1988.
6. Kumar PS, Anish PK, Rajmohan V. Olanzapine has better efficacy compared to risperidone for treatment of negative symptoms in schizophrenia. *Indian journal of psychiatry*. 2016 Jul;58(3):311.
 7. Riskesdas. *Basic Health research*. Jakarta: Ministry of Health Republic of Indonesia; 2013.
 8. ShojaShafti S, Gilanipoor M. A comparative study between olanzapine and risperidone in the management of schizophrenia. *Schizophrenia research and treatment*. 2014;2014.
 9. Shah SK, Ojha SP, Koirala NR, Sharma VD, Yengkokpam B. A comparison of efficacy of risperidone and olanzapine in schizophrenia patients. *Journal of College of Medical Sciences-Nepal*. 2011;7(3):29-35.
 10. Stahl SM. *Prescriber's Guide: Stahl's Essential Psychopharmacology*. Cambridge University Press; 2017 Mar 31.
 11. Canive JM, Miller GA, Irwin JG, Moses SN, Thoma RJ, Edgar JC, Sherwood A, Torres F, Lanoue M, Lewis S, Hanlon FM. Efficacy of olanzapine and risperidone in schizophrenia: a randomized double-blind crossover design. *Psychopharmacology bulletin*. 2006;39(1):105-16.
 12. Mauri MC, Paletta S, Maffini M, Colasanti A, Dragogna F, Di Pace C, Altamura AC. Clinical pharmacology of atypical antipsychotics: an update. *EXCLI journal*. 2014;13:1163.

Study of Some Virulence Factors of *Candida Albicans* Causing Intestinal Infection

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Abstract

The incidence of systemic candidiasis which is caused by *Candida albicans* has increased so the present study sheds light on detecting some virulence factors of *Candida albicans* like production of phospholipases and proteinases, besides the adherence on epithelial cells (from human mouth) and drug tolerance were concerned. Proteinase enzyme was produced by 20 *C.albicans* isolates (47.62%) out of 42 isolates. On the other hand, 18 out of 42 (42.86%) isolates of *C.albicans* could produce the phospholipase enzyme. The ability of the isolates for attachment onto the surface of epithelial cells was studied and found that 39 isolates of *C.albicans* could adherence epithelial cells and 20 isolates recorded percentage 95- 98%. As the resistance to antifungals concerned, we found that 32 isolates of *Candida* were resistant to nystatin. Amphotericin B was the most effective against all isolates of *Candida*. Microscopic examination results of histological section taken from rats' intestine tissues that artificially infected with *C.albicans* which included degeneration, necrosis, hemorrhage.

Keywords: Virulence factors, *Candida albicans*, Intestinal infection.

Introduction

The fungal infections caused by yeasts has increased over the past several decades. Among them, the imperfect yeast *Candida albicans* and several related *Candida* species are importance as opportunistic pathogens in immunocompromised hosts and may cause life-threatening infections. ⁽¹⁾The ability of *C. albicans* to infect host is supported by a wide range of virulence factors so that *C.albicans* shows various mechanisms that are suggestive of virulence such as ability to form hyphae (germ tube formation and pseudo hyphae), capacity to adhere to mucosal surfaces; produces hydrolytic enzymes; proteinases which hydrolyze peptides and phospholipases which hydrolyze phospholipids⁽²⁾. *C. albicans* is polyphonic. *C. albicans* grows as ovoid "yeast" cells, when cultured in standard yeast laboratory medium, however, mild environmental changes in temperature and pH can result in a morphological shift to pseudo hyphal growth. When *C. albicans* cells are grown in a medium that closed to the physiological environment of a human host, they grow as "true" hyphae. These structures are often observed in invading tissue⁽³⁻⁴⁾. *C. albicans* can cause

two types of infections in humans: superficial infections and life-threatening systemic infections ⁽⁵⁾. Adherence of *C. albicans* to host epithelial cells is a first step in the infection process, it is essential for colonization and mucosal disease. Colonization of mucosal surfaces is lead to disseminated Candidiasis ⁽⁶⁾.

Materials and Method

One hundred and stool samples were taken from patient with intestinal infection during the period of first of June 2015 till the end of April 2016. All samples were inoculated on the suitable culture media including (SDA, MRS, CHROM) agar. All plates were incubated aerobically at 37° C for 24 hr.

Yeast Identification: Single colonies were isolated from primary positive cultures and identified according to the criteria of ⁽⁷⁾, that were included the following tests: Morphological tests, germ tube test, production of chlamyospore, Gram stain, biochemical test sugar fermentation and assimilation test Chromogenic agar culture, growth at 45°C, API Candida system Diagnostic kit of *Candida*

Virulence factors tests:

Detection of protease production: *Candida albicans* isolates were inoculated the medium Trypticase Soya agar, after then the medium was incubated at 37° C for (24-48) hr., positive result it was observed when clear zone around the colony was appeared (8).

Detection of Phospholipase production: Yeast suspension was inoculated the Egg- Yolk agar medium after then the medium was incubated at 37° C for (24-48)hr., positive result it was observed when clear zone around the colony was appeared (8).

Adhesion assay:

1. Preparation of yeast suspension

- Apart of yeast culture which growing on SDA in aged 24 hrs was the transferred to test tubes, the test tubes containing SDB and incubated at 30°C for 24 hrs.
- The yeast culture centrifuged at 500 cycle/minute
- The precipitated cells were washed by PBS then centrifuged them and washing three times
- PBS solution was added to precipitate cells until the concentration of cells became 1×10^5 by using heamocytometer⁽⁹⁾.

2. Preparation of epithelial cells suspension

- By using cotton swabs the epithelial cells which found in buccal cavity endothelial cells were obtained from healthy women after washing their mouth by using sterile normal saline three times, then cotton swabs infused in PBS for 10 minutes
- The solution contain epithelial cells centrifuged at 300 cycle/minute and then washed it with PBS three times
- The PBS was added to precipitate cells to preparation epithelial supernatant with concentration 1×10^4 by using heamocytometer.
- The 0.5ml of candida suspension and 0.5ml of epithelial cells suspension were mixed in test tube and incubated at 37°C for 1h in Shaking incubator 40 rpm.
- The mixture was centrifuged and washing with PBS three times then PBS added to precipitate cells to prepared supernatant.
- The supernatant was centrifuged at 1000 cycle/

minute for 5 minutes, then PBS added to precipitate cells

- Drop of supernatant cells was taken and spread onto clean slid then let to dry and fixed by flame. The percentage of epithelial cells attached by yeast cells were calculated as flow: Adherence percentage = the number of epithelial cells attached by yeast cells /total epithelial cells × 100. (9).

Susceptibility to antifungal agent's tests: It was used for study yeast susceptibility to antifungal agents Disk diffusion method that by transferred part of colony of yeast were grown in SDA by loop to test tube that contained 5 ml of normal saline and count the fungal cells by using Haemocytometer to obtain concentration 1×10^5 , and then transferring 0.1 ml of the yeast suspension has been spread on the surface of Emmons medium plate and left to dry. Antibiotic disks have been placed and incubated for 24 hr. at 37°C, Then the zones of inhibition have been measured using a ruler and compared with the zones of inhibition determined by National Committee for Clinical Laboratory standards (NCCLS, 2003) or ⁽¹⁰⁾

1. Yeast suspension: *Candida albicans* that contained most virulence factors. obtained from a culture on SDB medium and incubated for 24 hrs. at 37 °C, cells were precipitated by centrifuging and the sediment was suspended in normal saline to result 5×10^5 cell/ml ⁽¹¹⁾.

2. Intestine Candida inoculation: Rats were given 5×10^5 cell/ml in drinking water from day 1 to day 15 induce intestine inflammation. Inoculated control rats were oral gavage inoculated with sterile PBS ⁽¹¹⁾. After 24 hr of injection the rats were divided into four groups each group contain 10 rats, group 1, 2 and 3 were prepared to study *Candida* infection and group 4 as control group, animal of each group were killed after (5, 10, and 15) days. Then the rat scarified after 15 days and removed intestine tissue then fixed with 10% formalin.

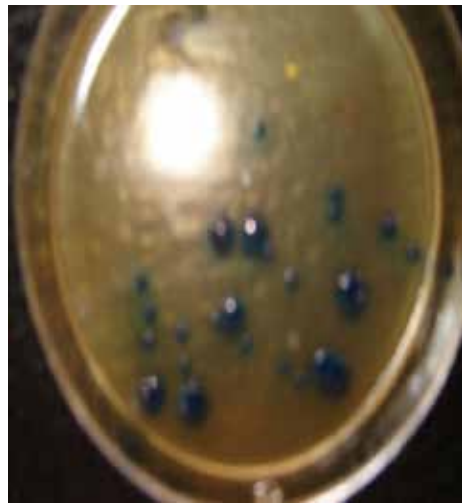
Results and Dissection

Isolation and Identification of Candida spp: Out of 100 stool samples, 95 isolates of *Candida* species were isolated from patient with fungal intestinal infection and diagnostic 8 isolates of *Candida* spp from 30 stool samples as control group. The types and numbers of these isolates, listed in (Table 1), were identified by using the CHROMagar, Biochemical tests, API20.

The majority of *Candida* species amongst the *Candida* isolates were *Candida albicans* (44.4%) followed by *C. tropicalis*, *C. krusei*, *C. parapsilosis* and *C. glabrata*. The color used to identify the *Candida spp* figure (1). *C. albicans* isolates produced green smooth-type colonies after incubation for 24, 48 and 72 h. the present study found CA to be useful for the identification of non- *C. albicans* species. This agreed with ⁽¹²⁾ who found that the chromogenic agar medium can be identification of not only *Candida* species but also other medically important non *Candida* yeast species, based on the development of coloured colonies. ⁽¹³⁾ Found that Chromogenic *Candida* Agar to be the most effective for distinguishing between different *Candida* species. The identification of clinically relevant yeasts by chromogenic medium is highly reliable and can be used as an accurate alternative to conventional identification method⁽¹²⁾.

Table 1: Frequency of isolation of important *Candida spp*.

Types of <i>Candida</i>	Number of Isolates		
	Healthy (%)	FII	%
<i>Candida. albicans</i>	5(62.5)	42	44.2
<i>Candida glabrata</i>	0(0.00)	4	4.2
<i>Candida tropicalis</i>	2(25)	20	21.1
<i>Candida parapsilosis</i>	1(12.5)	11	18.9
<i>Candida krusei</i>	0(0.00)	18	11.6
Total	8 (100)	95	100



B



C



A



D

Figure 1: *Candida spp* growing on chromogen agar (A: *C. albicans*, B: *C. krusei*, C: *C. glabrata*)

Detection of virulence factors for *Candida* species:

Adherence ability: The results showed that the ability of *Candida spp* for attachment onto the surface of epithelial cells and showed that the highest percentage of adherence was for *C.albicans* 98% and followed by *C.tropicalis* 95% while the lowest percentage of adherence was for *C.glabrata* 72%. The results showed that 39 isolates of *C.albicans* could adhere on oral cavity epithelial cells and 20 isolates recorded percentage 95- 98% (Table, 2), (Figure, 2).

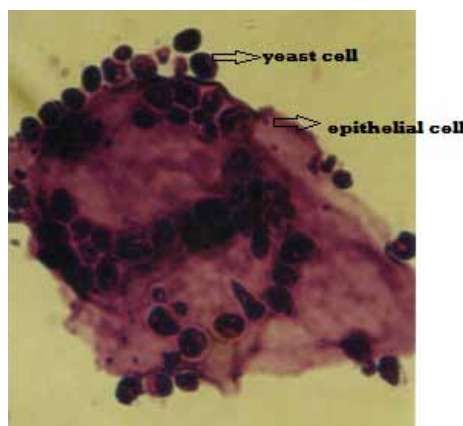


Figure 2: epithelial cells attached by *Candida albicans* yeast cells, slid staining by safranin (Light microscope, 100x).

Table 2: A- Percentage ability of some candida spp for attachment onto the surface of epithelial cells. B- Percentage of candida albicans adherence on oral cavity epithelial cells

A. Percentage ability of some candida spp for attachment onto the surface of epithelial cells.

Types of isolates	Highest of adherence (%)	Lowest of adherence (%)
<i>Candida. albicans</i>	98	85
<i>Candida glabrata</i>	72	48
<i>Candida tropicalis</i>	95	77
<i>Candida krusei</i>	88	60
<i>Candida parapsilosis</i>	78	52

B. Percentage of candida albicans adherence on oral cavity epithelial cells

Range (%)	Number of Isolates
95-98	20
90-94	8
85-89	11
Total	39

Resistance of *C.albicans* to antifungal agents:

Sensitive test for all isolates of *C.albicans* was done against four antifungal agents (Amphotericin B, Miconazole, Econazole, Nystatine) by cell diffusion method and the results are compared with ⁽¹⁰⁾. *C.albicans* showed the major resistance to Nystatine with percentage 76.19 followed by Econazole 71.43 Miconazole 66.7 and then Amphotericin B 42.86 (Figure,3). The result was close to the result of b⁽¹⁴⁾ who showed that Nystatine had the highest percentage of resistance reached to 57.5% compared with other antifungal agents. The mechanism of resistance will be different depending on the mode of action of antifungal compounds. Cellular and molecular mechanisms supporting resistance against antifungal classes⁽¹⁵⁻¹⁶⁾. Resistance was probably due to a decrease or lack of ergosterol content in cell membranes. Mitochondrial dysfunction was one of the possible mechanisms by which azole resistance can occur in *Candida glabrata* and *C.albicans*⁽¹⁷⁾ (Table, 3 A)

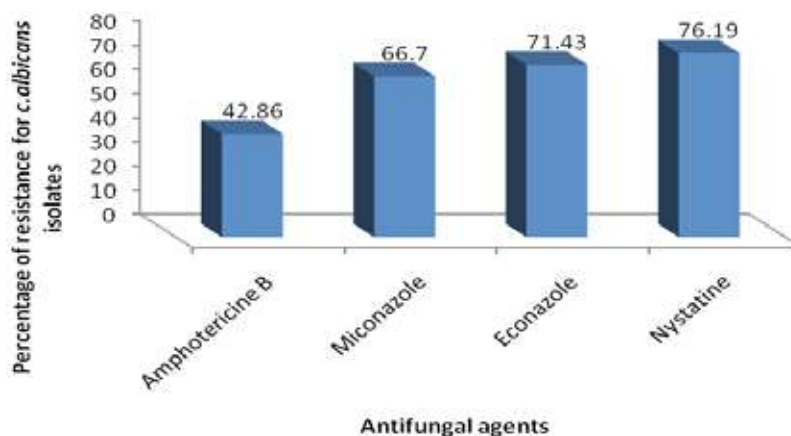


Figure 3: Percentage of antifungal resistance to *C.albicans*

Production of proteinase and phospholipase enzyme: The results revealed that proteinase enzyme was produced by 20 *C. albicans* isolates (47.62%) out of 42 isolates (Table 3 B). That is similar to the observation⁽¹⁸⁾ who found that proteinase production was also seen in *C. albicans* (82.1%). proteinase activity was detected in *C. albicans*, *C. tropicalis*, and *C. parapsilosis*⁽¹⁹⁾. The non-*Candida albicans* produced more proteinase than *C. albicans*. *C. albicans* produced higher levels of phospholipase than non-*Candida albicans* in the study of⁽¹⁹⁾. The enzyme phospholipase was produced by 18 out of 42 (42.86%) isolates of *C. albicans*. The result is close to the result of ⁽²⁰⁾ who detected Phospholipase

activity in 75% (9 out of 12) of the *C. albicans* isolates. Several studies have shown that phospholipase activity is observed only in *C. albicans* strains⁽²¹⁾. However, other researchers described that other *Candida* species such as *C. glabrata*, *C. guilliermondii*, *C. tropicalis*, *C. famata* and *C. inconspicua* secreted smaller amounts of phospholipase⁽²²⁾. Phospholipase enzyme digests the host cell membrane phospholipid causing cell lysis and changes in the surface features that enhance adherence and consequent infection and hence phospholipase production may be used as one of the parameters to distinguish virulent invasive strains from non-invasive colonies⁽²²⁾.

Table 3: A. Ability of candida albicans to produce proteinase and Phospholipase enzyme. B-Antifungal sensitivity of C.albicans.

A. Ability of candida albicans to produce proteinase and Phospholipase enzyme.								
Number	Amphotericin B	%	Miconazole	%	Econazole	%	Nystatine	%
R	18	42.86	28	66.7	30	71.43	32	76.19
S	24	57.14	14	33.3	12	28.57	10	23.81
B- Antifungal sensitivity of C.albicans.								
Types of enzyme	Positive		%		Negative		%	
Proteinase	20		47.62		22		52.38	
Phospholipase	18		42.86		24		57.14	

Conclusion

As resistance to fungi involved, it was found that 32 isolates of *Candida* were resistant to nystatin. Amphotericin B was the most effective against all *Candida* isolates.

Conflict of Interest: None

Funding: Self

Ethical Clearance: Not required.

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References

1. Pfaller MA, Rhine-Chalberg J, Redding W, Smith J, Farinacci G, Fothergill AW, Rinaldi MG. Variations in fluconazole susceptibility and electrophoretic karyotype among oral isolates of

2. Namking LA. Diversity of Pathogenic *Candida* Species Colonizing Women with and without *Candida* Vaginitis in Dar es Salaam Region, Tanzania Journal of Biology and Life Science. 2013. Vol. 4, No. 1:p:138-143.
3. Berman J, Sudbery PE. *Candida albicans*: a molecular revolution built on lessons from budding yeast. Nature Reviews Genetics. 2002. 3 (12): 918–930.
4. Peter E, Sudbery PE. Growth of *Candida albicans* hyphae. Nature Reviews Microbiology. 2011. 9 (10): 737–748.
5. Calderone RA, Clancy CJ. *Candida* and Candidiasis: ASM Press, Washington. 2012.
6. Takesue Y, Kakehashi M, Ohge H, Imamura Y, Murakami Y, Sasaki M. Combined assessment of Beta-D-glucan and degree of *Candida* colonization

Candida albicans from patients with AIDS and oral candidiasis. J Clin Microbiol, 1994. 32: 59-64.

- before starting empiric therapy for candidiasis in surgical patients. *World J Surg*, 2004. 28:625–630.
7. Milan EP, Zaror, L. Laboratory diagnosis of some types of fungi: Medical mycology. Rio de Janeiro: Guanabara Koogan, 2004. 4 :89-101.
 8. Elsner HA, Sobottka I, Mack D, Claussen M, Laufs R, Wirth, R. Virulence factors of *Enterococcus faecalis* and *Enterococcus faecium* blood culture isolates. *Eur. J. Clin. Microbiol. Infect. Dis.*, 2000. 19: 39-42.
 9. Chritchley IA, Douglas JL. Isolation & partial characterization of an adhesin from *Candida albicans*. *J. of General Microbiol*, 1987. 133:629-633.
 10. Himedia Laboratories Limited. Performance standards for antimicrobial disk susceptibility test. 4th ed, 1993. Vol.10.
 11. Fidel PL. History and update on host defense against vaginal candidiasis. *Am. J. Reprod. Immunol*, 2007. 57:2-12.
 12. Agrwal V, Bhagwat AM, Vishalakshi V, Gode V, Sawant CS. Exploring the potential of chromogenic medium for the identification of medically important yeast species other than *Candida*. *International Journal of Pharmacy and Pharmaceutical Sciences*, *Int J Pharm Pharm Sci*, 2014. Vol 6, Issue 3, 291-294.
 13. Messeir I, Abrantes P, Africa CW. Strengths and Limitations of different Chromogenic Media for the Identification of *Candida* Species. *Journal of Microbiology Research*, 2012. 2(5): 133-140.
 14. Al-Waaily ER. Study the inhibitory effect of some plant extracts and antibiotics on some microbial causing genital tract infections. Master thesis, University of Thi-Qar, Iraq, Education College for Pure Science, 2014. pp.1-126 (in Arabic)
 15. Vandeputte P, Ferrari S, Coste AT. Antifungal resistance and new strategies to control fungal infections, *International Journal of Microbiology*, 2012. 12: 1-26.
 16. Razzaghi-Abyaneh M, Sadeghi G, Zeinali E, Alirezaee M, Shams-Ghahfarokhi M, Amani A, Mirahmadi R, Tolouei R. Species distribution and antifungal susceptibility of *Candida* spp. isolated from superficial candidiasis in outpatients in Iran. *J Mycol Med*. 2014. (14) 5-10.
 17. Ferrari S, Sanguinetti M, Torelli R, Posteraro B, Sanglard D. Contribution of CgPDR1-regulated genes in enhanced virulence of azole-resistant *Candida glabrata*, *PLoS One*, 2011. 6 (3) 1-13.
 18. Riceto EB, Menezes RP, Penatti MP, Pedroso RS. Enzymatic and hemolytic activity in different *Candida* species. *Rev Iberoam Micol*. 2014. 63 (14): 19-9.
 19. Mohandas V, Ballal M. Distribution of *Candida* species in different clinical samples and their virulence: biofilm formation, proteinase and phospholipase production: a study on hospitalized patients in southern India. *J Glob Infect Dis*, 2011, 3(1):4-8.
 20. Chin VK, Foong KJ, Maha A, Rusliza B, Norhafizah M, Ng KP, Chong PP. *Candida albicans* isolates from a Malaysian hospital exhibit more potent phospholipase and haemolysin activities than non-*albicans* *Candida* isolates. *Trop Biomed*. 2013. 30(4):654-62.
 21. Pinto E, Ribeiro IC, Ferreira NJ, Fortes CE, Fonseca PA, Figueiral MH. Correlation between enzyme production, germ tube formation and susceptibility to fluconazole in *Candida* species isolated from patients with denture-related stomatitis and control individuals. *J Oral Pathol Med*. 2008. 37:587-592.
 22. Farina C, Saleri N, Lombart JP. Epidemiological phenotypic characteristics of vaginal yeasts at the Comoros. *Mycoses*, 2009. 52: 458-461.

The Effectiveness of National Early Warning Score (News) as Predictor of Mortality in Heart Failure Patients in Emergency Department

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Abstract

Introduction: Heart failure is one of the global health problems for society characterized by a high mortality rate, increased hospitalization and rehospitalization. National Early Warning Score (NEWS) is one who has the EWS development of physiological parameters include pulse rate, systolic blood pressure (SBP), respiratory rate, body temperature, level of consciousness (AVPU), oxygen saturation and the use of supplemental oxygen in the range of 0-3 on each parameter

Objective: This study aimed to analyze NEWS effectiveness as a predictor of mortality of heart failure patients in the Emergency Department (ED) of General Hospital of Dr. Slamet Martodirdjo Pamekasan.

Method: This study using observational analytic design with prospective cohort approach. The respondents in this study were 64 patients in *quota sampling*. The research instrument is observation sheet. ROC analysis and multivariate used multiple logistic regression test

Results: ROC test showed that NEWS has value of $p=0.000$ and AUC of 0.856 which describes NEWS can be a strong predictor related mortality in heart failure patients with CI of 95%, sensitivity value of 0.85 (85%) and specificity of 0.818 (81.8%). Logistic regression analysis explained the SBP became independent variables that most associated with mortality of heart failure patients with $\text{Exp}(B)$ of 10.208 which describes the high score of SBP has greater risk 10.208 times to death compared with a normal score of SBP after controlled by SPO_2 .

Conclusion: NEWS is an effective predictor of mortality of heart failure patients.

Keywords: *National Early Warning Score, heart failure, mortality, ED.*

Introduction

Heart failure is one of the global health problem for society characterized by a high mortality rate, increased hospitalization and rehospitalization¹. Patients with heart failure who have the condition decompensation come with a return visit to the installation of emergency and have high rates of hospitalization, resulting in an increase in health care costs². WHO (2016) recorded more than 17.5 million people in the world die of cardiovascular disease³.

Based on data from basic medical research in 2013, the prevalence of heart failure are diagnosed by a doctor or symptoms by 0.3%, or about 530 068 people, with

a prevalence of heart failure is based on the highest diagnosis in Yogyakarta (0.25%), followed by East Java (0.18%), while the prevalence of heart failure in North Sulawesi (0.14%), the prevalence of heart failure increases with age and the highest prevalence occurs at age 65-74 years (0.5%) and are more prevalent in urban areas⁴.

The treatment of patients with heart failure remains a problem for doctors and nurses in the ED, in terms of setting priorities, monitoring and assessing on an ongoing basis on the condition of the patient, and provide support to patients and families in a limited time⁵. One of strategy for detecting deterioration of non-trauma patients in

the ER is the implementation of Early Warning Score (EWS). National Early Warning Score (NEWS) is one of the development of EWS by the Royal College of Physicians that have physiological parameters include pulse rate, systolic blood pressure, respiratory rate, body temperature, level of consciousness (AVPU), oxygen saturation and the use of supplemental oxygen in the range 0-3 on each parameter. NEWS recommended to assess patients in acute pain conditions⁶. Currently there are limited studies that address the application NEWS in heart failure patients in the ED. EWS research in the ED just focused on predicting mortality and referral to the ICU and the study was conducted retrospectively⁷⁸.

Based on preliminary studies, the number of visits a patient in the ED of General Hospital of Dr. Slamet Martodirdjo Pamekasan in 2017 as many as 15.689 patients, while in 2018 until September as many as 111.276 patients. Heart failure among the 10 major diseases in the ED in 2017 until 2018. Interviews with ED nurse that there are some patients with heart failure who suddenly experience worsening and nurses require early detection system to predict the deterioration of the patient so that they can be addressed early and prevent death. Therefore, this research needs to be carried out.

Methodology of Research: This study used observational analytic design with prospective cohort approach. The respondents in this study were 64 patients in *quota sampling*. The research was conducted in the ED of General Hospital of Dr. Slamet Martodirdjo Pamekasan. The research instrument is observation

sheet. ROC analysis and multivariate used logistic regression test.

Research Result:

Table 1: Characteristics of Respondents based on NEWS, Age, Systolic Blood Pressure, Heart Rate, Respiration, Temperature and Oxygen Saturation

Variables	N	Mean ± SD	Min-Max
News	64	6.83 ±2.815	0-13
Age	64	58.25 ±14.46	25-85
Systolic blood pressure	64	154.36 ±37.33	95-261
Heart rate	64	97.36 ±21.69	53-149
Respiration	64	27.02 ±4.981	16-40
Temperature	64	36.5 ±0.61	34.9-38.5
Oxygen saturation	64	94.08 ±4.25	77-100

Table 1 shows the highest NEWS is 13 and the lowest is 0 with the average value is 6.83. The oldest respondent is 85 years old and the youngest is 25 years old with an average of 58.25 years old. A maximum systolic blood pressure on patients is 261 mm Hg and the lowest is 95 mmHg with an average of 154.36 mmHg. The maximum heart rate of patient is 149 and lowest is 53 with an average of 97.36. The maximum respiration rate on patient is 40x/minute and the lowest is 16x/min with an average of 27.02x/min. The highest temperature of the patient is 38.5⁰C and the lowest is 34.9⁰C with an average of 36.5⁰C. The maximum oxygen saturation of patient is 100% and the minimum is 77% with an average of 94.69%.

Table 2: Characteristics of Respondents based on Gender and Mortality

Variables	Category	f	%
Gender	Male	32	50
	Female	32	50
Mortality	Die	20	31.2
	Survive	44	68.8
Level of consciousness	Alert	58	90.6
	Verbal	2	3.1
	Pain	3	4.7
	Unresponsive	1	1.6
Oxygen	Use	61	95.3
	Do not use	3	4.7

Table 2 describes the gender of the respondents have an equal number of male and female with each number of 32 people. The survive respondents in this study were

44. The most respondents with alert awareness level were 58 people. The most respondent that use oxygen were 61 people.

Table 3: Description The Value of Area Under Curve (AUC) of NEWS

	AUC	Std. Error	p-value	CI 95%	
				LB	UB
News	0.856	0.059	0.000	0.741	0.971

Table 3 shows the NEWS has a value of p=0.000 and the AUC of 0.856 which describes NEWS can be a strong predictor related to mortality in patients with heart failure.

Table 4. Cut off Point, Sensitivity and Specificity NEWS

	Cut off Point	Sensitivity	Specificity
NEWS	6.5	0.85	0.818

Table 4 shows the cut off point of NEWS is at a point 6.5 which means that the detection of mortality of heart failure patients in the score of 6.5 with the sensitivity of 0.85 and specificity of 0.818. The sensitivity of 0.85 indicates the NEWS ability clinically to generate positive value or their mortality of heart failure patients by 85%. The specificity of 0.818 showed NEWS ability clinically to produce a negative value or the patient's life in case of heart failure by 81.8%.

Table 5. The results of multiple logistic regression test between the scores of systolic blood pressure (SBP), respiratory rate (RR), temperature, oxygen saturation (SPO₂), level of consciousness (AVPU) and use of oxygen to mortality in heart failure patients in the ED

Variables	Coefficient	The p-value	Exp (B)
Step 1			
Systolic blood pressure	2.109	0.017	8.237
Respiratory rate	0.775	0.239	2.171
Temperature	0.613	0.307	1.847
SPO ₂	0.987	0.016	2.684
Level of consciousness (AVPU)	7.276	0.999	1.445E3
The use of O ₂	8.624	0.999	5.565E3
Constants	-21.939	0.999	0.000
Step 2			
Systolic blood pressure	2.118	0.017	8.318
Respiratory rate	0.810	0.210	2.248
Temperature	0.629	0.297	1.876
SPO ₂	0.999	0.015	2.717
Level of consciousness (AVPU)	7.277	0.999	1.447E3
Constants	-4.812	0.013	0.008
Step 3			
Systolic blood pressure	2.177	0.021	8.816
Respiratory rate	0.771	0.267	2.162
SPO ₂	1.100	0.004	3.003
Level of consciousness (AVPU)	7.352	0.999	1.560E3
Constants	-4.478	0.022	0.011
Step 4			
Systolic blood pressure	2.323	0.013	10.208
SPO ₂	1.060	0.003	2.886
Level of consciousness (AVPU)	7.462	0.999	1.741E3
Constants	-2.529	0.000	0.080

Table 5 shown the final results of the multiple logistic regression test indicate the calculated value Exp (B) systolic blood pressure is 10.208, the value of Exp(B) of SPO₂ is 2.886 and the value of Exp(B) of the level of consciousness (AVPU) is 1.741. Based on the results of this analysis, the variables SBP became independent variables that associated with mortality of heart failure patients with Exp(B) value of 10.208 which describes high score of SBP has greater risk of 10.208 times to the death compared with a normal score of systolic blood pressure (SBP) after being controlled by oxygen saturation (SPO₂).

Discussion

The results of this study indicate that the NEWS is effective in detecting the occurrence of mortality in heart failure patients in the ER. Based on Table 5.4 shows that NEWS has the Area Under the Curve (AUC) of 0.856 (0.741-0.971), which means NEWS can be a strong predictor related mortality. Furthermore, the cut off point values of NEWS obtained at a point 6.5 which means that the detection of mortality of heart failure patients in the score of 6.5 with the sensitivity of 0.85 and specificity of 0.818. Supported by the positive predictive value of 0.68 indicates clinically NEWS ability to generate positive value or their mortality of heart failure patients by 68%.

According to the study results Alam et al., 2015 with a prospective design, explained NEWS as a good predictor of death with AUC value 0.768 (0.618 to 0.919)⁹. Powered studies Smith et al., 2012 retrospectively say that NEWS is an effective predictor to detect unexpected death compared with 33 EWS others with mean AUC value of 0.894 were strong¹⁰ (Smith et al., 2012). The study by Pimentel et al., (2018) retrospectively to detect mortality in patients in the ER told NEWS has a value of 0.862 which means strong AUC as a predictor of mortality¹¹. The purpose of NEWS including the assessment of acute illness, clinical deterioration detection, and enable timely clinical response. NEWS should be used for a preliminary assessment of acute illness and for further monitoring of patients during hospital stay. By NEWS regularly noted, the clinical response of patients can be identified when there is a potential patient's clinical deterioration and the need to obtain clinical care. Likewise Scoring NEWS will provide guidance on patient recovery and re-stabilized, thereby reducing the frequency and intensity of clinical monitoring to discharge patients⁶.

NEWS has seven physiological parameters include heart rate (HR), systolic blood pressure (SBP), respiratory rate (RR), body temperature, level of consciousness (AVPU), oxygen saturation and the use of supplemental oxygen in the range of 0-3 on each parameter⁶. On multivariate analysis, obtained the variable component of the NEWS of the most influential is the component of systolic blood pressure (SBP) with Exp (B) 10 208 which describes score SBP high 10 208 times greater risk of death compared with a score of SBP normal after being controlled by the oxygen saturation (SPO₂).

Blood pressure is one of the hemodynamic parameters were simple and easy to do measurement¹². According to Jones & Hall (2006), high blood pressure (hypertension) is an important risk factor for cardiovascular disease¹³. The results showed that patients with systolic blood pressure of 261 mmHg highest and the lowest was 95 mmHg with an average reach 154.36 mmHg. The study results Britton et al., (2009) says there is an increased risk of heart failure by 35% among subjects with systolic blood pressure of 130-139 mmHg compared to subjects with normal systolic blood pressure of 120 mmHg¹⁴. However, systolic blood pressure low (hypotension) an assessment of the worsening of the acute illness of the most significant because of hypotension may indicate compensation blood circulation due to a decrease in the volume of cardiac output, heart failure or heart rhythm disorders, and the effects of blood pressure lowering drugs¹³. Low systolic blood pressure (<120 mmHg) at admission showed a worse prognosis. In the scoring system NEWS hypotension condition is given a higher assessment scores (a score of 1 and 2) than hypertension <200 mmHg given a low score (a score of 0). Described in severe hypertension (systolic blood pressure ≥200 mmHg), can occur as a result of the pain experienced by the patient but it is important to consider the impact of acute disease or be exacerbated by severe hypertension and selection of clinical measures⁶.

Furthermore, oxygen saturation is a powerful tool for the assessment of pulmonary function and cardiac integrated⁶. Measurement of oxygen saturation is one of the non-invasive procedure using pulse oximetry are routinely be used in the clinical assessment of acute illness but are still rarely included in the EWS system. Because the measurements are considered practical, the oxygen saturation is considered as an important parameter in NEWS⁶. On the condition of heart failure with shortness of breath conditions can cause a decrease in oxygen saturation of the patient. In the

study Sittichanbuncha et al., 2015 says that the oxygen saturation including predictors of mortality. Oxygen saturation has a negative correlation with prehospital mortality¹⁵. In the results in Table 5.1 oxygen saturation values obtained for heart failure patients when entering the ED is 77-100%. There are still patients with heart failure had oxygen saturation below 94%. Studies have shown that the lower the patient's oxygen saturation owned by the increased risk of death in patients. Each 1% increase in oxygen saturation, it will be followed by a decrease in the risk of death by 8%¹⁵. By observing the oxygen saturation levels will be known needs oxygen delivery. Giving oxygen to patients would increase survival in patients so it will give good results. Oxygen saturation has a positive correlation with the amount of oxygen supplied which means higher oxygen levels given the higher levels of oxygen saturation¹⁶.

Conclusion

NEWS is effective as a predictor of mortality of heart failure patients in the ED as well as systolic blood pressure (SBP) is the most closely related to NEWS parameters as predictors of mortality of heart failure patients in the ED.

Conflicts of Interest: None

Ethical Clearance: This research has passed the test of ethics with No: 070/219/432.603/2019 implemented in general hospitals dr. Slamet Martodirdjo Pamekasan, East Java.

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References

1. Imaligy EU. Gagal Jantung pada Geriatri. CDK-212. 2014;41(1).
2. Lee DS, Stitt A, Austin PC, Stukel TA, Schull MJ, Chong A, et al. Prediction of Heart Failure Mortality in Emergent Care. *Annals of Internal Medicine*. 2012;155(11).
3. WHO. Cardiovascular diseases (CVDs) 2016 [cited 2018 September 3th]. Available from: [https://www.who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases-\(cvds\)#.VrIw5CcYeDI.mend](https://www.who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)#.VrIw5CcYeDI.mend).
4. Kemenkes. Republik Indonesia Badan Penelitian dan Pengembangan Kesehatan: Riset Kesehatan Dasar. 2013.
5. Salters CR, Bailey AL, Whayne TF. Current treatment of heart failure in the USA. *Expert Reviews Cardiovascular*. 2010;8(2).
6. Williams B, Alberti G, Ball C, Bell D, Durham L. National Early Warning Score (NEWS): Standardising the assessment of acute illness severity in the NHS. London: The Royal College of Physicians. 2012.
7. Subbe CP, Slater A, Menon D, Gemmel L. Validation of physiological scoring systems in the accident and emergency department. *Emergency medicine journal*. 2006;23(11):841-5.
8. Ho I, Li H, Shahidah N, Koh ZX, Sultana P, Hock Ong ME. Poor performance of the modified early warning score for predicting mortality in critically ill patients presenting to an emergency department. *World journal of emergency medicine*. 2013;4(4):273-8. PubMed PMID: 25215131.
9. Alam N, Vegting IL, Houben E, van Berkel B, Vaughan L, Kramer MH, et al. Exploring the performance of the National Early Warning Score (NEWS) in a European emergency department. *Resuscitation*. 2015 May;90:111-5. PubMed PMID: 25748878. Epub 2015/03/10. eng.
10. Smith GB, Prytherch DR, Meredith P, Schmidt PE, Featherstone PI. The ability of the National Early Warning Score (NEWS) to discriminate patients at risk of early cardiac arrest, unanticipated intensive care unit admission, and death. *Resuscitation*. 2013 2013/04/01/;84(4):465-70.
11. Pimentel MAF, Redfern OC, Gerry S, Collins GS, Malycha J, Prytherch D, et al. A comparison of the ability of the National Early Warning Score and the National Early Warning Score 2 to identify patients at risk of in-hospital mortality: A multi-centre database study. *Resuscitation*. 2019;134:147-56.
12. Muttaqin A. Pengantar Asuhan Keperawatan Klien Dengan Gangguan Sistem Kardiovaskuler. Jakarta: Salemba Medika; 2009.
13. Jones DW, Hall JE. Racial and Ethnic Differences in Blood Pressure. *American Heart Association*. 2006;114(25).
14. Britton AK, Gaziano MJ, Djoussé L. Normal systolic blood pressure and risk of heart failure in

US male physicians 2009. 1129-34 p.

15. Sittichanbuncha Y, Sanpha-asa P, Thongkrau T, Keeratikasikorn C, Aekphachaisawat N, Sawanyawisuth K. An Online Tool for Nurse Triage to Evaluate Risk for Acute Coronary Syndrome at Emergency Department. *Emergency Medicine International*. 2015;2015:4.
16. Silvestri LA. *Saunders Comprehensive Review For The NCLEXRN Examination*. US: Elsevier Inc; 2011.

Breast Cancer and Hormonal Level Changes

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Abstract

Purpose: Study of Surgical procedure used in treating Breast Cancers – Mastectomy, Bilateral Mastectomy and Adjuvant procedures and the rise in the blood hormonal levels of the breast cancer patients. The purpose of the study is to understand breast cancer and to delve into various factors that increase the risk of contracting breast cancer. It describes various surgical procedures like mastectomy, bilateral mastectomy and adjuvant procedures. It also describes the various serums that body secretes that can cause cancer. It sees the genetic factors and other risk factors that can cause cancer.

Method: It studied 30 breast cancer cases from private Clinicat Babylon. Only those patients who had undergone mastectomy or had tumors removed from breast were considered. These patients were in the age group of 25 to 65. Statistical data was arrived at by questionnaires and interviews with surgeons, nurses and patients. The paper also describes changes in the blood hormones of cancer patients. Complete blood tests were done on 30 patients that included the measurement of various serum and blood plasma cells such as Estrogen hormone, Progesterone hormone (Prog. H), Serum total cholesterol, Serum triglyceride, Serum HDL-cholesterol, the concentration of LDL cholesterol and other proteins in serum as IgG, IgM, and IgA.

Interpretations: Cancer if detected at a young age need not lead to mastectomy, but surgically removing tumors will suffice. As the age progresses the incidence of mastectomy and bilateral mastectomy also increases. The blood hormones of cancer patients showed abnormal readings and a conclusion can be drawn that BC can be detected from the abnormal levels of blood hormones.

Keywords: Blood hormones, breast cancer, tumors.

Introduction

According to Cancer.Net (2019)² & ³ Breast Cancer kills around 42000 women and at least 500 men every year. The number of women who are diagnosed for invasive breast cancer is approximately 268,600 in United States alone and 62000 women have in situ breast cancer. Though there have been many innovations in the medical science, women and to a lesser degree men continue to die or suffer because of this cancer.

According to Holst-Hansson, Idvall, Bolmsjö & Wennick, (2018)¹² say that cancer is gaining attention in Iraq as a significant health problem, this is because there is an increase in the cases of incidence as well mortality. Iraqi Cancer Board also echoes the same concerns. The reasons for the increase in cancer cases is attributed to many factors like improvement of case detection, early detection programs, rising awareness amongst the population and better registration of cases.

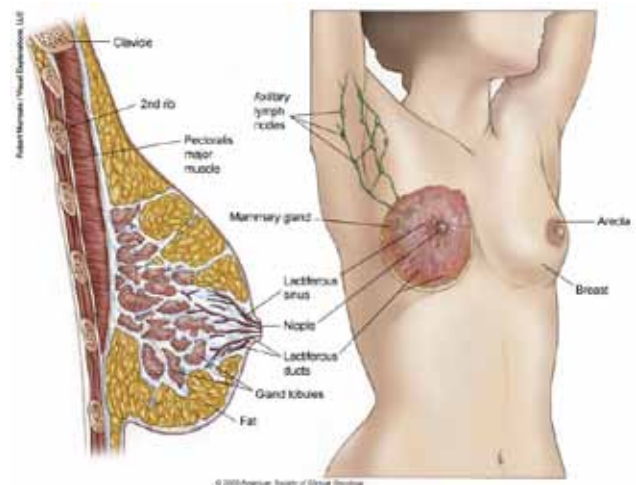


Fig. 1: American Society of Clinical Oncology.

Fisher et al (2014)⁹ opine that breast cancer (BC) is kind of malignancy that appears in the tissues of the breast. It occurs in both pre-menopausal and post-

menopausal women. BC forms in those tissues of the breast that usually carry milk and milk producing glands called lobules. Females with a history of breast cancer are at a risk having breast cancer too. Fisher et al (2014)⁹

Malvia, Bagadi, Dubey & Saxena (2017)⁸ opine that breast cancer (BC) starts with a development of tumor in the breast. There are 2 types' tumors benign and malignant.

Malignant tumors are aggressive and cancerous. In case malignancy is suspected the doctor will perform biopsy to understand the aggressiveness and severity of tumor. Coles et al (2017)¹³

Metastatic cancer happens when the cancerous cells of the malignant tumor spread to the other parts of the body via lymph system to form secondary tumors.

Anampa, Makower & Sparano (2015)¹² say that there is only one cure for advanced breast that is mastectomy, if cancer is detected earlier then only the tumor can be removed with some healthy tissue surrounding it called margin.

Cancer Detection: Hosseini, et al (2016)¹³ says that detection of cancer is very difficult as normal hormones and chemicals that are useful to the healthy body go on to fuel cancer cells also. Some of them are listed below.

Estrogen: Estrogen which is essential for growth and normal development of breast and its tissues is known to cause cancer if there is a higher exposure of the hormone. 2 types of cancers can be formed when there is a high exposure to estrogen as genotoxin and mitogen. Samavat, & Kurzer, (2015)¹¹

Lipids: It is believed that the changes in the lipid profile also causes cancer. Lipids have an important role in the maintenance of the cell integrity. It is hypothesized that when there are changes in the lipoprotein levels and plasma lipid there is malignant proliferation in the tissues of the breast. It has been further postulated that because of concentration in serum lipid in cancer patients can bring about increase production of tumor necrosis factor. Garg, et al (2016)¹¹

HER₂:

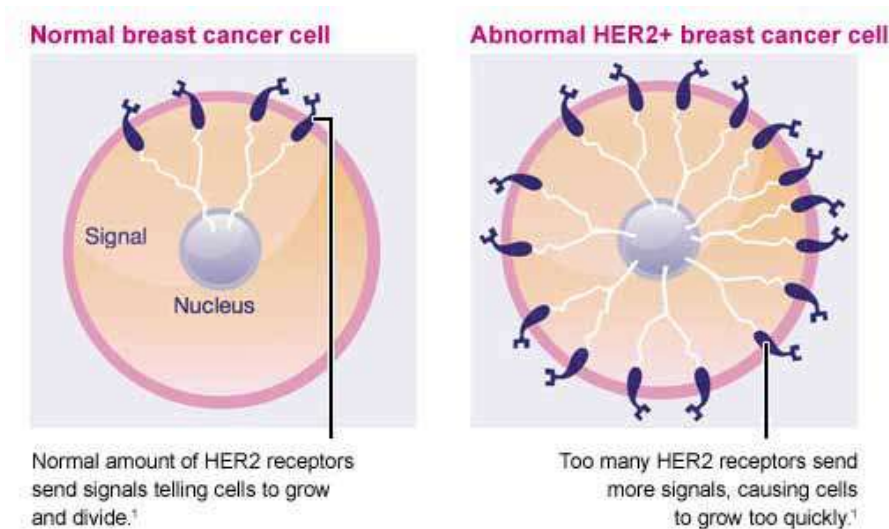


Fig 2. HER₂ (Source Cancer Research UK)

In fig 2. Shown HER₂/neu gene is a growth hormone. Healthy HER₂ receptors are proteins which are put in use when the breast cell grows, divides and in repairs. It was observed that in at least 25% of breast cancer patients this gene is not functioning properly. It makes excessive copies of itself in a process known

as “HER₂ gene amplification.” These extra cells then make the cells to make many HER₂ receptors. This is called “HER₂ protein overexpression.” It is because of these processes that breast cells divide and grow in an uncontrollable fashion. Katayama et al (2019)¹⁴

The Lymph System:

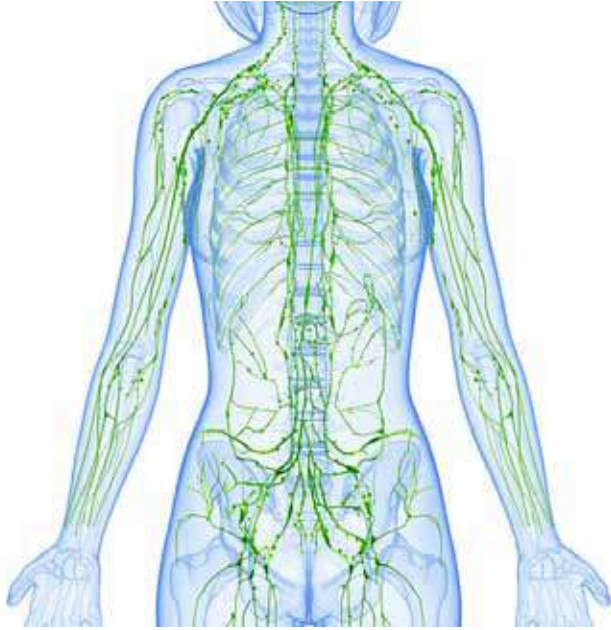


Fig 3. The Lymph Systems (Source cancer research UK.)

The network of lymph (fig. 3) nodes and lymph vessels run throughout the body and are part of the immune system. Just as the circulatory system of blood which distributes elements across the body. This system transports fluids and disease fighting cells.

Cancer cells typically grown in the ducts, lobules and the lobes within the lymph network. Katayama et al (2019)¹⁴

Genetic Factors: Lahart, Metsios, Nevill, & Carmichael, (2015)¹⁵ say that the following genetic factors are associated with BC

- *Gender: Female*
- *Age: 55.*
- *Race:* Caucasian women are more vulnerable to BC than any other race.
- *Family History and Genetic Factors:* If there has been a case of cancer (either breast or ovarian) in the immediate family such mother, sister then the chances of having cancer increase. If the relative had cancer before 50 then the risk increases.
- *Personal Health History:* If the patient has been diagnosed with BC in one breast, then the chances of having BC in the other breast increases in the future. The risk also increases if abnormal breast cells have

been found before (such as lobular carcinoma in situ (LCIS), atypical hyperplasia, or ductal carcinoma in situ (DCIS)).

- *Menstrual and Reproductive History:* Late menopause (after 55), Early menstruation (before age 12) having the first child at an older age, or if a women has never been pregnant also increases the risk for breast cancer.
- *Certain Genome Changes:* Mutations in some genes, like BRCA1 and BRCA2, can increase the risk of breast cancer. This is determined through a genetic test, which patients can consider taking if they have a family history of BC. Those who have these mutations may pass them to their children.
- *Dense Breast Tissue:* Dense breast tissue also increases risk for BC. It also makes the lumps harder to detect.
- *Radiation therapy on the chest:* If the woman has been given radiation therapy to the chest before the age of 30 then there is risk of contracting BC.
- *Combined Hormone Replacement Therapy (HRT):* Having combined hormone replacement therapy, as prescribed for menopause, increases the risk for BC and It also increases the risk that the cancer will be difficult to detect in the earlier stages.

Cancer treatment: Rheinbay et al (2017)⁹ opines in case there is BC is found then the surgery is the only effective treatment. In case the cancer is detected in early stages then lumpectomy is done where only the tumour is removed and the rest of the breast is conserved.

Decision to perform mastectomy (removal of the breast) or lumpectomy (removal of the tumour) is done with through consultation and permission of the patient.

Nowadays there are better method to perform mastectomy which preserve the breast skin and allows for a natural breast appearance following the surgery.

When do doctors advise mastectomy?

- In case of multiple tumours in the breast
- There are widespread or malignant-appearing micro calcifications (calcium deposits) that have been identified as cancerous after biopsy.
- In case of recurrence of breast cancer after radiation therapy

- Even after undergoing lumpectomy; cancer is found on the edges of the operated area.
- The size of the tumour is large compared to the size of the breast
- In case of pregnancy where radiation will harm the fetus. Coles et al (2017)¹³

Material and Method

A cross-sectional of 30 female breast cancer patients both young and old from hospitals and daily clinics in Babylon province were studied. They were presented with questionnaires and the physicians and nurses were

interviewed. Their ages varied from 25 to 65 as shown in the table and pie chart below.

Table 1 and pie chart about age of patients

Age	No. of patients
25-35	1
36-45	5
46-55	11
56-65	13
Gender	All females

Surgeries and Adjuvant procedures performed on the study group

Table 2.

Age	Mastectomy of single breast	Bilateral Mastectomy	Removal of tumor	Chemotherapy	Radiation Therapy
25- 35	0	0	1	1	0
36-45	4	0	1	1	1
46-55	7	3	1	11	11
56-65	8	5	0	13	13

Discussion on Surgical Procedures: The female aged 25-35 had tumour which was surgically removed, biopsy showed it was malignant in nature and so chemotherapy was prescribed to her. Hosseini et al (2016)¹³

Tumour also removed from 1 patient in the age group 36-45, but radiation was used before surgery to reduce the size of the tumour. Holst-Hansson Idvall, Bolmsjö, & Wennick, (2018) ¹²

Tumour was also removed from the age group 46-55. All the patients had to undergo adjuvant procedures to prevent the disease from appearing again. Holst-Hansson Idvall, Bolmsjö, & Wennick, (2018) ¹²

19 females had to undergo single mastectomy and also adjuvant therapy and 8 patients had to undergo bilateral mastectomy and adjuvant procedures to arrest the spread and re-occurrence of the disease.

Study of the blood samples for serum/hormonal imbalance

Blood contains different types of cells in definite proportions in normal human beings, however in case of diseases or infections these proportions change

dramatically. The same holds true for cancer patients also. Therefore the hematological and bio-chemical parameters of these 30 women were also studied.

Findings:

Table 3 shows the results of hematological parameters received from 30 BC patients

TEST	Patient
ESR mm/hr	17.355 ±6.154*
WBC X103 /µL	4.509 ±0.8839*
RBC x106 /µL	4.372 ±0.7995*
Packed cell volume (%)	35.206 ±4.105*
Platelets X103 /µL	180.27 ±32.158*
Lymphocytes (%)	46.009 ±4.7399*

*Values expressed as Mean +/-SD P value <0.05 was considered as significant.

The mean red blood cell count, packed cell volume, platelets count, white blood cell count, and lymphocytes are lower than what is observed in healthy women. Whereas the mean ESR values of the breast cancer patients were considerably higher than normal healthy women.

Table 4: Biochemical parameters of 30 female BC patients

Test	Patients
Est. H (Pg/ml)	92.286 ±20.407
Prog. H. (ng/ml)	2.347 ±0.850
Cholesterol(mg/dl)	182.14 ±16.868
Triglyceride(mg/dl)	120.77 ±10.152
H.D.L. (mg/dL)	55.148 ±20.486
L.D.L. (mg/dl)	74.605 ±13.050
IgA (g/L)	3.550 ±0.411
IgM (g/L)	1.685 ±0.351
IgG (g/L)	18.478 ±1.834

*Values expressed as Mean +/-SD P value <0.05 was considered as significant.

Table 3 shows the biochemical profile (Mean ±SD) in women with breast cancer. The data indicated higher levels of estrogen and progesterone than normal healthy women. Also total cholesterol, triglycerides level HDL were at higher than normal healthy levels. LDL levels were lower than those found in healthy women. Immunoglobulin’s IgG, IgA and IgM were also at higher than normal levels.

Discussion on blood tests: Physicians routinely use complete blood picture in diagnosing various diseases and infections like anemia, hemorrhagic states, cancers, allergic disorders and immunity disorders. Lahart, MetsiosNevill, & Carmichael (2015)¹⁵ In this study the low hematocrit levels show that cancer patients are suffer from anemia. This observation is in sync with other studies of similar nature.

With regards to age BC patients above the age 40 have significant reduction in RBC count and hematocrit level than healthy individuals of the same age. Medicinal Chemistry¹² opine that this could be because these parameters tend to reduce after the 5th decade or it could be that because of cancer also causes immune suppression and bone marrow suppression. It is also found that BC tends to be more aggressive in the younger patients. The low blood counts can also be attributed to side effect of chemotherapies that patients had to undergo as post-operative procedure. Chemotherapy also reduces the lymphocyte and it is considered as an adverse effect of this procedure Anampa, Makower, & Sparano (2015)¹²

There is a significant increase serum estrogen in patients of breast cancer women than normal healthy women. These results are also in sync to those obtained

by other investigators.

According to Rheinbay et al (2017)⁹It can be concluded that increased estrogen levels is a good marker in for increasing the risk factor of BC. Estrogen levels play an important role in the development of BC.

The results of table 3 show that there is noticeable increase in progesterone hormone in BC women compared to healthy women. Other investigators have also reported the same results. It is believed that increase in ovarian secretion of progesterone hormone could lead to BC. There is a marked increase in serum cholesterol in BC women than normal levels. However this may be because there is positive correlation between increased cholesterol levels and menopausal status. Rheinbay et al (2017)⁹ There is an increase in serum Triglyceride in the BC patients, but this could be attributed to the intake of tamoxifen, which is prescribed for patients having BC Rheinbay et al (2017)⁹

Finally it was observed that there were marked differences in BC women and healthy women in serum immunoglobulin IgA, IgG. However the results also showed that there was marked difference in serum immunoglobulin IgM. Some investigations have reported that the advancing metastatic BC is associated with high serum immunoglobulin levels of IgG and IgA, other investigators believe that a defense reaction against increasing tumor load or the secretion of immunoglobulin by the tumor Garg, et al (2016)¹¹

Conclusion

This study shows that all these women had contracted with breast cancer which was in different stages. All had undergone surgery as described above and also adjuvant procedures to arrest the spread of the disease.

Further blood samples were taken from the study group it was found that anemia; thrombocytopenia and leucopenia were usual basic features to be found in breast cancer patients.

This study also measured various biochemical factors like cholesterol, level of estrogen, progesterone hormones, lipoproteins (HDL, LDL), triglycerides and some immunoglobulin’s (IgG, IgA and IgM). The results show that there was a huge increase in cholesterol, level of estrogen, progesterone hormones, lipoproteins (HDL, LDL), triglycerides and high levels were also recorded in immunoglobulin’s (IgG, IgA and IgM).

Conflict of Interest: The author would like to state that there was no conflict of interest whatsoever.

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References

1. Anampa J, Makower D, Sparano J. Progress in adjuvant chemotherapy for breast cancer: an overview. *BMC Medicine*. 2015;13(1).
2. Cancer.Net. (2019). Breast Cancer - Introduction. [online] Available at: <https://www.cancer.net/cancer-types/breast-cancer/introduction> [Accessed 6 May 2019].
3. Cancer.Net. (2019). Breast Cancer - Types of Treatment. [online] Available at: <https://www.cancer.net/cancer-types/breast-cancer/types-treatment> [Accessed 11 May 2019].
4. Coles C, Griffin C, Kirby A, Agrawal R, Alhasso A, Bhattacharya I et al. SP-0314: Partial breast radiotherapy after breast conservation: 5 year outcomes from the IMPORT LOW (CRUK/06/003) phase III trial. *Radiotherapy and Oncology*. 2017;123:S162-S163.
5. Fisher B, Costantino J, Wickerham D, Redmond C, Kavanah M, Cronin W et al. Tamoxifen for Prevention of Breast Cancer: Report of the National Surgical Adjuvant Breast and Bowel Project P-1 Study. *JNCI: Journal of the National Cancer Institute*. 1998;90(18):1371-1388.
6. Garg N, Singh B, Jain A, Nirbhavane P, Sharma R, Tyagi R et al. Fucose decorated solid-lipid nanocarriers mediate efficient delivery of methotrexate in breast cancer therapeutics. *Colloids and Surfaces B: Biointerfaces*. 2016;146:114-126.
7. Holst-Hansson A, Idvall E, Bolmsjö I, Wennick A. The narrow treatment road to survival: Everyday life perspectives of women with breast cancer from Iraq and the former Yugoslavia undergoing radiation therapy in Sweden. *European Journal of Cancer Care*. 2018;27(2):e12825.
8. Hosseini H, Obradović M, Hoffmann M, Harper K, Sosa M, Werner-Klein M et al. Early dissemination seeds metastasis in breast cancer. *Nature*. 2016;540(7634):552-558.
9. Katayama H, Tsou P, Kobayashi M, Capello M, Wang H, Esteva F et al. A plasma protein derived TGFβ signature is a prognostic indicator in triple negative breast cancer. *npj Precision Oncology*. 2019;3(1).
10. Lahart I, Metsios G, Nevill A, Carmichael A. Physical activity, risk of death and recurrence in breast cancer survivors: A systematic review and meta-analysis of epidemiological studies. *Acta Oncologica*. 2015;54(5):635-654.
11. Malvia S, Bagadi S, Dubey U, Saxena S. Epidemiology of breast cancer in Indian women. *Asia-Pacific Journal of Clinical Oncology*. 2017;13(4):289-295. *Medicinal Chemistry (Formerly Current Medicinal Chemistry-Anti-Cancer Agents)*, 16(4), 519-525.
12. Rheinbay E, Parasuraman P, Grimsby J, Tiao G, Engreitz J, Kim J et al. Recurrent and functional regulatory mutations in breast cancer. *Nature*. 2017;547(7661):55-60.
13. Rosenberg M, Bikadi Z, Hazai E, Starborg T, Kelley L, Chayen N et al. Three-dimensional structure of the human breast cancer resistance protein (BCRP/ABCG2) in an inward-facing conformation. *Acta Crystallographica Section D Biological Crystallography*. 2015;71(8):1725-1735.
14. Samavat H, Kurzer M. Estrogen metabolism and breast cancer. *Cancer Letters*. 2015;356(2):231-243.

Socio-demographic Characteristics and Caregiver's Quality of Life Associated with Suspected Developmental Delay among Early Childhood in Northeast of Thailand

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Abstract

The first 5 years was possibly the most critical and extremely important in child development. Development problem of Thai children are not improve to standard.

This research aimed to analyze about association between Socio-demographic Characteristics, Caregiver's quality of life and suspected developmental delay among early childhood. A Cross-sectional analytical study, there are 1,168 sampling groups; caregivers 584 persons, early childhood 584 persons, between April to May 2019. The multivariable analysis was used by multiple logistic regression.

Early childhood aged average 36.1 months, males are 53.1%, and with suspected developmental delay 48.1%. There are 4 factors which are associated with the suspected developmental delay; 1) monthly self-income of caregiver (AOR= 1.9; 95%CI: 1.24 to 2.87; p= 0.003) 2) gender (AOR= 1.9; 95%CI: 1.33 to 2.64; p<0.001) 3) age range (AOR= 2.5; 95%CI: 1.54 to 4.09; p<0.001) and 4) quality of life about social relationship (AOR= 1.6; 95%CI: 1.23 to 2.01; p= 0.020).

Prevalence of suspected developmental delay is quite high, Socio-demographic Characteristics and caregiver's quality of life has influenced to the early childhood development.

Keywords: *Early childhood, Developmental, Quality of life.*

Introduction

Children are important resource in society; therefore, the children should have efficient development so that they can grow up to be good children learn qualities that will help them become happy, and be able to create and do anything benefit to our society in the future. The children are significant to our county which we should invest them to get high number of returns around 6.7-17.6 times¹.

In the first five years of life, it's the most important time at any other time in their lives; their developments will go faster including their brain develop more and faster around 80% comparing to adults. Besides, it's also related to the foundation for children developments and their quality of life. Window of opportunity points us that if we evaluate or notice their delayed development in early before age of 6 years, that can stimulate their development and help them to be their normal developments².

A report from World Health Organization found out that the children all around the world 15-20%, their development are not appropriate³. In addition, department of health, ministry of public health 2017 has observed that children normal developments for

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early children in Thailand are in their rate at 70%, the children in Northeast of Thailand is at only 50-60%⁴. Regarding to family structure, some parents move out from rural area to city and leave their children to stay with grandparents, this situation has occurred so much in Northeast region, the children do not live with their own parents are 30%⁵, so family structure are members of grandparents and grandchildren which without parents.

After literature review, there are risk factors which effect to the children developments involve with biological and economic and social. Regarding to biological risk factor composes of health and mothers' nutrition status, complication during intra partum and postpartum periods including health and nutrition status of the children⁶. Relating to economic and social factors compose of age, occupation of mothers, including family income and the way how they raise the children, especially mothers' education level is quite so much affect to the children than fathers^{7,8}. In the past, there are many studies related to risk factors which effects to the early children developments which still be problem. A part of this issue might cause of biological and economical and social risk factors. However, there is not any study about socio-demographic characteristics, caregiver's quality of life and early children developments in Northeast of Thailand.

Therefore, this study aimed to analyze about association between socio-demographic characteristics, caregiver's quality of life and suspected developmental delay among early childhood in Northeast of Thailand.

Material and Method

Study Design and Sampling: A cross-sectional analytical study and collect data from April through May 2019. The sample size was calculated following formula to specify sampling size by multiple logistic regression, Hsieh FY⁹. ρ of 0.70, VIF= 3.33. The sampling size of this study is 584 persons.

Using Multi Stages random sampling did in research for 20 provinces in Northeast region. Simple random sampling is used for 5 provinces at 25% out of all provinces in this region, next, for selected 2 districts out of each sampling province. Then, do random sampling group from name list of the early children (0-6 years) from public health department of sampling district (HosxP PCU program), according to proportional to size for 10 districts, get sampling group 58-60 persons each.

Inclusion criteria are Thai nationality children aged 0-6 years and been live in Northeast of Thailand. The caregivers are look after children at least 6 months up, their profiles can be given us completely and they must have the maternal and child health handbook. Regarding to exclusion criteria are disable children from birth which effect to their developments such as down syndromes, autism, cerebral palsy and children with seizure history, children with no cooperative to check development, children with no any age history and children who are not raised by their own blood relatives.

Material: Socio-demographic Characteristics which compose of age, gender, occupation, education level, self-income, family income, income sufficiency, number of children per family and living with their own parents.

Evaluation of Caregiver's quality of life by WHOQOL-BREF¹⁰: there are 4 domains; physical, psychological, social relationship and Environmental. Divide quality of life in each domain and overall for 3 levels which are poor, medium and good.

Suspected developmental delay test by Denver II is used to screen children's development. Four domains (gross motor, fine motor adaptive, language and personal-social). It consists of 125 items, testing time is around 10-20 minutes. The testing results are divided into 2 levels; Normal, develop a child without a delayed test and no more than one caution tests. Suspected has a test two or more cautions and one or more than one delay tests. This study uses Denver II in Thai¹¹ to do developmental tests. In addition, assessor has been passed children development training from the National Institute for Child and Family Mahidol University.

Data analysis: Relating to analysis of association between socio-demographic characteristics, caregiver's quality of life and suspected developmental delay, a simple logistic regression, was used for bivariate analysis to identify individual factors associated with suspected developmental delay. The factors that had p-value <0.25 were processed into the multivariable analysis using multiple logistic regression by backward elimination method which statistical significance is (p-value= 0.05), reported the adjusted odds ratio (AOR), 95% confidence interval (95% CI) and using Stata version 13.1 program (Stata Corp, College Station, TX)

Result

Socio-demographic Characteristics: The total 1,168 sampling; 584 caregivers and 584 childhood found most of caregivers are female 93.3%, average age is 40.4 years with a range of 16-74, their occupation is agriculturist 44.4%. Education level is primary school 46.4%, average monthly self-income 6,394.8 THB, average monthly family income 15,029.8 THB. Early childhood are males 53.1%; average age is 36.1 months with a range of 9-72 months, the children aged 36-76 months is 46.7%. The child living with their own parents is 51.4%. (Table 1).

Table 1: Socio-demographic characteristic

Factors	Number	(%)
1. Caregiver's age (Years)		
16 - 29	165	28.2
30 - 59	359	61.5
60 - 74	60	10.3
Mean: SD	40.4	13.8
Median (Min: Max)	39.0	16: 74
2. Occupation		
housewife	147	25.2
agriculturist	259	44.4
governmental officer	120	20.5
businessman, trader	58	9.9
3. Education level		
primary school	271	46.4
high school/vocational	213	36.5
bachelor's degree up	100	17.1
4. Monthly self-income (THB)		
< 10,000 (325 US dollars)	455	77.9
> 10,000	129	22.1
Mean: SD	6,394.8	7,922.9
Median (Min: Max)	4,000.0	0: 70,000
5. Monthly family income (THB)		
< 10,000	244	41.8
> 10,000	340	58.2
Mean: SD	15,029.8	15,706.5
Median (Min: Max)	10,000.0	1,000: 200,000
6. Income's sufficiency		
sufficient	299	51.2
insufficient	285	48.8
7. Gender of child		
male	310	53.1
female	274	46.9
8. Age range (months)		
0 - 12	105	18.0

13 - 35	206	35.3
36 - 72	273	46.7
Mean: SD	36.1	15.7
Median (Min: Max)	36	9:72
9. Number of children per family		
1	276	47.3
2	257	44.0
3 - 5	51	8.7
10. living with parent		
living with parents	300	51.4
not living with parents	284	48.6

Caregivers' quality of life: It found average score of their quality of life in good level 77.7%. When consider in each domain, their psychological domain is in good level 75.7%, next on down environmental domain is 71.7%, social relationship is 68.5% and physical is 66.3%. (Table 2).

Table 2: Caregiver's quality of life

Factors	Number	(%)
Quality of life in overall		
medium	130	22.3
good	454	77.7
Mean: SD	104.9	13.0
Median (Min: Max)	104.0	71: 130
Quality of life in each domain		
Physical		
medium	197	33.7
good	387	66.3
Psychological		
poor	2	0.3
medium	140	24.0
good	442	75.7
Social relationships		
poor	6	1.0
medium	178	30.5
good	400	68.5
Environmental		
poor	1	0.2
medium	164	28.1
good	419	71.7

Children development: The early childhood development in Northeast of Thailand found they are in suspected developmental delay 48.1%. If consider each domain development, language domain tends to be delayed the most 39.4%, next, it's fine motor adaptive 27.2%. (Table 3).

Table 3: Denver II Results

Denver II	Number	%
Normal	303	51.9
Suspect	281	48.1
Gross motor	79	13.5
Language	230	39.4
Fine motor adaptive	159	27.2
Personal-social	74	12.7

Factors associated with suspected developmental delay: Bivariate analysis: Bivariate analysis on the association between each independent variable and suspected developmental delay in early childhood was performed presenting the crude odds ratio (OR) with 95% CI, and p-value. All factors that had p-value <0.25 were proceeded to multivariable analysis by using multiple logistic regression. (Table 4)

Table 4: Factors associated with suspected developmental delay: Bivariate analysis

Factors	Number	% of Event	Crude OR	95%CI	P-value
1. Monthly self-income (THB)					0.003
> 10,000	129	36.4	1		
< 10,000	455	48.1	1.8	1.23-2.76	
2. Gender of child					<0.001
Female	274	39.8	1		
Male	310	55.5	1.9	1.36-2.62	
3. Age range (months)					<0.001
0 – 12	105	31.4	1		
13 – 35	206	46.6	1.9	1.16-3.12	
36-72	273	55.7	2.7	1.70-4.41	
4. living with parent					0.011
Living with parents	300	43.0	1		
Not living with parents	284	53.5	1.5	1.10-2.12	
5. Quality of life in physical domain					0.049
Good	387	45.2	1		
Medium	197	53.8	1.4	1.00-1.99	
6. Quality of life in social relationship domain					0.016
Good	400	44.7	1		
Medium and poor	184	55.4	1.5	1.18-2.18	

Factors associated with suspected developmental delay: Multiple logistic regression: Multiple logistic regression analysis by Backward elimination indicated that The children who are raised by the caregiver who has monthly self-income lesser than 10,000 THB, tend to be suspected developmental delay more than the ones who are taken cared by the caregiver with monthly self-income over than 10,000 THB for 1.9 times. (AOR= 1.9; 95% CI: 1.24 to 2.87). Boys tends to be suspected developmental delay more than girls for 1.9 times (AOR= 1.9; 95% CI: 1.33 to 2.64).

The child aged 13-35 months has a chance to suspected developmental delay more than the ones aged 0-12 months in double fold. (AOR= 2.0; 95% CI: 1.21 to 3.34). In addition to the children aged 36-72 months tends to be suspected developmental delay more than the children aged 0-12 months in 2.5 times (AOR= 2.5; 95% CI: 1.54 to 4.09)

The children who are raised by the caregiver with social relationship in medium and poor level, it has chance to reflect the children be suspected developmental delay more than the ones who are in good level for 1.6 times. (AOR= 1.6; 95%CI: 1.23 to 2.01). (Table 5).

Table 5: Factors associated with suspected developmental delay: Multivariate analysis

Factors	Number	% of event	Crude OR	Adjusted OR	95%CI	P -value
1. Monthly self-income						0.003
> 10,000	129	36.4	1	1		
< 10,000	455	48.1	1.8	1.9	1.24-2.87	
2. Gender						<0.001
Female	274	39.8	1	1		
Male	310	55.5	1.9	1.9	1.33-2.64	
3. Age range						<0.001
0-12	105	31.4	1	1		
13-35	206	46.6	1.9	2.0	1.21-3.34	
36-72	273	55.7	2.7	2.5	1.54-4.09	
4. Quality of life in social relationship						0.020
Good	400	44.7	1	1		
Medium and poor	184	55.4	1.5	1.6	1.23-2.01	

Discussion

This study revealed that the suspected developmental delay among early childhood in Northeast of Thailand were 48.1%. The associated factors with suspected developmental delay were found 4 factors including: monthly self-income, gender, age range and quality of life in social relationship domain.

The association between Monthly self-income of caregivers and suspected developmental delay was consistent with Ozkan et.al¹², they found that economic and social factor effected to the delayed development.

Girls who are in normal development greater than boys were concordant with a study of Bhattacharya and Brito et al^{13,14}. They found that boys were suspected developmental delay greater than girls. Nevertheless, it was different from a study of Ozkan et.al¹² reported that there was not difference on gender with suspected developmental delay.

Age range of the early childhood with developmental delay the most was 35-72 months which this result was consistent with problem about developmental delay on language domain which tended to increase up. A part of problem is environmental circumstance was not propitious to support the children development; for example, eating food following advertisement, leaving kids to use electric media alone, so the kid aged 3-5 years were slightly risky greater than the kid aged 0-2 years which were consistent with a study of Brito et al.

and Celikkiran et al^{14,15}, they found that infant stage had normal developmental better than preschool age.

Regarding to the caregiver's quality of life in social relationship is related to children development which also conformed to a study of Yamada et al¹⁶, especially mother who was in poor quality of life which her might get lower social support, it also affected to another family members on development, personality and children behavior.

Conclusion

The risky factors affected to the children development issue, biological factor slightly was lowering significant, but the socio-demographic characteristics factor was more important. Therefore, we should closely pay more attention to the risk factors which were biological, social and environmental factors which cause of children development issues. As a result, we should monitor these risk factors which might affect to the children in first five year in order to solve the problem and did any activities to stimulate and do support their normal developmental and being main human resource to develop our country in the future.

Research Ethics approval for this study was obtained from the Khon Kaen University Ethics Committee for human Research (HE622051).

Conflict of Interest Statement: The authors declare that no conflict of interest.

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References

1. Walker SP, Wachs TD, Grantham-McGregor S, Black MM, Nelson CA, Huffman SL, et al. Inequality in early childhood: risk and protective factors for early child development. Elsevier Ltd all Rights Reserved 2011; 378(9799): 1325-1338.
2. Kachapakdee N. Child development. Developmental textbooks and child behavior for general practice. Bangkok: Beach Enterprise Co Ltd; 2009.
3. World Health Organization. Developmental Difficulties in Early Childhood: Prevention, early identification, assessment and intervention in low and middle-income countries: A Review. Child and Adolescent Health and Development. Turkey: Turkey Country Office and CEECIS Regional Office; 2012.
4. Department of Health, Ministry of Public Health. Development of the situation survey and early child rearing behavior of Thai families in 2017. Bureau of Health Promotion, Ministry of Public Health; 2017.
5. National Statistical Organization. Thailand multiple Indicator cluster survey. In Bangkok: National Statistical Organization and UNICEF; 2012.
6. Meungrungsarat T, Fuengfu A. Factors affecting child development. Developmental textbooks and child behavior book 4. Bangkok: PA Living Limited; 2018. p. 44.
7. Dubow EF, Boxer F, Huesmann LR. Long-term effects of parent' Education on children's educational and Occupational Success: Mediation by Family Interaction, Child Aggress, and Teenage Aspiration. *Merrill-Palmer Q* 2009; 55(3):224-49.
8. Bradley RH, Corwyn RF. Socioeconomic Status and Child Development. *Annu Rev Psychol* 2002; 53:371-99.
9. Hsieh FY, Bloch DA, Larsen MD. A simple method of sample size calculation for linear and logistic regression. *Stat Med* 1998; 17:1623-34.
10. Mahatnirunkul S, Tuntipivatanaskul W, Pumpisanchai W, et al. Comparison of the WHOQOL100 and the WHOQOL-BREF (26 items). *J Ment Health Thai* 1998; 5: 4-15.
11. Kachapakdee N, Lertwadadrakul O. Training manual the Denver Developmental Screening Test II. 4thed. Nakhon Pathom: National Institute for Child and Family Development, Mahidol University; 2013.
12. Ozkan M, Senel S, Arslan EA, Karacan CD. The socioeconomic and biological risk factors for developmental delay in early childhood. *Eur J Pediatrics* 2012; 171(12): 1815-21.
13. Bhattacharya T, Ray S, Das DK. Developmental delay among children below two years of age: a cross-sectional study in a community development block of Burdwan district, West Bengal. *Int J Community Med Public Health* 2017; 4:1762-7.
14. Brito CM, Vieira GO, Costa MC, Oliveira NF. Neuropsychomotor development: the Denver scale for screening cognitive and neuromotor delays in preschoolers. *Cad Saude Publica* 2011; 27(7):1403-14.
15. Celikkiran S, Bozkurt H, Coskun M. Denver Developmental Test Findings and their Relationship with Sociodemographic Variables in a Large Community Sample of 0-4-Year-Old Children. *Arch Neuropsychiatr* 2015; 52: 180-4.
16. Yamada A, Kato M, Suzuki M, Watanabe N, Akechi T, Furukawa TA. Quality of life of parents raising children with pervasive developmental disorders. *BMC Psychiatry* 2012;12: 119.

Lapin Stealth Citrobacter Urogenital Infection Model

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Abstract

A lapin stealth *C. freundii* urogenital infection models were being developed. Three groups each of five rabbits were assigned as group I for stealth *C. freundii*, group II for intact *C. freundii* and group III for control. The infectious dose was rated to, 1×10 to 7 CFU/ml . The dosing program was through transurethral route. From the time zero day up to the day eight post infection the rabbits was watched for signs of disease. The changes in the whole animal beings were found as; rise up in body temperature, loss of appetite, loss of body weight and sluggishness. Postmortem gross urogenital organ/tissue matrix changes were congestion and haemorrhage. Tissue changes were noted as an acute to sub-acute urethritis, cystitis and testiculitis. To this end rabbits were proved to be suitable experimental models for evidence of stealth *C. freundii* pathogenicity. The developed models are being novel so far *C. freundii* is concerned.

Keywords: Acute, body, Infection, model, transurethral, urogenital.

Introduction

Citrobacter freundii in classical medical microbiology literature have been mentioned as commensal organism with an opportunistic pathogenic potentials^[1,2]. Current published works have been assuring more than once clinical proves that *C. freundii* stands as an emerging human pathogens causing; enteritis, colitis, arthritis, urinary tract infections and meningitis^[3]. Though most of the workers hold the idea that it stands as an opportunistic human uropathogen^[2,4]. The objective of the present work was to develop a lapin models for *C. freundii* urogenital pathogenicity.

Materials and Method

Pathogens: The infectious *C. freundii* was a confirmed urinary isolate from human being that was identified using classical and API20E system. It was used in two forms; stealth and intact whole infectious units per fixed volumes. In both of the cases the stock was revived onto fluid overnight broth culture then onto quadrante streak 24 hr. culture valid for more processing. For intact, five similar colony morpho-types onto selective enteric solid media were elected and transferred to 25ml. flask culture containing brain heart infusion broth. The inoculated broth was incubated for 24 hr at

37C then centrifuged at 5000rpm for 10 mints. Pellet was washed twice with sterile normal saline the reconstituted to the rate of 1×10 to 7 CFU/ml .^[3,4,5]

Stealth Pathogen: The isolate was grown onto variant medium with 62.5 ug/ml. Impenim at 37C for; 24, 48, 72, 96 and 120 hrs., with continual shake every now and then during incubation period. The transformation percentages to cell wall defective stealth form was checked at the aforementioned periods by direct microscopic exam of methylene blue stained films of inocula from the cultures. Reasonable high percentages were considered for preparing the infectious doses and rated to 1×10 to 7 CFU/ml .^[6]

Lapin Models: The experimental rabbits were checked for absence of common pathogens and their specific antibodies. Among the negatives, three groups each of five were adapted for the housing conditions for one week then assigned as group I for stealth, group II for the intact and group III for saline controls. The stealth *C. freundii* infectious doses were prepared as 10 days variant culture with 62.5 ug/ml. Impinim, checked and rated to 1×10 to 7 CFU/ml . Intact infectious *C. freundii* doses were made as in paragraph 1. The infection route was through transurethral mini-catheters made as two

sided open polyethylene tubing of 0.5mm diameters fitted to needle-less disposable syringes inserted to urethra^[6,7,8]. Tissue section preparations were performed as in ^[9].

Results

Stealth Infection Model: The whole animal being gross changes observed onto stealth infected rabbits were;rise up in body temperature,loss of appetite,loss of weight, sluggish-ness, polyuria as compared to the normal beings in saline control rabbits. The gross postmortem organ/tissue changes were;congested hyper-atrophized urinary bladder with marked vein congestion and pan patchy haemorrhage in bladder tissue matrix. The urethral tissue sections was shown an inflammatory cell infiltrate of mixed macrophages and lymphocytes with urethral epithelial tissue damage indicating sub-acute urethritis. The whole mark of urinary bladder tissue section diffuse patches of haemorrhages, Figure 1. Renal tissue changes were as; thickening and damage of the mucosal layer of the renal tubules with an apparent derrangement of mucosal congestion, Figure 2. Testicle tissue changes were as marked derrangement in the mucosal layer of the semi-neferous tubules and inflammatory cell infiltrates, Figure 3.

Intact Infection Model: The intact infected rabbits model have expressed animal whole being changes as; rise up body temperature, loss of appetite, loss of

weight,sluggishness, polyuria as compared to the normal being saline injected rabbits. The gross postmortem changes were congested hyper-atrophized urinary bladder with an apparent mild congestion in the urogenital tissue matrix. The urethral histologic tissue changes were infiltration of macrophages and lymphocytes in the tissue matrix with an evident urethral epithelial damage indicating sub-acute urethritis . Urinary bladder was showing dense inflammatory cell infiltrates together with translocation of bacterial populations into sub-mucosal tissue regions which is consistent with cystitis. Renal tissue sections were showing mild inflammatory cell responses in renal cortical area nearby the glomeruli with renal tubular damage. Testicular tissue sections have shown inflammatory cell infiltrates with epithelial damage in the semineferous tubules.

Control Model: The control rabbits were showing normal animal beings of body temperature, body weight,appetite and mobility,normal tissue cellularity and tissue contours,Figures 4,5,6.

Comparative View: Both of the infection models have shown inflammatory responses in urethra,urinary bladder, kidneys and testicles. The pathologic entities of these inflammations were spanning between acute to sub-acute inflammations with an apparent mucosal epithelial layer of the tubular structures. Though the tense damage was evident stealth than in intact infection models, Table 1.

Table 1: Pathogenicity of Stealth and intact C.freundii in rabbits

Pathogenicity features	Stealth infection Model	Intact infection model	Saline controls
Morbidity			
Body Temperature	High	High	Normal
Loss of Appetite	Present	Present	Normal
Loss of Weight	Present	Present	Normal
Mobility	Sluggish	Sluggish	Normal
Urination frequency	Polyuria	Polyuria	Normal
Postmortem			
Urinary bladder	Hyperatrophized	Hyperatrophized	Normal
Urinary bladder main venous supply	Congested	Normal	Normal
Bladder wall	Marked haemorrhagic	Mild haemorrhagic	Normal
Histology			
Urethra	Sub-acute urethritis	Sub-acute urethritis	Normal
Bladder	Cystitis	Cystitis	Normal
Kidneys	Renitis	Renitis	Normal
Testicles	Testiculitis	Testiculitis	Normal

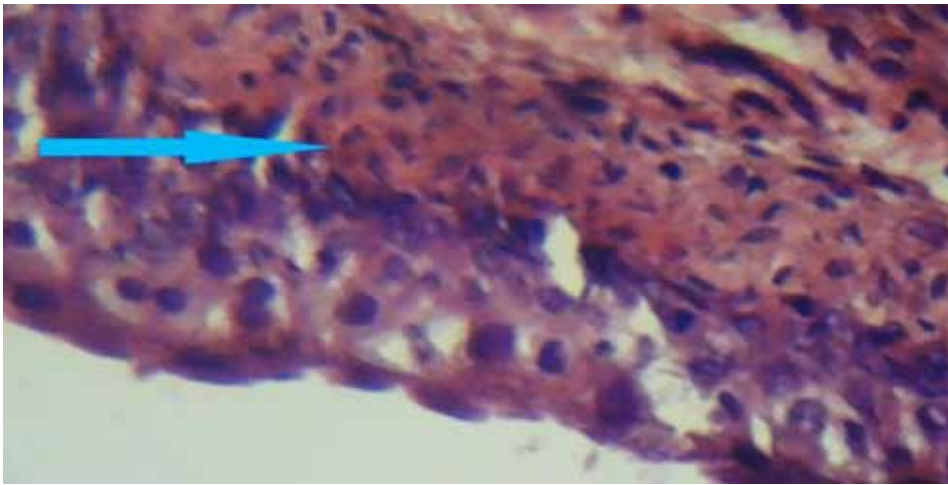


Figure 1: Urinary bladder tissue section H & E 1000X,from Stealth C. freundii transurethral infected rabbits showing haemorrhagic reactions[Arrow].

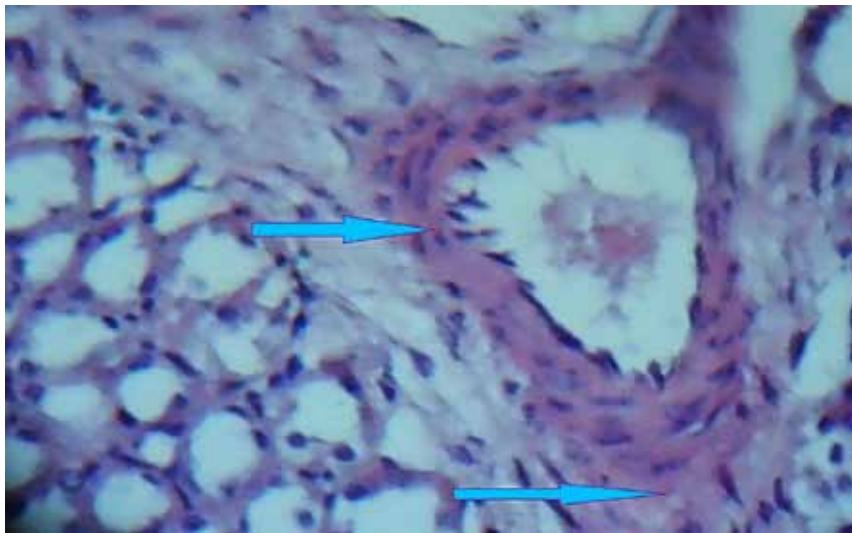


Figure 2: Kindney tissue section H & E,1000X from Stealth C.fruendii transurethral infected rabbits showing congestion and tissue derrangement.

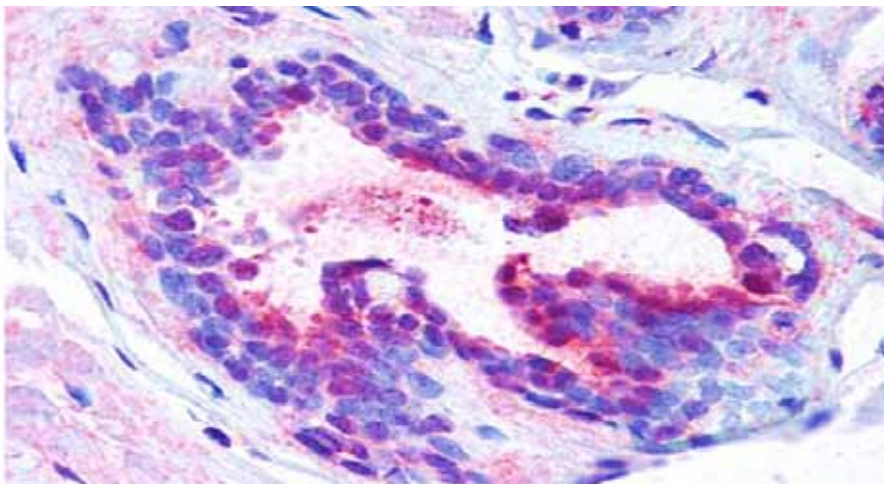


Figure 3: Testicle tissue section H & E 400X,from a Stealth C.fruendii transurethral infected rabbits,showing congestion and seminiferous tubule derrangement.

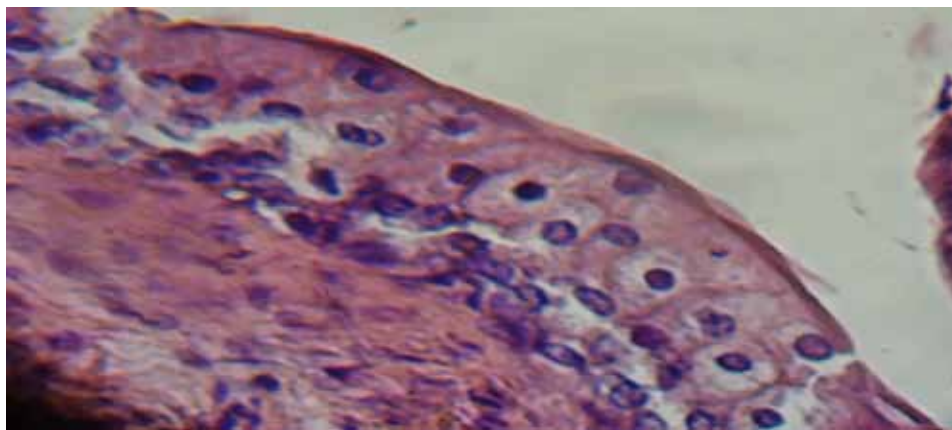


Figure 4: Urinary bladder tissue section H & E, 400x, from control rabbits showing normal tissue cellularity and normal contour.

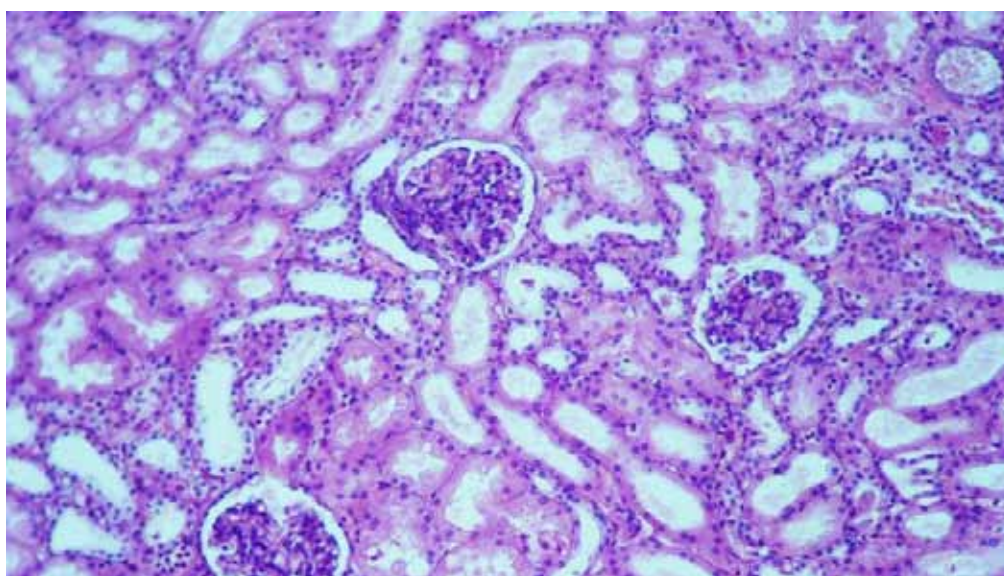


Figure 5: Kidney tissue section H & E 400X, from control rabbits showing normal cellularity and normal contour.

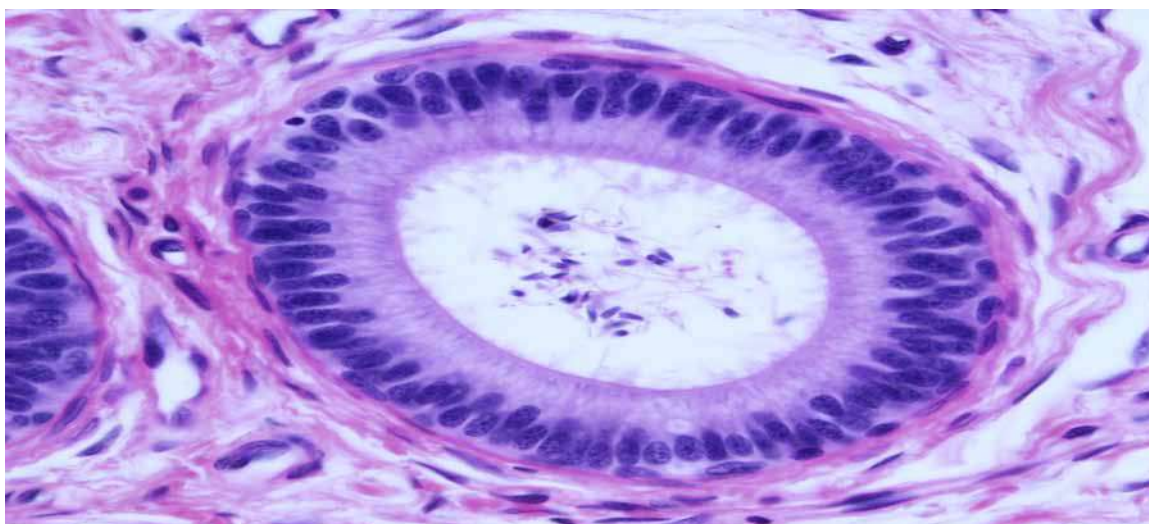


Figure 6: Testicle tissue section H & E 400X, from control rabbits, showing normal cellularity and normal contour.

Discussion

The pathogenesis of urinary tract infection in mammals including man is starting through three main routes; the ascending urethral, the descending haematogenous and lympho-genous^[1]. The theme of the present work was via the ascending urethral rout. The presence of *C.freundii* populations in the lapin urogenital tract tissues can be an indications to their ability to penetrate, invade, adhere and populate in to urinary and genital tissues. When *C.freundii* grow up in populations may be in form of biofilms, producing quorum sensing signals^[10], attaching, effacing, and/or other pathogenicity factors^[2] that may avoid local mucosal defense mechanisms as well as mechanical urine voiding mechanisms leading to initiation of an inflammatory processes which may be terminated by tissue damage and urogenital disease in urethra, urinary bladder, kidney and testicles and this was clear from the morbidity, postmortem and histological changes of the infected rabbits, Table 1 and figures 1-6. From this contribution it was evident that the intact *C.freundii* have tissue tropism towards lapin urogenital tract and its pathogenicity was more potentiated in case of losing their cell walls^[13,14,15]. To this end one can theorize the host range of *C.freundii* pathogenicity covers mammalian vertebrates including lapin and human beings. From the practical point of view rabbit were proved to be of value as an experimental *C.freundii* urogenital infection models through transurethral infection routes^[7,8]. The present models are novel since lapin models of *C.freundii* infection seemed to be rare^[7,8,11,12,13,14,15].

Conclusion

Transurethral as ending infection rout for both of stealth *C. fuendii* and *C. fruendii* in a lapin model was proved to be valid for the urogenital pathogenicity study. Stealth *C. fruendii* appeared to be more potent urogenital pathogen than intact *C. fruendii* in a lapin model.

Conflict of Interest: Non

Source of Fund: Personal

Ethical Issue: The research project is registered in the Afilated Department Ethical. Rabbits were reared and kept under standard Add Libitum conditions during experimentation period. On handling of rabbits authors followed the international athecal guidelines for laboratory animals.

References

1. Carroll KC, Morse SA, Mietzner S, Jawetz, Melnick, Adelbergs Medical Microbiology, 27th ed. McGraw-Hill Lange, New York, 2016. 153-165.
2. Kamada N, Sakamoto K, Puente, Munez G, Humoral immunity in the gut selectivity targets phenotypically virulent Attaching-Effacing Bacteria for inteluminal elimination, Cell Host Microbe, 2015, 17:621-627.
3. Government of Canada, Pathogen safety data sheet, infectious substances-Citrobacter spp., 2017, 1-7.
4. Gopal SD, Raj S, Incidence of Citrobacter urinary tract infection in Type 2 Diabetes and its relationships to glycemia control Int. J. Contemp. Med. Res., 2017, 49(1):60-62.
5. MacF Fadin JC, Individual Biochemical Tests for Identification of Medical Bacteria, 3rd ed. Lippincotte Williams and Wilkins, 2000, 27-439.
6. Thewaini QNO, Biology of Cell Wall Defective Microbes, Ph.D. thesis, University of Babylon, 2000, Iraq.
7. Hung C-S, Dason KW, Hultgren SJ, A murine model for urinary tract infection. Nat. Protoc. 2009, 4(8):1230-1234.
8. Barber AE, Norton JP, Wiles TJ, Mulvey M, Strength and limitations of model systems for study of urinary tract infections and related pathologies, Microbiol. Mol. Biol. Rev., 2016, 80(2):351-367.
9. Cardiff, RD, Manual of hematoxylen and eosin stainig mouse tissue sections, Cold Spring Harbar. Proto, 2014, 6:655-658.
10. Burton RW, Engelkrik PG, Microbiology For health Science, 6th ed., Williams and Wilkins, 2001, London, 296-304.
11. Harvey RA, Champ PC, Fisher BD, Microbiology 2nd ed, lippicotte Illustrated Reviews, Lippincotte Williams and Wilkins, 2007, London, 101-109.
12. Parija SC, Textbook of Microbiology And Immunology Vol. 3, Elsever, 2009, India, 70.
13. Domingue GS, Woody DS, Bacterial Persistence and expression of disease, J. Clin. Microbiol, Rev., 1977, 10(2):320-344.
14. Rangan KP, Ranjan N, Citrobacter, An emerging health care associated urinary pathogens, Urolo. Int., 2013, 5(4):313-314.
15. Bartholod SW, Citrobacter fruendii infection, Spriger Verlage, 1985, Berlin Heidelberg, 337-338.

Dosing of Erythropoietin Stimulating Agents in Patients on Hemodialysis: A Single-Center Study

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Abstract

Objective: Study the relationship of dialysis adequacy with the effectiveness of erythropoietin for the management of anemia in hemodialysis patients.

Materials and Method: A retrospective cohort study, conducted in the Medical city complex from January 2019 to June 2019, the study involved 162 ESRD patients on regular hemodialysis sessions.

Results: Change in Hb (percentage and value), was significantly higher in patients receiving once-weekly erythropoietin compared to both twice and thrice and more dosing per week. Overall only 33 (21.2%) of the patients achieved target Hb (10 – 11 mg/dL) with 6 months of follow-up. There was an inverse significant correlation between percentage change after 6 months with baseline Hb, baseline ferritin, and baseline albumin. While with urea at baseline, number of weekly sessions, and Kt/V the relationship becomes direct and significant. There is an increased risk (2 folds) of not achieving target Hb (10-11 mg/dL) in patients with DM compared to those without DM.

Conclusion: Once weekly regimen appeared to superior to other regimens (twice or more per week).

Keywords: Erythropoietin, dialysis, hemoglobin, anemia, weekly dosing.

Introduction

End-stage renal disease (ESRD) occurs when there is a progressive loss of kidney function over a period of months to years to the point where the kidneys can no longer maintain normal function¹. Anemia is common among patients with chronic kidney disease (CKD). Anemia underlies many of the symptoms associated with reduced kidney function and is associated with increased mortality and hospitalizations². The anemia of CKD is, in most patients, normocytic and normochromic and is due primarily to reduced production of erythropoietin

by the kidney (a presumed reflection of the reduction in functioning renal mass) and to shortened red cell survival³. The primary therapeutic options for the anemia of CKD include iron, erythropoiesis-stimulating agents (ESAs), and, rarely, red blood cell (RBC) transfusions. The treatment depends on the severity of anemia and iron deficiency. ESAs are administered to most CKD patients who have hemoglobin (Hb) <10 g/dL, providing the transferrin saturation (TSAT) is >25 percent and ferritin >200 ng/mL⁴. The current work aimed to study the relationship of dialysis adequacy with the effectiveness of erythropoietin for the management of anemia in hemodialysis patients.

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Method

Patients: A single-center study involved 162 ESRD patients on regular hemodialysis sessions

Data Collection: Demographic characteristics, cause of end-stage renal disease, time on dialysis, and

type (epoetin alpha) and the dose of erythropoietin (50 to 100 units/kg/dose 3 times weekly, SC), type and dose of iron preparation.

Two consecutive (every 6 months) laboratory records of the patients were collected by trained nurses and data were entered into a specifically designed datasheet.

Laboratory analysis: Laboratory data collected from patients' charts included hemoglobin level, serum ferritin, and single-pool Kt/V, serum albumin, blood urea, and serum creatinine.

Inclusion criteria:

1. Age above 18 years
2. Patients on regular hemodialysis
3. End-stage renal disease

Exclusion criteria:

1. Pregnant women
2. History of hematologic disorders such as thalassemia, sickle cell disease, and hematologic malignancies
3. Patients with active or past cancer

Statistical analysis: Discrete variables presented using their number and percentage, chi-square test used to analyze the discrete variable. One-way ANOVA used to analyze the differences between more than two groups after that in the results is significant post hoc Tukey test will be used. Linear regression analysis performed to assess the relationship between different variables, r (correlation coefficient or standardized beta is a representative of magnitude and direction of the relationship), negative sign indicates inverse relationship, but positive sign represents direct relationship. SPSS 22.0.0 (Chicago, IL), Minitab 17.1.0, software package used to make the statistical analysis, p-value considered when appropriate to be significant if less than 0.05

Results

The study included 162 patients, with mean age of 52.7 ± 15.9 years, 57.4% of them were males. There was no significant difference in the age of patients

when divided by gender (50.6 ± 13.6 vs. 54.3 ± 17.3 years, female vs. male, p-value = 0.128), as illustrated in table 1.

Table 1: Baseline Characteristics and Demographic Data

Variables	Value
Number	162
Age (years), mean ± SD	52.7 ± 15.9
Gender, n (%)	
Female	69 (42.6%)
Male	93 (57.4%)
Medical diseases	
Hypertension, n (%)	147 (90.7%)
Dry weight (kg), mean ± SD	70.2 ± 14.7
Cause of end-stage renal disease, n (%)	
Diabetic nephropathy	66 (40.7%)
Glomerulonephritis	27 (16.7%)
Polycystic kidney disease	21 (13.0%)
Hypertensive nephropathy	36 (22.2%)
Obstructive uropathy	24 (14.8%)
Dialysis duration, n (%)	
<1 year	72 (44.4%)
≥ year	90 (55.6%)
Vascular access	
Temporary double-lumen	126 (77.8%)
Tunneled	12 (7.4%)
Fistula	24 (14.8%)
T/V	0.85 ± 0.31
Dialysis adequacy (Kt/V ≥1.2)	30 (18.5%)

After 6 months of therapy with EPO, 6 patients (3.7%) stop their EPO since they maintain Hb level above 10 mg/dL during this period, the rest of the patients (156, 96.3%) categorized according to dosing intervals, in which 27 (17.3%) used single weekly dose, 63 (40.4%) used twice weekly doing, and 66 (42.3%) used trice weekly dosing.

Change in Hb (percentage and value), was significantly higher in patients receiving once-weekly EPO compared to both twice and thrice dosing per week (see Figures 3 and 4). Overall only 33 (21.2%) of the patients achieved target Hb (10 – 11 mg/dL) with 6 months of follow-up, as illustrated in table 2, figures 1.

Table 2: assessment of the effect of EPO on Hb

	Once Weekly	Twice Weekly	Trice Weekly	p-value
Number	27	63	66	-
Baseline Hb	8.6 ±2.0	8.6 ±1.5	7.4 ±1.2	<0.001
Hb% change	26.6 ±35.1	6.4 ±21.4	9.9 ±23.8	0.003
Hb change	1.7 ±2.1	0.3 ±1.6	0.6 ±1.7	0.002
Patients achieved 10-11 mg/dL	15 (55.6%)	9 (14.3%)	9 (13.6%)	<0.001
Hypertension, n (%)	24 (88.9%)	57 (90.5%)	60 (90.9%)	0.956
DM, n (%)	6 (22.2%)	30 (47.6%)	33 (50.0%)	0.039

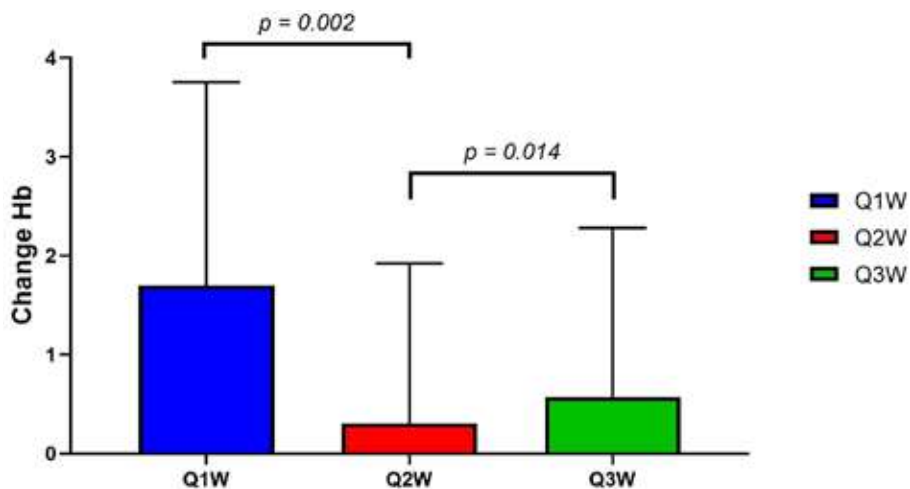


Figure 1: Assessment of the change in Hb from baseline to 6 months

There was a direct relationship between baseline urea, number of sessions per week, and Kt/V with percentage of Hb change.

There was an inverse relationship between baseline hemoglobin, baseline ferritin, and baseline albumin with percentage of Hb change, as illustrated in table 3.

Table 3: The relationship between change in Hb after 6 months and various variables

Variables	Percentage change in Hb	
	r	p-value
Age	0.084	0.288
Dry Weight	-0.088	0.266
Dosing Interval	-0.122	0.130
Hb at baseline	-0.629	<0.001 [S]
Ferritin at baseline	-0.194	0.013 [S]
Albumin at baseline	-0.284	<0.001 [S]
Urea at baseline	0.270	0.001 [S]
Creatinine at baseline	0.116	0.141
Ferritin after 6 months	-0.091	0.247
Albumin after 6 months	-0.110	0.162
Urea after 6 months	-0.060	0.448
Creatinine after 6 months	0.099	0.210
Session Per week	0.214	0.007 [S]
Kt/V	0.263	0.001 [S]

There an increased risk (1.943 folds) of not achieving target Hb (10-11 mg/dL) in patients with DM compared to those without DM, as illustrated in table 4.

Table 4: The relationship between DM and patients achieving target Hb

	Not DM	DM	OR	95% CI	p-value
Achieved target (%)	27 (29.0%)	12 (17.4%)	1.943	0.903 – 4.183	0.090
OR: odds ratio, CI: confidence interval					

Patients with higher Kt/V value had increased odd of achieving target Hb (1.5 folds), however, it did not reach statistical significance, as illustrated in table 5.

Table 5: The relationship between targets Hb with Kt/V

Variable	Target Hb		OR	95%CI	p-value
	Not achieved	Achieved			
Kt/V	0.84 ± 0.33	0.88 ± 0.24	1.548	0.498-4.809	0.450
OR: odds ratio, CI: confidence interval					

Discussion

In the current study, only 33 (21.2%) of the patients achieved target Hb (10 – 11 mg/dL) with 6 months of follow-up , with mean Hb after 6 months (8.8 ± 1.5 mg/dL), which lower than reported by international studies⁵⁻⁹.

In the present study, there was a direct relationship between number of sessions with change in Hb ($r = 0.238$, $p\text{-value} = 0.001$), indicating that patients offered higher number of sessions had better anemic response. Although iron deficiency is probably the most important factor affecting the response to erythropoiesis-stimulating agents (ESA) in most patients, occult blood loss, infection, and inflammation also are important. Adequate dialysis can contribute to anemia correction by removing small and possibly medium/large molecules that may inhibit erythropoiesis ¹⁰.

Several metabolites have been implicated as potential EPO toxins, including various polyamines, such as spermine, spermidine, putrescine, and cadaverine, and parathyroid hormone. However, these substances have been found to be general bone marrow toxins and not specific suppressors of erythropoiesis. More recently, polymeric polyamine-protein conjugates have been shown to have a selective inhibitory effect on colony-forming units-erythroid proliferation without any appreciable effect on burst-forming units-erythroid¹⁰.

In the present study we found that a once-weekly regimen is better than two or three times per week's

regimens. This finding is unique since it is not reported in the literature.

In the present study patients with diabetes had two folds (OR = 1.94 3 , 95%CI: 0.903 – 4.183) increased risk of not achieving target Hb (10 – 11 mg/dL). Diabetes is known to be a risk factor for the severity of anemia in non-dialyzed patients with renal failure, as well as in patients who require maintenance dialysis. Few studies have evaluated the difference in response to erythropoietin therapy in diabetic and non-diabetic patients ^{11, 12}.

Despite the similarity of the response offered by erythropoietin therapy on Hb among various regimen, the overall percentage of patients achieving target Hb (10 – 11 mg/dL) was low 33 (21.2%), with once-weekly regimen offered the highest proportion (55.6%) within target, while the rest of the regimens offered lower percentage (14.3%, and 13.6% for Q2W, and Q3W respectively). This was in disagreement with previous studies in which the percentage of achieving target was higher (80 – 90% in most studies)⁶⁻⁸.

In the present study Dialysis adequacy (defined at Kt/V ≥1.2 according to KDOQI guideline ¹³) achieved in 30 (18.5%) of the participants, which is lower than other reported studies like Nafar et al with 58% achieving dialysis adequacy ¹⁴, and once-weekly than Amini et al with 43.3% achieving dialysis adequacy¹⁵.

Because anemia improves after the start of dialysis, adequate dialysis is of paramount importance

in correcting anemia by removing small, and possibly medium/large molecules that may inhibit erythropoiesis. Even if previously underestimated, the role of dialysis dose per se on anemia and response to ESA has progressively come to the scene. In a previous study a direct relationship between hematocrit level and urea reduction ratio (URR) after adjustment for other factors; at logistic regression analysis, an 11% increase in URR doubled the odds that a patient would have a hematocrit higher than 30%. Twenty consecutive patients receiving inadequate dialysis (baseline URR, 65%) received an increase in dialysis dose and were compared with another 20 End-stage patients receiving inadequate dialysis and in whom the dialysis schedule was not modified.¹⁹ After 6 weeks, in parallel with an increase of mean URR to 72%, the hematocrit level increased from $28.4\% \pm 0.78\%$ to $32.3\% \pm 0.71\%$ (P-value 0.002), whereas it remained unmodified in the control group, without any difference in ESA dose in the 2 groups explained¹⁰.

Data on the possible role of dialysis dose on anemia correction also come from the dialysis center in Tassin, France. In this facility, patients are treated with long hemodialysis sessions lasting 8 hours. Fifty-nine of these patients were compared with 53 patients from Sweden receiving conventional hemodialysis lasting 3 to 5 hours.²³ Even if the mean hematocrit level was similar in the 2 groups, the proportion of patients treated with rh-EPO was much higher and the mean Kt/V was significantly lower in the Swedish than in the Tassin group. The better control of anemia observed in the patients from Tassin mainly is owing to a higher deuration rate, but it also is possible to hypothesize an effect of dialysis time per se, independent from dialysis adequacy¹⁰.

In the present study, there is direct correlation between dialysis adequacy with increase in Hb ($r = 0.263$, p-value = 0.001), which is in agreement with other studies^{16,17}.

One of the major determinants of anemia severity and ESA responsiveness is dialysis adequacy¹⁸. Patients with an inadequate dialysis dose are resistant to ESA, and their target Hb is harder to reach¹⁹. In hemodialysis, there is an inverse relationship between the achieved Kt/V and ESA dose, while increasing the dialysis dose is associated with an increase in hematocrit level²⁰. Uremic toxicity in general and/or retention of some direct inhibitors of erythropoiesis results in aggravated anemia and poor response to ESA treatment¹⁷.

Conclusion

Once weekly regimen appeared to superior to other regimens (twice or more per week).

Conflict of Interest: None

Ethical Clearance: Informed written consent was obtained from all the participants in the study, and the study and all its procedure were done in accordance with the Helsinki Declaration of 1975, as revised in 2000. The study was approved by the Arabic Board of Medical Specializations.

Source of Funding: Self

References

1. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *American journal of kidney diseases: the official journal of the National Kidney Foundation*. 2002;39(2 Suppl 1):S1-266
2. Collins AJ, Li S, St Peter W, Ebben J, Roberts T, Ma JZ, et al. Death, hospitalization, and economic associations among incident hemodialysis patients with hematocrit values of 36 to 39%. *Journal of the American Society of Nephrology : JASN*. 2001;12(11):2465-73
3. Eschbach JW. Erythropoietin 1991--an overview. *American journal of kidney diseases : the official journal of the National Kidney Foundation*. 1991;18(4 Suppl 1):3-9
4. Stirnadel-Farrant HA, Luo J, Kler L, Cizman B, Jones D, Brunelli SM, et al. Anemia and mortality in patients with nondialysis-dependent chronic kidney disease. *BMC nephrology*. 2018;19(1):135.10.1186/s12882-018-0925-2
5. Fishbane S, Besarab A. Mechanism of Increased Mortality Risk with Erythropoietin Treatment to Higher Hemoglobin Targets. *Clinical Journal of the American Society of Nephrology*. 2007;2(6):1274-82.10.2215/cjn.02380607
6. Germain M, Ram CV, Bhaduri S, Tang KL, Klausner M, Curzi M. Extended epoetin alfa dosing in chronic kidney disease patients: a retrospective review. *Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association*. 2005;20(10):2146-52.10.1093/ndt/gfh919

7. Pergola PE, Gartenberg G, Fu M, Sun S, Wolfson M, Bowers P. A randomized controlled study comparing once-weekly to every-2-week and every-4-week dosing of epoetin alfa in CKD patients with anemia. *Clinical journal of the American Society of Nephrology : CJASN*. 2010;5(4):598-606.10.2215/cjn.06770909
8. Spinowitz B, Germain M, Benz R, Wolfson M, McGowan T, Tang KL, et al. A randomized study of extended dosing regimens for initiation of epoetin alfa treatment for anemia of chronic kidney disease. *Clinical journal of the American Society of Nephrology : CJASN*. 2008;3(4):1015-21.10.2215/cjn.05681207
9. Kuragano T, Matsumura O, Matsuda A, Hara T, Kiyomoto H, Murata T, et al. Association between hemoglobin variability, serum ferritin levels, and adverse events/mortality in maintenance hemodialysis patients. *Kidney international*. 2014;86(4):845-54.10.1038/ki.2014.114
10. Locatelli F, Del Vecchio L, Pozzoni P, Andrulli S. Dialysis adequacy and response to erythropoiesis-stimulating agents: what is the evidence base? *Seminars in nephrology*. 2006;26(4):269-74.10.1016/j.semnephrol.2006.05.002
11. Inaba M, Okuno S, Kumeda Y, Yamada S, Imanishi Y, Tabata T, et al. Glycated albumin is a better glycemic indicator than glycated hemoglobin values in hemodialysis patients with diabetes: effect of anemia and erythropoietin injection. *Journal of the American Society of Nephrology : JASN*. 2007;18(3):896-903.10.1681/asn.2006070772
12. Fernandez-Reyes MJ, Selgas R, Bajo MA, Jimenez C, Del Peso G, Sanchez MC, et al. Increased response to subcutaneous erythropoietin on type I diabetic patients on CAPD: is there a synergistic effect with insulin? *Peritoneal dialysis international : journal of the International Society for Peritoneal Dialysis*. 1995;15(6):231-5
13. KDOQI Clinical Practice Guideline for Hemodialysis Adequacy: 2015 update. *American journal of kidney diseases : the official journal of the National Kidney Foundation*. 2015;66(5):884-930.10.1053/j.ajkd.2015.07.015
14. Nafar M, Samavat S, Khoshdel A, Alipour-Abedi B. Anemia Evaluation and Erythropoietin Dose Requirement Among Hemodialysis Patients: a Multicenter Study. *Iranian journal of kidney diseases*. 2017;11(1):56-65
15. Amini M, Aghighi M, Masoudkabar F, Zamyadi M, Norouzi S, Rajolani H, et al. Hemodialysis adequacy and treatment in Iranian patients: a national multicenter study. *Iranian journal of kidney diseases*. 2011;5(2):103-9
16. Malyszko J, Milkowski A, Benedyk-Lorens E, Dryl-Rydzynska T. Effects of dialyzer reuse on dialysis adequacy, anemia control, erythropoietin-stimulating agents use and phosphate level. *Archives of medical science : AMS*. 2016;12(1):219-21.10.5114/aoms.2016.57599
17. Ryta A, Chmielewski M, Debska-Slizien A, Jagodzinski P, Sikorska-Wisniewska M, Lichodziejewska-Niemierko M. Impact of gender and dialysis adequacy on anaemia in peritoneal dialysis. *Int Urol Nephrol*. 2017;49(5):903-8.10.1007/s11255-016-1499-1
18. Locatelli F, Del Vecchio L. Dialysis adequacy and response to erythropoietic agents: what is the evidence base? *Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association*. 2003;18 Suppl 8:viii29-35.10.1093/ndt/gfg1089
19. Richardson D. Clinical factors influencing sensitivity and response to epoetin. *Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association*. 2002;17 Suppl 1:53-9.10.1093/ndt/17.suppl_1.53
20. Movilli E, Cancarini GC, Zani R, Camerini C, Sandrini M, Maiorca R. Adequacy of dialysis reduces the doses of recombinant erythropoietin independently from the use of biocompatible membranes in haemodialysis patients. *Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association*. 2001;16(1):111-4.10.1093/ndt/16.1.111

Analysis of Risk Factors Occurrence of Juvenile Delinquency Behavior

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Introduction

Now a days juvenile delinquency is increasing in terms of number and type. Delinquency and criminality among teenagers are generally categorized as deviant behavior in society and can be interpreted as a form of teenage resistance to normative rules and values that apply in society. Many risk factors are related to deviant behavior.

Objective: This study aimed to analyze the risk factors that influence the occurrence of juvenile delinquency.

Method: This study used a cross-sectional design and a simple random sampling technique. The calculation results involved 295 samples. The independent variables were individuals, families, school environments, peer groups, coping mechanisms, lifestyles, and technologies. The dependent variable was juvenile delinquency. The data was collected using a questionnaire. The analysis used a multiple linear regression test with a significance level of $\alpha \leq 0.05$.

Results: Of the seven variables, six of them significantly influence juvenile delinquency. Technology is the variable that has the greatest influence on the occurrence of teenager wear.

Conclusion: Technology is the most influential factor. These results indicate a significant shift in the causes of juvenile delinquency from family and peer factors to technological factors. This is quite reasonable because technology is a major need and is a trend for teenagers at this time.

Keywords: Risk factors, delinquency, juvenile.

Introduction

Juvenile delinquency has occurred since the early 19th century and has become a world problem, including in Indonesia. Juvenile delinquency is included in social disorders and now the incidence rate continues to increase¹. Delinquency and crime among teenagers are generally categorized as deviant behavior in society. These behavioral deviations can be interpreted as a form of teenage resistance to normative rules and values that apply in society². Juvenile delinquency is one form of mental health disorder in the community, which directly or indirectly can affect the degree of mental health of the community. Short-term impacts can be dangerous directly to safety teenagers and groups themselves. Fights, brawls, speeding will potentially lead to injury and possibly even death. Narcotics can threaten their

lives and society, potential free sex behavior for sexually transmitted diseases, and other harmful effects. The long-term impact is the threat of future loss so that they cannot take part in the development of the nation and state. This is not in line with the expectation that teenagers are the spearhead of development and the next generation of the nation³.

Adolescence is a period of transition from childhood to adulthood that is full of responsibility, where they are required to be able to adapt to these changes⁴. Adaptation failure will lead to problems and behavioral disturbances in the future. This is relevant to coping mechanisms owned by individuals because coping mechanisms are a measure of the ability of teenagers to solve problems.

Furthermore, the factors that play a role in juvenile

delinquency are actors who originate from their own teenagers or individual factors. Individual factors are internal factors that are related to the abilities and abilities of individuals in running their roles and social activities. Factors that also act as risk factors for juvenile delinquency are family. This family factors related to the attitudes and habits of parents in educating and caring for children, including how parents in facilitating the economic needs of the child, personal communication patterns and proximity (bonding)^{4,5}. The next external factor is the school environment and peer groups. School factors that become a risk factor for juvenile delinquency, related to various things that exist in the school environment include child relationships with teachers and peer group, the presence of children in school, and adherence to school rules. For peer group factors which are risk factors for juvenile delinquency is the frequency of children seeing exposure to harmful substances, both directly seeing and seeing events in the mass media. Included also in peer group factors are attitudes and relationship patterns⁵.

Technology use today also play a role in the occurrence of delinquency. Incorrect use of technology can have the effect of deviating behavior including violence, theft, and so on. Research shows that playing violent video games correlates with the occurrence of aggression in juvenile delinquents imprisoned⁶. Another factor that contributes to juvenile delinquency is a lifestyle. Changes in lifestyle due to environmental differences in the past and present will affect psychological well-being. Individuals who are not able to adapt to these lifestyle changes will lead to welfare problems⁷. A bad lifestyle has the potential to trigger juvenile delinquency. Based on the background above, it is necessary to analyze various risk factors that play a role in juvenile delinquency. The purpose of the study was to analyze risk factors that influence juvenile delinquency.

Materials and Method

Design: This type of research was observational with a cross-sectional design⁸.

Population and Samples: The population was all teenagers aged 12-19 years. The number of samples was 295 teenagers who attended schools in Malang City, East Java - Indonesia, and teenagers who were undergoing coaching in class I LPKA Blitar City.

Procedures: After getting permission, followed by

retrieval of data that begins with providing explanations and informed consent to students as respondents with parents and or teachers representing parents, as well as to teenagers in LPKA with prison providers or parents. To provide explanations and request parental consent through telephone contact or direct interaction.

Instrument: Data collected using questionnaire that has been tested for validity and reliability. The instrument was developed referring to the Juvenile Counseling and Assessment Program Model (JCAP Model) as risk factors including the factors the individual, family, school, and peer group, coping mechanisms, lifestyle and technology^{4,5,7,9-11}. Juvenile delinquency instruments were developed based on theory^{3,12,13}.

Respondents assessed the independent variable associated himself to be risk factors and its behavior as the dependent variable. Subject given a goal by circling number 1 (strongly disagree), 2 (disagree), 3 (agree) or 4 (strongly agree) regarding the measured independent variables. For instruments related to the dependent variable, respondents were asked to rate the degree of frequency associated with their behavior by circling the numbers 0 (never), 1 (sometimes), 2 (often) and 3 (always).

Data Analysis: Original data were inputted into an excel spreadsheet and checked by the researcher. All data were analyzed using the SPSS 20.00 software. The analysis is done in two ways, Bivariate analysis risk factors (independent variables) on juvenile delinquency (dependent variable) with Chi-square test analysis (X^2) after the data is converted into category data and then Analysis of the logistic regression test using the enter method to find out the magnitude of the influence (Odds Ratio) of each risk factor for the occurrence of juvenile delinquency .

Result

The following is described the results of the descriptive analysis of each variable and the results of the bivariate analysis of the effect of modern and dependent-independent variables.

Juvenile Delinquency (Juvenile Delinquency): The juvenile delinquency which is the indicator in this study contains the 6 most types of hate based on the results of previous studies. Description of juvenile delinquency based on the type as in table 1.

Table 1: Overview of Juvenile Delinquency Based Type Naughty Behavior

No.	Variable	There is No	Low-Moderate	Weight
1.	Violent Behavior	101 (34.2%)	126 (42.7%)	68 (23.1%)
2.	Theft/Deprivation	143 (48.5%)	103 (34.9%)	49 (16.6%)
3.	Use of substances/drugs	140 (47.5%)	84 (28.5%)	71 (24.1%)
4.	Destructive- an Property	80 (27.1%)	174 (59.0%)	41 (13.9%)
5.	Sexual Abuse/Harassment	120 (40.7%)	115 (39.0%)	60 (20.3%)
6	Murder	250(84.7%)	33(11.2%)	12(4.1%)

Based on table 8 it is known that the most juvenile behavior is substance use or included in narcotics, alcohol, psychotropic, and other addictive substances (NAPZA) groups, then violent and sexual abuse/abuse. Next, to find out the effect strength of the independent variable on the occurrence of juvenile delinquency, logistic regression tests were conducted with the enter method.

Logistic Regression Test Analysis Risk Factors for Juvenile Delinquency: Analysis results to determine the power of influence risk factor (independent variable) on juvenile delinquency (dependent variable) can be identified based on the value of *Odds Ratio* (OR) such as table 2.

Table 2: Test Analysis Results in Logistic Regression Risk Factors for Teenager

Variable	B	P-value (sig)	Odds Ratio (Exp B)
Individual	-0.039	0.008	0.962
Coping Mechanism	-0.038	0.186	0.963
Family	-0.020	0.005	0.980
School Environment	-0.116	0.000	0.891
Peers	0.268	0.000	1.307
Lifestyle	-0.111	0.000	0.895
Technology	0.346	0.000	1.413

Based on table 2 it is known that of the seven risk factors, which have a significant effect on juvenile delinquency there are six, namely the variables of the individual, family, school environment, peers, lifestyle and technology. Coping mechanisms do not have a significant influence on the occurrence of juvenile delinquency. The results of the analysis also show that technology is the most influential factor in the occurrence of juvenile delinquency with an Odds Ratio (OR) of 1.413. This means that technological factors have an effect 1,413 times on juvenile delinquency. Based on the OR value it is known that after technological factors, the factors that influence juvenile delinquency are peers, family, individuals, lifestyle and school environment.

Individuals who do not have the ability, do not have confidence in their success in the future, do not have a good foundation of faith that has the potential to act according to their wishes. This is in accordance with the researcher's opinion, that life skills or individual competence affect juvenile delinquency⁵. This is in line with the opinion of Robles that life skills in the form of soft skills are interpersonal qualities and personal attributes that a person has¹⁴. Soft skills are personal and interpersonal behavior to develop and maximize human appearance or performance. Coping mechanism factors also significantly influence juvenile delinquency. Individual failure in solving problems will have the potential for behavioral disorders including juvenile delinquency. Coping mechanisms can be constructive or destructive⁴. The results of family factor analysis found no significant effect on juvenile delinquency. This is not in accordance with the opinion of experts that the family

Discussion

The results of the analysis it is known that individual factors significantly influence juvenile delinquency.

is a risk factor that affects the occurrence of juvenile delinquency. Families that influence juvenile delinquency are high levels of family dynamics, violence, poverty, family dysfunction, and poor family communication and relations⁹. This result is also not in accordance with the opinion of experts who stated that parenting and bonding effects on children's development. Poor parenting results in poor mother-child bonding (poor bonding) which can eventually lead to criminal behavior in children¹⁵.

Family factors are still a risk factor that has great potential for juvenile delinquency and should get serious attention. Families have a significant role in the success of children in the present and future. School environment factors significantly influence juvenile delinquency⁵. The incompatibility of school policies or rules, the pattern of teacher-student relations, has the potential for adolescents to rebellion or against existing rules. Peers have a significant effect on juvenile delinquency. This is also in line with the researcher that juvenile delinquency is related to peer influence, antisocial behavior, and the quality and level of relationships in the group¹⁶. Further explained by other experts that bad friendships can result in problems in schools which can eventually lead to criminal behavior in children¹⁵.

At the age of adolescence, children are more likely to gather with peers than with parents. Teenagers are comfortable if they gather with their peers because they have the same problems. Thus, if the peer group is bad, it will also have a negative impact on adolescents. Lifestyle factors significantly influence juvenile delinquency. This is in accordance with the theory that a good lifestyle will have a good impact on adolescents. Conversely, a bad lifestyle will have an adverse effect on adolescents. Associated with sleep rest patterns explained that sleep disorders or poor sleep patterns will interfere with emotional stability, individuals become irritable and irritable. Emotional disorders that occur due to disturbances or sleep patterns that are not good will have the potential for violence¹⁷. Likewise, the habit of exercise activities or recreation can reduce tension so as to make individual behavior adaptive. The inappropriate use of leisure time and recreational culture will have an impact on health¹⁸.

Technological factors significantly influence juvenile delinquency¹¹. This result is quite relevant because of the phenomena of life in today's technological era, making the internet and cellphones a necessity. Individuals are more pleased with cyberspace than the world of reality

by using the internet and cell phone facilities they have. Related to the six indicators of juvenile delinquency behavior, it is known that the most juvenile behavior is the use of substances or included in narcotics, alcohol, psychotropic and other addictive substances (NAPZA), then violent behavior and sexual abuse. Furthermore, the results of the logistic regression test with the enter method are known that there are six risk factors that significantly influence juvenile delinquency, namely individual, family, school environment, peers, lifestyle and technology variables, while coping mechanisms do not have a significant influence.

The logistic regression test results are different from the bivariate test results with the chi-square test which shows that the coping mechanism has a significant effect, while the family does not significantly influence. In the opinion of researchers, these results indicate that the family is a factor that still must be considered and also determines the occurrence of juvenile delinquency. The family is the first place for individuals to learn and the golden age is formed early in the family. This is explained by Wiyani that the beginning of a child's life (early age) is a golden age ("Golden Age")¹⁹. Golden Age is a period of growth and development of children that occurs at the age of 0 to 6 years, where this time a child is in a family environment. Associated with coping mechanisms do not have a significant effect, in the opinion of researchers because these factors are not dominant in influencing adolescent attitudes and are internal. As is known that external factors are factors that are a more and more powerful influence on adolescents. So that the possibility of coping mechanisms will be maladaptive if the external push is too strong in adolescents. The results of the analysis also show that technology is the most influential factor in juvenile delinquency when compared to other factors. This is in accordance with the opinion which explains that the development of information and communication technology through the internet and cellphones (cellphones) is a phenomenon of modern society that can have an impact on society both positively and negatively¹¹.

Conclusions

Technology is a factor that has the most influence on juvenile delinquency. Inappropriate use of technology, for example, the wrong use of gadgets has the potential for juvenile delinquency. This shows that in this digital era there has been a significant shift in the causes of juvenile delinquency, from family and peer factors

to technological factors. This is reasonable because technology is now a major need for teenagers. Based on these results, further analysis is needed regarding the indicators of the factors that influence juvenile delinquency in order to develop new instruments in the early detection of juvenile delinquency behavior.

Ethical Clearance: This research was approved by the Health Research Ethics Commission (KEPK) of the Faculty of Public Health, Airlangga University Surabaya, number 534/EA/KEPK/2018.

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Reference

1. Steketee M, Gruszczynska B. Juvenile delinquency in six new EU member states. *Eur J Crim Policy Res.* 2010;16(2):111–25.
2. Badan Pusat Statistik. Profil kriminalitas remaja 2010: Studi di Lembaga Pemasyarakatan (Lapas) Anak di Palembang, Tangerang, Kutoarjo, dan Blitar. Badan Pusat Statistik. 2010.
3. Anjaswarni T. Juvenile Delinquency, Kenakalan Remaja: Teori, Hasil Penelitian Dan Aplikasi Asuhan Keperawatan. Sidoarjo Zifatama Publ. 2014;
4. Stuart GW. Principles and Practice of Psychiatric Nursing-E-Book. Elsevier Health Sciences; 2014.
5. Calhoun GB, Glaser BA, Bartolomucci CL. Practice & theory: The juvenile counseling and assessment model and program: A conceptualization and intervention for juvenile delinquency. *J Couns Dev.* 2001;79:3–13.
6. DeLisi M, Vaughn MG, Gentile DA, Anderson CA, Shook JJ. Violent video games, delinquency, and youth violence: New evidence. *Youth Violence Juv Justice.* 2013;11(2):132–42.
7. Heath CJ, Berman JS. Evolutionary lifestyle and mental health. *Evol Psychol.* 2008;6(1):147470490800600100.
8. Nursalam M. Metodologi Penelitian Ilmu Keperawatan Edisi 3. Jakarta. Penerbit Salemba Medika; 2014.
9. Henggeler SW, Edwards J, Borduin CM. The family relations of female juvenile delinquents. *J Abnorm Child Psychol.* 1987;15(2):199–209.
10. Baqutayan SMS. Stress and coping mechanisms: A historical overview. *Mediterr J Soc Sci.* 2015;6(2 S1):479.
11. Abdulkarim A, Zainul A, Maryani E. Perilaku Asertif dan Kecenderungan Kenakalan Remaja Berdasarkan Pola Asuh dan Peran Media Massa. *J Psikol.* 2014;41(1):74–88.
12. Kratcoski PC, Kratcoski LD. Juvenile delinquency. Prentice-Hall Englewood Cliffs, NJ; 1990.
13. Heilbrun K, Goldstein NES, Redding RE. Juvenile delinquency: Prevention, assessment, and intervention. Oxford University Press; 2005.
14. Robles MM. Executive perceptions of the top 10 soft skills needed in today's workplace. *Bus Commun Q.* 2012;75(4):453–65.
15. Tremblay RE, Craig WM. Developmental juvenile delinquency prevention. *Eur J Crim Policy Res.* 1997;5(2):33–49.
16. Howell JC, Lipsey MW. based guidelines for juvenile justice programs. *Justice Res Policy.* 2012;14(1):17–34.
17. Taylor C, Lillis C, LeMone P, Lynn PA. Fundamentals of nursing: The art and science of nursing care. Lippincott-Raven; 1997.
18. Tekin A. Wild life recreation: Utilizing wilderness adventure therapy to prevent delinquency in minors. *J Hum Sci.* 2010;7(2):640–54.
19. Wiyani NA. Psikologi perkembangan anak usia dini. Yogyakarta Gava Media. 2014;

A Case Study of the Health Adaptation of Former Schizophrenics in Communicating with the Bugis Makassar Community in the South Sulawesi Province

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Abstract

Objective: This study aims to identify and categorize the cases of health adaptation of former schizophrenic patients in the process of interaction and communication with the community after experiencing a healing phase.

Method: This research uses a qualitative method with the type of case study. The technique of determining informants using non probability sampling is purposive sampling intentionally characterizing former schizophrenics who have interacted and communicated directly with the internal and external environment. Field data collection techniques through primary data, such as participant observation and in-depth interviews with former schizophrenics. The informants selected and analyzed were nine cases of former sufferers who, on average, were aged 34 to 60 years.

Results: This study found a categorization of health adaptation cases of former schizophrenics who had been cured medically and had initial interactions with the internal and external environment. Based on the analysis of health adaptation cases, four phases are categorized, namely: the healing phase, the interaction phase, the acceptance phase, and the openness phase. After going through these four phases, it was found a pattern of health adaptation of former schizophrenic patients in interacting and communicating with the Bugis-Makassar community. First, the manifest pattern is the ability of former schizophrenics to deal with and overcome internal and external environmental problems. The manifest pattern is characterized by positive self concepts and self disclosure is increasingly open. Second, latent patterns indicate the inability of former schizophrenics to overcome problems in the external environment. This gives rise to negative self concepts and closed self disclosure to communicate with the Bugis-Makassar community.

Conclusions: Based on an analysis of nine cases of health adaptation of former schizophrenic patients in communicating with the Bugis-Makassar community, it was more dominant in the latent pattern than the manifest pattern. This is due to the higher openness in the internal environment compared to the external environment due to the shame of 'siri' in themselves and the nuclear family. As a result, fear arises when their families who are former schizophrenics suffer from lack or are not accepted in the Bugis-Makassar community.

Keywords: Health Adaptation, former schizophrenics, Communication, Bugis Makassar.

Introduction

Schizophrenia is a mental picture due to disharmony in the thought process, feelings and actions so that it affects social behavior. Schizophrenia is a schizophrenic reaction suffered by individuals and is regressive to avoid tension and anxiety in the self so as to cause delusions

and hallucinations.¹ In the Bugis-Makassar community, the type of schizophrenia is still considered a psychiatric disease that although it has been declared medically cured from a doctor, people's perceptions of this disease still cause negative stigma. As a result, the nuclear family and community have a fear of schizophrenia.^{1,2}

A very interesting factor is that South Sulawesi is in third place with a prevalence of 0.26% after Yogyakarta on Java and Aceh on Sumatra. Data of the South Sulawesi Special Region Hospital indicates that the data for schizophrenia patients tends to increase every year. This increase was shown by patients from the Toraja area. Medical record data of South Sulawesi Province Special Region Hospital in 2016 of 348 patients recovered with an initial diagnosis of a rage with 240 patients and anxious 108 patients.

Schizophrenia is an interesting phenomenon in South Sulawesi, where the majority of the population is ethnic Bugis-Makassar. Stereotype factors and personal prejudice against schizophrenia cause the Bugis-Makassar community to tackle this type of disease through non-medical treatment, such as traditional healers and even 'inclusion'. The term shaman or 'sanro' in the Bugis-Makassar community, is a person who is an expert in treating diseases traditionally.^{5,6,8}

The specification of the focus of this research is to find, categorize the process of interaction of health adaptation carried out by former Schizophrenic patients in communicating with the Bugis-Makassar community.

Method

Research Location: The health adaptation case study of a former schizophrenic sufferer in communicating with the Bugis-Makassar community is located in South Sulawesi, namely; Parepare City, Makassar City and Wajo District..

Types and Sources of Data: This type of research uses qualitative method referring to case studies. The aim is to reveal the health adaptation process of former Schizophrenia sufferers in communicating with the Bugis-Makassar community. The technique for determining informants through non probability sampling is purposive sampling based on the terms and objectives of the study. The informant's requirements are first, a former schizophrenic who has interacted directly with the community at least 3 months after being medically recovered from a doctor. Second, former schizophrenics who are willing to analyze their cases sequentially and in detail. Informant cases are based on research data sources, namely direct observation of social life. In depth interview techniques by collecting individual narratives of former schizophrenics based on medical records, recover, interact and communicate with their environment. This technique can explore deeply the

lives of former schizophrenics before and after recovery.

Data Collection Techniques

In analyzing the identification and categorization data of health adaptation cases of former schizophrenic patients in the process of communication and interaction is done through the analysis of Miles.¹² The steps of Huberman's analysis in qualitative research are: data condensation steps (data condensation), presenting data (data display), and conclusion drawing and verification. Data condensation refers to the process of selecting, focusing, simplifying, abstracting, and transforming.

Results

Humans are social creatures who need direct interaction and communication with their environment. The need to communicate with other individuals, such as family, and peers is a basic need that must be met. Former schizophrenics are individuals who need a process of direct interaction and communication with the internal and external environment. Human psychological needs to communicate and need other people in social life.

Research informants are former schizophrenics who have been medically recovered from mental disorders due to physical, psychological and socio-cultural changes. Schizophrenics have a negative stigma in the views of some Bugis-Makassar people. Public perception assumes that Schizophrenia is a curse that must be avoided. As a result, people tend to keep their distance and direct contact with them. This is due to the myth of schizophrenia which is considered a "crazy" disease in which individuals experience hallucinations, illogical thoughts, cause aggressive behavior, and often scream hysterically. Even schizophrenics lose their ability to think, hallucinating causing them to be seen talking to certain objects that are not in front of them.

The results of tracing the case were carried out in three locations in South Sulawesi Province, namely Makassar City, Parepare City and Wajo Regency. In tracking down informants who were willing and open to be observed and interviewed on an ongoing basis found only nine people. This factor is caused by the closure of former schizophrenics when first interacting with the external environment. Shame or known as 'siri' in the Bugis-Makassar community is a barrier to the openness of the causes of the illness. The findings of informant characteristics based on the medical records of former schizophrenics can be seen in the following Table 1:

Table 1: Medical Records of Former Schizophrenics

Informant Number	Informant Former Schizophrenic Patient	Age (Years)	Gender	First Age Category Suffering from Schizophrenia (Years)	Age of Medical Treatment Period (Years)	Alternative Early Treatment
1.	Andi	60	Male	35	37	Shaman
2.	Lia	45	Female	37	37	Medical
3.	Baso	40	Male	30	31	Shaman
4.	Arlina	43	Female	22	22	Medical
5.	Adi	45	Male	21	26	Shaman
6.	Rafi	48	Male	33	33	Medical
7.	Elia	40	Female	35	35	Medical
8.	Ahmad	34	Male	22	29	Shaman
9.	Dani	50	Male	42	42	Medical

Source: Primary Data, 2019.

The data in Table 1, indicates that the informants of former schizophrenic patients had an average age of 40-45 years of age of 5 people. Age 46-60 years as many as 3 people and only 1 person aged 34 years. This condition is different from the results of Dindia’s research (2000b: 24) which found women to be more open than men. Dindia found cases that women were more open about expressing themselves to women than men to women; or women are more open about expressing themselves to men than men to women. Then, an analysis of 205 studies assessed gender differences in self disclosure.) find women more open than men.¹⁴ That when women told stories with their friends, they usually involved emotional feelings in expressing themselves.¹⁵

Analysis of the patient’s medical record when first experiencing initial symptoms tends to choose the hospital or medical treatment as many as 5 cases. There were 4 cases that used medical treatment or traditional medicine for 1 to 4 years. Pure schizophrenia is a medical disease that has the potential to affect everyone.

Health Adaptation Phase Process of Former Schizophrenic Patients in Communicating with the Bugis-Makassar Society: The case of health adaptation of former schizophrenics starts with self-concept as a mirror for the individual in seeing himself. Individuals will react to the environment according to their own self-concept. The phase is the healing phase, the interaction phase, the acceptance phase, the openness phase. The characteristics and characteristics of the four phases can be seen in Table 2 below:

Table 2. Health Adaptation Phase Former Schizophrenic Patients

Early Phase of Healing	Interaction Phase	Acceptance Phase	Openness Phase
Passive Individuals choose to remain silent and less interact and communicate with the external environment.	Internal Individuals tend to be open and interact with nuclear families.	Reception Individuals are personally accepted by the external environment.	Closed Individuals have gone through the process of healing, interaction, acceptance, but still closing themselves with the external environment.
Active Individuals are active and have their own initiative to open and interact, communicate with the external environment.	External Individuals tend to be closed or silent when interacting with the community in their environment	Rejection Individuals are personally denied the external environment.	Open Individuals have gone through the process of healing, interaction, acceptance, but still closing themselves with the external environment.

Source: Primary Data, 2019

Based on the findings and categorization of health adaptation cases of former schizophrenics in four phases: First, the healing phase. In this phase, former passive schizophrenics remain silent, lack of interaction and communication with the external environment. Passivity is caused by feelings of ‘siri’ shame in the self so that it affects the negative self concept that is owned. That one’s self-concept is oriented towards positive self-concept and negative self concept.^{16,17} Former schizophrenics in the passive phase are in the category of negative self-concept. The behavioral characteristics of former schizophrenics consider themselves helpless, diseased and afraid of being ostracized in society.

Second, the interaction phase. This phase is marked by the motivation of former schizophrenics to interact and communicate with the internal and external environment.

Third, the acceptance phase. This phase is marked by the feeling of being accepted or rejected by the Bugis-Makassar people who still believe the myths of the history of schizophrenia.

Fourth, the openness phase. This phase category is characterized after the individual goes through a process of healing, interaction, acceptance. Although, the internal and external environment has been open to receiving former schizophrenics, there are still some who remain closed, especially in the external environment.

Pattern of Health Adaptation Former Schizophrenic Patients in Communicating with the Bugis-Makassar Society: Health adaptation is a way for former schizophrenics to adapt themselves to the internal and external environment to communicate with the Bugis-Makassar community. Based on the analysis of nine cases found two patterns of health adaptation of former schizophrenics communicating with the Bugis-Makassar community, namely the manifest pattern and the latent pattern. The manifest pattern is openness and positive self acceptance..

Furthermore, the latent pattern is marked by the closure of former schizophrenics who do not interact with the Bugis-Makassar community. The reason is that former schizophrenics fear the risk of resistance from the surrounding community. Former schizophrenics

prefer to stay at home or do homework activities. Factors of self confidence and embarrassment ‘siri’ cause them to choose to close themselves with the surrounding environment. Former schizophrenics perceive that mental illness suffered will never be completely healed and must continue to take medication for life. Medical control through drugs makes former schizophrenics feel that the illness can recur. Finally, they have a negative self concept that tends to live in fear and not trust others too much. Based on tracing the cases of former schizophrenics, there were two patterns of health adaptation of former schizophrenics in communicating with the Bugis-Makassar community, as shown in the following Table 3:

Table 3. Pattern of Health Adaptation Former Schizophrenic Patients

Informant	Pattern of Health Adaptation	Former Schizophrenic Patient
Former Schizophrenic Patient	Manifest Pattern	Latent Pattern
Andi	√	
Lia		√
Baso		√
Arlina		√
Adi		√
Rafi	√	
Elia		√
Ahmad		√
Dani	√	√

Source: Primary Data, 2019

The results found that the pattern of health adaptation cases of former schizophrenics in communicating with the Bugis-Makassar community was more dominant than the latent pattern of manifest patterns. Latent patterns indicate an inability to overcome the problems of self concept and self disclosure in former schizophrenics. There are only three informants in the manifest pattern category who are able to face and overcome problems to interact and communicate with the internal and external environment. former schizophrenics who are in the manifest pattern have had positive concepts and increasingly open self disclosure, such as, Table 4 follows:

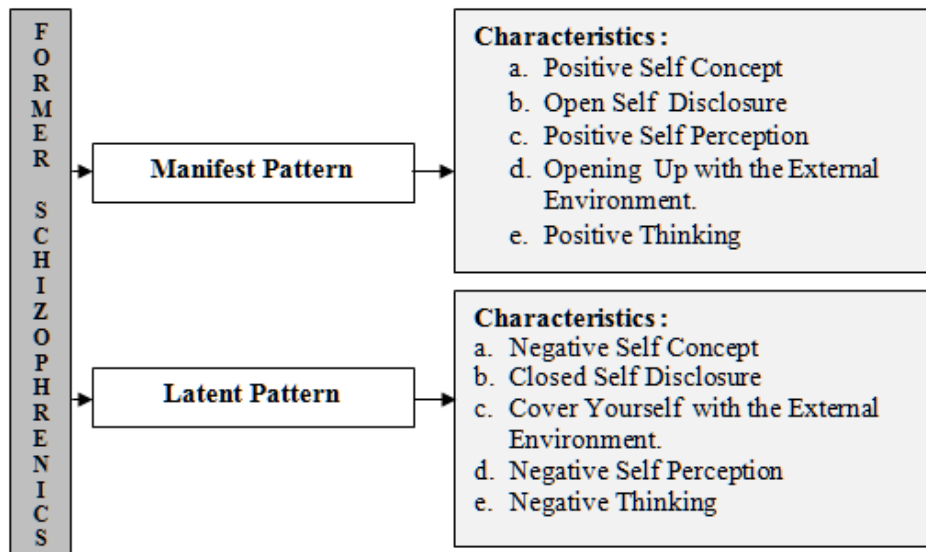


Figure 1. Characteristics of Health Adaptation Patterns of Former Schizophrenic Patients

In the case of former schizophrenics, community acceptance factors become a variable that can cause them to be in manifest or latent patterns. That is, the more positive acceptance of the internal and external environment of former schizophrenics, the more positive self concept and self disclosure they have. Positive self concept can lead to more effective individual interpersonal abilities, intellectual abilities and environmental mastery. The concept of self is not innate but rather through a process of learning and experience of interaction with others. Self concept is a life cycle that can change the mindset, positive outlook, culture, and socialization with the environment. For example, nuclear family, peers, and the community.

Conclusions

This study found the categorization of health adaptation cases of former schizophrenic patients in four phases, namely: the healing phase, the interaction phase, the acceptance phase, and the openness phase. The phase process of the former schizophrenic patient is a different health adaptation for each individual in interacting and communicating with the Bugis-Makassar community. The manifest pattern has the characteristics of a positive self concept and self disclosure is increasingly open. Latent patterns are characterized by negative self concepts and closed self disclosure to communicate with the Bugis-Makassar community. The results show that the health adaptation of former schizophrenics is more dominant in the latent pattern than the manifest

pattern. The condition is caused by self concepts and self disclosure of former schizophrenics, nuclear family, and the perception of acceptance of the Bugis-Makassar community.

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References

1. Stuart, G.W., and Sundeen, S.J. *The Book of Psychiatric Nursing (Translation)*. Issue 5: Jakarta;EGC. 2007.
2. WHO. *Schizophrenia*. [internet]. 2019 [accessed August 1, 2019]. Available from: <http://www.who>

- int/mental_health/management/schizophrenia/en/
3. Ministry of Health of the Republic of Indonesia. [internet]. 2019 [accessed August 5, 2019]. Available from: <http://www.depkes.go.id/article/print/16100700005/peran-keluarga-dukung-kesehatan-jiwa-masyarakat.html>.
 4. Mental disorders continue to rise. [internet]. 2019 [accessed August 5, 2019]. Available from: <http://www.jawapos.com/baca/artikel/7989/Gangguan-Jiwa-Terus-Naik>.
 5. Said, M.,Basir. Shaman. A Socio-Cultural Study of FunctionMakassar Bugis Shaman in Ujung Pandang Municipality. (Thesis not yet published). Jakarta: Postgraduate Program in Anthropology, University of Indonesia.1996.
 6. Rahman, Nurhayati. Love, Sea, and Power in the Epoch of La Galigo (Episode of Sawerigading Services to the Land of China; Perspective of Philology and Semiotics). Makassar;Publisher of La Galigo Press.2006.
 7. Agoes, Azwar. Indonesian Health Anthropology Volume I, Traditional Medicine. Jakarta: Buku Kedokteran B.G.C.1996.
 8. Alhumami, Amich. Herbalist and Politics. [internet]. 2009 [Accessed August 27 Agustus 2010]. Available from: URL: HYPERLINK <http://www.bernardsimamora.info/?p=3780>.
 9. Kalangie, Nico S. Culture and Health; Development of Primary Health Services Through the Sociocultural Approach. Jakarta;PT Kesaint Blanc Indah Corp. 1994.
 10. Rahmadewi, Ida. Traditional Treatment of Broken Lion Teacher's Bones. (Essay). Jakarta: University of Indonesia. 2009.
 11. Fadhillah, S Nurul. Self Concept and Self Disclosure Former Schizophrenic Patient in Wajo District (Interpersonal Communication Study). Makassar. Hasanuddin University.2017.
 12. Miles,M.B, Huberman, A.M, dan Saldana, J. Qualitative Data Analysis, A Method Sourcebook, Edition 3. USA: Sage Publications. Tjetjep Rohindi Rohidi, UI-Press. 2014.
 13. Kaplan, H.I., Sadock B.J. Sinopsis psikiatri Edisi ke-7, Terjemahan. Binarupa Aksara, Jakarta. 1997.
 14. Dindia, K. & Allen, M. 1992. Sex-Differences In Self-Disclosure Meta-Analysis. Psychological Bulletin, 112, 106-124.
 15. Maccoby, E. E. Social Development Psychological Growth and The Parentalchild Relationship. New York: Harcourt Brace Javanovich. 1980.
 16. Hutagalung, Inge. Personality Development (Practical Review Towards Positive Persons). Index: Jakarta. 2007.

Anxiety Symptoms in a Sample of Iraqi School Teachers

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Abstract

Background: Anxiety at workplace is a learnt response to stress and it differs from generalized anxiety disorder as the symptoms are specifically related to the work environment. Excessive pressure from educational institutions, students and student parents, community attitude, work overload, students' poor behavior and role conflict make teachers always confused and this predispose to anxiety.

Aims of Study:

1. To estimate the prevalence of anxiety symptoms among an Iraqi sample teachers of primary and secondary schools.
2. To determine the socio demographic factors contributing to anxiety among teachers.

Subjects and Method: This is a cross-sectional study involving teachers from 16 primary and secondary schools in Baghdad, Iraq. Beck Anxiety Inventory (BAI) (Arabic Version) was used to measures anxiety symptoms and determine anxiety levels among school teachers. All teachers of both sexes in selected primary and secondary schools who agreed to participate in the study and responded with data required were included.

Results: Most of teachers showed levels of anxiety symptoms that are higher than normal cut off of anxiety according to BAI. There was significant higher average score for BAI among primary school teachers while no significant difference was found when comparing different categories of levels of anxiety symptoms between the two groups.

Conclusion: Teaching profession is associated with high levels of anxiety in Iraq . Further studies are needed to confirm whether this anxiety is general to all Iraqi population or it is unique to teaching profession.

Keywords: Anxiety, symptoms, occupational, school, teachers.

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Introduction

Anxiety is normally occurring emotion that is observed throughout human cultures and several animal species.⁽¹⁾Anxiety is a diffuse, unpleasant, vague sense of apprehension which is often a response to an imprecise or unknown threat.⁽²⁾ Anxiety is a normal human physiological mechanism that helps body respond to threat. The autonomic changes occurring in anxiety are essential to avoid danger and moderate anxiety

improves performance. When anxiety is associated with autonomic arousal, erroneous cognitions, exaggerated threat perceptions and dysfunctional coping strategies, it results in distress and impairment in activities of daily living. For most modern individuals, running from larger animals and imminent danger is a less pressing concern. Anxieties now revolve around work, money, family life, health, and other issues that demand a person's attention without necessarily requiring the 'fight-or-flight' reaction which is a physiological reaction that occurs in response to perceived harmful event, or threat to survival.⁽³⁾

Some people experience more anxiety than others. They misinterpret events and linger on their misinterpretation, thinking them through over and over again.⁽⁴⁾ Symptoms of anxiety include fear, uneasiness, insomnia, cold or sweaty hands and/or feet, shortness of breath, incapability to be steady and calm, dry mouth, numbness or tingling in the hands or feet, nausea, muscle tension and dizziness.⁽⁵⁾ Anxiety disorders are the most prevalent mental disorders around the world and are associated with significant comorbidity. Prevalence of anxiety disorders is estimated to be around 7.3% (4.8% to 10.9%).⁽⁶⁾

Occupational anxiety is a learnt response to stress. It differs from generalized anxiety disorder as the symptoms are specifically related to the work environment. It may develop as generalized fears, phobias, hypochondriacal anxieties regarding working conditions, and fears of inadequacy or judgment. Common anxieties include fear of public speaking, working in groups, fear of not meeting deadlines, worrying that work may not meet expectations of others.⁽⁷⁾

Excessive pressure from educational institutions, students and student parents, community attitude, work overload, students' poor behavior and role conflict make teachers always confused and this predispose to anxiety.⁽⁸⁾

Aims of the Study:

1. To estimate levels of anxiety symptoms among teachers of primary and secondary schools at Al Karkh province of Baghdad city, Iraq
2. To determine contributing sociodemographic factors associated with anxiety symptoms.

Subjects and Method: This is a cross-sectional study arranged from January 2018 till end of April 2018.

Data were collected during two working days a week (Sunday and Thursday) from 9 am o'clock to 1 pm o'clock.

Al Karkh 1 Directory of Education is one of three educational general directories responsible on administration of schools at Al Karkh province; Baghdad city, Iraq. A list of all primary and secondary schools within in Al Karkh 1 administration were taken from General Directory of Education/Baghdad/Alkarkh_1 records. Primary schools include classes of 1st to 6th grades while secondary schools include classes of 6th to 12th grades. 500 schools were eligible for the study. A cluster sample of 8 areas within Al Karkh 1 administration is selected and from these areas 16 schools were selected randomly.

A total number of teachers present at time of visit were 320. Fifty six teachers refused to participate in the study and 47 teachers returned incomplete information, 217 teachers fully responded to required data for the study; 75 being from primary schools and 142 from secondary schools, and were willing to participate in this study.

A self-administered questionnaire form is used. The first part of questionnaire included socio demographic characteristics; age, gender, marital status, years of work, educational degree, monthly income, number of classes per week.

The second part of questionnaire included the Beck Anxiety Inventory (BAI) (Arabic Version) which measures anxiety symptoms and determine anxiety levels⁽⁹⁾. A preliminary pilot study was carried out on small group of 10 teachers (this group of teachers was excluded from the study sample).

Ethical Approval: This study was approved by the Scientific Committee Supervising Study of Fellowship of Arab Board of Family Medicine in Iraq. Official approval was obtained from General Directory of Education Baghdad/Alkarkh_1 to collect data needed for the study

All teachers were informed about the aim of the study, the way of answering the study instruments, and their right not to participate. Before sharing in the study, informed consent was obtained from all participants.

Statistical Analysis: Analysis of data was carried out using the available statistical package of SPSS-24.

Data were presented in simple measures of frequency, percentage, mean, standard deviation, and range (minimum-maximum values).

T test was used to test significance of differences for continuous data while chi square or Fisher exact were used for categories. Statistical significance was considered whenever the P value was equal or less than 0.05.

Results

A total of (217) teachers from both primary and secondary schools were included with mean age of the teachers of primary schools was (44.7±8.8), while mean age of teachers of secondary schools was (43.3±9.3). Female teachers were more than male teachers in both groups and the numbers of females were significantly higher in secondary schools (p value 0.0027). Most of teachers were married compared to single and divorced or widowed with significant difference favoring married status for the secondary school teachers (p value 0.002). The means of number years of work were (19.1±9.4) and (15.6±8.0) for primary and secondary schools respectively and the difference was found to be significant (p value 0,012). Most of primary school teachers were of institute qualification while secondary school teachers were mostly of bachelor qualification. The monthly income was significantly higher among primary school teachers (p value 0,027) and both groups showed comparable average number of classes per week.

Most of teachers (72.8%) showed levels of anxiety symptoms that are higher than normal cut off of 8 according to BAI in both groups and 27.2% of teachers only showed normal or minimal levels of anxiety (table

1). Although there was significant higher average score for BAI among primary school teachers (table 2) there was no significant difference when comparing different categories of levels of anxiety symptoms between the two groups (figure 1).

The levels of anxiety symptoms were significantly associated with female gender in both groups (p value 0,0001 for both groups). There was significant relation between levels of anxiety symptoms and number of school years (p value 0.004), monthly income (p value 0.034) and number of classes per week(p value 0.0001) for primary school teachers but not secondary school teachers while other socio demographic characteristics showed no significant relation with levels of anxiety in both groups.

Table 1: Rates of anxiety among all participant school teachers.

BAI	No. of teachers	Prevalence
Normal-Minimal (0-9)	59	27.2%
Mild-Moderate (10-18)	63	29.9%
Moderate-Severe (19-29)	51	23.5%
Severe anxiety (30-36)	44	20.3%
Total	217	100%

Table 2: The difference of means and SD of BAI between primary and secondary school teachers.

Beck Anxiety Inventory (BAI)	Primary	Secondary
Mean±SD	22.0±12.4	18.0±12.1
Standard Error of Mean	1.43	1.02
P value	0.022*	

*Significant difference between two independent means using Students-t-test at 0.05 level.

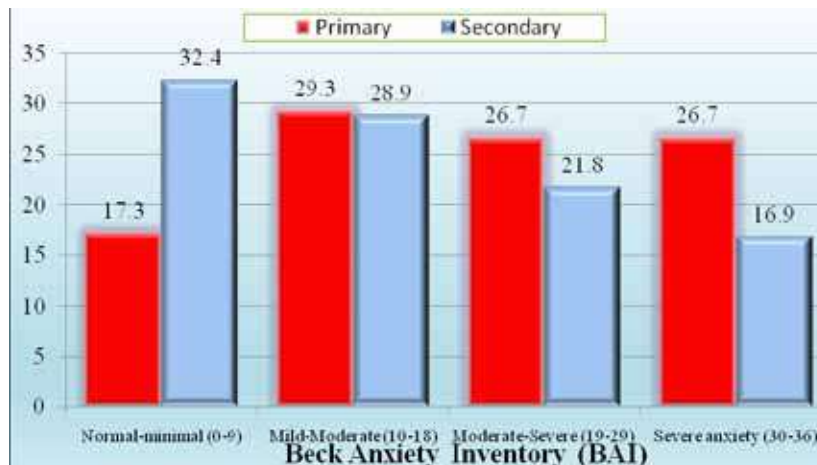


Figure 1: Comparison between rates of anxiety among primary and secondary school teachers. P value 0.05

Discussion

The overall rates of anxiety symptoms among this sample of school teachers are high. Such high rates are not unique to Iraqi population of teachers. Gonçalves GB et al (2015) in Brazil found comparably high anxiety rates.⁽¹⁰⁾ Dalia D. and Hiba A. (2017) in Egypt found prevalence of anxiety among school teachers to be of about 67.5%⁽¹¹⁾ and Sharron SK Leung et al (2009) in Hong Kong noted that prevalence of anxiety was even higher and moderate to extremely severe levels of anxiety were found in 57.2% of school teachers⁽¹²⁾ while Yousef A. Taher et al (2016) in Libya found that 61% of teachers had high rates of anxiety⁽¹³⁾. It is not known how much are the rates of anxiety symptoms among Iraqi population in general. In the Iraqi mental health survey arranged by world health organization at 2006-2007 it was found that 9.11% of Iraqi population had met the criteria of any anxiety disorder⁽¹⁴⁾. This survey examined the presence of disorders rather than symptoms and this can explain the much lower figure than one found in this study and the many other above mentioned studies. Further studies are needed to look for how much are the figures of prevalence of anxiety symptoms in the general Iraqi population and also in other profession to confirm how much anxiety is specifically related to school teaching in Iraq.

The number of female teachers in the current study is significantly high and there is significant association between gender and rates of anxiety. Inherently anxiety is more common among women than men⁽¹⁵⁾. Females prefer teaching as a job as its relatively short working hours saves time for other household responsibilities, on the other hand such dual role of house wife and working woman can predispose to stress that ultimately results in anxiety. This is supported by fact that most teachers in this study are married although no significant relationship was found between marital status and levels of anxiety. Marriage by itself is protective for both physical and mental health⁽¹⁶⁾ but it is possible that such dual role conflict between house and job duties of modern working woman that predispose to anxiety⁽¹⁷⁾

Further studies are needed to examine factors from home environment and school environment that contribute to such high figures of anxiety symptoms among school teachers, more over comparative studies are needed to be arranged with samples from other occupations to confirm this association between teaching career and anxiety.

Study limitations:

The limitations of this work include the use of a cross-sectional study where the causality and the direction of relationships couldn't be determined. Another limitation was the use of self-reported questionnaires where the responses to questionnaires could be affected by personal or social values leading to the probability of recall bias. A complete refusal of several teachers in many school lead to a reduction in sample size.

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Conflict of Interest: The authors and planners have disclosed no potential conflicts of interest, financial or otherwise.

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References:

1. Damasio A, Carvalho GB. The nature of feelings: evolutionary and neurobiological origins. *Nature Reviews Neuroscience*. 2013 Feb; 14(2):143.
2. Sadock B, Ruiz P. Kaplan & Sadock's. *Synopsis of psychiatry: behavioral sciences*. Walters Kluwer; 2015.
3. Balderston NL, Mathur A, Adu-Brimpong J, et al. Effect of anxiety on behavioral pattern separation in humans. *Cognition and Emotion*. 2017 Feb 17; 31(2):238-48.
4. Connolly S, Petty C, Simpson D, et al. *Anxiety disorders*. InfoBase Publishing; 2006.
5. American Psychiatric Association. *The Diagnostic and Statistical Manual of Mental Disorders*. 2013; 5.
6. Dan J. Stein, Kate M. Scott, Peter de Jonge, Ronald C. Kessler. *Epidemiology of anxiety disorders: from surveys to nosology and back*. *Dialogues Clin Neurosci*. 2017 Jun; 19(2): 127–136.
7. Hansen ÅM, Høgh A, Persson R, et al. *Bullying at work, health outcomes, and physiological stress*

- response. *Journal of psychosomatic research*. 2006 Jan 1;60(1):63-72.
8. Skaalvik EM, Skaalvik S. Teacher self-efficacy and teacher burnout: A study of relations. *Teaching and teacher education*. 2010 May 1;26(4):1059-69.
 9. Dr. Al-Shatti, Taghreed S. psychometric properties of the Arabic Version of the Beck Anxiety Inventory in the State of Kuwait *Journal of Educational and Psychological Sciences*. 2015;16th (2):431-63.
 10. Gonçalves GB, Fernandes MR, Beijo LA, et al. Assessment of Stress, Depressive, and Anxiety Symptoms in Teachers in the Public Education Network. *Ann Depress Anxiety*. 2015;2(3): 1051.
 11. Desouky D, Allam H. Occupational stress, anxiety and depression among Egyptian teachers. *Journal of epidemiology and global health*. 2017 Sep 1;7(3):191-8.
 12. Leung SS, Wah Mak Y, Yu Chui Y, Chiang VC, Lee AC. Occupational stress, mental health status and stress management behaviors among secondary school teachers in Hong Kong. *Health Education Journal*. 2009 Dec;68(4):328-43
 13. Yousef A. Taher, Awatef M, Massara M. Hashemi, etal. Prevalence of Depression, Anxiety and Stress among Libyan Primary and Secondary Schoolteachers: A Cross-Sectional Study. *Jordan Journal of Pharmaceutical Sciences*. 2016;9(2):131-2.
 14. WHO. Iraqi mental health survey 2006/7.2009:44
 15. Carmen P. McLean, Anu Asnaani, Brett T. Litz, and Stefan G. Hofmann. Gender Differences in Anxiety Disorders: Prevalence, Course of Illness, Comorbidity and Burden of Illness. *J Psychiatr Res*. 2011 Aug; 45(8): 1027–1035.
 16. Walter R Gove, Carolyn Briggs Style, Michael Hughes . The Effect of Marriage on the Well-Being of Adults: A Theoretical Analysis. *Journal of family issues*.1990; 11(1) : 4-35 .
 17. Swanson NG. Working women and stress. *J Am Med Womens Assoc*. 2000 spring; 55(2):76-9.

Psychosocial Experience of Diabetes Melitus Patients While Experiencing the Diabetes Feet Ulcer in Rumah Perawatan Luka Ubalan Pamotan Village Dampit Subdistrict Malang Regency

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Abstract

Introduction: This study reveals the psychosocial experience of diabetic mellitus patients with diabetic foot ulcers while undergoing treatment at *Rumah Perawatan Luka Ubalan* (Ubalan Ulcer Nursing Home).

Objective: Exploring the meaning of psychosocial experiences of diabetes mellitus patients with diabetic foot ulcers during treatment.

Method: Qualitative research uses phenomenological interpretive approach and is analyzed using IPA (Interpretive Phenomenological Analysis).

Findings: This study found 3 major themes: fear of facing death, loss of opportunity to interact socially with others, feeling insecure about the physical appearance of the disease.

Conclusion: Perceptions and psychosocial responses in diabetic foot ulcer patients have an impact on the life of social interactions.

Keyword: *Meaning of life, foot ulcer, diabetes mellitus.*

Introduction

Diabetes mellitus is a metabolic disorder characterized by an increasing of blood sugar levels⁽¹⁾. Diabetes mellitus to be considered as a serious public health problem, because it is one of the four dangerous non-spread diseases after cardiovascular disease, cancer, and chronic lung⁽²⁾. Diabetes mellitus which occurring lasts long may cause damage to organs such as heart problems, blood vessels, eyes, kidneys, and nerves⁽³⁾.

The occurrences number of Diabetes mellitus has increased each year. Huang reported that in 2015 there were 415 million people and an increase of 451 million in 2017⁽¹⁾. International Diabetes Federation found that Indonesia was ranked 7th in the world for the highest prevalence of patients with diabetes mellitus in the amount of 8.5 million, after China, India, America, Brazil, Russia and Mexico⁽⁴⁾.

Data obtained from the Malang District Health Office in July 2018, stated that diabetes mellitus is a disease that is ranked eighth in the category of 15 most diseases with a total of 1023 people. In 2017, the Pamotan Public Health Service, DampitSubdistrict, Malang Regency ranked 9th from 10th health centers which had the most cases of diabetes mellitus with 785 people. The researchers did not find patients suffering from diabetes mellitus with diabetic foot ulcers based on data provided, but empirically researchers found that many patients had diabetic foot ulcers in the society. Frykberg stated that estimated 15% among all patients with diabetes mellitus are suffering diabetic ulcers⁽⁵⁾.

Prolonged treatment processes in diabetic foot ulcer patients may affect physical, economic, emotional response, depression, unhappiness with social life and their quality of life resulting in psychosocial disorders⁽⁶⁾.

King in his research entitled 'Psychological Factors and Delayed Healing in Chronic Wounds' stated that there is an effect of psychosocial stress factors on the healing process of foot ulcers in diabetes mellitus and recommend nurses as medical teams to always pay attention to psychosocial aspects as an important part in treating diabetes mellitus foot ulcers by providing comprehensive services⁽⁷⁾.

Data obtained from preliminary studies conducted by researchers in October 2018 indicated that participants had diabetes for approximately 20 years, still undergoing ulcer treatment. Doctors recommend amputation of the left leg. The verdict of amputation given by the doctor made him feel scared and anxious because he would lose one of his legs. Participants feel inferior because cannot work any longer, worried about financing ulcer treatment even though it have been borne by their children, pitying their children and wife for their sacrifice in caring for him, disappointed with his closest friends who rarely communicate and stay away. He had stopped participating in society activities because of embarrassment with the condition of his leg ulcer. The only thing for his daily activities are watching TV and listening radio.

Mental care is essential for treating process for patients with psychosocial cases. Fulfillment of psychosocial needs is required to help patients return to their family and society to be able to continue their duties and functions in accordance with their roles. Providing health education to achieve life goals independently aimed at patients, families, and groups and communities by improving their abilities, attitudes and skill is the goal of mental nursing⁽⁸⁾.

The purpose of this study is to explore the meaning of the patient's experience of perceptions and psychosocial responses while undergoing wound care in Rumah Perawatan Luka Ubalan, Pamotan Village, Dampit District.

Research Method

This research is a qualitative research with an interpretive phenomenology approach. Participants in this study were persons with diabetes mellitus with diabetic foot ulcers, in total 5 (five) persons. The participant selection procedure was carried out using a purposive sampling technique, in accordance with inclusion criteria, specifically undergoing diabetic foot ulcer treatment at Ubalan Ulcer Nursing Home regularly,

level 4 diabetic foot ulcer classification, have married and aged between 40-65 years old.

Research Findings: This study found 3 main themes and the researcher described the overall themes formed from the results of the analysis based on the expressions of the participants.

Theme: Fear of facing death: Fear according to Indonesia Dictionary (KBBI) means "feeling afraid (horrified) to face something that is considered to bring disaster". The researcher interpreted this theme that participants felt afraid of death due to their illness. This theme is arranged on sub themes Fear of death. This sub theme describes the concerns of participants in the process of diabetes itself. This was conveyed by participants through the following quote:

"Worried about how the person with diabetes, I saw my friend who died (because of diabetes)..." (P4)

"Yes, I am afraid of death, fear of death, I am afraid ... but I am not ready ... not ready yet ..." (P5)

"I was dumbfounded ... scared if there was a relapse of the disease (diabetic foot ulcer), suddenly died" (P4)

Theme: Loss of opportunity to interact socially with other people: The loss according to KBBI is "no more; vanished; invisible". The researcher interpreted what was conveyed by the participants that participants expressed disappointment that they could not socialize with others because of their physical limitations. This theme is composed of two sub-themes described by the researcher as follows:

Feeling disappointed can't socialize: It describes a condition in which participants feel disappointed because they are unable to relate socially to other people around them. The condition of diabetic foot ulcers limits the movement of participants socialize with others. This has an impact on his mentality, participant feels regret because he has lost the opportunity to interact with others. The participant's statement is illustrated as follows:

"Yes ... if I can't come (to recitation), I feel regretful ..." (P4)

"Actually, it is unfortunate (regretting) that you cannot attend (recitation) ... gathering with people like our own family ... and being friends" (P3)

Feeling physical limitations prevents interaction with others: It was interpreted by researchers based on the participants' expressions that with their diabetic foot ulcer condition, participants felt they were not free in associating with friends and the community around their home. Participants reveal the condition of his body at this time causing physical disturbances that can interfere with the interaction of his life. The following is a quote from participants regarding the statement above:

"... when I want to get out I find it difficult to wear sandals, and actually there is also a desire to sunbathe under the sun" (P1)

"... Yeah no, I am sick ... I can't walk, so I can't go anywhere, just at home" (P2)

Theme: Feeling insecure about the physical appearance of the disease: It describes a situation which participants feel insecure about the condition of their foot ulcer. This condition may arise because diabetic foot ulcers have a characteristic that makes this disease shunned by people around him as the presence of a distinctive smell. This has an impact on the emergence of insecurity when interacting with others. Confident according to KBBI, is "absolutely sure or ensuring the ability or strength of someone or something". Lack of confidence means individuals who do not have confidence in their abilities or strengths. The theme of feeling insecure about the physical appearance of the disease is composed of two sub themes, namely:

Worried about gangrenous ulcer conditions, this sub-theme provides a picture of the feelings experienced by participants regarding the distinctive odor of the ulcer's leg. Participants express these feelings through the following quote:

"... The fear is, people said diabetes is a deadly disease that is difficult to heal ... it is difficult to recover, continue to wet (ulcer) ..." (P5)

"Yes, I feel worried (ulcer odor) ... I'm worried like this ..." (P1)

The second sub theme which was composed from the theme above was **feeling inferior because of their illness condition,** participants felt embarrassed when they gathered with other people because of the condition of the wound in the leg with bandage dressing. This was revealed from the participant's statement, as follows:

"Yes, my feeling when wearing there a bandage ...

and when there are flies ... I feel more reluctant ... I'm ashamed of this" (P4)

"..... It means that I don't seem to have function anymore, it's my feelings ... but this is only my own feeling, because you say it's not like that, people think, it's just my feeling"(P1)

The other sub-theme is **fear of disability,** the meaning of this sub-theme is the participants are afraid of amputation if the condition of diabetic foot ulcer is getting bigger (and worse). The quote as follows:

"... What I can do sir. If going to be like this, it's hard for me ... later if getting bigger, shall go to see doctor. It will be amputated, my troubles "(P4)

Discussion

Theme: Fear of facing death: Contextually the fear of facing death reflects the feelings of participants who are afraid of death. This is due to diabetic foot ulcer conditions. Fear of the disease that began to be felt when the victim was convicted of suffering from an illness, this has an impact on worry and anxiety. Taylor revealed that feelings of anxiety or fear of chronic health problems (diabetes mellitus) caused by imagination of potential life changes and the possibility of death may worsen glucose control and symptoms of diabetes ⁽⁹⁾.

Other research reveals the same phenomenon, as conducted by Ismail through his research, found results that one third of people with diabetes mellitus experience depression which is directly related to death⁽¹⁰⁾. The results of the study also provide the same picture that participants were worried about the disease, because some of the participant's friends eventually died because of the same disease. Other feelings of fear of death are also felt by participants but psychologically, participants are not ready to face it. This condition is in line with the expression of Lehto, that many factors make an individual feel anxious about death. Amongst them they do not know what he is facing after death, a picture of the pain of death, worry about the family that will be left after and lack of understanding the meaning of life and death ⁽¹¹⁾.

The condition of fear of death is physiologically described in patients with diabetes mellitus will cause failure in treatment such as fear of glucose monitoring, failure in self-control related to dietary habits, memory failure and perceived self-failure in controlling diabetes

can inhibit diabetes self-management behavior so that it interferes with the process daily treatment and care ⁽¹²⁾.

Theme: Loss of opportunity to interact socially with other people: This theme has a contextual meaning, that's participants have a dilemma towards the condition of diabetic foot ulcers which limits their social interaction with others. The results of a study conducted by Trisnawati revealed that foot ulcer patients diabetes will feel cautious in carrying out their activities because they are afraid they will cause more severe conditions⁽¹³⁾. This situation causes patients to be stressed and may interfere with their social interactions with others. In line with research, Astrada stated that social interaction is one of the risks that may occur in diabetic foot ulcer patients ⁽¹⁴⁾.

Participants expressed feelings of disappointment cannot interact because the condition of diabetic foot ulcers that cause odor, pain and cannot walk so they depends on the child and spouse for daily activities. According to Agustin, she revealed the results of her research, if diabetic patients suffer injuries, they will experience disruption of activity, emotions, and pain due to the smell of diabetic foot ulcers ⁽¹⁵⁾.

Physical limitations cause participants unavailable to socialize with the society. Participants revealed that his condition was still not healthy enough so he felt uncomfortable to interact socially with other people. Social interaction can be disrupted due to physical weakness, feeling bad and dirty wounds that affect the feeling of comfort both physically, psychologically and socially.

Other participants felt sad and sorry that they could not interact socially. Participants assume that by gathering together there will be many benefits, such as the existence of a sense of pleasure in being able to share and exchange ideas and remind each other in self-improvement. Another thing illustrated by this theme is the existence of desire but is limited by the physical conditions suffered by the participants, he is aware about his physical difference with others. Brown said patients with chronic diabetic foot ulcers did not seems to suffer a higher level of loneliness than their healthy counterparts, but with their present conditions they felt different from others ⁽¹⁶⁾.

Theme: Feeling insecure about the physical appearance of the disease: It has contextual meaning, namely participants with diabetic foot ulcer conditions

feel inferior due to diabetic foot ulcer conditions that cause unpleasant odors, and this has an impact on the low self-esteem of a person. This low self-esteem may occur when a person has physical limitations or deficiencies and disrupts his life ⁽⁸⁾. The results of this study illustrate that participants were afraid if their legs would be amputated if diabetic foot ulcers were not immediately treated. This makes participants feel shy and worried to interact socially with others.

The feeling of inferiority over the condition of diabetic foot ulcers has made participants uncomfortable, unsatisfied with their abilities, lacked self-confidence, and unable to express themselves in the social environment so they feel insecure even in their own environment and vice versa if the individual has self-esteem high, they will feel satisfied and comfortable and be able to get positive appreciation from the environment ⁽¹⁵⁾. Diabetic foot ulcers can worsen the patient's psychosocial condition. This is in line with the report Ningsih about the psychosocial experience of diabetic patients who stated that complications of diabetic foot ulcers cause patients to feel scared, blame themselves, helpless, and feel insecure in socializing ⁽¹⁷⁾.

Conclusion

Psychosocial problems may occur in individuals who have a disease or suffer from a particular disease. This problem does not only have an individual impact, but in a broad sense, this problem will affect his social life. Diabetes ulcer sufferers have fears and anxieties for their illness, various limitations that have resulted in changes in the sufferer such as low self-esteem. These problems must be addressed immediately to prevent other health problems occurring. Various efforts need to be made by health workers to prevent this psychosocial problem to have a further impact on behavioral irregularities.

Conflict of Interest: None

Ethical Clearance: This study has received ethical approval from the Medical Faculty of Brawijaya University with No. 257/EC/KEPK-S2/10/2018.

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References

1. Cho N, Shaw J, Karuranga S, et al. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. *Diabetes Research and Clinical Practice*. 2018;138:271-281.

2. Chan M. Global report on diabetes. World Health Organization. 2014; 58(12):1–88.
3. Punthakee Z, Goldenberg R, Katz, P. Definition, classification and diagnosis of diabetes, prediabetes and metabolic syndrome. *Canadian J of Diabetes*. 2018; 42:10–15.
4. IDF. International Diabetes Federation. *IDF Diabetes Atlas, 7th ed.* Brussels, Belgium: International Diabetes Federation. 2015;1-163.
5. Frykberg R, Armstrong D, Giurini J, et al. Diabetic foot disorders: A clinical practice guideline. *J ofFoot and Ankle Surgery*. 2006; 45(5):S1–S66.
6. Jaksa P J, Mahoney JL. Quality of life in patients with diabetic foot ulcers :Validation of the Cardiff Wound Impact Schedule in a Canadian population. *International Wound J*. Blackwell Publishing Ltd and Medicalhelplines.com Inc. 2010;7(6).
7. King Ac, Gordon K. Psychological factors and delayed healing in chronic wounds. In *Psychosomatic Medicine*. 2001.
8. Keliat BA. *Community mental health nursing: CMHN (Basic Course)*. Jakarta: EGC 2011.
9. Taylor MR. *Health Psychology*. 6th. ed. Singapore: Mc. Graw Hill Book Company. 2006;(6).
10. Ismail A. Cohort study of people with diabetes and their first foot ulcer. *Diabetes Care*. 2007 June;30(6).
11. Lehto RH, Stein KF. Death anxiety: An Analysis of an evolving concept. *Research and Theory for Nursing Practice: An International J*. 2009;23(1):23-41.
12. Chlebowy OD, HoodS, La Joie AS. Facilitators and barriers to self-management of type 2 diabetes among urban African American adults: Focus group findings. *Diabetes Educator*. 2010;36(6):897–905.
13. Trisnawati. Risk Factors for Type 2 Diabetes mellitus in the community Health Centers Cengkareng District, West Jakarta, *Health Scientific J*. 2013;5(1).
14. Adam A, Suriadi. Factors that influence the occurrence of diabetic foot injuries in patients with type 2 diabetes mellitus in the treatment center and wound care specialist, the stoma and Pontianak “Kitamura” incontensia.2014.
15. Agustin Y, Nurachmah E, Kariasa IM. Experience clients with type 2 diabetes mellitus post major lower limb amputations. *Indonesian Nursing J*. 2013;16(2).
16. Brown A. Chronic leg ulcers, part 2: do they affect a patient’s social life?.*British J of Nursing*. 2005;14(18):986-89.
17. Ningsih ES. Psychosocial experience of patients with ulcers diabetikumin diabetes mellitus nursing carecontext. Depok: Indonesian University Medical Science Faculty. 2008.

Is Osteopontine of Value in Diagnosis of Knee Osteoarthritis?

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Abstract

Background: Osteoarthritis is a painful chronic joint disease characterized by structural changes to the whole joint, including loss of articular cartilage, development of osteophytes, synovial inflammation, subchondral bone changes, meniscal damage, muscle weakness, and ligamentous laxity.

Aim of the Work: To detect osteopontine (OPN) in knee osteoarthritis.

Method: 60 patients diagnosed as primary knee OA fulfilling Arthritis Rheum 1986 OA classification criteria, And 60 healthy control were included. All patients subjected to through history taking and full examination, body mass index, plain x ray knees PA view to assess severity according to Kellgren and Laurence grading, plasma and synovial fluid OPN levels, and plasma OPN for control. Assessment of pain for OA patients by patient pain visual analogue scale (VAS) and for functional status by Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), ESR, CRP were done.

Results: there was significant difference between both groups regarding plasma osteopontine ($p < 0.0001$), OPN levels in OA patients in plasma and synovial fluid was correlated with each other ($p < 0.0001$), patient pain VAS, WOMAC score, K-L grading were correlated with plasma OPN levels with p value (0.001, < 0.001 , < 0.001), and with synovial fluid OPN levels in primary OA patients with p value (0.008, < 0.001 , < 0.001) respectively. ESR positively correlated with plasma OPN $p = 0.004$.

Conclusion: OPN is higher in OA patients more than control, and it is higher in synovial fluid than plasma in knee OA patients, OPN correlated with markers of systemic inflammation and has impact on functional status so it can be used as a diagnostic and prognostic factor in knee osteoarthritis.

Keywords: Osteoarthritis–OPN, ESR, synovial.

Introduction

Osteoarthritis is a painful chronic joint disease characterised by structural changes to the whole joint including: loss of articular cartilage, development of osteophytes, synovial inflammation, subchondral bone

changes, meniscal damage, muscle weakness, and ligamentous laxity. It results from a complex interplay of genetic, metabolic, biomechanical, and biochemical factors. At the knee, osteoarthritis most commonly affects the medial tibiofemoral and patellofemoral joint compartments.⁽¹⁾ Biochemical markers can be used to detect the disease and determine its severity. Therefore the extracellular matrix proteins were crucial to the occurrence and development of osteoarthritis. some extracellular matrix proteins such as osteopontin (OPN) was found to play important roles in promoting the inflammatory occurrence of cartilage cells in knee osteoarthritis, As an important extracellular matrix protein, OPN can mediate cellular growth, survival, adhesion and migration in osteoarthritis⁽²⁾.

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Aim of the work: To detect osteopontine (OPN) in knee osteoarthritis.

Patients and Method

The study conducted in Minia university hospital, included 60 patients with primary knee osteoarthritis (group I) and 60 apparently healthy controls (group II), patients in group I was complaining of knee effusion candidate for aspiration for detection of synovial fluid OPN level, both groups also were tested for plasma OPN level. All patients fulfilled criteria for diagnosis of primary knee osteoarthritis⁽³⁾ were included as (group I). Sixty apparently healthy volunteers were served as a control group (group II). Patients with other rheumatological diseases as rheumatoid arthritis, systemic lupus, gouty arthritis, Other forms of arthritis, cancer or other chronic inflammatory diseases, Secondary knee osteoarthritis, Diabetes mellitus were **excluded** from the study

Statistical analysis: Analysis of data was done by personal computer using SPSS (Statistical program for social science) version 16. The data of all software patients and controls were fed into an IBM personal computer. Data were expressed as mean ± SD for parametric variables and as number and percent for non-parametric variable. Comparison between groups for parametric data was done by independent samples t-test (unpaired t-test). The difference was considered significant if P <0.05. The Bivariate Correlations procedure computes Pearson’s correlation coefficient with its significance levels. Pearson’s correlation coefficient is a measure of linear association for parametric variables and Spearman-rho correlation coefficient for nonparametric variables.

Results

Characters of OA patients; demographic data, laboratory investigation, functional status and radiological KL grading in table 1

Table 1: Characters of OA patients

Parameters Mean±SD and/or n (%)		OA patient n = 60
Age (y)		46-72(56.3±7.95)
DD (y)		2-10 (5.8 ±2.33)
BMI	Over weight	4 (6.7%)
	Obese I	16 (26.7%)
	Obese II	24 (40%)
	Obese III	16 (26.7%)
VAS		5-10 (7.53±1.22)
WOMAC total score		45-96 (74.26±14.07)

Parameters Mean±SD and/or n (%)		OA patient n = 60
KL grading	I	5%
	II	35%
	III	38.33%
	IV	21.67%
Plasma OPN		92-222 (136.67±35.1)
Synovial fluid OPN		162-298 (218.4±37.7)
ESR mm/1 st hour		8-36 (23.97±7.4)
CRP		53 (88.3%)

Functional status and severity in group I (OA patients): Table 2 shows that patient pain VAS, WOMAC score, K-L grading were correlated with plasma OPN levels with p value (0.001, <0.001, <0.001), and with synovial fluid OPN levels in primary OA patients with p value (0.008, <0.001, <0.001) respectively. ESR positively correlated with plasma OPN p= 0.004.

Table 2: Correlation between plasma & synovial osteopontine with demographic data, disease functional and severity indices in OA patients:

Parameters r (p)	Plasma OPN	Synovial fluid OPN
Age	0.032 (0.730)	0.800 (<0.0001)
DD	0.155 (0.236)	0.390 (0.002)
BMI	0.629 (<0.0001)	0.074 (0.574)
Patient pain VAS	0.431(0.001)	0.338 (0.008)
WOMAC total score	0.342 (<0.001)	0.358 (<0.001)
KL grading	0.358 (<0.001)	0.680 (<0.001)
ESR	0.362 (0.004)	0.087 (0.510)
CRP	0.895)) 0.017	0.689 (0.455)

Discussion

Osteoarthritis (OA) is a low-grade inflammatory disease of synovial joints and the most common form of arthritis⁽⁴⁾. It is a leading cause of chronic pain and physical disability in older individuals. OA is one of the most costly and disabling forms of joint disease, being far more common than rheumatoid arthritis (RA) and other forms of joint disease ⁽⁵⁾.

The increased expression of OPN has been observed in the joints of patients that were reported to be correlated with the severity of joint lesion and inflammatory status in the OA patients ⁽⁶⁾.

In our study patient pain VAS, WOMAC score, KL grading was positively correlated with plasma and synovial OPN levels.

Plasma osteopontine show statistically significant difference between both groups ($p < 0.001$), and synovial fluid OPN was significantly higher than paired plasma level in primary OA patients.

In agreement with⁽⁷⁾ who found in a similar study on Plasma OPN (in patients and control) and in synovial fluid OPN (in patients) levels in knee OA patients, that patients had higher plasma OPN concentrations compared to healthy controls ($P < 0.0001$). Also OPN levels in synovial fluid were significantly higher with respect to paired plasma samples ($p < 0.001$).

In another study done by **Qin et al.**,⁽²⁾ who examined the synovial fluid from 42 patients with knee OA and 40 cases of the normal control group had effusion due to traumatic causes as meniscus injury or lower extremity fracture surgery in the hospital at the same period for OPN level and demonstrated that the expression levels of OPN in OA group was significantly higher than those in the control (post traumatic) group, ($P < 0.05$)

In agreement with **Haider et al.**,⁽⁸⁾ who found In their study about OPN in knee OA patients and control, that plasma OPN level significantly correlated with synovial OPN in OA patients ($r = 0.806$, $P < 0.001$), a significant difference between patients and controls as regards the plasma OPN levels ($t = 8.534$, $P < 0.001$), OPN in synovial fluid was higher with respect to paired plasma. Also, OPN level in both plasma and synovial fluid was significantly correlated with severity of knee pain ($r = 0.878$, $r = 0.795$, $p < 0.001$).

In Conclusion: This study suggests that OPN is an inflammatory marker that can be used as a diagnostic and prognostic marker in knee OA.

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References

1. Zhang, W., Moskowitz, R. W., Nuki, G., Abramson, S., Altman, R.D., Arden, N., Bierma-Zeinstra, S., Brandt, K, D., Croft, P., Doherty, M., & Dougados, M. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis and cartilage*; 2008; 16 (2): 137-162.
2. Qin, L. F., Wang, W. C., Fang, H., Mao, X. Z., Huang, G. L., Chen, Y., ... & Peng, D. Expression of NF- κ B and osteopontin of synovial fluid of patients with knee osteoarthritis. *Asian Pacific journal of tropical medicine*, 2013; 6(5), 379-382.
3. Altman, R., Alarcon, G., Appelrouth, D., Bloch, D., Borenstein, D., Brandt, K., Brown, C., Cooke, T, D., Daniel, W., Feldman, D., & Greenwald, R. The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hip. *Arthritis & Rheumatology*; 1991; 34 (5): 505-514.
4. Berenbaum, F. Osteoarthritis as an inflammatory disease (osteoarthritis is not osteoarthrosis!). *Osteoarthritis and Cartilage*; 2013; 21 (1): 16-21.
5. Cross, M., Smith, E., Hoy, D., Nolte, S., Ackerman, I., Fransen, M., & Laslett, L. L. The global burden of hip and knee osteoarthritis: estimates from the global burden of disease 2010 study. *Annals of the rheumatic diseases*; 2014; 73 (4): 2047-2063.
6. Tanamas, S. K., Wluka, A. E., Pelletier, J. P., Martel-Pelletier, J., Abram, F., Wang, Y., & Cicuttini, F. M. The association between subchondral bone cysts and tibial cartilage volume and risk of joint replacement in people with knee osteoarthritis: a longitudinal study. *Arthritis research & therapy*; 2010; 12 (2): 58.
7. Honsawek, S., Tanavalee, A., Sakdinakiattikoon, M., Chayanupatkul, M., & Yuktanandana, P. Correlation of plasma and synovial fluid osteopontin with disease severity in knee osteoarthritis. *Clinical biochemistry*, 2009; 42(9), 808-812.
8. Haider, H. M., Amin, I. R., & Ahmad, K. A. Plasma and synovial osteopontin levels, are they associated with disease severity of primary knee osteoarthritis in Egyptian patients?. *The Egyptian rheumatologist*, 2015; 37(1), 29-34. one, 7(11), e49014.

Coal Dust Exposure and Gingival Lead Line in Coal Miners

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Abstract

Coal dust contains less than 1% lead (Pb). This dust can enter the body through breathing, mouth and skin. Lead contained in coal dust can react with Sulfur and form gingival leadline. The study was an observational study with cross-sectional design. The research subjects were coal miners in Sambung Makmur Sub-District, Banjar District, amounting to 100 people. The number of samples was calculated by the Slovin formula and obtained 80 people as samples and determined by simple random sampling technique. The sample obtained then determined the value of the gingival lead line score as done by Sudibyo. The degree of gingival lead line is assessed based on the score as follows: 0 = no gingival lead line; 1 = gingival lead line found in 1-2 marginal gingival anterior teeth labial surface; 2 = gingival lead line found at 3-4 marginal gingival anterior teeth labial surface; 3 = gingival lead line at >4 marginal gingival anterior teeth labial surface. In addition, age, working period (tenure), and smoking habits are the variables measured in this study. The data obtained were analyzed using the chi-square test with $\alpha = 5\%$. The conclusion is the incidence of gingival leadline of coal miners was related to age, tenure, and smoking habits.

Keywords: *Gingival leadline, lead, coal dust, coal miners.*

Introduction

Kalimantan Selatan is one of the provinces in Indonesia which has the largest coal mining with locations spread throughout the region. One of the problems arising from mining is the issue of coal dust which can have an impact on health. This is due to the metal content found in coal dust, namely Fe 36.9%; Si 17.9%; Mo 15%; Al 10%; Ca 8.67%; S 4.7%; Ti 3.65%. Some heavy metal content of less than 1% includes K, V, Cr, Mn, Ni, Cu, and Pb.¹

Coal dust containing metals can enter the body through breathing, mouth and skin. Furthermore, metals

contained in coal dust, especially Lead and Sulfur will accumulate in gum tissue through systemic and local processes, namely direct absorption by the oral mucosa. Lead and Sulfur produce lead sulfate which is deposited in the basement membrane of gum.² These deposits provide a picture of the lead line in the gums. Various factors that are thought to influence the occurrence of gingival lead line, such as working period, age, use of personal protective equipment (PPE), smoking habits, etc.³

The working period (tenure) affects the incidence of gingival lead line, because the working period shows the length of time someone is exposed to coal dust. The longer the exposure time, the incidence of gingival lead line will be more severe. Likewise, increasing age causes the detoxification rate to slow down, resulting in a buildup of lead from coal dust. This incident gingival lead line will be more severe.⁴

Previous research has revealed that the working period has a relationship with the incidence of gingival lead line in traffic police.⁴ Other studies have also

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revealed that the workshop workers have a risk of gingival lead line, because every day they are exposed to fumes that contain lead.⁵ Coal miners are a group at risk of developing gingival lead lines. This is due to his daily exposure to coal dust containing lead and sulfur. However, not many studies have revealed this. Therefore in this study we will examine the relationship of working period, age, and smoking habits to the incidence of gingival lead line of coal miners.

Materials and Method

The study was an observational study with cross-sectional design. The research subjects were coal miners in Sambung Makmur Sub-District, Banjar District, amounting to 100 people. The number of samples was calculated by the Slovin formula and obtained 80 people as samples and determined by simple random sampling technique.

The sample obtained is then determined by the value of the gingival lead line score as done by Sudibyo.⁶ The degree of gingival lead line is assessed based on the score as follows:

- 0 = no gingival lead line
- 1 = gingival lead line found in 1-2 marginal gingival anterior teeth labial surface
- 2 = gingival lead line found in 3-4 marginal gingival anterior teeth labial surface
- 3 = gingival lead line at >4 marginal gingival anterior teeth labial surface

In addition, age, working period, and smoking habits are the variables measured in this study. The data obtained were analyzed using the chi-square test with $\alpha = 5\%$.

Findings and Discussion

This study involve 80 male who were willing to be sample in the study. The lowest age is 19 years and the highest is 45 years. The existence of gingival lead line can be seen in Figure 1.



(a)



(b)

Figure 1. Normal gum looks reddish (a) and gingival lead line (b)

Gingival leadline, also called Burton's Line, is a pigment in the form of gray-blue lines at the border between teeth and gums.^{7,8} Leadline occurs due to a reaction between lead and sulfur ions released by the bacterial oral cavity, leading to lead sulfid at the tooth and gingival surface.⁸

Relationship between age and gingival lead line:

The relationship between age and the gingival lead line is presented in table 1. Gingival lead line is found in >4 marginal gingival anterior teeth labial surfaces. It is found more at the age of 30-45 years.

Table 1. Relationship of Age with Gingival Lead Line

Age (Years)	Gingival Lead Line Score			
	0	1	2	3
15-30	15%	23.75%	7.5%	6.25%
30-45	7.5%	8.75%	15%	16.25%

Based on the results of the chi-square test obtained $p = 0.005$ ($p < 0.05$), it was concluded that age was associated with the incidence of gingival lead lines in coal miners. The relationship between age and

gingival lead line caused by in the young age more sensitive to lead activity. It is closely related to organ development and function are not perfect. In the old age the sensitivity is higher, this is caused by the activity of the biotransformase enzyme decreases with increasing age and the resistance of certain organs decreases to the effects of coal dust containing lead. The older the person, the higher the amount of lead accumulated in the body tissues.

On the other hand, the activity metaloprotein (metal-binding protein) in the oral cavity will slowly decrease the activity. This causes lead contained in coal dust can not be transported optimally by metalloproteins. As a result, lead reacts with sulfur in the oral cavity and leadline is formed. The results of this study are in accordance with the study by Vera⁹, which states that the age of street vendors in the city of Semarang affects the incidence of gingival leadline.

Relationship between working period and gingiviallead line: Working period of more than 12 months caused 16% of the study subjects have gingivial lead line at>4 marginal gingival anterior teeth labial surface. The relationship between the working period and the gingivial lead line is presented in table 2.

Table 2: Relationship between Tenure and Gingivial Lead Line

Working period (month)	Gingivial Lead Line Score			
	0	1	2	3
<3	12.5%	3.75%	1.25%	1.25%
3-6	5%	7.5%	1.25%	1.25%
6-9	1.25%	6.0%	6.25%	1.25%
9-12	2.5%	2.5%	1.25%	2.5%
>12	1.25%	13.5%	12.5%	16.25%

Based on the results of the chi-square test obtained $p = 0.000$ ($p < 0.05$), it was concluded that the working period of coal miners was related to the incidence of gingivial lead line. The working period shows the length of exposure to coal dust containing lead. Lead as the cause of many lead lines accumulates in gum tissue through systemic processes or local processes, namely direct absorption by the oral mucosa. This lead will only form a lead line after reacting with sulfur ions produced by anaerobic bacteria in the oral cavity.¹⁰ The results of the reaction are lead sulfate compounds which are then deposited on the gum basement membrane. These deposits provide a picture of the lead line in the gums. Thus, it can be concluded that indirectly the Oral

Hygiene Index (OHI) and Gingivitis Index (GI) are important factors that determine the quality of lead line formation because these two factors are closely related to the presence of bacteria in the oral cavity.¹¹

Relationship between smoking habit and gingivial lead line: In table 3, the relationship between smoking habits and the incidence of gingivial lead line is presented.

Table 3: Relationship between Smoking Habit and Gingivial Lead Line

Smoking habit	Gingivial Lead Line Score			
	0	1	2	3
Not a smoker	7.5%	10.0%	7.5%	1.25%
Smoker	15.0%	22.5%	15.0%	21.25%

Based on the results of the chi-square test obtained $p = 0.158$ ($p < 0.05$), it was concluded that the smoking habits of coal miners were not related to the incidence of gingivial lead lines. The standard of cigarettes taken from tobacco, in the handling process often uses pesticides which also contain basic ingredients of lead (Pb).¹² Thus, research subjects who had a smoking habit of Pb levels increased the amount of Pb exposure both from the contents of the cigarette and from coal dust were also sucked. This can worsen the incidence of gingivial leadline.

Conclusion

The results of this study concluded that the incidence of gingivial leadline in coal miners was significantly related with age, working, and smoking habits. Thus, a comprehensive effort is needed to improve dental and oral health.

Ethical Clearance: This research has gone ethical feasibility testing by the Ethical Research Commission of the Faculty of Dentistry, University of Lambung Mangkurat and declared as ethical: no. 28/KEPKG-FKGULM/EC/IX/2017.

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References

1. Yuwono A, Setiawan B, Kania N, Nurdiana, Widodo MA. Subchronic Coal Dust Exposure

- to Lipid Peroxidation and Blood Sugar Levels in Diabetes Mellitus Mice. *Majalah Kedokteran Bandung*. 2011; 43 (4): 189-92.
2. Takwa A, Bujawati E, Mallapiang F. Overview of Lead Levels in urine and Gingival lead line incidences on gums of street children on Jl. AP. PettaraniMakassar. *Hygiene*. 2017; 3 (21): 114-123.
 3. Daeng Pasiga B, Samad R, Pratiwi R, Akbar FH, Identification of Lead Exposure Through Saliva and the Occurrence of Gingival Pigmentation at Fuel Station Indonesian Officers, *Pesquisa Brasileira em Odontopediatria e Clínica Integrada*. 2019;19(1):1-9.
 4. Oktaria PC. The Effect of Working with Gingival Leadline Incidences on Traffic Police in Semarang City. *Scientific papers*. 2009; 10-33.
 5. Hakim AF. The relationship between the working period and Gingival Leadline on Parking Attendants along the Malioboro Road in the city of Yogyakarta. *Scientific papers*. 2013: 1-37.
 6. Sudiby. *Gingivia as a measure of Black Tin Chronic Poisoning*. Dissertation. 1993; 1-21.
 7. Pearce JMS. Burton's Line in Lead Poisoning. *European Neurology*. 2007; 57: 118-119.
 8. Shetty Hospital, Al-Bayati SAAF, Suneja R. Oral Manifestation of Lead Posioning. *Aperito Journal of Oral Health and Dentistry*. 2015; 1 (2): 1-109.
 9. Putri VP, Munandar S, Nugroho T. Relationship Between Working Period and Gingival Lead Line Incidence at Street Vendors in Semarang City. *Scientific papers*. 2010: 2-13.
 10. Tort B, Youn-Hee Choi, Eun-Kyong Kim, Yun-Sook Jung, Mina Ha, Keun-Bae Song, and Young-Eun Lee. Lead exposure may affect gingival health in children. 2018; 18 (79): 1-7.
 11. Z Yetkin-Ay, B Çadır, E Uskun, FY Bozkurt, N Delibaş, FM Gültepe. The periodontal status of indirectly lead-exposed apprentices working in autorepair workshops. *Toxicology and Industrial Health* 2007; 23: 599–606.
 12. Istikomah NS, Santjaka A, Budiono Z. Several Determinants that Affect the Black Lead Level (Pb) in the Blood of Battery Smelting Industry Workers in the Village of Small Industries (Pik) Kebasen Village Talang Sub-District, Tegal District in 2016. *Scientific Writing*. 2016: 446-454.

Re-evaluation of Psoriatic Patients with Metabolic Syndrome: A Case Control Study Searching for the Highly Prevalent Criteria

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Abstract

Psoriasis is a common chronic inflammatory skin disorder, presented as erythematous plaques with salmon pink color and silvery white scales. The association between psoriasis and metabolic syndrome have recently demonstrated by many studies, and this link suggested by the presence of systemic inflammatory status with the high level of cytokines. The study aimed to evaluate psoriatic patient who have metabolic syndrome with recording of the frequency of the criteria of this syndrome. Sixty two cases of psoriasis involved in this study with age and gender matched controls. Patient was diagnosed as having metabolic syndrome if he has three or more of the criteria depend upon IDF/NHBLI/AHA/World Heart Federation/International Atherosclerosis Society/International Association. This study revealed that metabolic syndrome occur in a higher frequency among psoriatic patients (58%) than the controls (16%). The highly prevalent criteria among psoriatic patients with positive metabolic syndrome was increase waist circumference at the top (100%) and hypertriglyceridemia came next (69%), with low HDL, hypertension, and raised fasting blood glucose came successively. The study reiterates the fact that Metabolic Syndrome and psoriasis do have a close association. Our study shows that central obesity and hypertriglyceridemia occur with high frequency among psoriatic patients with positive metabolic syndrome.

Keywords: Psoriasis, metabolic syndrome.

Introduction

Psoriasis is a common chronic inflammatory skin disorder, presented as well defined plaques with salmon pink color and silvery white centrally attached scales. Psoriasis is considered to be a polygenic disorder⁽¹⁻³⁾. Recently, many studies demonstrated the association of psoriasis with systemic disorders like metabolic syndrome, cardiovascular disease, osteoporosis, inflammatory bowel disease, cancer, and depression. Systemic inflammation and the presence of interleukin-6 and tumor necrosis factor- α in high levels

suggested the link between psoriasis and associated systemic disorders⁽⁴⁾.

With regards to the immunopathogenesis of psoriasis and metabolic syndrome [chronic inflammation mediated by pro-inflammatory cytokines], both may develop “interdependently”. Additionally, “insulin-like growth factor 1” have implicated in psoriasis “as a shared mediator in the proliferation of keratinocyte” and the development of hyperlipidemia and diabetes⁽⁵⁻¹⁰⁾.

Chronic inflammation (Th-1 and Th-17) with cytokines dysregulation, in addition to promotion of hyperplasia of epidermis in psoriasis, may also antagonize insulin signaling leading to increase risk of obesity and insulin resistance. In addition, both psoriasis and metabolic syndrome sharing the genetic susceptibility by the existence of pleiotropic “PSORS2-4, CDKAL1, and ApoE4” genetic loci^(11,12). Significant clinical implications may be demonstrated in psoriatic patients with metabolic syndrome, especially those on chronic

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systemic treatments “use them with caution” because the coexisting metabolic disorders may be adversely affected⁽¹³⁾.

Aim of our study was to evaluate psoriatic patient who have metabolic syndrome with recording of the frequency of the criteria of this syndrome .

Patients and Method

This case control study was conducted over a period of nine months from October 2018 till march 2019. Sixty two cases of psoriasis involved in this study collected from Department of dermatology in AL-Yarmok teaching hospital in Baghdad province with age and gender matched controls. Psoriasis was diagnosed clinically and suspicious cases proved by histopathological study **Inclusion criteria** are those with plaque psoriasis of at least 3 months, more than 18 years old, and not received any systemic medication for psoriasis for at least three months while **Exclusion criteria** are pustular and erythrodermic psoriasis, those taking systemic drugs in the three months before enrolling, pregnant women and those complaining from other autoimmune diseases .

Questionnaire was designed to obtain the information age, gender, duration of psoriasis, family history, height, and weight . Waist circumference was measured by placing a tape measure around the abdomen at the level of uppermost part of the pelvic bone. Blood pressure was recorded by taking the average of two separated measurements. Body mass index was measured by dividing the weight in kilogram on the square of height in meter and psoriasis severity evaluated by using the psoriasis area and severity index (PASI). Venous blood samples were taken 12 hour fasting status in the morning to measure fasting blood sugar and serum triglyceride in our hospital laboratories .For diagnosis of metabolic syndrome I depend upon “IDF/NHBLI/AHA/World Heart Federation/International Atherosclerosis Society/International Association for the Study of Obesity, 2009”. Patient was diagnosed as having metabolic syndrome if he has three or more of the following :

- waist circumference [>94 cm in men and >80 cm in women].
- serum triglycerides [≥ 150 mg/dL] or lipid-lowering drugs.

- serum HDL [<40 mg/dL in male and <50 mg/dL in female].
- Blood pressure [$\geq 130/85$ mm Hg] or antihypertensive therapy.
- Fasting plasma glucose [≥ 100 mg/dL] or pharmacologic therapy.

To clarify the effect of difference factors in this study parameters, the “Statistical Analysis System 2012” program was used and Chi-square test applied to compare the significance .

Results

Sixty two psoriatic patients [34 male (55%) and 28 female (45%) with their matched control] enrolled in this study . Their age distribution : 46 (74.2%) between 21 years and 50 years, 10 (16.1%) above fifty years, and only six (9.7%) between 18 years and 20 years. Metabolic syndrome discovered to be presented in a higher frequency in psoriasis patients [36 (58%)] in comparison with controls [10 (16%)], the result is highly significant and the p -value was .000001. The highly prevalent criteria among psoriatic patients with positive metabolic syndrome was increase waist circumference [36 (100%)] with same percent in controls with positive metabolic syndrome. Serum triglyceride in the second place (25 patients 69%) with a nearly equal value in control group (7 control 70%) .

There were 12 (33%) psoriatic patients with positive metabolic syndrome found to have low S.HDL while in control group only two (20%) appeared to have low value of S. HDL . Elevated blood pressure was noticed in 22 patient (61%), in control group 6(60%) persons have elevated blood pressure . Sixteen (44%) psoriatic patients had elevated fasting blood sugar, in contrast to control group in which there were only 2 persons.

Regarding PASI score among psoriatic patients with positive metabolic syndrome: 32 (89%) subjects with a score less than 8, while only 4 (11%) subjects above 10 body mass index measurement revealed that 16 (44%) patients were obese, 10 patients (28%) were overweight and the another 10 (28%) patients presented with normal weight.

Table 1: The frequency of metabolic syndrome criteria among psoriatic patients in comparison with controls

Metabolic Syndrome criteria	Psoriasis Group = (62)					Contrpl Group = (62)				
	+ Metabolic syndrome 36		Metabolic syndrome 26		Chi-square (χ^2)	+ Metabolic syndrome 10		- Metabolic syndrome 52		Chi-square (χ^2)
	No.	%	No.	%		No.	%	No.	%	
↑ Waist circumference	36	100	12	46	10.38 **	10	100	22	42	10.16 **
S . triglyceride	25	69	9	35	9.02 **	7	70	26	50	7.25 **
S.HDL	12	33	4	15	6.19 **	2	20	10	19	0.037 NS
Blood pressure	22	61	0	0	12.72 **	6	60	10	19	10.26 **
Fasting blood sugar	16	44	2	8	9.41 **	2	20	4	8	4.39 *

* (P<0.05), ** (P<0.01).

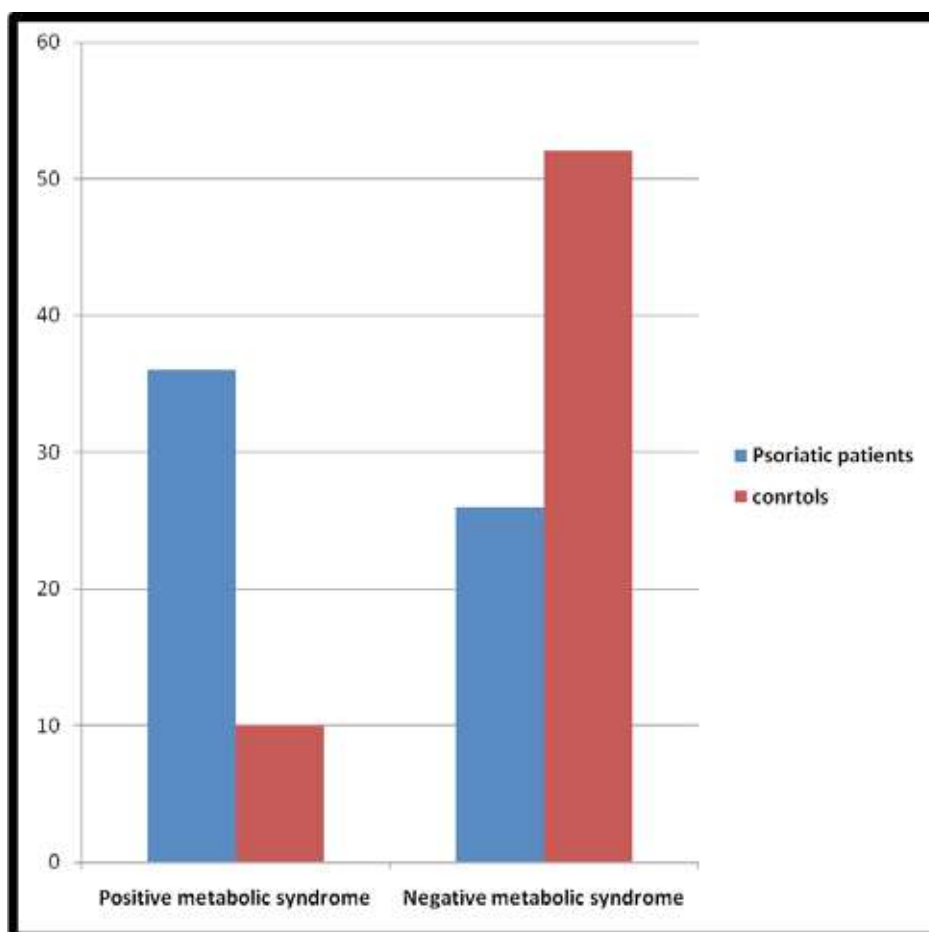


Fig. 1: Prevalence of metabolic syndrome among psoriatic patients in comparison with controls

Discussion

Recently, “the understanding of the role of inflammatory cells and mediators in the pathogenesis of psoriasis” have changed our look to psoriasis from being a cutaneous disease to that of a systemic disorder. (14) Psoriasis and metabolic syndrome are characterized by sharing inflammatory pathways display similar

inflammatory profiles with Th1 and over expression of IL-6 and TNF-alpha⁽¹⁵⁾. Epidemiological link of psoriasis to metabolic syndrome and it’s prevalence was suggested by several observational studies (15–25% in the general population)⁽¹⁶⁾.

In this study psoriatic patients examined for the presence of metabolic syndrome in comparison with

controls, and data was analyzed to clarify the prevalence of criteria of such syndrome. Males were the predominant sex and maximum number of psoriatic cases (74.2%) was noted in the age group of between 21 years and 50 years. This study revealed that metabolic syndrome occur with a higher percentage in psoriatic patients (58%) than controls (16%) this appear higher regarding recent case control study by Narendra Gangaiah, NS Aysa Roshin, et al (38% vs. 22%)⁽¹⁷⁾. Regarding the prevalence of metabolic syndrome criteria among patients :central obesity (Raised values of waist circumference) was at the top (100%) and hypertriglyceridemia came next (69%), with low HDL, hypertension, and raised fasting blood glucose came successively .

Visceral obesity and type 2 diabetes are the main components of metabolic syndrome. Adipose tissue pathologically has important effects as it infiltrated by macrophages that secrete cytokines in the systemic circulation resulting in a chronic inflammatory state which will lead to the development of numerous diseases associated with obesity⁽¹⁸⁾. In most international studies obesity appear to be more frequent among psoriatic patients than controls⁽¹⁹⁾. All psoriatic patients in the present study have increased Waist circumference and visceral obesity could be the possible mechanism that correlate psoriasis with metabolic syndrome and its comorbidities. It was also demonstrated that obesity is a risk factor [more than two times] for developing psoriasis⁽²⁰⁾. Middle or older age men with mild obesity are more likely to develop psoriasis as suggested by Naito and Imafuku⁽²¹⁾.

Significant elevation in serum triglyceride levels have shown in various studies done in Caucasians⁽²²⁻²⁴⁾. In the present study, psoriasis was strongly related with dyslipidaemia. Hypertriglyceridemia represent (69%) in psoriasis group with no difference among controls . Low value of S. HDL was found in 33% of psoriasis group, while it was found to be low in 20% of controls. Similar observations were documented in Lebanon study⁽²⁵⁾.

Hypertension was documented among 22 cases of psoriatic patients with positive metabolic syndrome, in comparison to controls with metabolic syndrome. Psoriasis patients in regards to the risk of developing hypertension showed modest increase in comparison with the general population^(26,27). No known mechanism explain the relation that link psoriasis to hypertension. Multiple researchers proposed that the major source of angiotensinogen is the adipose tissue and the derived

angiotensin II [in addition to its function in salt retention by kidneys] may act as stimulator for T-cell proliferation. Perivascular fat which result from increased visceral adipose tissue “can serve as a reservoir for activated effector T cells” which in turn lead to the promotion of dysfunction in the blood pressure⁽²⁸⁾.

Regarding the relation between psoriasis and hyperglycemia, there is high risk to develop diabetes in addition to metabolic syndrome⁽²⁹⁾. Elevated fasting blood sugar was present in 44% of Psoriatic patients and in 20% of controls. This finding is supported by a study conducted by Samer A Dhaher, and Alaa Abdul Hassen Naif^(18,30).

Both hypertension and dyslipidemia cause increase the “systemic inflammatory burden” together with obesity, all of these adds to the comorbidities of psoriasis⁽³¹⁾. PASI score among psoriatic patients with positive metabolic syndrome was less than 8 in nearly 90% of cases, this gave us a negative impression about the relation between the severity of disease and metabolic syndrome. Nisa and Qazi study also found no significant correlation⁽³²⁾.

While studying of body mass index and its association with metabolic syndrome in both groups shows no significance. This comparable with Korean and Norwegian studies where they found a non-statistically significant association with increment in the weight^(33,34).

Conclusion

The study reiterates the fact that Metabolic Syndrome and psoriasis do have a close association and showed that central obesity and hypertriglyceridemia occur with high frequency among psoriatic patients with positive metabolic syndrome

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References

1. William D James, Timothy G Berger, Dirk M Elston. Isaac M Neuhaus. Andrewes' Diseases of the skin; clinical Dermatology. 12th ed. China. Elsevier. 2015:190-198.
2. Peter C. M., van de Kerkhof, Frank O. Nestlé, Papuloacromous and eczematous dermatoses.

- in: Jean L. Bologna, Julie V. Schaffer, Lorenzo Cerroni. *Dermatology*. 4th edition. China. Elsevier, 2014; 8; 138-158.
3. Richard B. Weller, Hamish J.A. Hunter, Margaret W. Mann. *Clinical dermatology* 5th edition. John Wiley & Sons. 2015;5:52–67.
 4. Sristi Lakshmi, Amiya Kumar Nath, Carounanidy Udayashankar. Metabolic syndrome in patients with psoriasis: A comparative study. *Indian dermatology online journal*. 2014; 5(2):132-137.
 5. Armstrong EJ, Harskamp CT, Armstrong AW. Psoriasis and major adverse cardiovascular events: a systematic review and meta-analysis of observational studies [published Apr. 2013]. *J Am Heart Assoc*. doi: 10.1161/JAHA.113.000062.
 6. Esser N, Legrand-Poels S, Piette J, Scheen AJ, Paquot . Inflammation as a link between obesity, metabolic syndrome and type 2 diabetes. *Diabetes Res Clin Pr*. 2014;105(2):141–50.
 7. Moon YS, Kim DH, Song DK. Serum tumor necrosis factor-alpha levels and components of the metabolic syndrome in obese adolescents. *Metabolism*. 2004;53(7):863–7.
 8. Popa C, Netea MG, van Riel PL, et al. The role of TNF-alpha in chronic inflammatory conditions, intermediary metabolism, and cardiovascular risk. *J Lipid Res*. 2007;48(4):751–62.
 9. Azfar RS, Gelfand JM. Psoriasis and metabolic disease: epidemiology and pathophysiology. *Curr Opin Rheumatol*. 2008;20(4):416–22.
 10. Yoo H, Kim SJ, Kim Y, et al . Insulin-like growth factor-II regulates the 12-lipoxygenase gene expression and promotes cell proliferation in human keratinocytes via the extracellular regulatory kinase and phosphatidylinositol 3-kinase pathways. *Int J Biochem Cell B*. 2007;39(6):1248–59.
 11. Davidovici BB, Sattar N, Prinz JC, et al. Psoriasis and systemic inflammatory diseases: potential mechanistic links between skin disease and co-morbid conditions. *J Invest Dermatol*. 2010;130(7):1785–96.
 12. Azfar RS, Gelfand JM. Psoriasis and metabolic disease: epidemiology and pathophysiology. *Current opinion in rheumatology*. 2008;20(4):416-22.
 13. Paolo Gisondi, Anna Chiara Fostini, Irene Fossà, Giampiero Girolomoni, Giovanni Targher. Psoriasis and the metabolic syndrome. *Clinics in Dermatology* .2018;36(1) : 21-28 .
 14. Krueger G, Ellis CN. Psoriasis : Recent advances in understanding its pathogenesis and treatment. *J Am Acad Dermatol* . 2005;53:94-100.
 15. Ibrahim Mohammed abid Al-juboury. Evaluation of association between psoriasis and atherosclerosis in tikrit governorate :Genetic and Biochemical study. *Tikrit Medical Journal* . 2014:189-194.
 16. Davidovici BB, Sattar N, Prinz J, et al . Psoriasis and systemic inflammatory diseases: potential mechanistic links between skin disease and co-morbid conditions. *J Invest Dermatol*. 2010;130(7):1785–1796.
 17. Narendra Gangaiah, NS Aysha Roshin, Veena Thimmappa, Ragunatha Shivanna. Metabolic syndrome in patients with psoriasis: A hospital-based case–control study .*Clinical dermatology review* . 2018;2(2):64-68 .
 18. Samer A Dhaher, Zaineb Aljasim . Risk factors for cardiovascular diseases and metabolic syndrome in psoriatic patients: case - control study . *Medical journal of Basrah university* . 2015;33:100-106 .
 19. Bonomini F, Rodella LF, Rezzani R. Metabolic Syndrome, Aging and Involvement of Oxidative Stress. *Aging and Disease*. 2015;6(2):109-120.
 20. Balci, A., Balci, D.D., Yonden, Z., et al . Increased amount of visceral fat in patients with psoriasis contributes to metabolic syndrome . *Dermatology*. 2010;220:32–37.
 21. A. Baran, I. Flisiak, J. Jaroszewicz, M. Swiderska. Serum adiponectin and leptin levels in psoriatic patients according to topical treatment . *Journal of Dermatological Treatment* .2015; 26:134–138.
 22. P. Rocha-Pereira, A. Santos-Silva, I. Rebelo, et al. Dislipidemia and oxidative stress in mild and in severe psoriasis as a risk for cardiovascular disease. *Clinica Chimica Acta* .2001;303:33–39.
 23. B. S. Uyanik, Z. Ari, E. Onur, et al . Serum lipids and apolipoproteins in patients with psoriasis . *Clinical Chemistry and Laboratory Medicine* . 2002;40:65–68.
 24. Ahmed Abdul-Aziz Ahmed. Serum lipid profile in Psoriasis: a controlled study. *Tikrit Medical Journal*. 2011;17(1):38-42 .
 25. S. Itani, A. Arabi, D. Harb, et al . High prevalence of metabolic syndrome in patients with psoriasis in Lebanon: A prospective study. *International Journal of Dermatology* . 2016;55:390-395 .

26. Cohen AD, Weitzman D, Dreiherr J. Psoriasis and hypertension: a case-control study. *Acta Derm Venereol.* 2010;90:23–26.
27. Prodanovich S, Kirsner RS, Kravetz JD, et al. Association of psoriasis with coronary artery, cerebrovascular, and peripheral vascular diseases and mortality. *Arch Dermatol.* 2009;145:700–703.
28. April W. Armstrong, Steven W. Lin, Cynthia J. Chambers, et al . Psoriasis and Hypertension Severity: Results from a Case-Control Study [Published: March 29, 2011] . *PLoS One.* doi: 10.1371 .
29. Maddalena Napolitano, Matteo Megna, Giuseppe Monfrecola .Insulin Resistance and Skin Diseases [published online 2015] .*The Scientific World Journal.*2015. doi:10.1155/2015/479354.
30. Alaa Abdul Hassen Naif. Metabolic syndrome in Iraqi patients with psoriasis: A comparative study. *J.Thi-Qar Sci.* 2015;.5 (2):37-39.
31. Y. C. Nakhwa, R. Rashmi, and K. H. Basavaraj .Dyslipidemia in Psoriasis: A Case Controlled Study [Published 8 October 2014] . *International Scholarly Research Notices* . doi: 10.1155/2014/729157.
32. Nisa N, Qazi MA. Prevalence of metabolic syndrome in patients with psoriasis. *Indian J Dermatol Venereol Leprol* . 2010;76:662-5.
33. Kim ES, Han K, Kim MK, et al. Impact of metabolic status on the incidence of psoriasis: a Korean nationwide cohort study. *Sci Rep.* 2017;7:1989.
34. Danielsen K, Wilsgaard T, Olsen AO, et al. Overweight and weight gain predict psoriasis development in a population-based cohort. *Acta Derm Venereol.* 2016;97:332–9.

Analysis of Employee's Satisfaction in Efforts to Improve Service in Regional Public Hospital of Dok II Jayapura Papua

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Abstract

Dissatisfied employees tend to experience a decline in performance, so they can't provide good health services. Patient satisfaction is influenced by the good and bad health services provided by employees, so there may be problems with human resource management. The purpose of this study was to describe employee job satisfaction in an effort to improve services in the Regional Public Hospital of DOK II Jayapura Papua. The type of research was descriptive (case study). The number of samples of 74 samples with the sampling technique was random sampling. Results obtained by employees who stated that they were not satisfied 51.3%, very dissatisfied 1.4% while those who expressed satisfaction were 47.3%. Most employees were not satisfied with efforts to improve service. One form of human resource development can be done through the creation of a strategic plan. The Strategic Plan itself must be based on a SWOT analysis where systematic identification of various factors will be carried out to formulate a strategy by maximizing strengths, opportunities, and simultaneously minimizing weaknesses and threats.

Keywords: Patient satisfaction, Health Service, Hospital.

Introduction

Health service organizations are an organization that consists of various kinds of health professions and other professions related to health service activities to the community. In carrying out its functions, this organization requires a management system that is comprehensive and sustainable. An effective human resource management can create a work environment that gives a sense of togetherness, equals, supports productivity, encourages its members to work towards organizational goals, and is able to meet the needs of its members to actualize themselves and fulfill their individual expectations through appreciation, development and recognition

of their identity¹. The variety of health professions incorporated in an organization will be a challenge for human resource management. Different health education backgrounds will produce individual health practitioners with different egos and ideals. Health services are basically a complex and interrelated process between health practitioners. For this reason, collaboration between individuals or health professions is needed in an effort to provide maximum health services to the community².

A well functioning human resource management will have policies, rules, and programs in the activities of employee selection and recruitment (members), formulation of members' rights and obligations, training and organizational development, member safety guarantees, and succession systems in organizations. Strategic planning is the process of developing organizational goals, strategies and tactics to achieve the organization's mission and vision. An organization needs to determine short-term goals and long-term goals by using the organization's mission statement as a guide. The purpose of an organization can include

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sales targets, company profits, customer satisfaction, and increase organizational value (image branding). A health service organization must also have a plan to carry out its functions as an organization. The thing that must be considered in determining the health service organization policy is its function as a health service facility for the community³.

Efforts are needed to fulfill greater comfort so that patients are satisfied. Satisfaction and comfort causes the concerned to become a subscription. It is hoped that not only those concerned, but also their families and relatives may be interested⁴. The good and bad health services are influenced by the level of job satisfaction of hospital employees. Dissatisfied employees tend to experience a decrease in performance, so they can't provide good health services⁵.

Successful organizations are organizations that are capable of human resource management to become a force that can unite, have commitment and high work motivation through human resource management. It is a process of dealing with various problems for employees, managers and other workers to be able to support the activities of the organization in order to achieve the intended goals. One of the problems in managing human resource is the problem of job satisfaction. Job satisfaction is a positive attitude that involves healthy adjustments of employees to work conditions and situations, including salary issues, social, physical and psychological conditions. Job satisfaction is also defined as a pleasant emotional state or a general attitude towards differences in rewards that are accepted and should be accepted as well as for work factors, adjustment and social relations outside of work⁶.

Method

This study used descriptive survey design. This research was a case study in the Regional Public Hospital of DOK II Jayapura Papua. This research was conducted from April to May 2018. Total sample was 74 samples with using random sampling technique. Primary data was collected through filling out questionnaires submitted to employees to identify employee job satisfaction. The results of the data obtained from the questionnaire were analyzed to determine efforts to improve human resource management in health services.

Results

In this study, job satisfaction will be measured by

a structured questionnaire compiled by adopting and adapting the standardized translation questionnaire measuring tool, Minnesota Satisfaction (MSQ). The following are the results of the job satisfaction questionnaire:

Table 1: Distribution of Frequency of Employee Job Satisfaction in the Regional Public Hospital of DOK II Jayapura Papua

No.	Job Satisfaction	Frequency	Percentage
1	Satisfied	35	47.3
2	Dissatisfied	38	51.3
3	Very Dissatisfied	1	1.4
Total		74	100

Based on Table 1, Employees who stated that they were not satisfied were 51.3%, very dissatisfied 1.4% while those who expressed satisfaction were 47.3%. Good or bad health services are influenced by the level of job satisfaction of hospital employees⁷. According Soeroso (2003) that dissatisfied employees tend to experience a decrease in performance, so they can't provide good health services. It is known that patient satisfaction is influenced by the good and bad health services provided by employees, so there may be problems with human resource management.

Discussion

In managing human resource management must pay attention to the organization's demands, goals, vision, mission, organizational plan and human resource division as well as the supply of health workers in the community and prospective producer institutions. Soeroso (2003) said that There are two human resource planning, namely quantitative, namely the planning of the number of each health worker needed, and qualitative, namely the special aspects of each element of the human resources management cycle from planning to recruitment, selection, placement, utilization and development, career, supervision and control and evaluation performance.

Human resources management is increasingly important in the future, due to internal factors, namely the need for hospitals to get suitable employees, increasing human resource costs (compensation: salaries, incentives, facilities etc.), demands of managers and employees and the development and expansion of hospitals. Whereas because of external factors, namely government/stakeholder policies, the development

of Socio-Economic and Science and Technology, competition with competitors and market development and the impact of globalization.

According Soedarmo, *et.al* (1997) The success of the use and development of human resources is largely determined by various aspects of the organization such as; career management aspects, leadership, work relations, work motivation and job satisfaction, achievement and work productivity, compensation, transfer and promotion, education and training, rewards and punishments, employment and union regulations, supervision and control, work evaluation and evaluation. There is no standard and appropriate or appropriate human resources development and development pattern for all organizations. The most appropriate form is the use and development of human resources that must be sought, processed and can change from time to time or be dynamic.

Management is a function that deals with realizing certain results through the activities of people. This means that human resources play an important and dominant role in management. human resource management organizes and establishes a staffing program that covers the following issues: establish effective amount, quality, and work placement according to company needs based on job description, job specification, job requirements, and job evaluation, establish employee withdrawal, selection and placement based on the right man in the right place and the right man in the right job, establish a welfare program, development, promotion and dismissal, predicting the supply and demand of human resources in the future, estimating the state of the economy in general and the development of the company in particular, carefully monitor labor laws and policies for granting remuneration of similar companies, monitor technical progress and development of trade unions, carry out education, training, and employee performance appraisal, efforts to improve services in health service institutions are efforts to improve employee efficiency, efficiency of operational funds, fairness and ability of health services held in accordance with the development of the latest medical science and technology⁸.

Conclusions

Most employees were not satisfied with efforts to improve service in the Regional Public Hospital of

DOK II Jayapura Papua. One form of human resource development can be done through the creation of a strategic plan. The Strategic Plan itself must be based on a SWOT analysis where systematic identification of various factors will be carried out to formulate a strategy by maximizing strengths and opportunities, and simultaneously minimizing weaknesses and threats.

Conflict of Interest: None

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Ethical Clearance: This Study was approved by Health Research Ethics Committee of Public Health, Airlangga University.

References

1. Wuryanto E. Thesis on the Relationship of Work Environment and Characteristics of Individuals with Nurse Job Satisfaction at the Tugurejo Regional General Hospital Semarang. Depok: FIK Master of Nursing Program Specialization in Nursing Management. 2010
2. Supriyanto S, Wulandari R. Quality Management. Surabaya: Airlangga University. 2010
3. Simamora. Human Resource Management Edition III. Yogyakarta: YKPN College of Economics. 2006
4. Sabarguna B. S. Quality Assurance of Hospital Service. Edisi Kedua. Yogyakarta: Konsorsium Rumah Sakit Islam Jateng-DIY. 2004
5. Soeroso S. Human Resource Management in Hospitals, Jakarta: Edition I, EGC Publishers. 2003
6. Soedarmo S. S. P, Garna H, Hadinegoro S.R.S, Satari H.I. Organizational Behavior, Yogyakarta; Edition I, BPFE. 1997
7. Sahyuni R. Employee Job Satisfaction, SWOT Analysis, and Strategic Plan for Human Resource Development in an effort to Improve Services at H. Abdul Aziz Marabahan Regional Hospital in South Kalimantan in 2009. Semarang: Diponegoro University. 2009.
8. Hasibuan, M. S. P. Human Resource Management. Jakarta: Bumi Aksara. 2007

Identifying the Most Influential Variables in Breast Cancer Using Logistic Regression

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Abstract

Breast cancer has become recently the most common cancer and a major cause of death among women all over the world and especially in developing countries like Iraq. This study aims to identify the most important features that affect in deciding the type of breast cancer whether benign or malignant.

A predictive model was developed using binary logistic regression which is expected to be helpful for oncologists in diagnosing the type of breast cancer data set have been downloaded from UCI ml repository that consists of 9 attributes and 683 valid instances.

At first, some preprocessing was done to cleanse the data, then two models were built using two different LR method to find out which one will give the most suitable model and highest classification rate. The first one was the full model with all predictive variables, while the other called reduced model with only 5 predictive variables. Each model was validated with a different data set than that used for developing the two models. Both validated and trained models were evaluated using different performance metrics like ROC curves, AUC, sensitivity and specificity. The analysis of the results showed that the reduced model is the best classifier since it gives the higher classification rate.

Keyword: UCI ML repository, Logistic Regression, classification, validation, Breast Cancer.

Introduction

Breast cancer is one of the most common types of cancer in the world, especially in the developed countries and it has been the most common cancer in Iraq for the years (1986-2012). A study has shown that survival rate is 88% after 5 years of diagnosis and 80% after 10 years of diagnosis. Therefore it is necessary to detect breast cancer at earliest stage possible^[1].

Machine learning has become more influent in diagnosing cancer, because It allows deductions or inference to be made that classical statistical procedures could not make^[2].

In order to assist oncologists making the right diagnosis of biopsy in breast cancer, a classification model known as a classifier can be very helpful. The classification problem refers to predicting the target class of new observations, from a given set of predictive variables from the population data set.

Since the outcome of biopsy can confirm the existence/absence of the malignancy it is hence considered a binary outcome.

Logistic Regression LR have been applied increasingly in many fields particularly the medical fields, and is a perfect statistical algorithm for binary classification, that is evaluating the correlation between one or more categorical or continuous predictor variables and a dichotomous dependent variable^[3]. Logistic regression technique has the ability of assigning distinct data sets to predefined classes, the distinction is done by setting up the discrimination rules, these rules are estimated through the training phase and can be used to assign the new observations into the classes defined formerly^[4].

Method of variable selection differ according to the problem. It is essential to include all relevant variables in the model. Some researchers propose inclusion of

all clinical and other predictive variables in the model regardless of their significance to get a better model fit to the data. Yet, more variables will affect the coefficient in the model and lead to over-fitting model. Besides, a model with many insignificant predictors will produce less classification accuracy and it would be hard to explain the results. Commonly, statistical model building techniques attempt to minimize the number variables to get a numerically stable and generalized model, but this can cause in a large standard errors. Variables selection can be done in two ways filter and statistical^[5,6]. For filter method, the variables are reduced according to their importance as was done in similar research.

On the other hand, statistical method for variable selection can be done by either of the following method^[11];

- “Enter: A procedure for variable selection in which all variables in a block are entered in a single step.
- Forward Selection (Conditional).
- Forward Selection (Likelihood Ratio).
- Forward Selection (Wald).
- Backward Elimination (Conditional).
- Backward Elimination (Likelihood Ratio).
- Backward Elimination (Wald).”

In forward selection, the significant effects once entered then could not be removed from the model. For backward elimination, removed effects from the model, cannot be entered again. While, for stepwise selection which are the method of focus in our study the variables already included in the model do not need to remain, they can be entered into or eliminated from the model in a certain manner that every step of forward selection could be followed by a backward elimination step or more. The stepwise selection procedure stops if no additional effect is added to the model^[7].

In this study, two different variable selection procedures were implemented, namely Enter and Stepwise method to establish logistic regression models. This study aims to evaluate the performance of the two developed models in order to determine which of the used method is more powerful in identifying the most influential predicted variables in predicting breast cancer.

Materials and Method

The data set used in this study, is the breast-cancer-Wisconsin data file which was collected from UCI machine learning repository^[8].

The data set consists of observations of 699 patients diagnosed with cancerous tumors. It is arranged in 11 columns each row represents observations belong to a patient that was obtained from medical analysis. The first column is an identification code associated with each patient; the following 9 columns are the features used to analyze each patient; tumor thickness, uniformity of cell sizes, uniformity of cell forms, marginal adhesion, size of the simple epithelial cell, Bare nuclei, smooth chromatin, nucleolus normality, and mitosis^[9]. The last column is the dependant variable (cancer type; 4 for malign and 2 for benign tumors).

All the independent variables have numerical values ranging from 1 to 10, and these values were obtained through medical assessments or lab tests. The distribution of the dependant variable Class is; Benign: 458 (65.5%) and Malignant: 241 (34.5%).

The first step in this study was converting the data into Excel sheet to make it easier to build the statistical model which is generated and analyzed using SPSS, V19.0, SPSS Inc. using LR algorithm, then the data was imported to SPSS for processing.

The second step is data cleaning; missing values is a well known issue exists in datasets. There are several method to overcome missing values like list wise or case deletion, substituting the missing values with mean or mode of that variable and other method^[10]. For our study the case deletion method was applied to remove 16 cases having missing values. This leads to that the dataset size becomes 683 observations with 444 benign tumors and 239 malignant. As it is not required in the design and analysis of our model, the (Id) column was removed.

In order to identify the variables that count in investigating the type of breast cancer two LR models were established. The first one, named full model was developed using the standard ENTER method with all 9 attributes. The second model, which is the reduced model was developed using the stepwise forward selection (Wald) method. Stepwise selection method tests the entry of variables according to the significance of the score statistic, while removal testing is done according to the probability of the Wald statistic^[11],

the model was developed with only 5 attributes which are tumor thickness, uniformity of cell size, marginal adhesion, bare nuclei, and smooth chromatin since they were statistically significant at the level of 0.05 using Wald statistic.

Validation of the model is very important to measure the stability and robustness of the coefficients resulting from logistic regression and a crucial part of the process of model-building^[14]. Many statistical tools for model performance validation in binary logistic regression are available like data splitting, repeated data-splitting, jackknife technique and bootstrapping^[15]. For this purpose, the data-splitting technique was used in our study, where the data had been randomly divided into two groups; the first consisting of 80% of the data (550) sample was used for developing the LR model with 372 benign and 178 malignant, and the second group consisting of 20% of data (133) sample (72 benign, 61 malignant) was used for validating the two models.

The training data was used at first to fit both full and reduced models then we apply the validation data to the fitted models to evaluate the model's performance. The obtained posterior probability for malignant class was considered and its value was then classified into two categories; posterior probability in range of (0-0.5) = benign, and posterior probability in range of (0.5-1) = malignant. Results obtained are then evaluated in terms of measures such as ACC, Specificity, Sensitivity, and ROC curve area.

Logistic Regression Model: The conditional probability for dependent variable to occur is given by the logistic function^[16],

$$\text{Probability}(\text{dependant variable}(Y) = 1) = \frac{e^{-z}}{1+e^{-z}}$$

Where probability estimates are between 0 and 1 because of the logistic transformation.

z is also called logit. The logit is a linear multiple regression model of the independent variables

$$z = \hat{\beta}X = \beta_0 + \beta_1 * X_1 + \beta_2 * X_2 + \dots \beta_n * X_n$$

where $\beta_0 \dots \beta_n$ are coefficients of the independent variables calculated by estimation of the maximum likelihood, $X_1 \dots X_n$ are independent variables and n is the number of explanatory variables.

while reference probability is defined as

$$p(y = 0) = 1/(1 + e^{-z})$$

the log(odds), or log-odds ratio, is defined by

$$\log (\text{odds}) = \ln \left[\frac{p}{1-p} \right] = z$$

and expresses the natural logarithm of the ratio between the probability that an event will occur, p(Y=1), to the probability that it will not occur p(Y=0), it is found by calculating the probability of each event. Odds ratio measure the incidence when the independent variable increases by one unit. The odds ratio is defined as

$$\frac{p}{(1 - p)} = e^{\hat{\beta}x}$$

This study aims to identify the most important predictive variables in classification of patterns into benign or malignance classes, and to compare the performance of the full model and the reduced model using different performance metrics, finally to validate the capability of each model to recognize new cases.

Performance Metrics: Accuracy which is the percentage of correct predictions is the most used measure in classification task. Sensitivity and specificity have to be calculated because the first indicates the performance of classification for minority class, while the second indicates the proportion of majority samples that are correctly identified. Also the area under a ROC curve (AUC) was used to evaluate the performance of the feature selection method^[17]. For our work, the two models were evaluated using these metrics (Equations 1-4) based on the confusion matrix shown in Table 1.

Table 1. Confusion Matrix

	Predicted Class	
Actual Class	Benign (0)	Malignant (1)
Benign (0)	TN	FP
Malignant (1)	FN	TP

$$CCA = (TP+TN)/(TP+FP+TN+TP) \dots(1)$$

$$\text{Sensitivity} = TP/(TP+FN) \dots(2)$$

$$\text{Specificity} = TN/(TN+FP) \dots(3)$$

$$AUC = \frac{1+TP_{rate}-FP_{rate}}{2} \dots(4)$$

where, TP_{rate} is sensitivity and

$$FP_{rate} = \frac{FP}{FP + TN}$$

Results

The results of training full model using the training sample is shown in Table 2 where the values of logistic regression parameters, standard errors, Wald statistic and p-values of the logistic regression model are computed. Considering all available variables, the logit of the full model is given by,

$$\text{Logit 1} = -9.614 + 0.486 * \text{clump thickness} + 0.23 * \text{uniformity of cell size} + 0.166 * \text{uniformity of cell shape} + 0.271 * \text{marginal adhesion} + 0.019 * \text{single epithelial cell size} + 0.435 * \text{bare nuclei} + 0.401 * \text{bland chromatin} + 0.127 * \text{normal nucleoli} + 0.374 * \text{mitosis}$$

Table 2: Parameter Estimations of the Full logistic regression model fitted to the training sample.

Variable	Coefficient estimate	Standard error	Wald	Sig.
clump_thickness	.486	.175	7.728	.005*
uniformity_of_cell_size	.230	.252	.832	.362
uniformity_of_cell_shape	.166	.278	.358	.550
marginal_adhesion	.271	.129	4.381	.036*
single_epithelial_cell_size	.019	.237	.006	.938
bare_nuclei	.435	.112	14.925	.000*
bland_chromatin	.401	.211	3.625	.057
normal_nucleoli	.127	.142	.800	.371
metosis	.374	.501	.556	.456
Constant	-9.614	1.415	46.143	.000

*significant at level of 0.05

From Table 2, we find that small p-values of clump thickness, marginal adhesion, and bare nuclei indicate that they are most significant predictor of malignancy in the model at level of 0.05. Also, the p-value obtained for bland chromatin was noticeable (p=0.057) though it is not statistically significant. Hence, a reduced model can be derived by removing from the full model the variables that have the largest Wald test p-value^[18]. Using the mentioned significant variables along with bland chromatin, the logit of the full model can be modified into a reduced form as follows,

$$\text{Logit 2} = -9.614 + 0.486 * \text{clump thickness} + 0.271 * \text{marginal adhesion} + 0.435 * \text{bare nuclei} + 0.401 * \text{bland chromatin}$$

The evaluation of LR full model and modified model was done using logit 1 and logit 2.

The coefficients of the reduced model were computed from training the model by the stepwise method using the training sample is shown in Table 3. from which the logit of the reduced model is given by,

The coefficients of the reduced model were computed from training the model by the stepwise method using the training sample is shown in Table 3. from which the logit of the reduced model is given by,

$$\text{Logit (stepwise)} = -9.413 + 0.546 * \text{clump thickness} + 0.435 * \text{uniformity of cell size} + 0.266 * \text{marginal adhesion} + 0.436 * \text{bare nuclei} + 0.506 * \text{bland chromatin}$$

Table 3: Parameter Estimations of the reduced logistic regression model (stepwise) fitted to the training sample

Variable	Coefficient estimate	Standard error	Wald	Sig.
clump_thickness	.546	.167	10.617	.001*
uniformity_of_cell_size	.435	.162	7.237	.007*
marginal_adhesion	.266	.125	4.539	.033*
bare_nuclei	.436	.105	17.106	.000*
bland_chromatin	.506	.198	6.524	.011*
Constant	-9.413	1.230	58.603	.000*

*significant at level of 0.05

Table 4 and Fig. 1 show a comparison of performance of the logistic regression models on testing sample (n=133).

Table 4: Comparative performance of the full, modified and reduced modes l on validation sample (n=133)

Model	Full model	Model modified from full	Reduced model
Sensitivity	0.902	0.459	0.836
Specificity	0.972	1.000	0.972
CCA	0.908	0.752	0.940
AUC	0.904	0.730	0.937

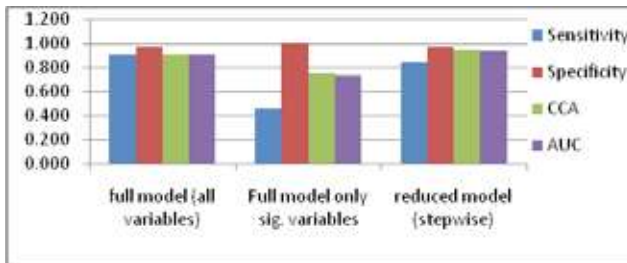


Figure 1: Comparative histogram of the average sensitivity, specificity and accuracy obtained for the full, modified and reduced models.

Discussion

In this work, the first model set was full model included all the nine covariates and the second was a reduced model. Based on guidelines for variables selection from the previous research, we removed the variables with the largest wald test p-value from the full model which were; uniformity of cell size, uniformity of cell shape, single epithelial cell size, metosis, and normal nucleoli, retaining the coefficients of the significant covariates as in the full model, but the output of the resulting model did not show any improvement in any of the metrics used except for specificity as shown in Table 4. & Fig. 1. The reduced model was established by the stepwise method resulting in a model with 5 predictive variables which were the same four in the modified model in addition to uniformity of cell size factor.

The results of the reduced model showed improvement (94%) in the correct classification rate in comparison with one obtained from the full regression model (90%); as for the specificity, it was about 97% for both. However, reduced model showed less sensitivity (84%) than the full model (90%) but it could still be considered as highly sensitive. These results showed

that if we use the most significant features in logistic regression model, its performance would be improved in comparison with a full model.

Limitations and Future Work: The size of the dataset affects the performance of the models so increasing the number of samples could lead to an improvement in performance. In order to have more than 2 classes a multinomial logistic regression could be implemented. Also other machine learning techniques such as different types of ANN could be tested.

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References

1. Ian H. Witten, Frank E. Data Mining: Practical machine learning tools and techniques. 3rd Ed. San Fransisco: Morgan Kaufmann; 2011.
2. Cruz JA, Wishart DS, Applications of Machine Learning in Cancer Prediction and Prognosis, Cancer Informatics. 2006; Vol.2: 2-21.
3. <https://science-network.tv/logistic-regression/>. Accessed September 24, 2019. Ronny Gunnarsson and first published June 22, 2014.Last revised August 30, 2019.
4. Hosmer DW, Lemeshow S.Applied logistic regression.New York: Wiley; 1989.
5. Austin PC,Tu JV. Automated variable selection method for logistic regression produced unstable models for predicting acute myocardial infarction mortality. Journal of Clinical Epidemiology. 2004; 57(11): 1138-1146.
6. Genuer R, Poggi JM, Tuleau-MalotC.Variable selection using random forests. Pattern Recognition Letters. 2010; 31(14):2225-2236. DOI:10.1016/j.patrec.2010.03.014
7. Bursac Z, Gauss CH, Williams DK, Hosmer DW. Purposeful selection of variables in logistic regression, Source Code for Biology and Medicine. 2008; 3(17), doi:10.1186/1751-0473-3-17
8. Dua D, Graff C. (2019). UCI Machine Learning Repository [<http://archive.ics.uci.edu/ml>]. Irvine, CA: University of California, School of Information and Computer Science.

9. Leisch F, Dimitriadou E. (2015). Machine learning benchmark problems. Viewed on 24.09.2019 from <https://cran.r-project.org/web/packages/mlbench/mlbench.pdf>.
10. Kang H. The prevention and handling of the missing data. *Korean journal of anesthesiology*. 2013; 64(5): 402–406. doi:10.4097/kjae.2013.64.5.402, available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3668100/>
11. IBM SPSS Regression 22. Copyright IBM Corporation 1989, 2013
12. Cox DR, Snell EJ. *The Analysis of Binary Data*, 2nd edition. London: Chapman and Hall; 1989.
13. Nagelkerke NJD. A note on the general definition of the coefficient of determination. *Biometrika*. 1991; Vol.78: 691-692.
14. Shao J. Linear Model Selection by Cross-Validation, *Journal of the American Statistical Association*. 1993; Vol.80, No.422: 486-494.
15. Rana S, Midi H, Sarkar SK. Validation and Performance Analysis of Binary Logistic Regression Model, *Proceedings of the WSEAS International Conference on Environment, medicine and health sciences*; Penang, Malaysia, 2010; 51-55
16. Schwarz J, Heidi Bruderer Enzler P. (2014). *Research Methodology: Tools; Applied Data Analysis (with SPSS)*. Lucern University. Available at <http://www.schwarzpartners.ch/extracted> on September 30, 2019.
17. Miri Rostami S, Ahmadzadeh M. Extracting Predictor Variables to Construct Breast Cancer Survivability Model with Class Imbalance Problem, *Journal of AI and Data Mining*. 2018; 6(2): 263-276. DOI: 10.22044/JADM.2017.5061.1609
18. Abdolmaleki P, Yarmohammadi M, Gity M. Comparison of logistic regression and neural network models in predicting the outcome of biopsy in breast cancer from MRI findings. *Iranian Journal of Radiation Research*. 2004;1(4), 217-228.

Lived Body Principle Police of the Regional Traffic Management Center (RTMC) of the East Java Regional Police to Their Families

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Abstract

Introduction: Guilt is the first and foremost in the form of emotional outbursts. Guilt is not a very good motivator. It is more accurate to regard guilt as an internal condition and a negative feeling. Happiness is a feeling of satisfaction, that life is as it should be and all needs have fulfilled.

Objective: It is to explore the meaning of feeling guilt and happiness experiences (Lived Body) police of the Regional Traffic Management Center (RTMC) to their families.

Method: The method are qualitative by using phenomenology interpretative approach and Interpretative Phenomenological Analysis (IPA).

Results: The emerging themes based on relationship principle are two: feeling guilty to the family and feeling happy with family.

Conclusion: The findings obtained were that members of the police at RTMC could be free from stress while working and were able to return and get support from the family. Being able to live happily, both happy at work and happy with the family that will reflect in the calmness in their life.

Keyword: Police; Regional Traffic Management Center (RTMC); Lived Body; Family; Phenomenology.

Introduction

More than 400 pairs of police officers were surveyed with a questionnaire to assess the impact of police work on the feelings and functions of their partners and families. The results of the study show that police work has an adverse effect, especially in terms of the social life of the couple. The leading causes are long working hours, work schedules, and canceled leave¹. Positive emotions such as excitement, interest, love, and receiving love contribute to human growth². About 50% of happiness is determined genetically³, so

each of us has a different level of joy, but it remains a regulatory point where our daily happiness experiences fluctuate. Thus, the development of positive emotions helps a person to return to a genetically determined position of happiness regulation⁴, after suffering from stress and trauma⁵. Positive emotions also indirectly help accumulate personal resources in four dimensions: physical, intellectual, social, and psychological, to enable one to overcome stress⁶. The development of positive emotions is obtained and collected through the functions of various emotions, so that feeling of fear, anger, and sadness are associated with danger, transgression, and despair, respectively, and this feeling triggers danger avoidance or flying behavior, while positive emotions are associated with expectations, and therefore, people build resources for long-term survival⁶.

A preliminary study conducted on seven police officers who were on duty at that time found that

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members of the police experienced a change of feelings to their families. The police caused the shift in feelings they experience as law enforcers who are required to be disciplined in carrying out their duties. Besides that, he or she was worried about safety at work, and work hours exceed time.

Police work and how it affects the family is very complicated. There was a feeling of guilt and a sense of happiness to his family caused by the impact of work as a police officer. This feeling will mainly be created by work stress. When examining this paper, it was found that there was no special education for officers to guide them in handling their beliefs, especially feelings of guilt to the family. There is also no education offered after assuming their professional role as police officers about effective techniques for using wisdom or dealing with stress. The pressure experienced by officers in his or her profession can be transferred to or shared by his or her family appropriately⁷. Aim of the study is to explore the meaning of feeling guilt and happiness experiences (Lived Body) police of the Regional Traffic Management Center (RTMC) to their families.

Method

This study used a qualitative research design with an interpretive phenomenology approach to explore the meaning in the experience of feeling guilt and happiness police of the Regional Traffic Management Center (RTMC) to their families. Participants involved in the five members of the police at RTMC were by the inclusion criteria determined through purposive sampling. Data collection by in-depth interviews using a semi-structured interview guide. During the meeting, the researcher used field notes. After the data collected, the researchers used Interpretive Phenomenological Analysis (IPA) to analyze the data.

Findings: Thematic aspects, such as the meaning of mental or psychological experience, can be found apart from the description of participant experience: A comprehensive approach, allowing researchers to read and analyze each sentence carefully to find the essence or meaning of the participants' experience. The holistic approach allows researchers to look at the whole text and try to find meaning from the text. The emotional experience of police officers at RTMC to their family gets these two themes:

Theme 1: Feelings of guilt in the family: Most participants expressed a sense of sin in the family. Guilty

according to Indonesia Dictionary is doing wrong; make mistakes (mistakes); has an error⁸. The theme was derived from several sub-themes as follows:

Sub-theme: feeling guilty for children because rarely at home, participants said feeling liable to children because they are seldom at home because of their work. The following are excerpts from the interview:

Sometimes I feel guilty about my child, and I am rarely at home because of my job. (P1)

Sub-theme: bestow resentment on family members, the first participant reveals present bitterness or anger at family members when emotional stress is increasing due to pressure. The following are excerpts from the interview:

Even though sometimes my husband was my target if I went berserk because of fear in the office. (): teary eyes (P1)*

Sub-theme: opposed by children because they rarely deliver school, the second participant said that he felt challenged or protested by children because he rarely drove to school. Protests according are statements that do not approve, oppose, deny, etc⁸. The following are excerpts from the interview:

But sometimes I was also protested by my child because I rarely drove to school. (): smiled while lowering head (P2)*

Sub-theme: feeling sorry for children because they rarely go home, feeling sorry is compassion⁽⁸⁾. The fourth participant's expression about this is as follows:

I'm sorry for that too. Usually, the first child, because I also rarely go home on time. (P4)

Sub-theme: feeling bad in the eyes of the family, the third participant said that they felt terrible in the eyes of the family. Feeling useless, not doing (behaving) is not good too; properly treating is the meaning of feeling bad⁽⁸⁾. The third participant's phrase about this is as follows:

Sometimes I think that I am not useful in my family's, especially my children. (): head down. (P3)*

Sub-theme: unable to make children happy, participants revealed that they thought they were not able to make children happy. Happy is satisfied and

relieved, without feeling awkward and disappointed, and so on(8). Quotation of the fourth participant interview as follows:

Sometimes I thought that I couldn't make my child happy (P4).

Theme 2. Feeling happy with the family: All participants revealed that there was a feeling of happiness when with family. Participants assume that family is one of the greatest gifts in his life. Together with the family, a sense of joy, a happy heart, peace of mind, there is a feeling of a miss, a family of removers and a stressed therapist, and can be various stories. Happiness means the situation or feeling happy and serene (free from all that is troublesome)⁸. The theme was obtained from several sub-themes as follows:

Sub-theme: feeling great happiness with my husband, the first participant said that he thought great satisfaction with her husband, especially the husband and police member who knew the workload. This sense of joy means circumstances or feelings of pleasure and serenity (free from all that is troublesome)⁸. The following are excerpts from the interview:

Indeed happy with my husband, mainly my husband also works as a member of the national police. (): laugh out loud. (P1)*

Sub-theme: feeling great happiness and lingering with the family, the third participant said that feeling happy was extraordinary and wanted to stay with the family. The following are excerpts from the interview:

The point is that my family always makes me want to linger at home. Happy extraordinary (): smile. (P3)*

Sub-theme: feeling great and pleased with the family, the second participant said that feeling comfortable and pleasant was exceptional with the family, but because of the demands of work it was obligatory to go home late. Excerpt of the interview as follows:

Wahh, if it's not asked, it's clear that the family is happy and extraordinarily happy. (P4)

Sub-theme: feeling great happiness with my husband and children; the second participant explained that he felt great pleasure with her husband and children. Feelings of desire define happy things; satisfaction; conveniences; happiness; relief (8). Excerpt of the interview as follows:

It's beautiful, especially if it's complete at home. There is a husband, and there are children. That's what makes me always excited about working. (): points to several angles with the right index finger (P2)*

Sub-theme: feel happy to be noticed and given advice by the wife, the fourth participant said that handle happy to be seen and offer information by the wife about health. Excerpt of the interview as follows:

I am so glad because my wife is always attentive and always gives advice to me. (P4)

Sub-theme: feel happy to meet parents and family; the fifth participant said that they felt comfortable to meet their parents and family at home. Excerpt of the interview as follows:

Indeed, I am delighted, mainly I also rarely meet my parents and family at home because of work that cannot be left behind. (P5)

Sub-theme: feeling happy and peaceful to reach children, the second participant said that feeling heart becomes comfortable and calm when meeting children at home. Excerpt of the interview as follows:

So, when I have met my children, my heart is peaceful and serene. (): smile. (P2)*

Sub-theme: feeling nostalgic for mother, the fifth participant explained that felt miss mother. Miss is eager to meet, miss. Excerpt of the interview as follows:

If there is my mother here, I will hug tightly, and I miss her. (P5).

Sub-theme: feel the medication is stressed and tired is family, the second participant said that the family is a stress medication and tiredness reliever. Healers mean something that is used to treat; people who treat; heart entertainers⁸. Excerpt of the interview as follows:

Whose name is tired, stress is whatever the title must go. The family is a stressed medication. (P2)

Sub-theme: feeling calm to be happy and tired when meeting family, participants said that when they met with their families, they felt relaxed, comfortable and bored. Excerpt of the interview as follows:

Anyway if I have reached my family, I am pleased and calm, like my tiredness is gone, even though I am exhausted. (P3)

Sub-theme: feeling forgetful with stress and stress at the office when with family, the fourth participant said that when with a family feeling tired and stressed at the office will forget. Excerpt of the interview as follows:

Yes, if you are with your family, tired and confirmed, the office has ignored. (P4)

Discussion

Feelings of Guilt in the Family: Guilt is a common emotion that everyone must experience. Guilt does contain not only positive values but also negative values if those who feel are too excessive⁹. These guilt feelings play an indispensable role in maintaining human behavior standards and maintaining personal, family, and community relationships¹⁰. Guilt Survivor is very complicated. They do not know what to do to make up for their misconduct.

Most participants have feelings of guilt in their families. The members of this police feel themselves guilty of his child, feeling challenged by his child, feeling bad in the eyes of his family, feeling unable to make his child happy, even from feeling guilty arose pity for his family members and also bestowed his frustration on the family. Evidence in psychology research suggests that even if there is a slight change in the condition of one's affection, it can affect cognitive processes and individual social behavior¹¹.

The guilt faced by police officers is not a mental disorder. But guilt is one of cause mental disorders. Excessive guilt causes neurotic problems such as obsessive-anxiety disorders, depression, and anxiety, and finally disturb their lives¹². People with extreme guilt are identical to people with disabilities; limited in self-actualization¹³. Proper identification will help the handling guilt appropriately. If his guilt is objective, the way out to experience a soul recovery is to apologize to someone where we have been guilty of him. If subjective, it is necessary to look at the problem in a more objective and intact perspective. After identifying guilt and resolving it, it is essential to release guilt and negative thoughts that have been suppressing the soul. Mistakes and failures that cause guilt are part of the life process to be wiser.

Feelings Happy with Family: Participants assume that with family they get a sense of happiness, a happy heart, peace, a feeling of nostalgia, a family of relievers

and stressors, and can be various stories. According to Compton¹⁴, individuals have different ways of finding happiness according to their culture. Javanese society is part of the Indonesian community that is fertile for the repertoire of the philosophy of life. In the Javanese cultural environment, the togetherness of all family members is one of the forms of happiness that exists in a family and means to have the same meaning as a collectivist culture.

Participant revealed that there was a feeling of happiness when with family. Participants assume that family is one of the greatest gifts in his life. Together with the family, the police officer will feel happy, calm, and nostalgic. Hurlock¹⁵, says that happiness is a combination of acceptance, affection, and achievement. The attitude of accepting others controlled by self-acceptance in social adjustment. Cultural adaptation requires physical attraction that can generate love and acceptance from others, while love is the result of the attitude of acceptance of others into the environment.

Mental health is a state of prosperity associated with happiness, excitement, satisfaction, achievement, optimism, or hope. This term is difficult to define, and meaning can change if it is associated with people and certain life situations¹². Assessment of stressors involves determining the meaning and understanding of the impact of a job that is stressful to the individual. An estimate is an evaluation of the significance of an event related to one's well-being. Stressors contain meaning, intensity, and importance with unique and meaningful interpretations given by a person who is at risk of illness¹².

Conclusions

The participants' feelings originate from within internal factor, which distinguishes them from fear and related to external factors such as job risk and regulations. Feeling happy and guilty resulting from workloads have an impact on the quality and effectiveness of their work.

Conflict of Interest: None

Source of Funding: None

Ethical Clearance: This study has passed the ethical approval from the Faculty of Medicine Universitas Brawijaya, with a reliability number 304/EC/KEPK-S2/11/2018.

References

1. Alexander DA, Walker, L.G. The Perceived Impact Of Police Work On Police Officers' Spouses And Families. *Stress Medicine Medical School University of Aberdeen Scotland*. 2014;12:239-46.
2. Fredrickson BL. The role of positive emotions in positive psychology: the broaden-and-build theory of positive emotions. *Am Psychol*. 2001;56(3):218-26.
3. Lykken D, Tellegen, A. Happiness is a stochastic phenomenon. *Psychol Sci*. 1996;7(3):186-9.
4. Sheldon KM, Lyubomirsky, S. . Achieving sustainable gains in happiness: change your actions, not your circumstances. *J Happiness Stud*. 2006;7(1):55-86.
5. Ong AD, Bergeman, C.S, Bisconti, T.L, Wallace, K.A. Psychological resilience, positive emotions, and successful adaptation to stress in later life. *J Pers Soc Psychol*. 2006;91(4):730-49.
6. Fredrickson BL. The broaden-and-build theory of positive emotions. *Philos Trans R Soc Lond B Biol Sci*. 2004;359:1367-78.
7. Pratesi D. *Police Work and Its Effects on the Family*. Washington, D.C, U.S. : 2002.
8. KBBI. *The Indonesian Dictionary* Jakarta: Kemdikbud; 2016 [cited 2019 20 Maret]. Available from: <http://kbbi.web.id/>.
9. Alwisol. *Personality Psychology Revised Edition*. Malang: UMM Press; 2014.
10. Winch G. *First Aid to Your Emotions: A Guide to Treating Everyday Failure, Rejection, Guilt, and Psychological Injuries*. Jakarta: Pustaka Alvabet; 2017.
11. Aaker DA, Stayman, D.M, Hagerty, M.R. Warmth in Advertising: Measuretent, Impact and Sequence Effects. *Journal of Consumer Research*. 2012;12(4).
12. Stuart GW. *Stuart's Principles and Practices in Mental Health Nursing*. Edisi Indonesia ed. Singapore: Elsevier; 2016.
13. Juanita D, R. *Recovery from Guilt*. Jakarta: Seminari Alkitab Asia Tenggara; 2016.
14. Compton WC. *Introduction to Positive Psychology*. USA: Malloy Incorporated; 2012.
15. Hurlock EB. *Developmental Psychology, An Approach Throughout the Life Range*. Jakarta: Erlangga; 2012.

Infertility Causing Factors & the Success Rate of in Vitro Fertilization (IVF) in One of Fertility Center of Surabaya City, Indonesia

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Abstract

The success rate of in Vitro Fertilization (IVF) with ICSI depends on married couples factors such as maternal age, causes of infertility from the married couples, embryo status, reproductive history, lifestyle, ethnicity, and type of medical examination of infertility. The success rate of IVF was different among countries, rating from 21.4% to 51.7% meaning that the couples succeeded having a child, while in Indonesia the rate was unknown.

Objective: To analyze infertility causing factors in married couples who underwent IVF and the success rate of IVF in one fertility center in Surabaya, Indonesia. Method: This observational study was conducting during January to December 2017. All couples who visited the fertility center, the female ≤ 39 years old, and the couples finished medical examination in the study place were asked to participate this study. Their characteristics (female age and duration of marriage), type infertility causing factors as well as the success rate.

Results: Among 154 married couples, 64.3% of the female and 44.8% of the male had one or more abnormality in their reproductive status, while 26.6% of both (the couples) had the abnormalities, and 17.5% of both (the couples) had no abnormality (unexplained infertility). The success rate of IVF, meaning the female got pregnancy, was 37.7%. There was no significant association between male factors, female factors, more over the number of abnormalities were not associate to success rate. When correspondents divided in to 2 groups, having one or more abnormalities group vs. no abnormalities group (unexplained abnormality), we found that the success rate did not differ significantly between the two groups; suggesting additional examination were needed to predict the other factors for increasing the success rate in this study place.

Keyword: Infertility, Success Rate In Vitro Fertilization (IVF), Indonesia.

Introduction

Infertility is a problem in the reproductive system that is described by the failure to get a pregnancy after

12 months or more in which the couples have sexual intercourse at least 2-3 times per week regularly without using contraception.¹ Infertility occurs in 10-15% of couples², while in Indonesia was 12.5%. Infertility causing factors in married couples were 35% male factors, 35-50% female factors, 5% unusual problems, 10% unexplained infertility.² In Vitro Fertilization (IVF) is one of Assisted reproductive technologies (ART) that commonly used in infertility therapy. ART is used if other medicines failed to treat caused of infertility.³ Unfortunately, IVF is not always succesful⁴, it depends on variability factors such as maternal age, caused of

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infertility, embryo status, reproductive history, lifestyle, ethnicity, and type of medical examination.^{5,6,7} The IVF outcome based on live birth rates in the South-East Asian, African-Caribbean, and Middle-Eastern were 38%, 23.3%, 21.4%, respectively in contrast to the live birth rates in white European population 43.8% and America was 51.7%.⁶ However, in Korea, the pregnancy rate of IVF with ICSI was 34.1%.⁸ The success rate of IVF in developed and developing countries can be comparable, although each country had different factors that influence the success rate of IVF. So, this study was important to analyze the different causes of infertility that can influence the success rate of IVF in developed and developing countries.

Material and Method

Data collection from participants were gotten after they signed the informed consent. The protocol of this study was approved by the Health Research Ethic Committee Fertility Center in Surabaya, Indonesia.

The fertility center in Surabaya, Indonesia is a private hospital. Patients who visited this hospital come from many region of Indonesia, such as Surabaya, East Java, Kalimantan, Sulawesi and many east regions of Indonesia. Their background of Fertility center patients were middle-high socio-economic background. This observational study was conducting during January to December 2017. All couples who visited the fertility center and fulfilled inclusion criteria were asked to participate this study. The inclusion criteria were married couples who recorded in medical record; married couples had complete medical examination of sperm, ovarian, tuba, and uterus factors; married couples who underwent IVF; and female age ≤ 39 years old. Their characteristics (female age and duration of marriage), type of medical examination, infertility causing factors, and the success rate were recorded and analyzed.

This study used an observational analytic research. The data were collected from medical record of married couples who underwent IVF therapy at the fertility center in Surabaya Indonesia, in the period of January 2017 to December 2017. Samples were taken from population using total sampling method. The total of samples was 154 married couples who underwent IVF according to the inclusion criteria. Medical records were compiled based on the inclusion and exclusion criteria.

Variables in this study were infertility causing factors of male, infertility causing factors of female, and in vitro

fertilization (IVF). Infertility causing factors of male infertility was defined from normal and abnormal sperm analysis. Infertility causing factors of female infertility was defined from normal and abnormal ovarian, tuba, uterus, and endometriosis medical examination. In vitro fertilization (IVF) was defined based on pregnancy rate, success if the titer of β-hCG is ≥ 25 mIU/ml and failed if the titer of β-hCG is < 25 mIU/ml. The data analysis was tested by Chi-square test to analyze relation between infertility causing factors in married couples with the success rate of IVF.

Findings: Total of 213 medical records obtained, 154 medical records met fulfilled inclusion criteria. In samples that were used to analyze infertility causing factors in married couples with the success of IVF, the most frequent female age were 30-39 year and female factors were the most frequent cause of the infertility [Table 1]. Fallopian tube disorders were the most frequent infertility disorder followed by uterus disorders and endometriosis [Table 3]. Meanwhile in male factors, oligoasthenoteratozoospermia (OAT) were the most frequent cause of the infertility [Table 3]. The success rate of IVF based on pregnancy rate was 37.7% [Table 4]. Infertility causing factors in married couples were 17.5% unexplained infertility, 18.2% male factors, 37.7% female factors, 26.6% both factors [Table 5]. Analysis showed that there was no significant relation between infertility causing factors in married couples with the success of IVF (p = 0.586) [Table 5]. When correspondents divided in to 2 groups, having one or more vs. no abnormalities (unexplained abnormality), we found that the success rate did not differ significantly (p = 0.216) [Table 6]. There was no differ significant between female age and number of abnormalities in the success rate of IVF [Table 7, Table 8].

Table 1: Characteristic and Status of Infertility factors of Respondents

Characteristics	n	%
Female age	32.6±4(20-39)*	
20-29 years	36	23,4
30-39 years	118	76,6
Duration of Marriage	6.3±3.9(0.5-22)*	
≤5years	69	47
6-10 years	59	40.1
>10 years	19	12.9

Note: *Mean±SD (minimum-maximum)

Table 2: Status of Infertility factors

Factors	n	%
Male		
Normal	85	55.2
Abnormal	69	44.8
Female		
Normal	55	35.7
Abnormal	99	64.3
Male and Female		
Normal	27	17.5
Abnormal	127	82.5

Table 3: Status of Infertility factors based on sex and type of abnormality and pregnancy rate

Infertility causing factors	n	%
Male	154	
Normal of sperm analysis	85	55.2
One disorders of sperm analysis	42	27.3
Azoospermia	12	7.8
Oligozoospermia	10	6.5
Teratozoospermia	13	8.4
Astenozoospermia	7	4.6
Two disorders of sperm analysis	12	7.8
Astenoteratozoospermia	8	5.2

Infertility causing factors	n	%
Oligoastenozoospermia	4	2.6
Three disorders of sperm analysis	15	9.7
Oligoastenoteratozoospermia (OAT)	15	9.7
Female	154	
Ovarian function disorders		
Normal	132	85.7
Abnormal	22	14.3
Fallopian Tube disorders		
Normal	111	72.1
Obstruction	43	27.9
Uterus disorders		
Normal	117	76
Abnormal	37	24
Endometriosis		
Normal	120	77.9
Endometriosis	34	22.1
Unexplained infertility	27	17.5

Table 4: Frequency of IVF success

IVF Success	n	%
Success	58	37.7
Failed	96	62.3
Total	154	100

Table 5: Association between infertility causing factors in married couples with the success rate of IVF

Infertility causing factors	IVF Success				Total		p value*
	Success		Failed		n	%	
	n	%	n	%			
Male factors	10	6.5	18	11.7	28	18.2	0.586
Female factors	19	12.4	39	25.3	58	37.7	
Male and female factors	16	10.4	25	16.2	41	26.6	
Unexplained infertility	13	8.4	14	9.1	27	17.5	
Total	58	37.7	96	62.3	154	100	

Note: *Chi-Square Test

Table 6: Comparison of IVF success rate in normal vs. abnormal of married couples disorders

	IVF Success				Total		p value*
	Success		Failed		n	%	
	n	%	n	%			
No abnormalities	13	8.5	14	9	27	17.5	0.216
Have abnormalities	45	29.2	82	53.3	127	82.5	
Total	58	37.7	96	62.3	154	100	

Note: *Chi-Square Test

The research from Monash University, Australia which states that motility is one of the most important parameters in determining fertility levels. Sperm concentration does not significantly influence fertility levels when the motility and morphology of abnormal sperm can be controlled.⁹ Another study, at hospital in Bandung also stated that there was a significant relation between sperm motility and the success of IVF. However, there was no significant relation between sperm morphology and the success of IVF. Motility have role in the success of IVF, while morphology has no role in the success of IVF.¹⁰ In this hospital, azoospermia that diagnosed was caused by obstruction. In this study, the percentage of IVF success in the male factors who had sperm abnormalities, it was found that azoospermia had the biggest percentage of IVF success (3.9%) if compared to other sperm abnormalities. In this hospital, azoospermia that diagnosed was caused by obstruction. This can occur because the therapy for male infertility in the Fertility Center was done by intracytoplasmic sperm injection (ICSI), but might different in other studies that using conventional IVF techniques. ICSI is process of selecting the most qualified sperm for fertilization with oocytes. So, we can found the best quality of sperm from the azoospermia that caused by obstruction.

In this study, the success of IVF in women 20-29 years (5.9%) and 30-39 years (31.8%). This study was different from research in the UK in 2010, the success of IVF in women under 35 years of age (32.2%), ages 35-37 (27.7%), ages 38-39 (20.8%), above the age of 40-42 years (13.6%), while the age of more than 43 years (<5%).⁸ In contrast to previous studies, in this study using the age range of 20-29 years and 30-39 years, this was because infertile patients who underwent IVF the most frequent were more than 30 years of age. In this study also excluded the age of more than 39 years so that the study sample was reduced. A phenomenon that exists in Indonesia, in infertile couples who underwent IVF, the female age is mostly over 30 years old. It should be on screening or early detection, if for one year have been related to a husband and wife regularly and do not use any contraception but have not been pregnant, then it should be immediately consulted with an obstetrician. However, in fact, most married couples check up their fertility for more than 30 years because they are waiting for probability to get pregnant at less than 30 years of age by adhering to the socio-cultural conditions in each region.

Based on the results of the statistical test with chi-

square, it was found that there was no significant relation between infertility causing factors and the success of IVF. Infertility in married couples can be caused by 35% male factors, 35-50% female factors, 5% unusual problems, and 10% unexplained infertility.² Medical examination of the causes of infertility in this Fertility Center includes sperm analysis, laparoscopy, HSG, ultrasound, and menstrual disorder history. Medical examination of causes of infertility in abroad is almost the same as in Indonesia, however, there are additional of medical examination, post coitus cervical mucus tests, the aim of which is to determine the ability of sperm to reach the uterine cavity and the ability to survive cervical mucus.² In the other research explained that the post coital test (PCT) was a valuable test in daily practice, as a negative outcome is associated with a lower ongoing pregnancy rates (OPR) and higher need in IUI and ART (IVF). Moreover, the PCT was particularly useful in couples with male factors infertility.⁷

In vitro fertilization (IVF) is a technology that is still developing to continue to deal with infertility. Depending on the type of calculation used, the results may represent the number of confirmed pregnancies, called the pregnancy rate, or the number of live births, called the delivery rate. The success rate of IVF depends on various variable factors such as maternal age, causes of infertility, embryo status, reproductive history, and lifestyle factors.⁵ However, in the other research found that ethnicity, GDP, utilization, and type of medical examination could be influence of IVF success rate.^{5,6,7}

The success of IVF in this study was 37.7% at Fertility Center in 2017. In other research, the IVF outcome based on the ethnicity, live birth rates in the South-East Asian, African-Caribbean, Middle-Eastern and white European population were 38%, 23.3%, 21.4%, 43.8%.⁶ This study is comparable with research in Taipei, which shows a pregnancy rate of 47.7% and a delivery rate was 33.6%,¹² and in Korea, the pregnancy rate of IVF with ICSI was 34.1%.⁸ However, it was contrast with the research in USA shows a pregnancy rate was 51.7%.¹³ The relation between the causes of infertility in couples with the success rate of IVF in this study or research from abroad still not be explained yet. If there are no abnormalities found in male and female, infertility is categorized as unexplained infertility.¹⁴ However, the success of IVF in unexplained infertility is still not explained yet, too. Based a psychological perspective, research in New York shows that psychological stress affects the success of IVF. Much stress level of couples who underwent IVF

can affect success of IVF.¹⁵ Many factors can influence the success of IVF, could be related caused by ethnicity or other factors. However, the analysis of the causes of infertility in the success of IVF still not be explained yet.

This study had a number of limitations. The total number of samples collected was still low if compared with the other study. It recommended to use a large sample size and investigate other factors that influence the success rate of IVF or external factors of infertility in further study.

Conclusion

The conclusion of this study is that infertility causing factors influences the success rate of IVF. However, this study has not yet established relation between infertility causing factors in married couples with the success rate of IVF at the one of fertility center in Surabaya, Indonesia in 2017 with the success rate of IVF. The success rate of IVF depends on various variable factors such as maternal age, causes of infertility, embryo status, reproductive history, and lifestyle ethnicity, and type of medical examination.

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Ethical Clearance: Taken from Ethical Committee in Health Research Dr. Soetomo General Hospital Surabaya, Indonesia on 19 December 2018 (ref. no. 0853/KEPK/XII/2018).

Conflict of Interest: The authors declare that they have no competing interests.

Reference

1. Zegers-Hoshschild F, Adamson GD, de Mouzon J, Ishihara O, Mansour R, Nygren K, et al. International committee for monitoring assisted reproductive technology (ICMART) and the world health organization (WHO) revised glossary of art terminologi, 2009. *Fertil Steril.* 2009;92(5):1520-4.
2. Fritz MA, Speroff L. *Clinical gynecologic endocrinology and infertility.* 8th ed. Philadelphia: Woltres Kluwer Health/Lippincott William & Wilkins; 2011.
3. Nieschlag E, Behre HM, Nieschlag S. *Andrology: male reproductive health and dysfunction.* 3rd ed. Berlin: Springer; 2010.
4. Tournaye H. Male factor infertility and art. *Asian J Androl.* 2012;14(1):103-8.
5. Andon, H, et al. *Consensus Guidelines for Handling Infertility.* Jakarta; 2013
6. Jayaprakasan K, Pandian D, Hopkisson J, Campbell BK, Maalouf WE. Effect of ethnicity on live birth rates after in vitro fertilization or intracytoplasmic sperm injection treatment. *BJOG* 2014; 121:300-308.
7. Hessel M, Brandes M, de Bruin JP, Bots RSGM, Kremer JAM, Nelen WLDM, et al. Long term ongoing pregnancy rate and mode of conception after a positive and negative post-coital test. *Acta Obstet Gynecol Scand* 2014; 93: 913-920.
8. Choi YM, Chun SS, Han HD, et al. Current status of assisted reproductive technology in Korea, 2009. *Obstet Gynecol Sci* 2013; 56(6): 353-361.
9. Mahadevan MM, Alan OT, et al. The relationship of tubal blockage, infertility of unknown cause, suspected male infertility, and endometriosis to success of in vitro fertilization and embryo transfer. *Fertil and Steril.* 2016;40(6):755-762.
10. Rezano A, Ramadhan PV, Permadi W. Correlation between Sperm Motility and Morphology in the Success Rate of in Vitro Fertilization Procedure. *Althea Medical Journal.* 2016;3(4):520-525.
11. Ramalingam M, Durgadevi P, Mahmood T. In Vitro Fertilization. *Obstetrics, Gynaecology And Reproductive Medicine.* 2016;26(7):200-209.
12. Hsin-Fen L, Fu-Shiang P, et al. The Outcomes of Intracytoplasmic Sperm Injection and Laser Assisted Hatching in Women Undergoing In Vitro Fertilization Are Affected by The Cause of Infertility. *Royan Institute International Journal of Fertility and Sterility.* 2015;9(1): 33-40.
13. Centers for Disease Control and Prevention (CDC). *National Center for Chronic Disease Prevention and Health Promotion, Division of Reproductive Health.* USA; 2019
14. Hamada A, Esteves SC, Nizza M, Agarwal A. Unexplained Male infertility: Diagnosis and Management. *Int Braz J Urol.* 2012;38(5):576-94.
15. Quant HS, Zapantis A, Nihsen M, et al. Reproductive implications of psychological distress for couples undergoing IVF. *J Assist Reprod Genet.* 2013;30:1451-1458.

The Prevalence of *Entamoeba Gingivalis* and *Trichomonas Tenax* in Children Treated with Orthodontic Appliances in AL Muthanna Province, Iraq

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Abstract

The present study was aimed to determine the prevalence of *Entamoeba gingivalis* and *Trichomonas tenax* in children treated with Orthodontic appliances and their correlation with oral health. The study conducted on 95 children in age (9-12), treated by using orthodontic appliances (fixed or removable) in the pediatric oral center in dentistry faculty at AL Muthanna University, Iraq. Both microscopical method and PCR technique have been used in determining the presence of *Entamoeba gingivalis* and *Trichomonas tenax*. *T. tenax* hasn't detected by both diagnostic method the presence of *E. gingivalis* was in 9(9.47%) samples and 15(15.78%) samples by the microscopical method and PCR technique respectively. The higher percentage was in the age(9-10) by both method. The statistical analysis showed a significant correlation between the infection and age at $p \leq 0.05$. Furthermore, depending on oral health, the highest percentage was in the mild gingivitis by both method, statistically no significant correlation between oral health and the presence of the *E. gingivalis* at $p \leq 0.05$. The percentage of the parasite depends on the orthodontic appliance treatment was similar (9.58%) in the fixed and (9.09%) in the removable by microscopical method, while by PCR technique was (12.32%) in the fixed and (27.27%) in the removable table, statistically no correlation between the infection with the parasite and orthodontic appliances type at $p \leq 0.05$.

Keywords: *Entamoeba gingivalis*, Orthodontic appliances, Gingivitis.

Introduction

Human oral cavity is colonized by specific bacteria, fungi, and protozoa^{1,2}. Among these microorganisms *Entamoeba gingivalis* and *Trichomonas tenax*. *E. gingivalis* is a cosmopolitan and may be found on the teeth surface and gingival, in interdental spaces, carious lesions, gingival pockets and in dental plaque. Additionally can inhabit the tonsillar crypts and the bronchial mucus. Trophozoites are the infective forms³. The incidence of *E. gingivalis* in patients with periodontal

disease was assumed that it may participate in the etiology and development of this disease. Furthermore, the pathogenic perspective of *E. gingivalis* has been proven experimentally by the development of lesions in immunosuppressed animals⁴. Another protozoan of oral cavity *T. tenax* found in the oral cavity and patients with poor oral hygiene and periodontal disease. *T. tenax* is less often found in patients with the poor oral condition. However, it has been involved in different infections outside the oral cavity^{5,6}. Treatment with Orthodontic appliances which represent a new component in the oral cavity requires a high degree of oral hygiene. Moreover, the orthodontic appliance creates a surface for the accumulation of the microorganisms. Many signs of gingivitis may appear in patients with fixed orthodontic appliances⁷. Fixed and removable orthodontic appliances constitute an obstacle which prevents the maintenance of oral hygiene resulting in aggregation of plaque⁸.

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Material and Method

The samples were obtained from 95 children aged (9-12)year who treated with orthodontic appliances(fixed and removable) in the pediatric dental clinic in the Department of Pedodontics, Orthodontics and Preventive Dentistry (POP) of Dentistry faculty, University of AL Muthanna. From the first of October 2018 till March 2019. All the subjects were healthy with no antibiotic consumption for the last six months. For each patient, plaque and saliva samples were taken from the deepest sites of one front tooth and one molar by using two sterile cotton swabs, sterile curette, and scaler. Then examined by the wet mount direct smear and PCR technique. Questionnaires were done for age, gender, oral health, and orthodontic appliances type. The samples were collected from all patients in the morning, before any oral hygiene.

Microscopic Examination: The swabs were washed in 0.9% NaCl solution. A droplet of the samples was put on microscope slides, which were then examined under 100x, 200x and 400x magnification.

DNA Extraction: The DNA of the parasites

was extracted from the samples, according to the manufacturer’s instructions. (gSYNC™ DNA Mini Kit Blood/cultured cell/Protocol/Geneaid/Korea) was used. The DNA extracts were stored at -20°C till PCR executed.

PCR Amplification: The DNA extracts served as a template for the PCR amplification using the method formerly described by^{9,10,11}. In order to the detection of *E. gingivalis* and *T. tenax* the target DNA regions of the SSU rDNA gene and 18S rRNA gene respectively, were amplified using specific primers (mentioned in Table 1). The amplification products were visualized and photographed under UV light after 1 h of ethidium bromide staining. Typical bands of the *E. gingivalis*, is manifested in Fig. 1.

Ethics Statement: The approval has been taken from all the parents of children, informing them that the samples would be for the study purpose only and no more samples will be needed.

Statistical analysis: Data were analyzed by using SPSS version 22 software Fisher’s exact and Chi-square with a significant $P < 0.05$.

Table (1): The primer sequences and PCR conditions with their amplicon size (Base pair (BP)).

Parasite (Gene’s Name)	Primer Sequence (5’- 3’)	Size (BP)	Conditions	Reference
SSU rDNA gene of <i>E. gingivalis</i>	F: 5’-AGGAATGAACGGAACGTACA-3’ R: 5’-CCATTTCCTTCTTCTATTGTTTCAC-3’	203	initial denaturation at 94°C for 3.5min	(3)
			40 cycles of denaturation at 94 °C, 1min, annealing at 60 °C for 1min; and extension at 72°C for 1min)	
			final extension at 72°C for 1min and holding (4°C).	
18S rRNA gene of <i>T. tenax</i>	TGBK-F 5’-AGCAGCTGCGGTAATTCCAG-3’ TGBK-R 5’-CTTGTTACCACTTCTCCTTCC-3’	1000	Taq activation at 94°C for 5 min	(11)
			30cycles of denaturation at 93°C for 30 s, annealing at 55 °C for 30 s, and extension at 72°C for 2 min	
			final extension at 72 °C for 5 min	



Fig. 1: Agarose gel electrophoresis of the amplified band of SSU rDNA gene for Entamoeba gingivalis detection

Results

Out of 95 samples(49 girls and 46 boys) were examined to evaluate the prevalence of *E. gingivalis* and *T. tenax* in children aged (9-12) years treated with orthodontic appliances. *T. tenax* parasite wasn't detected by PCR and microscopical examination in this study while *E. gingivalis* has been detected by both method. For *E. gingivalis* by Microscopical method showed only 9(9.47%) samples were positive, while by PCR technique the percentage of the *E. gingivalis*, was 15(15.78%). Depend on the age the higher percentage was (23.52%) in the age(9-10) by microscopical method table(2,A), and 6 (35.29%) in the same age group by PCR technique table(2,B). The statistical analysis showed a significant

correlation between the infection and age at $p \leq 0.05$. Depend on oral health the highest percentage was in the mild gingivitis (20%) by microscopical method table(3) and by PCR the highest percentage of the infection was (26.66%) in mild gingivitis as well table(5). The statistical analysis showed no correlation between oral health and the presence of the *E. gingivalis* at $p \leq 0.05$. The percentage of the parasite depends on the orthodontic appliance treatment was similar (9.58%) in the fixed and (9.09%) in the removable by microscopical method (table 4, A) while by PCR technique was(12.32%) in the fixed and (27.27%) in the removable table(4, B), statistically no significant correlation between the infection with the parasite and orthodontic appliances type at $p \leq 0.05$.

Table (2) A: The number of positive and negative samples of *E. gingivalis* by Microscopical examination depends on age and gender. B: number of positive and negative samples of *E. gingivalis* by PCR depend on age and gender

A							
Age groups	Negative		negative Total	positive		Positive total (percentage)	Grand Total
	female	Male		female	male		
9-10	7	6	13	4	0	4 (23.52%)	17
11-12	37	36	73	1	4	5 (6.41%)	78
Grand Total	44	42	86	5	4	9 (9.47%)	95
B							
Age groups	Negative		negative Total	positive		Positive total (percentage)	Grand Total
	female	Male		female	male		
9-10	5	6	11	6	0	6 (35.29%)	17
11-12	35	34	69	3	6	9 (11.53%)	78
Grand Total	40	40	80	9	6	15 (15.78%)	95

Table (3): Number of negative and positive samples with Entamoeba gingivalis by Microscopical examination depends on Oral health

Oral Health	Negative	Positive (Percentage)	Grand Total
Healthy Mouth	15	0	15
Mild Gingivitis	24	6 (20%)	30
Moderate Gingivitis	35	3 (7.89%)	38
Severe Gingivitis	12	0	12
Grand Total	86	9 (9.47%)	95

Table (4) A: Number of positive and negative samples of E. gingivalis by Microscopical examination depend on Orthodontic appliance. B: number of positive and negative samples of E. gingivalis by PCR technique depend on Orthodontic appliances

A			
Orthodontic appliance	Negative	Positive (Percentage)	Grand Total
Fixed	66	7 (9.58%)	73
Removable	20	2 (9.09%)	22
Grand Total	86	9 (9.47%)	95
B			
Orthodontic appliances	Negative	Positive (Percentage)	Grand Total
Fixed	64	9 (12.32%)	73
Removable	16	6 (27.27%)	22
Grand Total	80	15 (15.78%)	95

Table (5): Number of negative and positive samples with Entamoeba gingivalis by PCR technique depend on Oral health

Oral Health	Negative Samples	Positive Samples (Percentage)	Total
Healthy Mouth	12	3 (20%)	15
Moderate Gingivitis	34	4 (10.52%)	38
Severe Gingivitis	12	0	12
Mild Gingivitis	22	8 (26.66%)	30
Total	80	15(15.78%)	95

Discussion

Oral protozoa have been detected in 95% of the population with poor oral hygiene. The present study was aimed to evaluate the presence of *E. gingivalis* and *T. tenax* in children aged 9-12 years treated by using orthodontic appliances, and their correlation with oral health. The study showed no prevalence for *T. tenax* in all examined samples by both Microscopical examination and PCR technique. On the contrary to many studies which were detected highly variable levels for the prevalence^{11,12}.

Out of 95 samples were examined only 9(9.47%) samples were positive by the microscopical method and 15(15.78%) positive samples by PCR technique. This percentage was compatible with many previous studies. ¹²found the average number of *E. gingivalis* in urban children was 12.84 unity and a lower number was found in rural children (10.74 unity) in Lublin, Poland. In Egypt, the study showed the infection percentage 23 (28.75%) conducted on 80 cases with gingivitis. While in the control group, *E. gingivalis* was 9 (11.25%)¹³.

Depend on the age the higher percentage was (23.52%) by microscopical method, and 6 (35.29%) in

the same age group by PCR technique, statistically there is a significant correlation between the infection and age. The study of ³ indicated that *E. gingivalis* occurs in the oral cavity of children. Our present study found the highest percentage of the infection with *E. gingivalis* was in the mild gingivitis but the statistical analysis showed no correlation between oral health and the presence of the *E. gingivalis* at $p \leq 0.05$. In fact, *E. gingivalis* live in the oral cavity as commensals and flourish in poor oral hygiene. According to some authors, this commensal has the potential to become opportunistic pathogens¹⁴. The study of ¹² found no significant correlation between the presence of *E. gingivalis* and dental caries. The study in Lublin, Poland found the presence of *E. gingivalis* (81,4%) in patients with some periodontal disease, and (62,5%) in people without oral diseases¹⁰. Another study in south India showed the presence of *E. gingivalis* was (88%) in patients with gingivitis, (76%) in patients with periodontitis and only 4% in healthy subjects¹⁶.

The percentage of the parasite depends on the orthodontic appliance treatment was similar (9.58%) in the fixed and (9.09%) in the removable by microscopical method while by PCR technique was (12.32%) in the fixed and (27.27%) in the removable, the statistical

analysis found no significant correlation between the infection and the orthodontic appliances type. Both fixed and removable orthodontic appliances are likely plaque retentive instruments and may have a risk for periodontal diseases. That may provide a good environment to flourish the parasite. It should be kept in mind the intimate contact of the orthodontic appliances with teeth and gingival tissues has a harmful effect on oral hygiene^{17,18}.

Conclusion

The result of the present study suggested the presence of *Entamoeba gingivalis* in the oral cavity with poor hygiene, which may provide by using orthodontic appliances. It's important for everyone have the orthodontic appliance to maintaining perfect oral hygiene.

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Funding: Self

Ethical Clearance: Not required.

References

- Bonner M, Fresno M, Gironès N, Guillen N, Santi-Rocca J. Reassessing the Role of *Entamoeba gingivalis* in Periodontitis. *Frontiers in cellular and infection microbiology*, (2018)8.
- Mehr AK, Ali ZArAnDi KA. Prevalence of oral trichomonas tenax in periodontal lesions of down syndrome in Tabriz, Iran. *Journal of clinical and diagnostic research: JCDR*, (2015). 9(7), ZC88.
- Mielnik-Błaszczak M, Rzymowska J, Michałowski A, Skawińska-Bednarczyk A, Błaszczak J. *Entamoeba gingivalis*—prevalence and correlation with dental caries in children from rural and urban regions of Lublin Province, Eastern Poland. *Annals of Agricultural and Environmental Medicine*, (2018).25(4), 656-658.
- Al-Saeed WM. Pathogenic effect of *Entamoeba gingivalis* on gingival tissues of rats. *Al-Rafidain Dental Journal*, (2003). 1(1), 70-73.
- Duboucher C, Farto-Bensasson F, Chéron M, Peltier JY, Beaufls F, Périé G. Lymph node infection by *Trichomonas tenax*: report of a case with co-infection by *Mycobacterium tuberculosis*. *Human pathology*, (2000).31(10), 1317-1321.
- El Kamel A, Rouetbi N, Chakroun M, Battikh M. Pulmonary eosinophilia due to *Trichomonas tenax*. *Thorax*, (1996). 51(5), 554-555.
- Cernochova P, Augustin P, Fassmann A, Izakovièová-Hollá L. Occurrence of periodontal pathogens in patients treated with fixed orthodontic appliances. *Scr Med (Brno)*, (2008). 81, 85-96.
- Tonetti MS, Mombelli A. Aggressive periodontitis. Lindhe J, Lang NP, Karring T. *Clinical Periodontology and Implant Dentistry*. 5th ed. Oxford: Blackwell Munksgaard, (2008). 428-58.
- Bonner M, Amard V, Bar-Pinatel C, CharpentierF, Chatard JM, Desmuyck Y, Ihler Y, Rochet S, de La Tribouille JP, Saladin VR, Verdy M. Detection of the amoeba *Entamoeba gingivalis* in periodontal pockets. *Parasite*, (2014). 21.
- HUSSIAN, R. S. (2017). MOLECULAR DETECTION OF ENTAMOEBA GINGIVALIS USING POLYMERASE CHAIN REACTION. *Pak. J. Biotechnol*. Vol, 14(3), 351-354.
- Athar A, Soghandi L, Haghighi A, Kazemi B. Prevalence of oral trichomoniasis in patients with periodontitis and gingivitis using PCR and direct smear. *Iranian Journal of Public Health*, (2007). 33-37.
- Yazar S, Çetinkaya Ü, Hamamci B, Alkan A, Sisman Y, Esen Ç, Kolay M. Investigation of *Entamoeba gingivalis* and *Trichomonas tenax* in Periodontitis or Gingivitis Patients in Kayseri. *Türkiye Parazitolojii Dergisi*, (2016). 40(1), 17.
- El-Dardiry MA, Shabaan SH. Detection of *Entamoeba gingivalis* trophozoites in patients suffering from gingivitis versus healthy. *Advances in Environmental Biology*, (2016). 10(12), 222-226.
- Vundela RR, Sisnity VS, Palaparthi RB, Guntakanla VR. Role of *Entamoeba gingivalis* in periodontitis: myth or reality!. *Indian Journal of Dental Advancements*, (2016). 8(2), 100-106.
- Luszczak J, Bartosik M, Rzymowska J, Sochaczewska-Dolecka A, Tomaszek E, Wysokinska-Miszczuk J, Bogucka-Kocka A. The occurrence of *Entamoeba gingivalis* among patients with periodontal disease. *Current Issues in Pharmacy and Medical Sciences*, (2016). 29(2), 86-89.
- Ramamurthy S, Sudarsana S, Sivasamy S, Ulaganathan A, Rathinasamy K, Govindarajan S. Incidence of the oral protozoa-*Entamoeba*

- gingivalis in a hospital-based population in South India-A preliminary study. *Journal of Oral Disease Markers*, (2018). 2, 1-4.
17. Slutzkey S, Levin L. Gingival recession in young adults: occurrence, severity, and relationship to past orthodontic treatment and oral piercing. *American Journal of Orthodontics and Dentofacial Orthopedics*, (2008). 134(5), 652-656.
 18. Türkkahraman H, Sayın M, Bozkurt FY, Yetkin Z, Kaya S, Önal S. Archwire ligation techniques, microbial colonization, and periodontal status in orthodontically treated patients. *The Angle Orthodontist*, (2005).75(2), 231-236.

Are Former Athletes Protected Against Obesity after Retirement?

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Abstract

The aim of this study is to assess the prevalence of overweight and obesity in retired athletes in Saudi Arabia. Seventy former athletes, aged from 20-60 years old, who had played in international and national competitions – and had since stopped competitive sport – were recruited for this study. Sports history, age, height, and weight were collected using an online questionnaire. The study results showed that 47.14% of the participants are overweight and 22.86% are obese. The results of this study indicated that many former athletes had high BMI after ceasing participation in competitive sport. Also, the results indicated that there is a significant difference between BMI before and after retirement.

Keywords: Former athletes; obesity; overweight; physical activity; body mass index.

Introduction

Being overweight and obese are increasingly recognised as a serious public health issue worldwide (1-3). Results from several studies have reported that overweight and obesity lead to a wide variety of health issues, such as type 2 diabetes, high blood pressure, and coronary heart disease, and that they shorten the life span (1-6). The relationship between high body mass index (BMI) and all-cause mortality and cardiovascular disease (CVD) mortality follows a U-shaped curve (7).

It is commonly acknowledged that engaging in regular physical activity (PA) and exercise in the early stage of life has a significant role in later life (8-10). This means that those who do so decrease the risk of high body fat and contribute to sustaining an ideal body weight. The high accumulation body fat could cause several diseases, such as type 2 diabetes, high blood pressure, and coronary heart disease (8,11,12).

Participating in sports in early life, as exemplified by top athletes, can lower the prevalence of several non-communicable diseases, such as type 2 diabetes and high blood pressure, as well as helping them maintain psychological wellbeing in late adulthood (8,13-16). According to Batista and Soares (2014), being an athlete at a high level is often associated with the possibility of decline for the occurrence of several non-communicable diseases. Batista and Soares (2013) have shown that former athletes may maintain appropriate levels of physical fitness (PF) in comparison with the general population, regardless of their participation in competitions or the level of PA.

However, a growing body of literature has emerged showing that the prevalence of obesity, which has experienced a remarkable increase among athletes after retiring from competition (11,17,18). It has been reported that many former athletes engage in sedentary behaviours after ceasing to participate in sport, which can cause a risk to their health (8,11). Functional capabilities in later life might be put at risk because of the negative consequences of injuries during exercises and competitions. The high demands of athleticism during adulthood probably make athletes unable to be as active as they become older, which could affect on their health (19). Top athletes normally exercise for many

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years or even several decades to reach their professional level, and when there is no longer any vigorous training motivation, they usually become affected both physically and mentally (20). However, less is known about the impact of regular training on obesity risk in former athletes. In this context, the aim of this study to assess the prevalence of overweight and obesity in retired athletes.

Method

An online questionnaire was administered to participants. The link to the questionnaire was sent to the Saudi Athletics Federation, asking them to send a request to former athletes to participate in this research. This study was approved by a panel of experts who were considered to be an ethical committee for the school of education at the University Technology Malaysia (UTM). All participants provided informed consent electronically before participation in this study. Subsequently, 70 individuals agreed to participate. The research participants were former male athletes who had played in international and national competitions and had ceased playing competitive sport. The inclusion criteria was that the participant be aged 20 years or older. The online, self-administered questionnaire collected data on sports history, age, height, and weight. BMI was defined as weight (in kilograms) divided by the square of the height (in meters). For the comparisons between our groups and data from the World Health Organization (WHO), overweight was defined as a BMI of 25-29.9, and obesity was defined as a BMI ≥ 30 kg/m².

Statistical Analysis: The Data are reported as mean, standard deviations, or number (percentage,%). A paired samples t-test was performed to compare the means of BMI in athletes before and after retirement. Statistical analysis was performed using software SPSS version 23. P-values of <0.05 were considered to be statistically significant.

Results

The results are derived from the data obtained from the online self-reported questionnaire. The total number

of participants in this study was 70, all of whom were former athletes from Saudi Arabia. Table 1 presents the demographic variables, and Figure 1 shows the prevalence of obesity classifications. As shown Table 1, the mean height and weight of the participants were 174.61 cm (SD = 7.605) and 83.99 kg (SD = 14.568), respectively. The mean age of the participants was 39.73 years old (SD = 7.75) and ranged from 24 to 59 years old. The majority of the participants were track & field players (34.3%), footballers (24.3%), and Karate practitioners (20.0%).

The findings, as shown in Figure 1, demonstrate that the majority of the former athletes were classified as overweight (47.14%), whereas, the prevalence of normal weight and obesity was 28.57% and 22.86%, respectively. In addition, the study results shown in Figure 3 reveal that there is a difference between the mean BMI before and after their retirement.

Table 1. Physical Variables

Demographic Variable	Mean +- SD
Age (years)	39.73+- 7.75 (24; 59)
Height (cm)	174.61 +- 7.605 (157; 194)
Weight (kg)	83.99 +- 14.568 (62; 130)
BMI (kg/m ²)	27.6244 +- .58630 (17.17; 43.94)

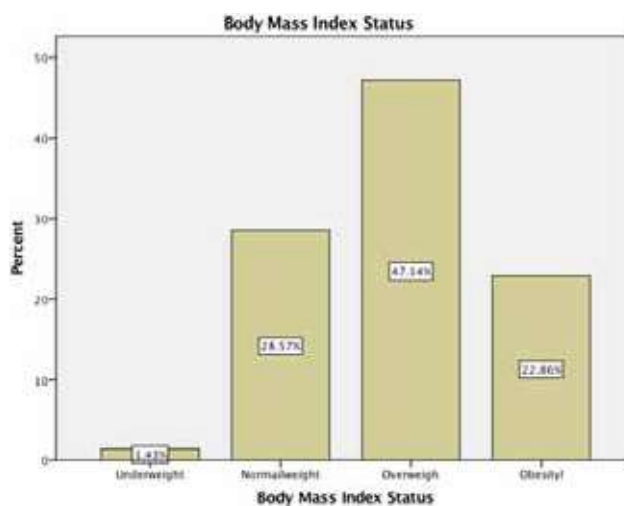


Fig. 1: Participant’s BMI as percentages of the overall sample

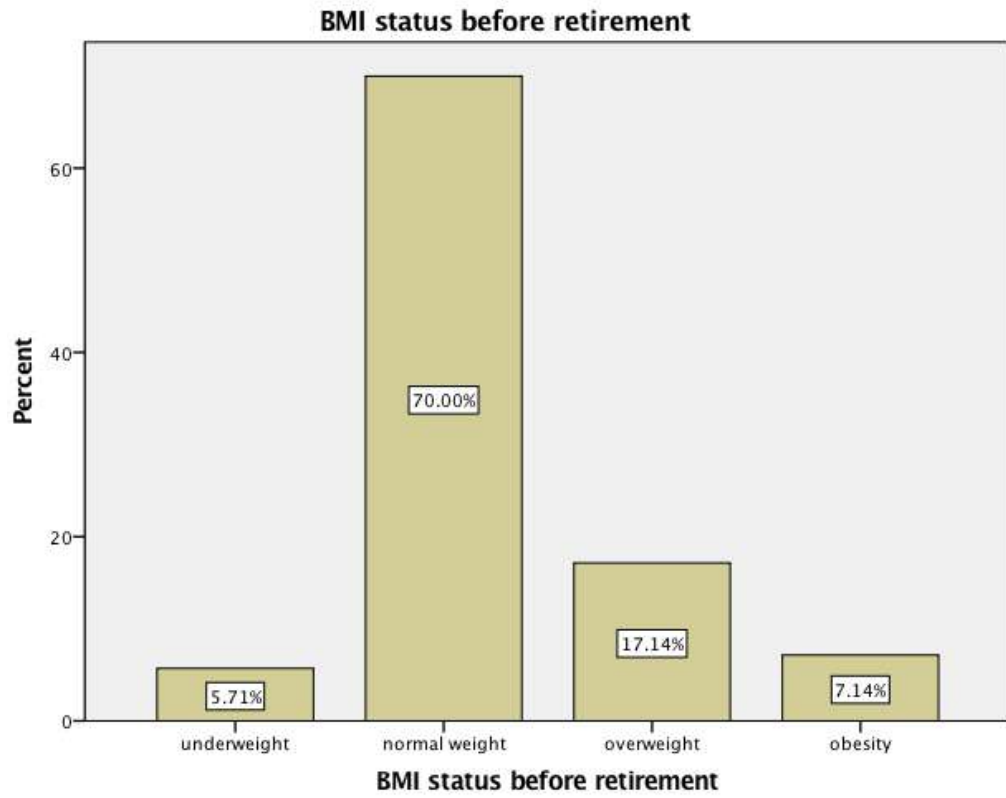


Fig. 2 Participant’s BMI as percentages of the overall sample before retirement

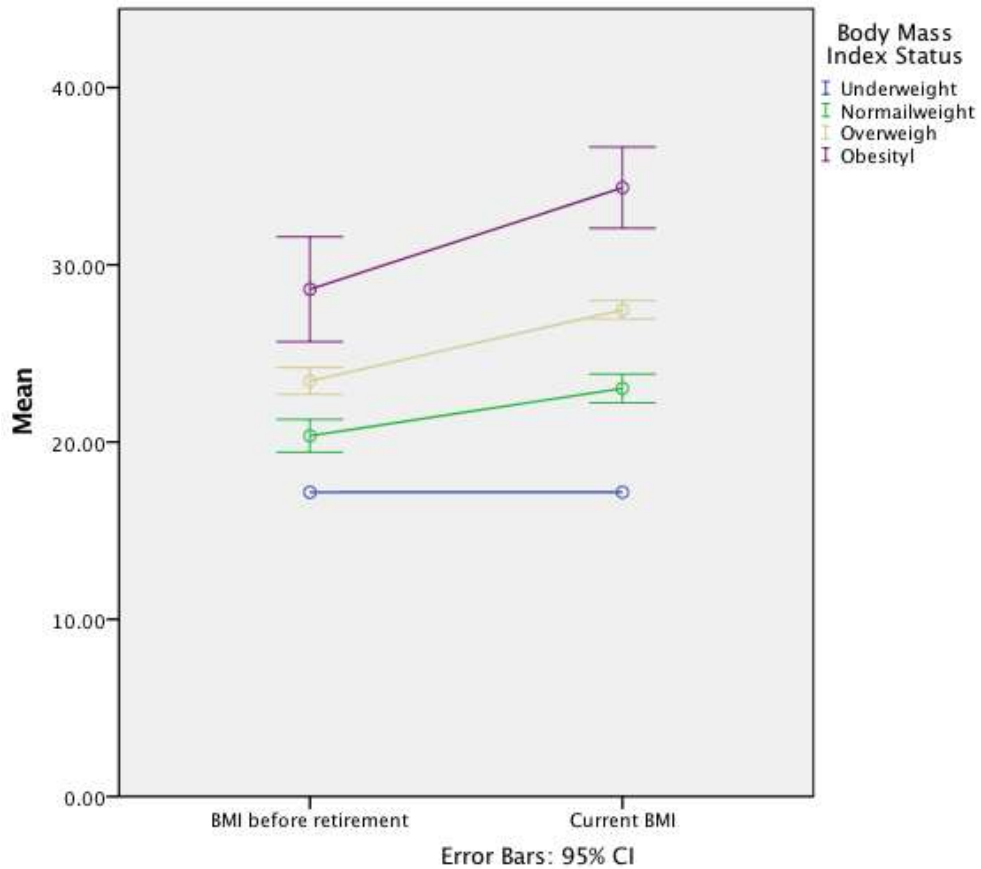


Fig. 3: The mean of BMI before and after retirement

Discussion

It is accepted that engagement in regular PA can lead a better health and a long life ^(12,19,21,22). For example, when the level of PA is increased, the risk of mortality might reduce by 20-35%. Moreover, the risk of mortality by CVD can reduce by half if the person is active or fit ^(19,23). However, several studies have reported that the risk of long-term diseases increase when the athletes adopted a sedentary lifestyle after ceasing to participate in competitive sport ^(9,11).

Regular exercise stimulates several physiological, biochemical and morphological adaptations in athletes ^(21,24). Athletes have to develop several physical fitness components, such as cardiorespiratory endurance and strength, to meet the demands of the sport. As a result of regular exercise, athletes develop versatile adaptations in their musculoskeletal and cardiovascular systems. For instance, Melekoğlu and colleagues indicated that footballers have greater muscle tissue than non-athletes and typical people. Regardless of the type of sports in which the athletes participated, various adaptations occur in their bodies. Therefore, in order to retain these bodily modifications, they have to remain active and fit even after retirement ⁽¹⁹⁾.

It has been reported that former athletes generally keep active and live a healthier lifestyle when they get older ^(8,9,12,22). However, several studies have indicated that a significant number of former athletes reduce their level of PA and or engage in sedentary behaviours after ceasing to participate in competitive sport ^(9,19). It has been reported that there are several reasons why former athletes do not participate in physical activities: for example, long-term injuries might prevent former athletes from carrying out physical activity ⁽¹⁹⁾. Furthermore, the process of ageing may play a significant role in increasing the body composition and reducing the cardiorespiratory functions ^(21,24,25).

Although many studies have focused on the current health of former athletes ^(8,10,11), there is a lack of research associated with athletes who had engaged in regular exercise before they had retired. The findings, which used a group of 70 former athletes that included men from 13 different sports, found that the percentages of overweight and obese individuals in the study sample were high, similar to those of the general Saudi population ^(1,3,26-29).

According to the study findings, a significant number

of former athletes are now overweight or obese in spite of gaining a normal BMI before retirement (Figure 2). Such gain weight is of concern given the associated boosted risk of CVD ^(11,19,30). Although having a high BMI may occur with age amongst the general population, athletes who had been retired from sports may reduce their physical activity, yet sustain their eating habits ⁽³¹⁾. Interventions towards the end of the athlete's career might assist former athletes to independently manage their levels of physical activity and nutritional requirements upon they leaving the sport ⁽³¹⁾.

The study findings are consistent with previous results ^(11,17,19), which show that athletes' body weight and BMI increase after retirement. According to Arliani and colleagues, 80% of former footballers were overweight. A recent results also stated that former professional footballers had higher body weight and BMI scores ⁽¹⁹⁾. It is accepted that obesity is a risk factor for several long-term disease, such as T2D, high blood pressure, CVD, and some cancers ^(11,25). Based on the study results, it seems that non-participation in sport and regular exercise results in higher BMI, and subsequently, this increases their risk for several chronic diseases. It has been reported that high BMI often occurs as a result of a lack of physical activity or high intake of foods ⁽¹⁹⁾.

Although this is a pilot study, it is in fact the first study to determine the prevalence of being overweight and obese in former athletes in Saudi Arabia. In addition, this is the first study to assess BMI before and after athletes retire, and therefore the outcomes are of great importance, in spite of the small number of participants.

Limitations: Some limitations need to be considered in this study. Firstly, the data on height and weight were reported by participants. Nonetheless, in spite of the problem with assessing this, the study reply rate offers useful data on former athletes, and the biases are unlikely to impact the study outcomes. Secondly, the absence of a control group for comparison represent another limitation for this study. Furthermore, the study did not take into account the participants' dietary habits. Although BMI is widely used to determine the prevalence of overweight and obesity in epidemiological research, this study is not a direct measure of fatness and can overestimate the prevalence of overweight and obesity in certain populations ⁽³²⁾. Therefore, using a waist circumference measure may provide a more accurate assessment of obesity than BMI amongst former athletes.

Conclusion

The results of this study of former athletes in Saudi Arabia indicated that these people had a high weight increase after retirement from sport, as well as a high prevalence of overweight and obesity. In addition, this study indicated that there are significant differences in BMI before and after retirement.

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References

1. Al-Qahtani AM. Prevalence and Predictors of Obesity and Overweight among Adults Visiting Primary Care Settings in the Southwestern Region, Saudi Arabia. *Biomed Res Int*. 2019;2019:1–5.
2. Lung T, Jan S, Tan EJ, Killedar A, Hayes A, Al-Qahtani AM. Impact of overweight, obesity and severe obesity on life expectancy of Australian adults. *Biomed Res Int* [Internet]. 2019;43(4):1–5. Available from: <http://dx.doi.org/10.1038/s41366-018-0210-2>
3. Al-Ghamdi S, Shubair MM, Aldiab A, Al-Zahrani JM, Aldossari KK, Househ M, et al. Prevalence of overweight and obesity based on the body mass index; A cross-sectional study in Alkharj, Saudi Arabia. *Lipids Health Dis* [Internet]. 2018;17(1):1–8. Available from: <http://www.embase.com/search/results?subaction=viewrecord & from=export & id=L622427875%0Ahttp://dx.doi.org/10.1186/s12944-018-0778-5>
4. Perreault L, Pi-Sunyer. FX, Kunins L. Overweight and obesity in adults: Health consequences. *UpToDate*. 2018;1–22.
5. Wang YC, McPherson K, Marsh T, Gortmaker SL, Brown M. Health and economic burden of the projected obesity trends in the USA and the UK. *Lancet* [Internet]. 2011;378(9793):815–25. Available from: [http://dx.doi.org/10.1016/S0140-6736\(11\)60814-3](http://dx.doi.org/10.1016/S0140-6736(11)60814-3)
6. Simon JE, Docherty CL. Current health-related quality of life in former national collegiate athletic association division i collision athletes compared with contact and limited-contact athletes. *J Athl Train*. 2016;51(3):205–12.
7. Kong KA, Park J, Hong S hyeon, Hong YS, Sung YA, Lee H. Associations between body mass index and mortality or cardiovascular events in a general Korean population. *PLoS One* [Internet]. 2017;12(9):1–17. Available from: <http://dx.doi.org/10.1371/journal.pone.0185024>
8. Batista C, Soares JM. Are former elite athletes more protected against metabolic syndrome? *J Cardiol* [Internet]. 2013;61(6):440–5. Available from: <http://dx.doi.org/10.1016/j.jjcc.2013.01.011>
9. Batista C, Soares JM. Is athletic background associated with a future lower prevalence of risk factors for chronic disease? *J Exerc Sci Fit*. 2014;12(2):47–54.
10. Laine MK, Eriksson JG, Kujala UM, Wasenius NS, Kaprio J, Bäckmand HM, et al. A former career as a male elite athlete — does it protect against type 2 diabetes in later life ? *Diabetologia*. 2014;57(2):270–4.
11. Emami M, Behforouz A, Jarahi L, Zarifian A, Rashidlamir A, Rashed MM, et al. The Risk of Developing Obesity, Insulin Resistance, and Metabolic Syndrome in Former Power - sports Athletes - Does Sports Career Termination Increase the Risk. *Indian J Endocrinol Metab*. 2018;515–9.
12. Teramoto M, Bungum TJ. Mortality and longevity of elite athletes. *J Sci Med Sport* [Internet]. 2010;13(4):410–6. Available from: <http://dx.doi.org/10.1016/j.jsams.2009.04.010>
13. Bäckmand H, Kaprio J, Kujala UM, Sarna S, Fogelholm M. Physical and psychological functioning of daily living in relation to physical activity. A longitudinal study among former elite male athletes and controls. *Aging Clin Exp Res*. 2006;18(1):40–9.
14. Laine MK, Kujala R, Eriksson JG, Kautiainen H, Sarna S, Kujala UM. Costs of diabetes medication among male former elite athletes in later life. *Acta Diabetol*. 2017;54(4):335–41.
15. Oliveira-Brochado A, Oliveira-brochado F, Brito PQ. Effects of personal, social and environmental factors on physical activity behavior among adults. *Políticas de Saúde*. 2010;28(1):7–17.
16. Ströhle A. Physical activity, exercise, depression

- and anxiety disorders. *J Neural Transm.* 2009;116(6):777–84.
17. Arliani GG, Lara PS, Astur DC, Cohen M, Gonçalves JPP, Ferretti M. Impact of sports on health of former professional soccer players in Brazil. *Acta Ortopédica Bras* [Internet]. 2014;22(4):188–90. Available from: http://www.scielo.br/scielo.php?script=sci_arttext & pid=S1413-78522014000400188 & lng=en & tlng=en
 18. Guo J, Zhang X, Wang L, Guo Y, Xie M. Prevalence of metabolic syndrome and its components among Chinese professional athletes of strength sports with different body weight categories. *PLoS One.* 2013;8(11):1–7.
 19. Melekoğlu T, Sezgin E, Işın A, Türk A. The Effects of a Physically Active Lifestyle on the Health of Former Professional Football Players. *Sports.* 2019;7(4):75.
 20. Sunčica Poček, Trivić T, Roklicer R, Ostojić SM, Drid P, Poček S, et al. Long-term outcomes of sports on health status : a mini review. *Exerc Qual Life* [Internet]. 2018;10(1):5–15. Available from: <http://www.eqoljournal.com/long-term-outcomes-of-sports-on-health-status-a-mini-review/>
 21. Gremeaux V, Gayda M, Lepers R, Sosner P, Juneau M, Nigam A. Exercise and longevity. *Maturitas* [Internet]. 2012;73(4):312–7. Available from: <http://dx.doi.org/10.1016/j.maturitas.2012.09.012>
 22. Gomez-Gallego F, Ruiz JR, Buxens A, Altmæ S, Artieda M, Santiago C, et al. Are elite endurance athletes genetically predisposed to lower disease risk? *Physiol Genomics* [Internet]. 2010;41(1):82–90. Available from: <http://physiolgenomics.physiology.org/cgi/doi/10.1152/physiolgenomics.00183.2009>
 23. Johansson JK, Kujala UM, Sarna S, Karanko H, Puukka PJ, Jula AM. Cardiovascular health in former elite male athletes. *Scand J Med Sci Sport.* 2016;26(5):535–43.
 24. Negrean V, Pascu C, Cheța IO, Alexescu T, Cioancă O. Metabolic diseases: the latest findings in sports. *Actual ale bolilor Metab în Sport* [Internet]. 2015;16(1):56–60. Available from: <http://search.ebscohost.com/login.aspx?direct=true & db=a9h & AN=102344004 & site=eds-live & scope=site>
 25. Fien S, Climstein M, Quilter C, Buckley G, Henwood T, Grigg J, et al. Anthropometric, physical function and general health markers of Masters athletes: a cross-sectional study. *PeerJ* [Internet]. 2017;5:e3768. Available from: <https://peerj.com/articles/3768>
 26. Al-Qahtani DA, Imtiaz ML, Shareef MM. Obesity and cardiovascular risk factors in Saudi adults soldiers. 2005;966(May).
 27. Al-Nozha MM, Al-Mazrou YY, Al-Maatouq MA, Arafah MR, Khalil MZ, Khan NB, et al. Obesity in Saudi Arabia. *Saudi Med J.* 2005;26(5):824–9.
 28. Al-Baghli N a, Al-Ghamdi a J, Al-Turki K a, El-Zubaier a G, Al-Ameer MM, Al-Baghli F a. Overweight and obesity in the eastern province of Saudi Arabia. *Saudi Med J* [Internet]. 2008;29(August):1319–25. Available from: <http://www.smj.org.sa/PDFFiles/Sep08/18Overweight20080438-p1319.pdf%5Cnhttp://ovidsp.ovid.com/athens/ovidweb.cgi?T=JS & CSC=Y & NEWS=N & PAGE=fulltext & D=emed8 & AN=2008610895%5Cnhttp://shelcat.org/sfxlcl3?sid=OVID:embase & id=pmid: & id=doi: & issn=0379-5284 & isbn= & volume=2>
 29. Horaib G Bin, Al-Khashan HI, Mishriky AM, Selim MA, AlNowaiser N, BinSaeed AA, et al. Prevalence of obesity among military personnel in Saudi Arabia and associated risk factors. *Saudi Med J.* 2013;34(4):401–7.
 30. Kerr ZY, DeFreese JD, Marshall SW. Current physical and mental health of former collegiate athletes. *Orthop J Sport Med.* 2014;2(8):1–9.
 31. Panayiotoglou A, Grammatikopoulou MG, Maraki MI, Chourdakis M, Gkiouras K, Theodoridis X, et al. Metabolic syndrome in retired soccer players: A pilot study. *Obes Med* [Internet]. 2017;8:15–22. Available from: <https://doi.org/10.1016/j.obmed.2017.09.004>
 32. Miller MA, Croft LB, Belanger AR, Romero-Corral A, Somers VK, Roberts AJ, et al. Prevalence of Metabolic Syndrome in Retired National Football League Players. *Am J Cardiol.* 2008;101(9):1281-4.

Safety Profile of Japanese Encephalitis Vaccine in Children and Adolescents in Bali Province: An Active Vaccine Safety Surveillance

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Abstract

Background: Indonesian Expanded Program of Immunization has implemented Japanese Encephalitis vaccination in endemic area in Indonesia such as Bali Province, was initiated by catch up campaign program in children 9 months to 15 years of age.

Objectives: The objectives of this study are to assess the immediate serious systemic reactions within 30 minutes after immunization and also local reactions, systemic events and any serious adverse event, until 28 days following immunization.

Method: An observational study was conducted in 1000 subjects. Local reactions and systemic events within 28 days following immunization, were recorded into daily cards and will be confirmed by trained primary health center staffs.

Result: Totally, 1000 children and adolescents completed the study and can be analyzed. The most common local reaction was pain, occurred in 21.1% subjects and mild swelling in 14.1% subjects within 30 minutes after vaccination. Redness occurred more frequent in 15.8% subjects at 24 hours following immunization. Fever, occurred only in 0.8%, no serious adverse event reported during the observation.

Conclusion: This JE live vaccine was safe and well tolerated in children and adolescents.

Keywords: JE, local reactions, systemic reactions, vaccines.

Introduction

Japanese encephalitis (JE), a mosquito-borne flaviviral infection, is the leading recognized cause of childhood encephalitis in Asia. After yellow fever (YF), JE is the second flavivirus that is vaccine preventable. JE is transmitted throughout Asia, in a region supporting

3.4 million people, 50% of the world population.¹ Even though on a global scale the incidence of JE may decline as a result of large-scale vaccination programs implemented in India and China, however, transmission of JE is likely to increase in several countries in Asia, such as, Indonesia, Laos, Myanmar, North Korea, Bangladesh, Cambodia and Pakistan because of population growth, yield increase in rice farming, pig rising and breeding, and the lack of immunization programs and surveillance.²

JE virus usually transmitted by Culex mosquitoes bite, and circulates in an enzootic cycle in pigs and birds as a breeding hosts. Culex tritaeniorhynchus, usually

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bites at night and plays the most important role as a vector, breeds in ponds and wetrice fields. JE virus has the reservoir for breeding and cannot be eliminated but disease can still be controlled by extensive immunization in endemic areas.³

The estimation of severe symptoms are estimated to occur 1 out of 250 infections by the JE virus.¹ More than three-quarters of pediatric patients will experience seizures, but will be less in adults. In pediatric patients, the most common symptom is abdominal pain accompanied by vomiting.⁴ Although the use of vaccines has begun to spread, it is estimated that around 67,900 cases occur each year, of which one quarter is a fatal case with an incidence of 1.8/100,000 in 24 countries at risk of disease due to JE infection..⁵

A study was conducted in 2001-2003 from 559,120 children under 12 years of age, 86 confirmed and 4 probable JE cases were identified. For children less than 10 years of age, the incidence rate of JE was 7.1 and adjusted to 8.2 per 100,000 over the 2.5 consecutive years of study. Among 96,920 children 10–11 years old (0.4per 100,000) only one JE case was found. The outcome of the patients were nine children (10%) died and 33 (37%) of the survivors had neurological sequele. Most of the cases (70%) were occurred in the rainy season, even though JE virus was transmitted in Bali year-round.⁶ A study was conducted in 15 districts from 12 provinces in Indonesia among the pig rearing location. All provinces found JE infections with the highest number from Central Sulawesi. Unfortunately Bali was not included in this study.⁷

At 2006 WHO recommended to gradually replaced the first generation vaccine by a new generation JE vaccines, with fewer side effects. This article describes this new generation of JE vaccine in depth.⁸ Indonesian government has decided to introduce JE vaccination in Bali province 2017-2018.⁹ The immunization program will be started with catch up campaign from 9 months to 15 years of age.

Method

We conducted an observational study design as an active vaccine safety surveillance, involving 1000 children between 9 months to 15 years of age. The study was conducted in period March – July 2018. This study was conducted in 2 primary health centers in Denpasar City (Denpasar Barat 1 and Denpasar Utara 3) and 2 primary health centers in Badung District (Mengwi 1

and Mengwi 3).

The sample size was calculated using formula for Post Marketing Surveillance/Phase IV study, from known adverse event; fever, 0.014 require 883 subjects, with drop out estimation 20%, this study require 1000 subjects.

Procedures: The study protocol has been reviewed and approved by the Health Research Ethics Committee of Faculty of Medicine of University of Indonesia (Reference number:03540/UN2.FI/ETIK/2018) prior the study.

After informed consent has been signed, the subjects who met inclusion criteria were allocated to an inclusion number from 001 to 1000. The subjects received Japanese Encephalitis Vaccine, Live[®](Chengdu Institute of Biological Products (CDIBP), Chengdu, China) and vaccination based on campaign base Immunization Program. All subjects/teachers/parents provided with diary card to assess and record information for local and systemic reactions within 28 days following immunization, with special attention in the first three days. Local reactions are reactions that arise at the injection site and systemic reactions are reactions that are experienced systemically outside the injection site. Safety assesments were confirmed by trained health care provider within 30 minutes after injection. Subjects received thermometers, plastic bangle and diary cards, to record the occurence of local and systemic reactions. The intensity (recorded as 1=mild, 2=moderate or 3=severe) of local (pain, redness, swelling and induration at injection site), and systemic reactions (fever $\geq 38^{\circ}\text{C}$, irritability and others) recorded from day 0 through 28 days after immunization.¹⁰⁻¹²

Results

We enrolled a total of 1000 children and adolescent aged 9 months to 15 years of aged, 424 female and 576 male, and all subjects completed the study and can be analyzed.

No serious adverse event observed during the study. Fever was observed, 0.25% – 0.8% according to the time of onset. Most of the fever were mild, one fever classified as moderate, and none of them was classified as severe. Irritability was observed in 0.6% subjects 30 minutes following immunization and was decreased to 0.3% at the following day with the intensity were mild. For local reaction, pain was the most commonly

reported reaction following JE immunization. Onset of pain occurred within 30 minutes in 211 subjects (21.1%), and most of the pain was mild to moderate intensity, and 0.7% was severe. Pain decreased within 24 hours after vaccination, and observed in 189 subjects (18.9%), the intensity was mostly mild to moderate and 0.4% was severe. At 30 minutes following immunization, 157 subjects experienced redness at the injection site, and increased 24 hours after immunization to 158 subjects (15.8%), mostly were mild in intensity, and decreased at the following day. Four subjects had severe redness. Mild swelling reported in 141 subjects (14.1%) within 30 minutes after immunization and were increased to 14.3% where 4 of them were severe in intensity. Swelling were decreased at the following day to 0.7% with the intensity mild.

If the adverse events were categorized based on the age group, the most frequent fever was in the 1 < 7 years age group, but for the local reactions, all of the local reactions were most frequent in 7 < 12 years of age, even though the highest number of participants were from 1 < 7 years age group.

Table 1. Age distribution of the study participants

No	Age (Years)	n	%
1	≤ 1	37	3.7
2	1 < 7	516	51.6
3	7 < 12	330	33.0
4	≥ 12	117	11.7
	Total	1000	100

Table 2. Fever and the intensity following JE immunization

No	Fever intensity	Observation Period									
		30 Minutes		1 day		2 days		3 days		4-28 days	
		n	%	n	%	n	%	n	%	n	%
1	Mild	2	0.2	2	0.2	2	0.2	3	0.3	8	0.8
2	Moderate	0	0	0	0	1	0.1	0	0	0	0
3	Severe	0	0	0	0	0	0	0	0	0	0
	Total	2	0.2	2	0.2	3	0.3	3	0.3	8	0.8

Table 3. Pain and the intensity following JE immunization

No	Local reaction	Observation Period									
		30 Minutes		1 day		2 days		3 days		4-28 days	
		n	%	n	%	n	%	n	%	n	%
1	Mild	177	17.7	171	17.1	19	1.9	14	1.4	5	0.5
2	Moderate	27	2.7	14	1.4	2	0.2	2	0.2	0	0
3	Severe	7	0.7	4	0.4	1	0.1	0	0	0	0
	Total	211	21.1	189	18.9	22	2.2	16	1.6	5	0.5

Table 4. Swelling and the intensity following JE immunization

No	Swelling	Observation Period									
		30 Minutes		1 day		2 days		3 days		4-28 days	
		n	%	n	%	n	%	n	%	n	%
1	Mild	141	14.1	143	14.3	7	0.7	5	0.5	3	0.3
2	Moderate	0	0	0	0	0	0	0	0	0	0
3	Severe	0	0	4	0.4	0	0	0	0	0	0
	Total	141	14.1	147	14.7	7	0.7	5	0.5	3	0.3

Table 5. Redness and intensity

No	Redness	Observation Period									
		30 Minutes		1 day		2 days		3 days		4-28 days	
		n	%	n	%	n	%	n	%	n	%
1	Mild	157	15.7	158	15.8	22	2.2	22	2.2	13	1.3
2	Moderate	0	0	0	0	0	0	0	0	0	0
3	Severe	0	0	4	0.4	0	0	0	0	0	0
	Total	157	15.7	162	16.2	22	2.2	22	2.2	13	1.3

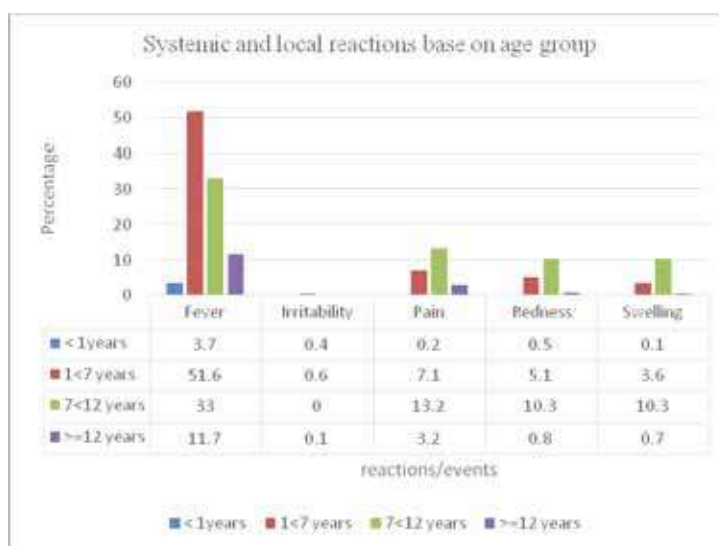


Figure 1. Systemic and local reactions based on age group

Discussion

Our study monitored the catch up campaign of live JE vaccine in 1000 subjects aged between 9 months to 15 years, in Bali. From 1000 subjects, all subjects completed the study visit. No serious adverse event occurred during the study. As the primary objective of this study, no immediate serious adverse event observed in this study.

The most common systemic event was fever. Fever was observed, 0.25% – 0.8% according to the time of onset. Most of the fever were mild, one fever classified as moderate, and none of them was classified as severe. Irritability was observed in 0.6% subjects 30 minutes following immunization and was decreased to 0.3% at the following day with the intensity were mild. For local reaction, pain was the most commonly reported reaction following JE immunization. Onset of pain occurred within 30 minutes in 211 subjects (21.1%), and most of the pain was mild to moderate intensity, and 0.7% was severe. Redness occurred more frequent in 15.8% subjects at 24

hours following immunization and swelling 14.3% at the same visit.

A study conducted in China to evaluate JE live and measles vaccine in 545 subjects, at 8 months of age infants received measles and JE live vaccination. The most common local reactions was redness 2%, and the other local reactions were <1%. The most common systemic event was fever 19%, followed by cough 5%, diarrhea, upper respiratory tract infections and others 3% for each event.¹³ Publication about safety review of JE vaccine was published in 2017. The frequency of erythema (0.2%–1.1%), swelling (0.4%–1.54%), pain (0.9–17%) as the local reactions and signs and/or symptoms at the injection site were reported approximately 3% across studies that administered only one JE live vaccine dose.¹⁴⁻¹⁷ A prospective cohort study among South Korean children, showed different profile, in which no local and systemic reactions were reported.^{14,18} Induration was reported in 12 from 2878 infants within 14 days follow-up period from a study in Srilanka.¹⁹ One dose administration of JE live vaccine

reported only mild and time-limited systemic reactions following immunization regardless of follow-up time in majority of the studies.¹³⁻¹⁶ Fever (>37.8°C) was found among 133 infants vaccinated with one dose of JE live vaccine, of whom 39% and 44% reported recovering within one day and 2 days, respectively which was conducted in Srilanka.¹⁹ According to WHO information sheet for JE live attenuated SA 14-14-2 vaccine redness and swelling at the site of injection was reported in <1% vaccinees. For systemic event, the incidence is very low, fever 5/10,000, skin rash 1/10,000 nausea and dizziness 3/1,000,000). In the same literature, but from different study found fever 5% and irritability 4%.²⁰

Compared to our study, all the systemic and local reactions observed in our study were mostly below or at least equal to that found in other studies above.

In conclusion, this JE live vaccine was safe and well tolerated in children and adolescents.

Conflict of Interests: Irawan Mangunatmadja, Julitasari Sundoro, I Made GDL Utama, Syafriyal, Hindra I. Satari, Sri R. Hadinegoro received grant support through their institutions. Rini M. Sari and Novilia S. Bachtiar were employees of PT Bio Farma at the time of the conduct of this study and manuscript preparation.

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Ethical Clearance: The study protocol has been reviewed and approved by the Health Research Ethics Committee of Faculty of Medicine of University of Indonesia (Reference number:03540/UN2.FI/ETIK/2018) prior the study.

Reference

- Halstead SB, Jacobson J, Dubischar-Kastner K. Japanese encephalitis vaccines. In: Plotkin SA, Orenstein WA, editor. *Vaccine*. 6th edition. Philadelphia: Saunders Company; 2013:313-751.
- Erlanger TE, Weiss S, Keiser J, Utzinger J, Widemayer K. Past, and future of Japanese encephalitis, *Emerg Infect Dis*. 2009;15(1):1-7.
- Background paper on JE Vaccines- SAGE working group. Available at http://www.who.int/immunization/sage/meetings/2014/october/1_JE_Vaccine_Background_Paper.pdf?ua=1, accessed November 2014.
- Solomon T, Dung NH, Kneen R, Thano LTT, Gainsborough M, Nisalak A, et al. Seizures and raised intracranial pressure in Vietnamese patients with Japanese encephalitis. *Brain*. 2002;125:1084-93.
- Campbell GL, Hills SL, Fischer M, Jacobson JA, Hoke CH, Hombach JM, et al. Estimated global incidence of Japanese encephalitis: a systematic review. *Bull World Health Organ*. 2011;89(10):766-74.
- Kari K, Liu W, Gautama K, Mammen MP, Clemens JD, Nisalak A, et al. A hospital-based surveillance for Japanese encephalitis in Bali, Indonesia. *BMC Medicine*. 2006;4(8):1-7.
- Ompusunggu S, Maha MS, Dewi RM, Subangkit. JE infection in pigs in some provinces in Indonesia. *Media Litbangkes*. 2012;25(2):1-8.
- World Health Organization. Immunization. Japanese encephalitis vaccines: WHO position paper- February 2015. <https://www.who.int/wer/2015/wer9009.pdf?ua=1>
- Ministry of Health of Indonesian Republic. Introduction of 3 new vaccines to the current immunization program. January 2017: <http://www.depkes.go.id/article/print/17020100001/ini-rencana-pelaksanaan-3-vaksinasi-baru-untuk-lengkap-imunisasi-dasar.html>
- Marcy S, Kohl K, Dagan R, Nalin D, Blum M, Jones M, et al. Fever as an adverse event following immunization: case definition and guidelines of data collection, analysis and presentation. *Vaccine*. 2004;22:551-556.
- Gidudu J, Kohl K, Halperin S, Hammer S, Heath P, Hennig R, et al. A local reaction at or near injection site: Case definition and guidelines for collection, analysis, and presentation of immunization safety data. *Vaccine*. 2008;26:6800-6813.

1. Halstead SB, Jacobson J, Dubischar-Kastner

12. Food and Drug Administration. Center for Biologic Evaluation and Research. U.S Department of Health and Human Services. Guidance for Industry. Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials. September 2007:1-8.
13. Li Y, Chu SY, Wannemuehler H, Xie S, Zhang F, Wang Y, et al. Immunogenicity and safety of measles-rubella vaccine co-administered with attenuated Japanese encephalitis SA 14-14-2 vaccine in infants aged 8 months in China: a non-inferiority randomised controlled trial. *Lancet Infect Dis.* 2019;1(3):1-8.
14. Gindburg AS, Meghani A, Halstead SB, Yaich M. Use of the live attenuated Japanese Encephalitis vaccine SA 14-14-2 in children: A review of safety and tolerability studies. *Human vaccines and immunotherapeutic.* 2017;13(10):2222-31.
15. Chotpitayasunondh T, Sohn YM, Yoksan S, Min J, Ohrr H. Immunizing children aged 9 to 15 months with live attenuated SA14-14-2 Japanese encephalitis vaccine in Thailand. *J Medical Association of Thailand D Chotmaihet Thangphaet.* 2011;94:S195-203
16. Ranganath BG, Hiremath SG. Adverse events following immunisation with SA 14-14-2 Japanese encephalitis vaccine in children of Kolar in Karnataka. *J Indian Medical Association.* 2012;110(1):10-12
17. Zaman K, Naser AM, Power M, Yaich M, Zhang L, Ginsburg AS, Luby SP, Rahman M, Hills S, Bhardwaj M, et al. Lot-to-lot consistency of live attenuated SA 14-14-2 Japanese encephalitis vaccine manufactured in a good manufacturing practice facility and non-inferiority with respect to an earlier product. *Vaccine.* 2014;32(46):6061-6. doi:10.1016/j.vaccine. 2014.09.012. PMID: 25239483
18. Sohn YM, Park MS, Rho HO, Chandler LJ, Shope RE, Tsai TF. Primary and booster immune responses to SA14-14-2 Japanese encephalitis vaccine in Korean infants. *Vaccine.* 1999;17(18):2259-64. doi:10.1016/S0264-410X(99)00006-7. PMID:10403593
19. Sanchayan K, Fernandopulle R, Amarasinghe A, Thiyahiny SN, Ranganathan SS. Safety of live attenuated Japanese encephalitis vaccine given at the age of 9 months in National Immunisation Programme of Sri Lanka. *Ceylon Medical J.* 2016;61(3):99-105. doi:10.4038/cmj.v61i3.8344
20. WHO. Information sheet: observed rate of vaccine reactions, Japanese Encephalitis vaccine. Available at: https://www.who.int/vaccine_safety/initiative/tools/JE_vaccine_rates_information_sheet.pdf

Heavy Metals Concentration and Biochemical Parameters in the Blood and Nails of Industrial Workers

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Abstract

This study aimed to measure the concentration of heavy metals (Pb, Cd) and certain biochemical variables in blood and nails of (50) samples (male and female) of workers (who were in risk of exposition to these heavy metals) from Northern Gas Company in Kirkuk city/Iraq. Flame atomic absorption spectrometer was used for measuring these elements. The results showed significant differences ($P < 0.01$) in the concentration of lead and cadmium in the studied samples (whole blood and nails) of workers compared to the control group. The concentration of lead and cadmium were higher in blood and Nails. As of the biochemical variables, significant differences ($P < 0.05$) showed in the concentration of antioxidant enzyme (SOD) in serum. As of oxidative stress (MDA), results showed significant differences ($P < 0.05$) in serum, the highest value of (MDA) was recorded in serum samples.

Keywords: Heavy metals, Antioxidant, Oxidative stress.

Introduction

Heavy metals have found as natural constituents of the Earth's crust and are non-degradable in nature and tend to form pollutants of living organisms in the environment,¹ and living organisms inhabiting contaminated sites may be exposed to very high amounts of heavy metals as they are toxic and may cause adverse effects, even if in small concentrations.²⁻³

Different sources of heavy metals were found in the environment (natural and industrial). Natural sources such as weathering and volcanic eruption contribute significantly to the pollution of heavy metals,⁴⁻⁶ and industrial sources such as; mineral processing in refineries, power plants, coal combustion, oil combustion, nuclear power plants, chemical and metal industries, in addition to the plants of wood preservation, and paper processing.^{7,8}

Malondialdehyde (MDA), one type of oxidant, is the final product for the oxidation of polyunsaturated fatty acids, which is an indicator for estimating oxidative stress.⁹ Antioxidants are of great importance as they are the first line of defence against free radicals, and the need for antioxidants becomes more critical with increasing exposure to free radicals.¹⁰ The human antioxidant defence system consists of enzymatic and non – enzymatic systems. Many enzymatic systems are stimulating reactions to neutralise free radicals. These enzymes include Superoxide Dismutases (SOD), Catalases (CAT), Glutathione Peroxidases (GPX), Glutathione Reductases (GRX), and these mechanisms form the internal defence mechanisms of the body to help protect against cell damage caused by free radicals.¹¹ These enzymes also require co-factors such as copper, zinc, and selenium as a stimulant to activate enzymes to maintain functions and prevent oxidation in human cells, and the need for antioxidants has become very important with increased exposure to free radicals.

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Materials and Method

The samples of blood and nails were collected from 50 employees (males and females) aged between 20-65 years of the Northern Gas Company in Kirkuk

governorate, while the duration of exposure or years of work ranged between (1-30) years. The control group was selected from 20 people outside the North Gas Company, which did not work in the industrial sector. The samples were collected in January 2019. The elements were estimated in all studied samples by an atomic absorption device (ASS), where the lead element was measured by the flame atomic absorption device (FAAS), while the Cd element by non-flammable atomic absorption device (GFAAS).¹²

Preparation and Sating Samples:

- Blood:** 10 ml of blood was collected from each person; blood samples were divided into two parts; in the first part, (5 ml) was placed in an anticoagulant tube and kept at room temperature to measure lead and cadmium. In the second part, (5 ml) was placed in plastic tubes with tight lids and free from any anticoagulant (Plain tube), and was left at room temperature (25 C) until coagulated, and then placed in the centrifuge for 10 minutes at a speed of 3000 rpm, afterword serum was collected by micropipette to measure biochemical tests. It was then transferred to dry plastic tubes and kept at 10 ° C using Deep Freezer¹³ until tests were carried out. The concentration of lead and cadmium in the blood of the workers was estimated by Haswell method.¹³
- Nails:** Each person's nails were trimmed with clean, sterile scissors, and then placed in sealed plastic bags. Nails were then washed with non-ionic cleaners. After a standard wash, the nail samples were soaked in acetone. Finally, the samples are rinsed five times with deionised water and then dried in the oven at 110 c and stored in the desiccant pending analysis. The samples were divided into two parts, the first part for measuring the heavy elements and the second part for measuring the biochemical variables. The heavy elements in the nail samples were estimated, according to Abdul-Rahman et al.¹⁴ method.

Statistical Analysis: Results were statistically analysed using ANOVA test and the results obtained were described in the tables as (mean and standard deviation) and with a probability level ($P < 0.05$) and $P < 0.01$).

Results and Discussion

1. Heavy metals:

Estimation of heavy metals in whole blood:

Table (1): Concentration of heavy metals (Pb $\mu\text{g/dl}$, Cd $\mu\text{g/dl}$) inworkers'whole blood and control group.

Elements	Groups	Mean \pm SD	P-Value
Pb	Workers	25.40 \pm 4.20	P<0.01
	Control	13.91 \pm 2.02	
Cd	Workers	1.0904 \pm 0.0416	P<0.01
	Control	0.2782 \pm 0.0291	

Lead-(Pb): The results of table (1) showed different concentrations of the lead element; the concentration of the lead in whole blood of workers during the study period was (25.40 \pm 4.20) and control (13.91 \pm 2.02), respectively (Figure 1). Statistically significant differences were found ($P < 0.01$) between the concentration of the lead in the whole blood of workers and the control group, that it was found to be higher than the control group. The reason for the high concentration of lead in the workers could be attributed to the tetraethyl lead, chemicals that emitted from North Gas Company. Furthermore, a study has shown that high concentrations of lead in industrial atmospheres are humanmade, as it is almost 100 times higher in industrial atmospheres compared to natural atmospheres¹⁵. Increasing the concentration of lead in the whole blood leads to many adverse consequences such as hypertension, renal failure, and brain damage.¹⁶ These findings are consistent with those reported by others^{17, 18}.

Cadmium-(Cd): The results of table (1) showed different concentrations of the Cadmium; the concentration of the Cadmium in whole blood of workers during the study period was (1.0904 \pm 0.0416) and control group (0.2782 \pm 0.0291), respectively (Figure 1). Statistically significant differences were found ($P < 0.01$) between the concentration of the lead in the whole blood of workers and the control group, that it was found to be higher than the control group. The high concentration of cadmium in workers was attributed to industrial emissions, especially the mining and mineral refining industry. Also, cadmium occurs naturally with zinc and lead in sulfide ores. Cadmium has a direct relationship with some chronic diseases, such as hypertension, which

is an excellent indicator of exposure to cadmium in occupationally exposed individuals. Cadmium leads to an increase in systolic and diastolic blood pressure, and thus an increase in high blood pressure.¹⁹

The results obtained were mostly consistent with studies conducted on gas station workers in Babil¹⁷ and Basrah¹⁸ governorates, where there was a decrease in the concentration of (Cu, Zn, Mg) and an increase in the concentration of (Cd, Pb) in the blood of gas station workers compared to the control group.

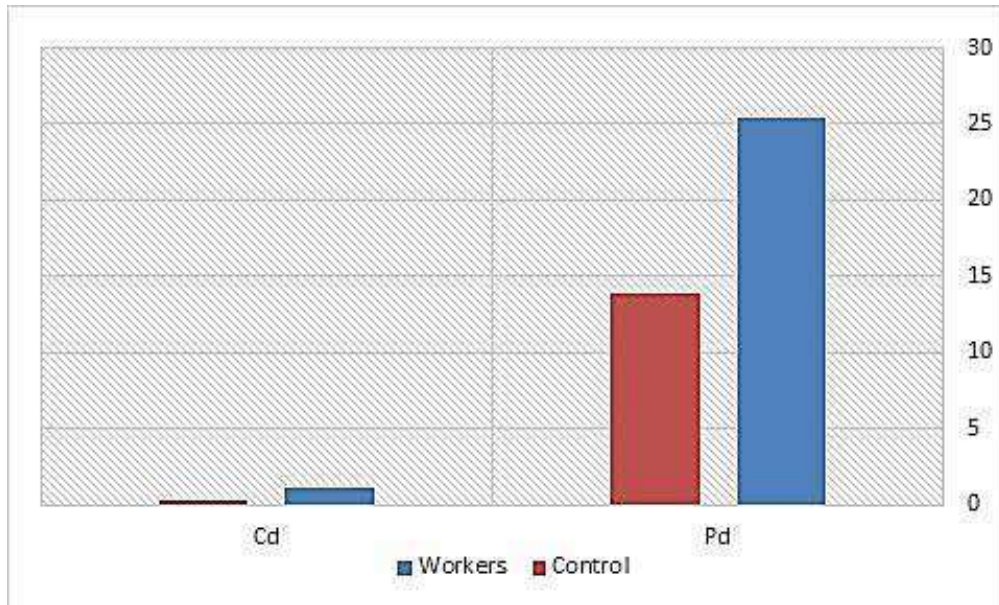


Figure 1: Concentration of Heavy Metals (Pb $\mu\text{g/dl}$, Cd $\mu\text{g/dl}$) in workers' Whole Blood and control group

Estimation of heavy metals in workers' hair compared to the control group:

Table (2): Concentration of heavy metals (Pb $\mu\text{g/dl}$, Cd $\mu\text{g/dl}$) in workers' hair and control group.

Elements	Groups	Mean \pm SD	P-Value
Pb	Workers	15.70 \pm 2.18	P<0.01
	Control	7.75 \pm 1.29	
Cd	Workers	0.1330 \pm 0.0264	P<0.01
	Control	0.0820 \pm 0.0194	

Lead-(Pb): The lead element poses a real concern among heavy metals because of its toxicity, and there is no primary function in the human body, the damage can occur only after its absorption from air or water²⁰.

The results of table (2) showed different concentrations of the lead element; the concentration of the lead in whole blood of workers during the study period was (15.70 \pm 2.18) and control (7.75 \pm 1.29), respectively (Figure 2).

Estimation of heavy metals in workers' nail compared to the control group:

Table (3): Concentration of heavy metals (Pb $\mu\text{g/dl}$, Cd $\mu\text{g/dl}$) in workers' nail and control group.

Elements	Groups	Mean \pm SD	P-Value
Pb	Workers	14.57 \pm 2.50	P<0.01
	Control	9.11 \pm 1.60	
Cd	Workers	0.1362 \pm 0.0217	P<0.01
	Control	0.0925 \pm 0.0189	

Lead-(Pb): The results obtained, shown in Table (3), indicate the concentration of the lead element in workers' nails compared to the control group, where the concentration of lead in workers' nails was 14.57 \pm 2.50), and in the control group (9.11 \pm 1.60), (Figure 3). Statistically, there were significant differences (P <0.01) for the average concentration of lead in workers' nails compared to the control group. This is due to occupational exposure, which contributes to the absorption of minerals, and these results are like those reported by others.^{21, 22}

Cadmium-(Cd): The results obtained, shown in Table (3), showed the concentration of cadmium in workers ‘nails compared with the control group, where the concentration of cadmium in workers’ nails was 0.1362 ± 0.0217), and in the control group (0.0925 ± 0.0189), (Figure 2). Statistically, there were significant

differences ($P < 0.01$) on the average concentration of cadmium in workers’ nails compared to the control group. The reason for the high concentration of cadmium is due to the complex occupational exposure of the elements, and the results obtained are consistent with the findings.^{21, 22}

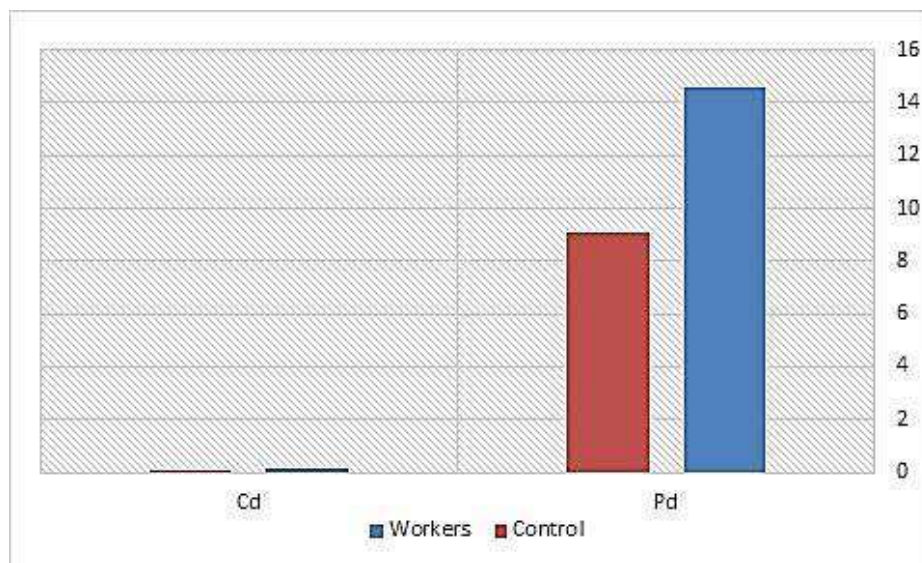


Figure 2. The concentration of heavy metals (Pb $\mu\text{g/dl}$, Cd $\mu\text{g/dl}$) in workers’ nail and control group.

Biochemical variables:

Estimation of oxidative and antioxidant concentrations in blood serum

Table (4): Concentration of Enzymes (SOD U/ML , MDA $\mu\text{mol/L}$) in the blood serum of workers and control group

Variables	Groups	Mean±SD	P-Value
SOD	Workers	30.7±3.1	P<0.05
	Control	49.3±10.5	
MDA	Workers	123.6±16.9	P<0.05
	Control	70.0±13.7	

The concentration of Superoxide dismutase (SOD) enzyme: The results of table (4) show the concentration of enzyme (SOD) in the serum of workers and the control group, where the concentration of enzyme in the serum of workers was (30.7 ± 3.1) which was lower than the control group was (49.3 ± 10.5), (Figure 4). Statistically, there were significant differences between the workers and the control group ($p < 0.05$). The reason for the decrease in the concentration of the enzyme SOD is that

it is common in contaminated environments because this enzyme is necessary to protect the body’s cells from free radicals and excessive oxygen that promote ageing or cell death.²³ Moreover, trace elements (Zn, Cu, Mg) are SOD components and are associated with antioxidant functions, so their deficiency may lead to poor control of free radicals, and all these elements are replaced by lead, which reduces the activity of (SOD).²⁴ The results obtained were in contrast with that reported in another study²⁵ and coincide with the others.^{17, 18, 26, 27}

Concentration Serum lipid peroxidation (MDA):

The results are shown in Table (4) indicate that the concentration of MDA in the serum of the workers (123.6 ± 16.9) was high in comparison to the control group (70.0 ± 13.7), (Figure 4). Statistically, there were significant differences between the workers and the control group ($p < 0.05$). The reason for this is that the rise in the level of heavy metals leads to the destruction of oxidative stress by increasing the production of free radicals (ROS), which reduces the system of antioxidant defence in cells and increase the concentration MDA.^{28,29} These results are consistent with other findings.^{17,18,26,30}

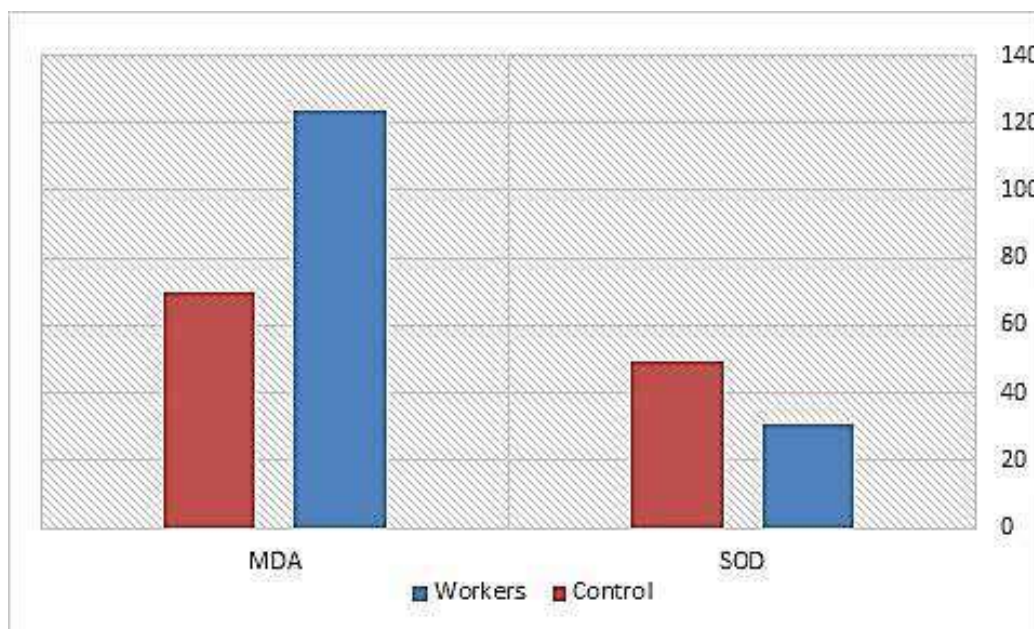


Figure 4. The concentration of Enzymes (SOD_{U/ML}, MDA _{$\mu\text{mol/L}$}) in the blood serum of workers and control group.

Conclusion

The results of this study concluded that the concentration of heavy metals (Pb, Cd) was high in the whole blood and nails of the workers in the North Gas Company. Moreover, the concentration of SOD enzyme in the blood and samples was low; the MDA was high in all samples of studied workers.

Conflict of Interest: None of the authors have any conflicts of interest to declare.

Source of Funding: The research was performed independently, there is no funding

Ethical Clearance: The project was approved by the local ethical committee in University of Kirkuk.

References

1. Bhagure, G. R. a Mirgane, S. R. . Heavy Metals Contaminations in groundwater and soils of Thane Region of Maharashtra, India, *Environ Mot Assess*, 2010; 1-10.
2. Aderinola, O.J., E. O. Clarke, O. M. Olarinmoya, V. Kusemiju and M. A. Anatekhai. Heavy Metals in Surface Water, Sediments, Fish and Perwinkles of Lagos. Lagoon. *American-Eurasian J.& Environ. Sci.*, 2009; 5(5), 609-617.
3. Yahaya A., Adegbe A. and Emurotu J. E. Assessment of Heavy Metals content in the Surface Water of Oke-Afa Canal Lsola Lagos, Nigeria. *Archives of Applied Science Research*, 2012; 4(6), 2322-2326.
4. Skaldina, O., & Sorvari, J. Ecotoxicological Effects of Heavy Metal Pollution on Economically Important Terrestrial Insects. In *Networking of Mutagens in Environmental Toxicology*, 2019; 137-144. Springer, Cham.]
5. Odum, H. T. Heavy metals in the environment: using wetlands for their removal, 2016. CRC Press.]
6. Nriagu JO. (1989). A global assessment of natural sources of atmospheric trace metals. *Nature*, 1989; 338:47-49.
7. Arruti A, Fernandez-Olmo I, Irabien A, Evaluation of the contribution of local sources to trace metals level in urban PM2.5 and PM10 in the Cantabria region (Northern Spain) *J Environ Monti*, 2010; 12(7):1451-1458.
8. Joshi, N. C. Biosorption: A green approach for heavy metals removal from water and waste waters. *RJLBPCS*, 2018; 4(1), 1-59.]
9. Bae S., Pan X., Kim S. et al. Exposures to particulate and polycyclic aromatic hydrocarbons and oxidative stress in school children, *Environ Health Perspect*, 2010; 118(4), 579-583 .
10. K. Bagchi. And S. Puri. Free radicals

- and antioxidants in healthy and disease. *Estranmediterrean health J.*, 1998; 4(2) ,pp: 350-360]
11. Burtis CA. and Ashwood ER. Tietz textbook of clinical chemistry «3rd ed. W.B. Saunders comp., 1999; Tokyo, 1034-1054.
 12. Haswell, S. J. Atomic absorption spectrometry Theory, Design And Application. 1991, Elsevier, Tokyo.
 13. Wilson, S. S., Guilan, R. A., &Hocker, E. V. Studies of the stability of 18 chemical constituents of human serum. *Clinical chemistry*, 1972; 18(12), 1498-1503.
 14. Abdulrahman, F. I., Akan, J. C., Chellube, Z. M., & Waziri, M. Levels of heavy metals in human hair and nail samples from Maiduguri Metropolis, Borno State, Nigeria. *World Environ*, 2012; 2(4), 81-89. 159.
 15. Bradl, H., Kim, C.,Kramar, U., &Stüben, D. Interactions of heavy metals. In *Interface science and technology*, 2005;6, 28-164.
 16. Tiwari, S., Tripathi, I. P., & Tiwari, H. L. Effects of lead onEnvironment. *International Journal of Emerging Research in Management &Technology*, 2013; 2(6).
 17. Azize S.Study of Heavy Metals and their effects on Oxidant/Antioxidant Status in Workers of fuel Station in Hilla city- Iraq . *Research J. Pharm . and Tech*, 2018; 11(1), 1-5 .
 18. Al-Fartosy, A. J., Awad, N. A., &Shanan, S. K. Biochemical Study of the Effects of Some Heavy Metals on Oxidant/Antioxidant Status in Gasoline Station Workers/Basra-Iraq . *Intarnational Journal of Scientific and Research*, 2017; 2(7), 83-88.
 19. Chen, G. C., Shan, X. Q., Wang, Y. S., Pei, Z. G., Shen, X. E., Wen, B., & Owens, G. Effects of copper, lead, and cadmium on the sorption and desorption of atrazine onto and from carbon nanotubes. *Environmental science & technology*, 2008; 42(22), 8297-8302.
 20. Pirsaraei, S. R. A. Lead exposure and hair lead level of workers in a lead refinery industry in Iran. *Indian journal of occupational and environmental medicine*, 2007; 11(1), 6.
 21. Al-Easawi N , Mahmood M , Hassoon H. Determination of heavy metal concentration in nail of car workshops workers in Baghdad. *Journal of American Science*, 2017; 13(6), 1-8 .
 22. Krishnamurthy, P., & Wadhvani, A. Antioxidant enzymes and human health. *Antioxidant enzyme*, 2012; 1-17.
 23. Negi, R., Pande, D., Karki, K., Kumar, A., Khanna, R. S., & Khanna, H. D. Trace elements and antioxidant enzymes associated with oxidative stress in the pre-eclamptic/eclamptic mothers during fetal circulation. *Clinical nutrition*, 2012; 31(6), 946-950]
 24. Gerli, G., Locatelli, G. F., Mongiat, R., Zenoni, L., Agostoni, A., Moschini, G., ... &Tarolo, G. Erythrocyte antioxidant activity, serum ceruloplasmin, and trace element levels in subjects with alcoholic liver disease. *American journal of clinical pathology*, 1992; 97(5), 614-618.
 25. Al-Fartosy, A. J., Awad, N. A., &Shanan, S. K. Biochemical correlation between some heavy metals, malondialdehyde and total antioxidant capacity in blood of gasoline station workers. *Int Res J Environment Sci*, 2014; 3(9), 56-60.
 26. Dewi, N. K., &Yuniastuti, A. Superoxide Dismutase Levels of Operator Gas Stations in Semarang, Central Java, Indonesia. *KnE Life Sciences*, 2017; 3(5), 167-172.
 27. Hussain S., Atkinson A., Thompson S.J. and Khan A.T. Accumulation of mercury and its effect on antioxidant enzymes in brain, liver and kidneys of mice, *J. Environ. Sci. Heal. B*, 1999;34(4), 645-660.
 28. Whaley-Connell A., McCullough P.A. and Sowers J.R. The role of oxidative stress in the metabolic syndrome, *Rev. Cardiovasc. Med.*,2011; 12, 21-29.
 29. Al-Fartosy, A. J., Awad, N. A., &Shanan, S. K. Biochemical correlation between some heavy metals, malondialdehyde and total antioxidant capacity in blood of gasoline station workers. *Int Res J Environment Sci*, 2014; 3(9), 56-60]
 30. Signori, V. Review of the current understanding of the effect of ultraviolet and visible radiation on hair structure and options for photoprotection, *Cosmet. Sci*, 2004; 55 ,95–113.

Dominant Factor Analysis of Medical Equipment and Device Affect Against Customers' Repeat Purchase Decision

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Abstract

This study is an attempt to identify what factors will affect customer to buy or do a repeat order of health equipment from them. Factors that define customer satisfaction are price, distribution channel, product quality, and service quality that will affect repeat purchase decision. Data were collected using observation and questionnaire method. A questionnaire sampling method was applied to 100 respondents. Data that has been collected was tested and processed with multiple regression analysis and sobel test method. This study has found that price and service quality affect customer satisfaction and customer satisfaction affect repurchase decision.

Keywords: Price, distribution channel, product quality, service quality, repurchase decision.

Introduction

Based on information taken from export.gov (2016), the market for medical equipment is very competitive market in Indonesia, one of the leading suppliers with shares above 10% in 2016^[1]. Other countries competing for market share of medical devices and equipment in Indonesia included are China, Germany, Japan, Korea and the Netherlands. Medical equipment products from China and Korea have the biggest markets in Indonesia. Unlike other ASEAN regulatory systems, before entering the Indonesian health market foreign markets must establish investment companies that cooperate in the form of PT or appoint local agents and distributors who can be trusted to serve the Indonesian market. Because only through local agents and distributors who can handle product registration and play an important role in developing the market in Indonesia^[2].

With the development of health services in Indonesia, the need for health equipment facilities in Indonesia is rapidly increasing. Health institutions continue to demand medical equipment to complete their facilities, so that a supply of medical devices is needed to meet the demand of a variety of health institution^[3]. The demand of medical devices in Indonesia is one of the businesses that is prestigious and will certainly lead to competition between companies in the same field. The company needs to be certain what are their customer need and pitch their products to win the competition^[4].

Based on the facts above, we tried to conduct a research to find out and identifies what are the driving factors that influence the customers repeat purchase decision? and what is the most influential factors that affect customers re-purchase decisions?

Hypothesis

H1 Ho: There is no significant effect between the price variable (X1) on Customer Satisfaction (Y1).

Ha: There is a significant effect between the price variable (X1) on Customer Satisfaction (Y1).

H2 Ho: There is no significant effect between the Distribution Channel variable (X2) on Customer Satisfaction (Y1).

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Ha: There is a significant effect between the Distribution Channel variable (X2) on Customer Satisfaction (Y1).

H3 Ho: There is no significant influence between the Product Quality variable (X3) on Customer Satisfaction (Y1).

Ha: There is a significant influence between the Product Quality variable (X3) on Customer Satisfaction (Y1).

H4 Ho: There is a significant difference between service quality (X4) against Customer Satisfaction (Y1).

Ha: There is a significant influence between service quality (X4) against Customer Satisfaction (Y1).

H5 Ho: There is no significant effect between the Customer Satisfaction variable (Y1) on Repurchase Interest (Y2).

Ha: There is a significant effect between the Customer Satisfaction variable (Y1) on Repurchase Interest (Y2).

Method

Survey and observation are utilized on this research. The study setting used is realtime situation, hence author is not altering any environment in the research and the result are purely from natural activities (non-contrived) [5,7,8]. This research was conducted only in one occasion, within a period of time selected (one shot). While the

data was collected by 2 method, the first is observation to know the past transaction that occurred before and see the pattern to be analyzed as a base foundation of hypothesis. To get the primary data, researchers require the do a survey while the secondary data can be obtained by visiting the library, study centers, archives or read many books related to the research. The second method is questionnaire. The measurement of all factors has been conducting using a 4-point Likert scale (1 = strongly disagree to 4= strongly agree). The final questionnaire was addressed to the selected past customer that we have done transaction with the company before. The size of the sample was 100 customers in Jakarta. The questionnaire contains 23 questions.

Result

Validity, Reliabilty, Normality: Based on the analysis using *Pearson product moment* obtained the results of validity for all instruments in this study $r^{count} >$ table, that can be concluded that the instrument in this study is valid. Based on the reliability test analysis on each of the independent and dependent variables, the results show that each variable gives a Cronbach alpha value > 0.60 , it can be concluded that the instrument in this study is reliable. Unstandardized Residual (Y1) dan Unstandardized Residual (Y2) data with Kolmogorov-Smirnov (Sig) > 0.05 so it can be concluded that the data is normally distributed.

a. Model 1:

Table 1. Result of F Test Model

ANOVA ^a					
Model	Sum of Squares	df	Mean Square	F	Sig.
Regression	4,207	4	1,052	89,187	,000 ^b
Residual	1,120	95	,012		
Total	5,328	99			

a. Dependent Variable: Customer Satisfaction, b. Predictors: (Constant), Service Quality, Distribution Chanel, Price, and Product Quality

Hypothesis:

Ho: There is no significant effect simultaneously between price (X1), Distribution Channels (X2), Product Quality (X3) and Service Quality (X4) on Customer Satisfaction (Y1).

Ha: There is significant effect simultaneously between price (X1), Distribution Channels (X2), Product Quality (X3) and Service Quality (X4) on Customer Satisfaction (Y1).

Conclusion

F-count 89,187 > F-table 2,47 → Ho rejected

b. Model 2:

Table 2. Result of F Test Model 2

ANOVA ^a					
Model	Sum of Squares	df	Mean Square	F	Sig.
Regression	301,296	1	301,296	465,260	,000 ^b
Residual	63,464	98	,648		
Total	364,760	99			

a. Dependent Variable: Re-purchase interest, b. Predictors: (Constant), Customer satisfaction

Hypothesis:

Ho: There is no simultaneous significant effect between the Customer Satisfaction (Y1) on Repurchase Interest (Y2).

Ha: There is simultaneous significant effect between the Customer Satisfaction (Y1) on Repurchase Interest (Y2).

Conclusion

F-count 465,260 > F-table 3,94 → Ho rejected

There is simultaneous significant effect between the Customer Satisfaction (Y1) on Repurchase Interest (Y2)^[21].

2. Multiple Regression Test

a. Model 1:

Table 3. Multiple Regression Test Model 1

Coefficients ^a					
Model	Unstandardized Coefficients		Standardized Coefficients	T	Sig.
	B	Std. Error	Beta		
(Constant)	,996	,093		10,705	,000
Price	,095	,006	,820	15,485	,000
Distribution Chanel	,002	,006	,020	,391	,697
Product Quality	,002	,004	,030	,550	,584
Service Quality	,017	,004	,191	3,971	,000

a. Dependent Variable: Customer Satisfaction

Multiple Regression Test Model 1:

$$Y_1 = 0,996 + 0,095X_1 + 0,002X_2 + 0,002X_3 + 0,017X_4$$

From the regression equation model 1 above it can be concluded that:

1. The constant coefficient 0 of 0.996 states that without the Price (X1), Distribution Channels (X2), Product

Quality (X3) and Service Quality (X4) variables, the Customer Satisfaction value (Y1) is 0.996.

- The coefficient of constant 1 worth + 0.095 states that the influence between Price (X1) and Customer Satisfaction (Y1) is positive.
- The coefficient of constant 2 is + 0.002 stating that the influence between Distribution Channels (X2) and Customer Satisfaction (Y1) is positive.

- 4. The coefficient of constant 3 value + 0.095 states that the influence between Product Quality (X3) and Customer Satisfaction (Y1) is positive.
- 5. The constant coefficient 4 is + 0.017 stating that the influence between Service Quality (X4) and Customer Satisfaction (Y1) is positive.

Hypothesis:

H1: Effect of Price (X1) on Customer Satisfaction (Y1)

Hypothesis:

Ho: There is no significant effect between the price variable (X1) on Customer Satisfaction (Y1).

Ha: There is a significant effect between the price variable (X1) on Customer Satisfaction (Y1).

Sig = 0,000 < 0,05 and t count 15,485 > t table 1,66 → Ho rejected

H2: Effect of Distribution Channels (X2) on Customer Satisfaction (Y1)

Hypothesis

Ho: There is no significant effect between the Distribution Channel variable (X2) on Customer Satisfaction (Y1).

Ha: There is a significant effect between the Distribution Channel variable (X2) on Customer Satisfaction (Y1).

Sig = 0,0697 > 0,05 and t count 0,391 < t table 1,66 → Ho accepted

H3: Effect of Product Quality (X3) on Customer Satisfaction (Y1)

Hypothesis

Ho: There is no significant influence between the Product Quality variable (X3) on Customer Satisfaction (Y1).

Ha: There is a significant influence between the Product Quality variable (X3) on Customer Satisfaction (Y1).

Sig = 0,584 > 0,05 and t count 0,550 < 1,66 → Ho accepted

H4: Effect of Service Quality (X4) on Customer Satisfaction (Y1)

Hypothesis

Ho: There is no significant influence between Service Quality variables (X4) on Customer Satisfaction (Y1).

Ha: There is a significant influence between Service Quality variables (X4) on Customer Satisfaction (Y1).

Sig = 0,000 < 0,05 and t count 3,971 > t table 1,66 → Ho rejected

b. Model 2

Table 4. Multiple Regression Test Model 2

Model	Coefficients ^a				
	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
(Constant)	-7,414	,757		-9,795	,000
Customer Satisfaction	7,520	,349	,909	21,570	,000

a. Dependent Variable: Repurchase Interest

Multiple Regression Test Model 2:

$Y_2 = -7,414 + 7,520Y_1$: The constant coefficient is negative -7.414 stating that by assuming the absence of the variable customer satisfaction (Y1), the interest in repurchasing tends to decrease by 7,414 units.

Hypothesis:

H5: Effect of Customer Satisfaction (Y1) on Repurchase Interests (Y1)

Hypothesis:

Ho: There is no significant effect between the Customer Satisfaction variable (Y1) on Repurchase Interest (Y2).

Ha: There is a significant effect between the Customer Satisfaction variable (Y1) on Repurchase Interest (Y2).

Sig = 0,001 < 0,05 and t-count 21,570 > t-table 1,66 → Ho rejected

3. Coefficient of Determination (R2)

Table 5. Coefficient of Determination Test

Model	R	R-sq	Adj R-sq	SE estimates
Model 1	,889 ^a	,790	,781	,10860
Model 2	,909 ^a	,826	,824	,805

The Adjusted R Square value in model 1 is 0.781. It means that 78.1% that the independent variables

such as price, Distribution Channels, product quality and service quality are able to explain the variables that occur in the variable customer satisfaction. While the remaining 21.9% is explained by factors outside the research variable. Likewise, the Adjusted R Square value in model 2 is 0.824, which means that 82.4% that the independent variable which is customer satisfaction can explain the dependent variable, namely the interest in repurchasing. While the remaining 17.6% is explained by factors outside the research variable.

4. Sobel Test (Mediation Test): In this study, the authors conducted a sobel test by using the Online Sobel Test Calculator^[22] for the Significance of Mediation from Daniel Soper at www.danielsoper.com to assess whether the tested variables were intervening variables that could mediate *P-value* < 0,05 or sobel test statistic > t-table 1,66

Table 6. Result of Sobel Test

Indirect Influence	Sobel test statistic	P-Value
Price → Customer Satisfaction → Repurchase Interest	12,759	0,000
Distribution Channel → Customer Satisfaction → Repurchase Interest	0,333	0,369
Product Quality → Customer Satisfaction → Repurchase Interest	0,499	0,308
Service Quality → Customer Satisfaction → Repurchase Interest	4,169	0,000

From the description of the sobel test above, it can be concluded that customer satisfaction can mediate the effect of variable prices and service quality on the repurchase interest.

Discussion

Price (X1) affects customer satisfaction (Y1): Based on the results of partial regression test, obtained a value of t-count (15.485) is greater than t-table (1.66) with sig 0.000, where the value of sig ≤ 0.05. Then, it can be stated that Ha is accepted which means that prices have a positive and significant effect on customer satisfaction.

Distribution Channels (X2) affect customer satisfaction (Y1): Based on partial regression test, obtained t-count is 0.391 (< t-table 1.66) with sig 0.697 (> 0.05). It means that Distribution Channels do not have a positive and significant effect on customer satisfaction.

This is contrary to previous research conducted, Tonny Sopan, et al. (2014: 10), that there is a significant effect of Distribution Channels on Customer Satisfaction.

Product Quality (X3) affects customer satisfaction (Y1): Based on partial regression test, obtained t-count is 0.550 (< t-table 1.66) with sig 0.584 (> 0.05). It means that product quality does not have a positive and significant effect on customer satisfaction. This is contrary to previous research conducted by Tristiana (2016: 21) that product quality has a positive and significant effect on customer satisfaction and research conducted by Putri and Astuti (2017: 8) that product quality has a positive and significant effect on customer satisfaction.

Service Quality (X4) has an effect on Customer Satisfaction (Y1): Based on partial regression test, obtained t-count is 3.971 (> t-table 1.66) with sig 0,000 (< 0.05). It defines that service quality has a positive

and significant effect on customer satisfaction. This is confirmed by previous research conducted by Putri and Astuti (2017: 8) that there is a service quality that has a positive and significant effect on customer satisfaction.

Customer Satisfaction (Y1) has an effect on Repurchase Interest (Y2): Based on partial regression test, obtained t-count is 21.590 ($> t$ -table 1.66) with sig 0.000 (< 0.05). It defines that Customer Satisfaction has a positive and significant effect on Repurchase Interest. This is reinforced by previous research conducted by Putri and Astuti (2017: 8) that customer satisfaction has a significant and positive effect on interest in repurchase.

Conclusions

Based on the data that has been collected and through the testing process with multiple regression analysis and sobel test method, we can know that distribution channels and product quality do not have a significant effect on customer satisfaction while price and service quality have a positive effect on customer satisfaction that influence customer to make repurchase decision^[23].

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Ethical Clearance: Taken from Jakarta Hospital Ethics Committee for Health Research, 11/03/2019, ref: 19/Panke.KKE/IX/2019. Further, all the subjects on this research are agreed to fill the consent form for this publication.

References

- Chinomona, R., & Dubihlela, D. Does customer satisfaction lead to customer trust, loyalty and repurchase intention of local store brands? The case of Gauteng Province of South Africa. *Mediterranean Journal of Social Sciences* MCSER Publishing, Rome-Italy. 2014; Vol. 5, No. 9.
- Direktorat Jenderal Kefarmasian dan Alat Kesehatan. *Aplikasi info alat kesehatan & PKRT*. 2018. Retrieved from <http://infoalkes.depkes.go.id>
- Ghezelbash, S., & Khodadi H. Evaluating the impact of promotion price, product quality, service quality, customer satisfaction and repeating purchase incentives (Case study: Amiran chain stores). *Journal of Internet Banking and Commerce*. 2017; Vol. 22, No. S8.
- Gomes, M. & Fernandes, T. & Brandão, A. Determinants of brand relevance in a B2B service purchasing context. *Journal of Business & Industrial Marketing*, 2016; Vol. 31 Iss 2 pp. 193 – 204
- Hamdan, H., Issa, Z. M., & Jusoff, K. Purchasing decisions among Muslim consumers of processed halal food products. *Journal of Food Products Marketing*. 2013; 19:54–61.
- Isaac, S., & Michael, W. B. *Handbook in research and evaluation: A collection of principles, method, and strategies useful in the planning, design, and evaluation of studies in education and the behavioral sciences*. (3rd Ed.). San Diego: Educational and Industrial Testing Services. 1997.
- Kellar, G. M., & Preis, M. W. *Academy of Information & Management Sciences Journal*. 2011; 14(2).
- Kementerian Kesehatan RI. *Rencana aksi kegiatan-tahun 2015 – 2019, Direktorat Jenderal Bina Kefarmasian dan Alat Kesehatan*. 2015. Retrieved from <http://www.kemkes.go.id/>
- Khuong, M. N., & Duyen, H. T. M. Personal factors affecting consumer purchase decision towards men skin care products: a study in Ho Chi Minh city, Vietnam. *International Journal of Trade, Economics and Finance*. 2016; Vol. 7, No. 2.
- Lin, S. J., Li, C. H., & You, C. S. Consumer behavior and perception of marketing strategy for amusement parks: A case study of Taiwan. *African Journal of Business Management*. 2012; Vol. 6(14), 4795-4803. L23
- Loukas, A., & Kavala. Purchase decisions of Greek consumers: An Empirical Study. *Iason Papafotikas et al./Procedia Economics and Finance*. 2014; 9, 456 – 465.
- Naumann, Earl; Williams, Paul; Khan, M. Sajid. Customer satisfaction and loyalty in B2B services: directions for future research. *The Marketing Review*, 2009; 9.4: 319-333.
- Khan, M. Sajid; Naumann, Earl; Williams, Paul. Identifying the key drivers of customer satisfaction and repurchase intentions: An empirical investigation of Japanese B2B services. *Journal of Consumer Satisfaction, Dissatisfaction and Complaining Behavior*, 2012; 25.3: 159-178.
- Oktaviani, N. Pengaruh-pengaruh kualitas pelayanan terhadap minat pembelian ulang. *E-Proceeding of*

- Management. 2015; Vol. 2, No.3.
15. Pohan, M., & Halim, R. Analisis ketersediaan infrastruktur kesehatan dan aksesibilitas terhadap pembangunan kesehatan penduduk di provinsi Sumatera Utara. *Jurnal Ilmu Ekonomi dan Studi Pembangunan*. 2016; Vol. 16, No. 1.
 16. Purnamasari, Y., & Suwena, K. R., & Haris, I. H. Pengaruh kualitas produk dan harga terhadap kepuasan konsumen produk M2 Fashion Online di Singarajata tahun 2015. *Jurnal Jurusan Pendidikan Ekonomi Undiksha*. 2016; Vol. 5, No. 1.
 17. Simbolon, F. Strategi pemasaran global di pasar Indonesia. *Binus Business Review*. 2013; Vol. 4, No. 1.
 18. Supiyadi, D. Strategi mengelola hubungan pelanggan B2B. Skripsi S2. Universitas Pendidikan Indonesia, Bandung. 2016.
 19. Suroto, K. S., Fanani, Z., & Nugroho, B. A. Factors influencing consumer's purchase decisions of formula milk in Malang city. *IOSR Journal of Business and Management*. 2013; Vol 9, Issue 3, 95-99.
 20. Uddin, M. R., Lopa, N.Z., & Md. Oheduzzaman. (2014). Factors affecting customers' buying decisions of mobile phone: A study on Khulna city, Bangladesh. *International Journal of Managing Value and Supply Chains (IJMVSC)*. 2014; Vol.5, No. 2.
 21. International Trade Administration. (n.d.). Healthcare Resource Guide: Indonesia. 2016. Retrieved from https://2016.export.gov/industry/health/healthcareresourceguide/eg_main_092295.asp.
 22. Yang, C., Chun, C. Gender and internet consumers' decision-making. *Cyberpsychology & Behavior*. 2007; Vol 10, Number 1. L24
 23. Yanuar, M. M., & Qomariah, N., & Santoso, B. Dampak kualitas produk, harga, promosi, dan kualitas pelayanan terhadap kepuasan pelanggan Optik Marlin cabang Jember. *Jurnal Manajemen Dan Bisnis Indonesia*. 2017; Vol. 3, No. 1.

Multimodal Hyperspectroscopy for Detection of Cervical Neoplasia

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Abstract

Objective: To provide a prospective evaluation of the sensitivity and specificity of MHS as a new test for detection of high grade cervical dysplasia.

Method: 203 women previously screened with liquid based cytology were evaluated with multimodal hyperspectroscopy (MHS), colposcopy and biopsy samples taken for histopathology.

Results: Sensitivity of MHS cervical scan for high grade intraepithelial neoplasia (CIN) 2+ was 86.6% and Specificity was 57.9%

Conclusions: MHS cervical scan is a noninvasive modality for detection of high grade cervical neoplasia with good efficacy.

Keywords: CIN, cervical cancer screening, multimodal hyperspectroscopy.

Introduction

Cervical cancer is the fourth most common female cancer worldwide.^[1] Pap smear and colposcopy are widely-used method for the detection of cervical cancer. 80% of all cervical cancer deaths are reported in developing countries, where these tests are not routinely practiced.^[2] This emphasizes the importance of effective screening and early detection techniques. However, the existing screening techniques have been shown to suffer from high false results, which could be attributed to the subjective interpretations and may lead to more unnecessary referrals^[3].

One of these approaches is light spectroscopy.^[4] Spectral imaging appears to be a powerful approach which is starting to become applied to medicine^[5] after it has been largely exploited in other areas, such as

mineralogy, remote sensing, drugs screening and food qualification^[6]. In fact, spectral imaging appears to be successful in distinguishing between tumor and normal tissues^[7], and has been used to study skin lesions^[8] and breast cancer^[9].

While cytology testing relies on morphological and staining patterns, biospectroscopy records the spectral information from tissues reflecting its biochemical composition at molecular levels, which occur before the changes in morphology are seen under the light microscope^[10].

Reflectance spectroscopy allows determination of the scattering and absorption properties of a turbid medium such as tissue. It indicates the presence of structural changes within tissue (cell size, arrangement and organelle density, Neoangiogenesis).^[11]

The fluorescence spectroscopy identifies metabolic changes associated with neoplasia. Intrinsic fluorophores can absorb light at different wavelengths and re-emit it, the most common fluorophores include collagen, elastin, tyrosine, nicotinamide Adenine Dinucleotide (NADH) and Flavin Adenine Dinucleotide (FAD).^[12] combining optical imaging techniques, referred to as

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multimodal imaging, allows for an improved diagnostic reliability due to the complementary nature of retrieved information [5].

Multimodal spectroscopy was implemented in a cost effective new device LuViva® that can be easily operated by trained medical personnel. It is supposed to have The advantage of early detection of cervical neoplasia^[13].

Aim of the work: To provide a prospective evaluation of the performance of MHS for detection of high grade cervical dysplasia

Methodology: This study included 203 women screened using liquid based cytology. a participant considered eligible for the study if they were 21 years old or above, and willing to undergo MHS cervical scan, colposcopy and biopsy. Patients were excluded if they had any pregnancy, menstruating, prior hysterectomy, congenitally abnormal cervix, or excessive blood or mucus in the examination field that cannot be removed.

Each participant had full history and clinical examination had been undertaken.

Cervical spectroscopy was performed using a noninvasive device (LuViva, Guided Therapeutics, Inc. Norcross, GA, USA). The system consisted of : base unit (light source, computer and monitor), handheld unit (optical systems), and the sight tube, (a hollow tube that is inserted into the vagina through a speculum).

The device collects and analyses fluorescence and reflectance spectra from the cervix without contrast agents. Light from the arc lamp is band passed, filtered to limit exposure of the cervix to three distinct color regions at wavelengths of 340 nm, 400nm and 460 nm, which excites fluorophores associated with neoplastic processes.

The resultant spectral output is imaged onto a charge coupled camera and stored for processing and analysis. In addition, the device contained a separate colposcopy quality imaging channel.

While patient in lithotomy position, speculum inserted, mucus or blood was removed by suction. the sight tube attached to the device to set the distance between the cervix and device while blocking ambient light. After calibrating the device, the tube was inserted into the vagina. This process was viewed on a monitor screen to ensure proper positioning and focus. Scan was

performed in a 1 minute procedure.

The output results were color coded : - Green (Low risk): negative, further evaluation is not necessary - Orange (Moderate risk): other medical factors should be considered before further evaluation - Red (High risk): positive, further evaluation is necessary.

Then, a conventional colposcopy with 5% acetic acid was performed. endocervical curettage was performed for subjects that had LSIL or HSIL cytology. Then , biopsy from the ectocervix from abnormal areas or from the quadrants if no obvious abnormality was observed. Biopsy specimens were sent to histopathology.

Results

Study included 203 cases with mean age of 42.80 ±8.5 years and parity of 3.2±1.5. participants were subjected to MHS cervical scan based on different indications, 88 case (43.3%) were referred following result of abnormal cytology, 22 cases (10.84%) had history of contact bleeding, 26 cases (12.8%) were referred due to suspicious cervix, 3 cases were presented for follow up after LEEP biopsy for CIN 1, another 2 with mastectomy, one case known as HIV patient. And 61 cases (30%) were referred for routine screening. 11 cases had history of HPV infection, none of the included cases had history of HPV vaccination.

Cytology was normal in 46.7%, ASCUS was the most prevalent abnormality found in 22.6% , followed by ASCUH (8.9%) then LISL and HSIL (10.8% and 6.4%). and one case with AGC.

Colposcopy was negative in 60.1% of cases, 24 cases (11.82%) showed signs of chronic infection while CIN was detected in 32 cases (15.76%). Unsatisfactory colposcopy in 4 cases (1.97%), Acetowhite areas and abnormal vascularity were seen in 15 and 6 cases respectively.

For MHS: 108 cases were low risk (53.2%), 27 cases were with moderate risk (13.3%), and 65 cases were with high risk for cervical neoplasia (32%).

Test failed in 3 cases (1.48%) due to failed visualization of the cervix. 2 of them due to excessive blood, the device reported “poor contact”, the 3rd case failed due to abnormal light reflection from the threads of IUCD, the device reported “excessive light” . although, the test was performed in many cases with IUCD with no errors.

Normal histopathology was reported in 45.81% of cases, benign conditions included: inflammatory changes (17.73%), polyps (3.45%), and metaplastic changes (11.33%). CIN 1 in 29 case (14.29%), and CIN2+in 15 cases (7.39%).

MHS was “high” in 46% of cases with abnormal cytology, while it was ‘low’ in 67.9% of cases with normal cytology.

Table 1: MHS correlated to cytology

MHS	Cytology						Total
	Negative	ASC-US	ASC-H	LSIL	HISIL	AGC	
Low	70	17	5	11	4	1	108
Moderate	12	8	2	2	3	0	27
High	19	21	10	9	6	0	65
Failed	2	0	1	0	0	0	3
Total	103	46	18	22	13	1	203

MHS reported high risk in 72.72% of abnormal colposcopic findings, it showed low risk in 70.83% of cases with normal colposcopy.

Table 2: MHS correlated to colposcopy

MHS	Colposcopy			Total
	Normal	Abnormal	Unsatisfactory	
Low	102	6	0	108
Moderate	17	8	2	27
High	23	40	2	65
Failed	2	1	0	3
Total	144	55	4	203

MHS was found ‘high’ in 30 cases out of 44 cases of dysplasia (75%). Adding the moderate risk MHS as a positive screening result, so 39 case were considered as positive out of 44 (88.6%).

In cases with severe dysplasia (CIN2+) MHS was positive in 13 case out of 15 (86.6)

Table 3: MHS correlated to histopathology

MHS	Histopathology				Total
	Benign	AGC	CIN1	CIN2+	
Low	104	1	2	1	108
Moderate	18	0	6	3	27
High	35	0	20	10	65
Failed	2	0	0	1	3
Total	159	1	28	15	203

Sensitivity of MHS for detection of 'any' dysplasia was 88.63%, and it had a specificity of 67.94%, with PP and NP values of 42.39% and 95.49% respectively

For high grade lesions (CIN 2+) MHS had a 86.66% Sensitivity, 57.97% specificity, 14.13% PPV and 98.19% NPV. Excluding the failed cases increased the sensitivity to 92.85%, with 58.6% specificity, 14.44% PPV, and 99% NPV

Combining cytology and MHS results, The sensitivity raised to 100% for high grade lesions.

One case was examined post LEEP biopsy, reported as high risk with MHS despite being negative histopathology.

Using the kappa test, cervical spectroscopy showed 56.3% agreement with liquid-based cytology, and 74.5% with colposcopy, with high significance ($p=0.001$).

Discussion

This study included 203 women presented to the outpatient clinic either for primary (routine) screening or secondary screening or to be followed after treatment of cervical neoplasia.

We included this category of patients to our study for research reasons, as colposcopy and biopsy are parts of our evaluation.

In this study, The Sensitivity of MHS for detection of any degree of dysplasia was 88.63%, and its specificity was 67.94%. While, For high grade lesions MHS cervical scan had a little lower Sensitivity (86.66%), but much lower specificity (57.97%).

Several previous studies examined the performance of cervical spectroscopy using histopathology as a gold standard endpoint

The early pre-clinical trials, the largest was carried on 572 patients, The sensitivity was 95.1% for CIN2+ with a corresponding 55.2% specificity for benign lesions.^[14]

A study of 113 women, compared results of cervical spectroscopy and HPV testing, concluded that Spectroscopic scanning of the cervix is equally sensitive (95%), and 2-fold more specific than HPV testing (66%, 27% respectively). Thus the use of cervical spectroscopy may reduce the number of false positive HPV test

results.^[15]

The largest phase 3 study was carried on 1850 women either presented for regular screening or referred for colposcopy, the sensitivity of MHS was 100% for detection of high grade lesions, 71% specificity. The device performance was best in the diagnostic rather than screening population^[16]

A multi-centre study of 1,607 women with positive cervical screening test; compared the results of HPV testing, colposcopy and biopsy, with MHS. The Sensitivity of MHS for CIN2+ was 91.3%, the potential reduction in referrals to colposcopy and biopsy was 38.9% for women with benign histology and 30.3% for women with CIN1^[17]. In a complimentary study by the same authors, 802 women were followed up for two years. MHS identified 89.6% of CIN2 + prior to their discovery during the follow-up period. They concluded that MHS as a triage would have reduced the need for further testing.

In our results MHS showed better performance in low grade lesions than with high grade lesions, This is in contrast to the results reported by *Twiggs et al* who found higher performance of MHS in higher grade lesions^[17]. But in our study there was one case of CIN 2 which was missed due to test failure, which considered as false negative and it affected the test performance.

Combining cytology and MHS results for detection of high grade cervical lesions, The sensitivity raised to 100%. this is in agreement with results from the study by *Werner et al.*^[15] however, *Twiggs et al.* combined both test results and found no increase in the sensitivity but the specificity increased by 30% in detection of neoplasia^[17].

Also, *Louwers et al.* studied the colposcopic dynamic spectral imaging in 275 women, they reported sensitivity of 79% in detection of high grade lesions, and 77% specificity, while sensitivity of conventional colposcopy was only 55%, combining both test results gave higher sensitivity 88% but lower specificity 69%^[18]

post launch trials reported variable results. in a pilot study by *Adewole et al.*^[19] the sensitivity of MHS was 92.3%. MHS reduced the percentage of unnecessary colposcopy and biopsy by 37.5%.

Another report indicated that LuViva performed with a specificity of 87% in a screening population and

it had potential as primary screening tool, especially in areas with no infrastructure for cervical cancer screening^[20]. However, *Cantor et al.* reported that the device performed best in diagnostic population.^[21]

In the current work, findings of MHS showed better agreement with those of colposcopy (74.5%) than with liquid-based cytology (56.3%).

In a recent study with similar methodology, good correlation between spectroscopy and both cytology and colposcopy was noticed (79.3%, 47.9% respectively)^[13].

In our study, 3 cases were examined for follow up after LEEP cervical biopsy, one of them had false positive result by MHS. It was noticed that this case was scanned no more than 6 months after the procedure. This may be attributed to the distorted anatomy in the early post-operative period.

In the current work one case with AGC by cytology underwent fractional endometrial curettage and cervical cone biopsy, histopathology reported CGIN. While it was reported as low risk by MHS. It puts a question on the ability of the device to detect endocervical lesions. However, other reports recorded high sensitivity for intracervical lesions up to 100%. As that by *Wade et al.* they reported that the emerging light can penetrate and detect the deep epithelial, superepithelial or endocervical lesions in contrast to cytology which only smears the superficial layers of cells.^[22]

Conclusions

MHS cervical scan had good efficacy in detection of high grade cervical neoplasia. It may be used as a triage for women who have low grade cervical cytology. And it can be used as screening tool for routine screening.

Ethical Statement: The material has not been published anywhere. Authors of the manuscript have no financial ties to disclose and have met the ethical adherence.

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Declaration of Authorship: All authors have directly participated in the planning, execution, analysis or reporting of this research paper. All authors have read and approved the final version of the manuscript.

References

1. World Health Organization (February 2014). "Fact sheet No. 297: Cancer". 2014-06-24. http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx
2. Torre LA, Bray F, Siegel RL. Global cancer statistics, 2012. *CA Cancer J Clin* 2015; 65:87.
3. Koliopoulos G, Nyaga VN, Santesso N. Cytology versus HPV testing for cervical cancer screening in the general population. *Cochrane Database Syst Rev*. 2017;8(8): 1-119.CD008587.
4. Gajjar K, Ahmadzai AA, Valasoulis G, Trevisan J. Histology Verification Demonstrates That Biospectroscopy Analysis of Cervical Cytology Identifies Underlying Disease More Accurately than Conventional Screening: Removing the Confounder of Discordance. *PLoS ONE* 2013; 9(1): e82416.
5. Vogler N, Heuke S, Bocklitz TW, Schmitt M. Multimodal Imaging Spectroscopy of Tissue. *Annu Rev Anal Chem (Palo Alto Calif)*. 2015;8:359-87.
6. Guolan Lua, Baowei Fei. Medical hyperspectral imaging: a review. *J Biomed Opt*. 2014; 19(1): 1-23.
7. Riccardo Cicchi, Suresh Anand, Riccardo Fantechi, Flavio Giordano, Valerio Conti, Gabriella Nesi. Multimodal fiber-probe spectroscopy as a clinical tool for diagnosing and classifying biological tissues. *Clinical and Preclinical Optical Diagnostics*. SPIE 10411, (2017); doi.org/10.1117/12.2283278
8. Moy, Austin, Feng, Xu, Markey, Mia, Reichenberg, Tunnell, James. Noninvasive skin cancer diagnosis using multimodal optical spectroscopy. *Photonic Therapeutics and Diagnostics*. 2016; 9689: 1605-7422.
9. Alchab L, Dupuis G, Balleyguier C, Mathieu MC, Farcy R. Towards an optical biopsy for the diagnosis of breast cancer in vivo by endogenous fluorescence spectroscopy. *J Biophotonics*. 2010 ;3(5-6):373-84.
10. Kelly JG, Angelov PP, Trevisan J, Vlachopoulou A, Paraskevaidis. Robust classification of low-grade cervical cytology following analysis with ATRFTIR spectroscopy and subsequent application of self-learning classifier. *Anal Bioanal Chem*. 2010; 398: 2191–2201.

11. Tatiana Novikova. Optical techniques for cervical neoplasia detection. *Beilstein J Nanotechnol.* 2017; 8: 1844–1862.
12. Drezek R, Brookner C, Pavlova I, Boiko I, Malpica A. Autofluorescence microscopy of fresh cervical tissue sections reveals alterations in tissue biochemistry with dysplasia. *Photochem Photobiol.* 2001;73:636–41
13. Trahmono, Lusiana, Indarti. The performance of multimodal hyperspectral spectroscopy in the detection of precancerous cervical lesions. *J. Phys.: Conf. Ser.* 2017; 884: 012152.
14. DeSantis T, Chakhtoura N, Twiggs L, Ferris D, Lashgari M, Flowers L. 2007 Spectroscopic imaging as a triage test for cervical disease: A prospective multicentre clinical trial. *J. Low. Gen. Tract. Dis.* 11 18-24.
15. Werner L., Griffith F., Ashfaq R, Wilkinson E, Faupel M. Comparison of Human Papilloma Virus Testing and Spectroscopy Combined With Cervical Cytology for the Detection of High-grade Cervical Neoplasia. *Journal of Lower Genital Tract Disease.* 2007; 11(2):73-79
16. Cantor SB, Yamal JM, Guillaud M. Accuracy of optical spectroscopy for the detection of cervical intraepithelial neoplasia: Testing a device as an adjunct to colposcopy. *Int J Cancer.* 2011;128(5):1151–1168
17. Twiggs L., Chakhtoura, N., Ferris G., Flowers C., Winter L., Sternfeld R., . Wilkinson, J. Multimodal hyperspectroscopy as a triage test for cervical neoplasia: Pivotal clinical trial results. *Gynecologic Oncology.* 2013; 130(1):147-151.
18. Louwers J, Zaal A, Harmsel WT, Graziosi G, Spruijt J, Papagiannakis E, Meijer C, Kemenade FV, Verheijenb R. Dynamic spectral imaging colposcopy: higher sensitivity for detection of premalignant cervical lesions. *BJOG* 2011; 118:309–318
19. Adewole F Isaac, Awolude A Olutosin, Akinwunmi O Babatunde. Multimodal hyperspectroscopy screening in women at risk of cervical cancer: Results of a pilot study in a developing country. *Trop J Obstet Gynaecol.* 2017; 34 (2): 134-139
20. Omoya SO, Obimakinde AM, Fasubaa OB, Olomojobi OG, Alabi OO. Cervical screening with Luviva machine for early detection of cervical dysplasia: Experience from Ekiti state, Nigeria. *Trop J Obstet Gynaecol* 2014;31:82-9.
21. Cantor Scott, José-Miguel, Martial Guillaud, Dennis. Accuracy of optical spectroscopy for the detection of cervical intraepithelial neoplasia: Testing a device as an adjunct to colposcopy. *International journal of cancer.* 2011; 128. 1151-68.
22. Wade R, Spackman E, Corbett M, Walker S, Light K. Adjunctive colposcopy technologies for examination of the uterine cervix – DySIS, LuViva Advanced Cervical Scan and Niris Imaging System: a systematic review and economic evaluation. *Health Technol Assess.* 2013;17(8):1-240

MR Diffusion and MR Perfusion in Characterization of Ovarian Tumors; the Problem and the Solution

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Abstract

Objective: To test and compare the sensitivity and accuracy of diffusion weighted imaging (DWI) and MR perfusion in women having ovarian tumors.

Patients and Method: Fifty women with ovarian masses were collected after meeting the inclusion criteria depending on gray scale sonographic findings which suggested the presence of ovarian masses. Conventional MRI, Diffusion weighted imaging (DWI) and MR perfusion (MRP) were done for all patient cohort after the approval of ethical committee of our institution. The sensitivity and accuracy of the techniques were compared.

Results: The surgical and pathological reports of our patients proved non tumorous lesion in three patients. They proved benign ovarian tumors in 18/47 (38.3%) patients, borderline tumors in 4/47 (8.5%) patients and malignant ovarian tumors in 25/47 (53.2%) patients. According to conventional MRI ovarian tumors could be diagnosed with sensitivity 92%, specificity 61.11%, PPV 76.7%, NPV 84.6% and accuracy 79.1%. DWI and MR perfusion showed the same results where they showed sensitivity 98%, specificity 83%, PPV 90%, NPV 98% and accuracy 93% with ADC cut off value $1 \times 10^{-3} \text{ mm}^2/\text{sec}$.

Conclusion: Diffusion weighted imaging and MR perfusion are useful in diagnosis of ovarian tumors with approximately the same sensitivity and positive impact on the operative management.

Keywords: MRI ovarian cancer, MR diffusion, MR perfusion, ovarian tumors characterization.

Introduction

Ovarian tumors are the fifth commonest tumor in women and the leading indication for gynecologic surgery. The therapeutic strategy depends on whether the tumor is benign, borderline or malignant.^{1, 2, 3}

Late diagnosis of ovarian cancer is due to lack of specific symptoms.^{4, 5}

MRI diffusion weighted imaging (DWI) and MRI perfusion (MRP) increased the technical capabilities for preoperative characterization of ovarian masses.^{6, 7}

The fast “wash-in” of contrast coupled with the rapid “wash-out” through tumors more than normal tissue allows a functional analysis of the tumor microcirculation.^{3, 8}

Multi-parametric calculations of permeability and perfusion are used to characterize the tumor vasculature within a tumor “microenvironment”. The malignant

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lesions enhance in contrast quickly and have more intense signals, compared to benign lesions.^{9, 10, 11}

DWI is a non-invasive imaging modality depends on the Brownian motion of water molecules in tissues. Diffusion-weighted imaging provides qualitative and quantitative information about tissue cellularity.¹²

Aim of the Work: The aim of this study is to evaluate the benefit of application of diffusion weighted imaging (DWI) and MR perfusion (MRP) in characterization of ovarian tumors.

Patients and Method

Study design and population: This study was a prospective study. The study population comprised 50 consecutive women who were suspected to have ovarian neoplastic mass. Patients were collected between January 2018 and December 2018. They underwent MRI imaging after meeting the inclusion criteria. All patients signed a written informed consent before MRI examination.

Inclusion and exclusion criteria: All patients included in this study had previous trans-abdominal or trans-vaginal real time ultrasonography with diagnosis of complex ovarian lesions, cystic lesion with solid vegetation or thick septa or soft tissue component (figure 2), solid ovarian lesions (figure 3) or suspicious adnexal lesions. Patients with simple cystic ovarian lesions, ovarian lesions with pure fatty component, impaired renal functions or general contraindications to MRI as the presence of any paramagnetic substances such as pacemakers, metallic clips or claustrophobic patients were excluded from the study.

Method

MRI technique: MR imaging was performed using 1.5 Tesla MR Scanner (Ingenia, Philips Healthcare, Netherlands). All patients were imaged in the supine position using pelvic phased array coil. The MRI examination was conducted on the female pelvis including conventional MRI sequences; Axial, sagittal and coronal T2WIs using the following parameters (TR 5000/TE 110 ms, echo train length 13–15, slice thickness 5–7 mm, gap 1–2 mm, Field of view 24–38 cm, excitations (NSA) 3 and matrix 304 • 512). Followed by axial T1WI spin echo MR images (TR 162, TE 10–14 ms, slice thickness 5–7 mm, gap 1–2 mm, field of view 24–38 cm, flip angle of 90°, excitations (NSA) 1–2 and matrix 256 • 256).

Diffusion weighted imaging was acquired in the axial plane prior to administration of contrast medium by using a single shot echo-planar imaging sequence with b values (0, 800, 1000) (TR/TE 2871/78, Slice thickness 5 mm, Gap 1 mm), FOV 375 x 312 x 161 mm and matrix 124x105).

MRI perfusion was done for all patients using Gadolinium chelate (Dimegluminegadopentate) that was given at a dose of 0.2 ml per kilogram of body weight by using a power injector (Medrad, spectrissolaris R) at a rate of 2ml/sec, followed by 20 ml of normal saline to flush the tubing. Images were obtained sequentially every 14 seconds beginning 14 seconds (first phase) before the bolus injection. 40 sequential slices were taken with slice thickness 2 mm. Rapid acquisition (every 14 seconds) was performed for 30 consecutive phases with the whole time of the sequence 7 minutes. The images stack should include part of the soft tissue inside the ovarian lesion and the adjacent external myometrium in optimal plane.

Data processing and image interpretation: The images were transformed to Philips 881030 IntelliSpace IX/LX Workstation. Each MR sequence findings were evaluated as following:

(A) Analysis of conventional sequences: Conventional MRI sequences were evaluated for the morphologic features of the lesion including the lesion laterality, size, shape, and complexity of the tumor, T2 signal intensity of the solid part inside the mass and the presence of ascites and peritoneal deposits.

(B) Analysis of MRI perfusion: For ovarian tumor characterization, two regions of interest (ROI) were placed. One on external myometrium and one on the most enhancing part of solid tissue of the ovarian mass. The most enhanced solid part was determined by the use of maximum enhancement colored generated map by the workstation. The enhancement of the solid tissue was classified by using a time-signal intensity curve classification (figure 1):

1. A gradual increase in the signal intensity of the solid tissue, without a well-defined shoulder was defined as type 1 curve.
2. A moderate initial increase in the signal intensity of the solid tissue relative to that of myometrium followed by a plateau was defined as type 2 curve.

3. An initial increase in the signal intensity of the solid tissue that was steeper than that of the myometrium was defined as type 3 curve.

Enhancement measures:

Maximum enhancement (SI max): Difference between peak intensity S1 and S0.

Maximum relative enhancement: (MRE) Maximum of all relative enhancements

Wash in rate (WIR): Maximum slope between T0 and the time of peak intensity.

Wash out rate (WOR): Maximum slope between the time of peak intensity T1 and the end of measurement.

Histopathological evaluation: All of the patients underwent surgical management. Twenty seven patients underwent radical hysterectomy with bilateral salpingo-oophorectomy, 5 cases underwent simple oophorectomy, 10 cases underwent ovarian cystectomy and 8 cases underwent simple oophorectomy. All results were correlated to final post-operative histopathological data.

Statistical analysis: Statistical analysis was performed using the SPSS software for Windows v. 20 (SPSS Inc., Chicago, IL). For comparing quantitative data, Kruskal Wallis test and Mann Whitney tests were performed. For comparing qualitative data, Fisher exact test was performed. Accuracy of the studied diagnostic test in predicting malignancy was represented using the terms sensitivity, specificity, overall accuracy, negative and positive predictive values. A probability value (p=0.05) was considered statistically significant. Receiver operating curve ROC curve was used to determine the cutoff values of the semi- quantitative parameters.

Results

Our study included 50 female patients, three of them found to have non-ovarian tumors on histo-pathological evaluation, two of them were tubo-ovarian abscesses and one was cyst with hemorrhagic infarction. Those three cases were excluded from the study to avoid bias.

Diffusion weighted magnetic resonance imaging was done for all patients before contrast injection. Among our patients 37/47 cases (78.7%) showed diffusion restriction and 10/47 cases (21.3%) showed facilitated

diffusion. The cut off value of ADC value below which malignancy is expected is less than $1 \times 10^{-3} \text{ mm}^2/\text{sec}$. There was statistical significance between ADC value and pathological diagnosis (P value <0.001).

Regarding MRP,SI_{max}, MRE% , WIR and WOR were evaluated and correlated to the final histopathological results. There was statistical significance between SI_{max}, WIR & WOR and pathological diagnosis with higher sensitivity specificity and accuracy in relation to WOR. There was no statistical significant difference between MRE% and pathological diagnosis. (Table I).

Regarding the time signal intensity curves of MRP; we found that Curves type 2 and 3 carry malignant probability with accuracy 95%, sensitivity 88% and specificity 92%. NPV 100%

ROC curve analysis was used for prediction of malignancy depending on conventional based diagnosis, DWI diagnosis, MRP and combined conventional MRI with DWI and with MRP.

There was statistical significant difference between the three method of diagnosis and the pathological diagnosis. However; the AUC, sensitivity, specificity and accuracy were higher on DWI and MRP- based diagnosis than those on conventional based diagnosis. Statistical correlation between results of conventional MRI, DWI and MRP to evaluate, the sensitivity, specificity, PPV, NPP and accuracy. (Table II)

Final pathological diagnosis after surgery revealed that 24/47 cases showed epithelial tumors (6 benign cases, 4 borderline cases and 14 malignant cases), 8/47 cases showed sex cord stromal tumors (5 benign cases and 3 malignant cases) and 15/47 cases showed germ cell tumors (7 benign cases and 8 malignant cases).

Table I: ROC curve analysis for prediction of malignancy according to MR perfusion measurements in correlation with histopathological diagnosis:

	SI max	WIR	WOR
Sensitivity	100	92	100
Specificity	94.44	94.44	100
PPV	96.2	95.8	100
NPV	100	89.5	100
Accuracy	97.67	93.02	100

Table II: ROC curve analysis for prediction of malignancy among various MRI techniques in correlation to the final histopathological diagnosis

	Conventional MRI	DWI	MRP	Combined conventional+ DWI OR Conventional+ MRI perfusion
Sensitivity	92%	98%	98%	97%
Specificity	61.11%	83%	83%	92%
PPV	76.7%	90%	90%	90%
NPV	84.6%	98%	98%	98%
Accuracy	79.1%	93%	93%	93%

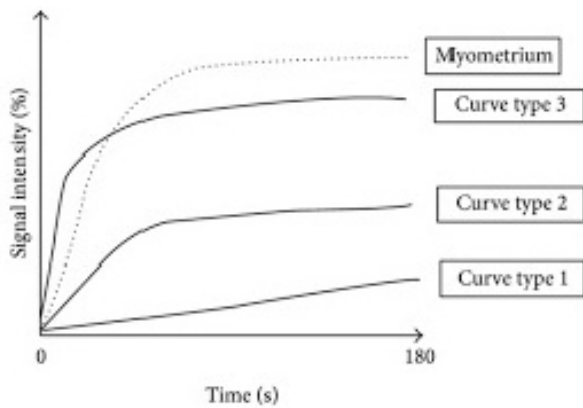


Figure 1: Time intensity curves

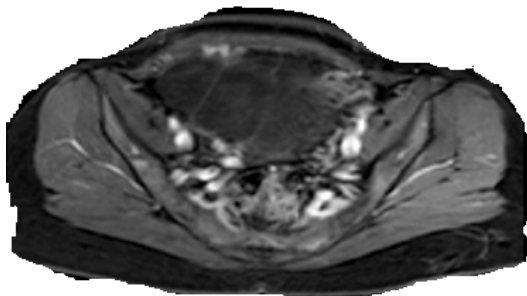


Figure 2: Axial T1WI shows cystic lesion with enhanced septae and enhanced posterior mural nodule. Diagnosis is strumaovarii.

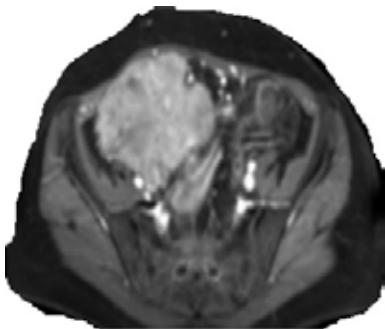


Figure 3: Axial T1WI fat sat. shows moderate enhancement of the right sided ovarian lesion. Diagnosis is ovarian clear cell carcinoma.

Discussion

Adnexal masses are challenging diagnostic problem because of the overlapping imaging features between benign and malignant tumors.^{13, 14}

In our study, DWI based diagnosis showed 100% sensitivity while specificity remains low 88%. Such low specificity elicited in our study can be explained by the presence of eight benign masses that mimicked malignancy. These masses included mature cystic teratomas, strumaovarii and benign sclerosing tumor. They all showed restricted diffusion and mean ADC values $0.8 \times 10^{-3} \text{ mm}^2/\text{s}$, $1 \times 10^{-3} \text{ mm}^2/\text{s}$ and $0.9 \times 10^{-3} \text{ mm}^2/\text{s}$ respectively presenting false positive cases due to mixed cellularity of the lesions. The mean ADC values for benign lesions were $1.7 \pm 0.6 \times 10^{-3} \text{ mm}^2/\text{s}$ and for borderline and malignant lesions were $0.9 \pm 0.2 \times 10^{-3} \text{ mm}^2/\text{s}$ and 0.8 ± 0.1 respectively. Cutoff value for ADC in malignancy is $\leq 1 \times 10^{-3} \text{ mm}^2/\text{sec}$. This agreed with Thomassin-Naggara et al., where they attributed the presence of low mean ADC values elicited by benign fibrous tumors as fibromas, Brenner tumors, and cystadeno-fibromas are due to dense network of collagen fibers within the extracellular matrix.¹⁵

In a study done by Zhang P et al., they show higher sensitivity and specificity of DWI than our study because they excluded endometriomas, mature cystic teratomas and pure cystic adenomas from their study.¹⁶

In our study, Curve type I was found to be specific for benign ovarian tumors with 100% specificity. Curves type II and III were more in favor of borderline/malignant tumors. From all cases with curve type III, only one case was benign which was pathologically diagnosed as benign sclerosing tumor of the ovary. The explanation for such result is the high vascularity of sclerosing stromal tumors.

In our study, the perfusion parameters that showed highest accuracy were WOR (100%) followed by SI_{max} (97%) then WIR (93%). The cut off value for WOR in our study was >6 (lesions with WOR more than 6 is likely to be malignant). The PPV and NPV were 100%.

In our study, the cut off value of SI_{max} was >1285 (tumors with SI_{max} more than that number is considered malignant). The sensitivity was 100% and specificity was 94%. Those measurements do not agree with Dilks et al. that suggested a threshold value of >250 for prediction of malignancy with a sensitivity and specificity 100%. This difference can be explained by the unequal distribution of cases in our study. WIR showed less sensitivity, specificity, NPV, PPV and accuracy (92%, 94%, 89.5%, 95.8% and 93% respectively) than WOR and SI_{max}. Bernardin et al. applied a cut off value > 9.5 for WIR where lesions with WIR more than 9.5 are considered malignant. In our study, the cut off value was higher than that value (>17.9) and this also can be explained by the unequal distribution of cases with increased number of cases with hypervascular nature.^{13, 17}

Our study had several limitations. The unequal distribution of pathology included in the study. Some relatively common pathological entities were not included in the study as ovarian metastasis. Also there is small number of cases of ovarian epithelial borderline tumors included in the study. Also, the method of the ROI drawing that may be subject to human error, which may affect the performance.

Conclusion

The application of MR diffusion and MR perfusion are proved accurate in characterization of malignant and benign ovarian tumors. Improvements in evaluation of SI_{max} and WI and WO lead to more accurate evaluation of ovarian tumors with high sensitivity and specificity and reduce false positive results.

Ethical Clearance: Taken from ethical committee in El-Minia university hospital.

Source of Funding: Self funding.

Conflict of Interest: Nil.

References

1. Chornokur G, Amankwah EK, Schildkraut JM, Phelan CM. Global ovarian cancer health disparities. *Gynecol Oncol.* 2013; 129 (1):258–64.

2. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. *CA Cancer J Clin.* 2013; 63 (1):11–30.
3. Thomassin-Naggara I, Daraï E, Cuenod CA, Rouzier R, Callard P, Bazot M. Dynamic contrast-enhanced magnetic resonance imaging: a useful tool for characterizing ovarian epithelial tumors. *MagnReson Imaging.* 2008 ;28 (1):111-20.
4. Lutz AM, Willmann JK, Drescher CW, Ray P, Cochran FV, Urban N, et al. Early diagnosis of ovarian carcinoma: is a solution in sight? *Radiology.* 2011; 259(2):329–45.
5. Cesario S. Advances in the early detection of ovarian cancer: how to hear the whispers early. *NursWomens Health.* 2010; 14 (3):222–34.
6. Medeiros LR, Freitas LB, Rosa DD, Silva FR, Silva LS, Birtencourt LT, et al. Accuracy of magnetic resonance imaging in ovarian tumor: a systematic quantitative review. *Am J Obstet Gynecol.* 2011; 204 (1):67.
7. Bazot M, Darai E, Nassar-Slaba J, Lafont C, Thomassin-Naggara I. Value of magnetic resonance imaging for the diagnosis of ovarian tumors: a review. *J Comput Assist Tomogr.* 2008; 32 (5):712–23.
8. Yankeelov TE, Gore JC. Dynamic contrast enhanced magnetic resonance imaging in oncology: theory, data acquisition, analysis, and examples. *Curr Med Imaging Rev.* 2009;3(2):91–107.
9. Tofts PS. T1-weighted DCE imaging concepts: modelling, acquisition and analysis. *Signal.* 2010;500(450):400
10. Kyriazi S, Kaye SB, deSouza NM. Imaging ovarian cancer and peritoneal metastases—current and emerging techniques. *Nat Rev Clin Oncol.* 2010;7(7):381–93.
11. Li X, Hu J, Zhu L M, Sun X H, Sheng H Q, Zhai N, Hu X B, Sun CR and Zhao B. The clinical value of dynamic contrast-enhanced MRI in differential diagnosis of malignant and benign ovarian lesions .*Tumor Biology.* 2015; 36,(7) : 5515–5522.
12. Kyriazi S, Kaye SB, deSouza NM. Imaging ovarian cancer and peritoneal metastases—current and emerging techniques. *Nat Rev Clin Oncol.* 2010;7(7):381–93.
13. Bernardin L, Dilks P, Liyanage S, Miquel M, Sahdev A, Rockall A. Effectiveness of semi-quantitative multiphase dynamic contrast-enhanced MRI as a predictor of malignancy in complex

- adnexal masses: radiological and pathological correlation. *Eur Radiol* 2012., 22:880-890
14. Maarof RA, Abdelrahman AS and Habeeb DA. Dynamic Contrast-Enhanced Magnetic Resonance Imaging; A Useful Tool for Characterization and Assessment of Ovarian Masses. *The Egyptian Journal of Hospital Medicine* 2018; 71 (2): 2620-2625
 15. Thomassin-Naggara I, Toussaint I, Perrot N, Rouzier R, Cuenod CA, Bazot M and Daraï, E. Characterization of complex adnexal masses: value of adding perfusion-and diffusion-weighted MR imaging to conventional MR imaging. *Radiology* 2011; 258(3), pp.793-803.
 16. Forstner R, Thomassin-Naggara I, Cunha TM, Kinkel K, Masselli G, Kubik-Huch R, Spencer J A and Rockall A. ESUR recommendations for MR imaging of the sonographically indeterminate adnexal mass: an update. *European radiology* 2017; 27(6), pp.2248-2257
 17. Zhang P, Li W, Chu C, Cui Y and Zhu, M. Diffusion-weighted MRI: a useful technique to discriminate benign versus malignant ovarian surface epithelial tumors with solid and cystic components. *Abdominal Radiology* 2012; 37(5), pp.897-90

The Diagnostic Accuracy of Different Echocardiographic Predictors of Subtle Myocardial Dysfunction in Asymptomatic Duchenne Muscular Dystrophy Patients

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Abstract

Introduction: Duchennemuscular dystrophy (DMD) is an uncommon X-linked disease affecting in average 1 in 3600 live male births. Cardiac disease is the major cause of mortality in affected patients. Several Echocardiographic parameters are available for evaluation of systolic and diastolic function among Duchenne patients. The aim of this paper is to determine which of those parameters has the highest accuracy in detection subtle myocardial affection in asymptomatic Duchenne patients. **Method:** 28 asymptomatic Duchenne patients as well as 28 age and sex matched healthy controls have been screened with Echocardiography including Motion mode, conventional and Tissue Doppler, 2 Dimensional (2D) and 3 Dimensional (3D) speckle tracking Echocardiography. **Results:** Conventional Echocardiographic parameters failed to differentiate cases from controls while Tissue Doppler derived parameter such as the ratio between Transmitral flow velocity in early diastole and Left Ventricular averaged basal septal and lateral tissue velocity (LV E/E') as well as global longitudinal (GLS) and Global Circumferential strain (GCS) (2D and 3D) proved to be useful in differentiation between them. 3D derived ejection fraction also showed statistically significant difference between cases and controls (54.2±4.5 vs. 70.2±6.1, P Value<0.001) respectively, 3D derived parameters showed the highest sensitivities and specificities among relevant parameters (100%) for detection of subtle myocardial affection in Duchenne patients. **Conclusion:** This paper concludes that 3 D derived EF, GCS and GLS can be reliably used in detection of subtle myocardial affection in Duchenne patients.

Keywords: Duchenne, Cardiac affection, 3D speckle tracking, 3D Ejection Fraction.

Introduction

Duchenne muscular dystrophy (DMD) is an X-linked disease that affects 1 in 3600–6000 live male births.⁽¹⁾ The majority of DMD patients after their

third decade of age have established cardiomyopathy. Although clinically overt heart failure may be delayed or absent (due to relative physical inactivity), cardiac disease is a major cause of death in patients with muscular dystrophies.⁽²⁾ In young patients (aged <12 years) with DMD, cardiac systolic function is generally at normal range. Recent studies have suggested the presence of subclinical dysfunction in those young patients. Detecting latent myocardial involvement is essential in this disease because early use of drugs like angiotensin - converting enzyme inhibitors may delay the progression of heart disease.⁽³⁾

Several echocardiographic tools have been used for early detection of subtle myocardial dysfunction in patients with DMD. Traditionally, assessment of global

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cardiac function has been evaluated via transthoracic echocardiography (TTE). However, the use of LVEF (Left ventricular Ejection Fraction) as a standalone method to predict myocardial affection in patients with DMD cannot be relied upon since affection of LVEF by M-Mode (Motion Mode) Echocardiography and cannot predict the earliest forms of affection.⁽⁴⁾ Hence the need for newer techniques that can unleash myocardial affection the earliest the possible to initiate anti-failure treatment and other forms of therapy that can slow down the progression of myocardial affection.

Promising results of earlier detection have been offered by Tissue Doppler imaging and 2D (2 dimensional) strain. In early stages, subclinical diastolic function has been reported in DMD pediatric population, preceding the LV systolic dysfunction. However, thorax deformities and difficulties to have optimal images in wheelchair-bound patients technically limit Doppler echocardiography.⁽⁵⁾ The use of 2D strain derived Global longitudinal and circumferential strain (GLS and GCS respectively) has also proved useful in early detection of systolic dysfunction before affection of conventional echocardiographic parameters.⁽⁶⁾ To our knowledge no study has explored the role of 3D (3 dimensional) derived strain role in detection of early myocardial affection in patients with DMD.

The aim of the current study is to compare the statistical power of different echocardiographic markers derived from M-Mode Echocardiography, Tissue Doppler, 2D and 3D strain in early detection of myocardial affection in DMD patients.

Method

Study Population: This study was designed as a case-control, cross-sectional study on pediatric asymptomatic patients with DMD and was performed between February 2016 and October 2017. The patients were recruited from neurometabolic Clinic of Cairo University Children Hospital, Egypt (a tertiary care center)

Study Method:

Echocardiographic assessment: Transthoracic echocardiography was performed using General Electric (Vivid-7/9, Horten, Norway) machine with a 3 and 5MHZ (megahertz) transducers according to the age of the patient and having tissue velocity imaging capabilities. **Conventional echocardiography** included M-mode,

2D and Doppler echocardiographic parameters were averaged over 3 cardiac cycles and all measurements were performed according to the guidelines for performance of echocardiogram by American Society of Echocardiography.⁽⁷⁾ Left ventricular fraction shortening (FS%) and ejection fraction (EF%) were calculated by M-mode echocardiography according to Teicholtz method.⁽⁸⁾ Pulsed Doppler method was used for blood flow measurements from mitral valve: flow velocity during early filling (E), flow velocity during atrial contraction (A) and then E/A was calculated. The global myocardial performance index (MPI or Tei index) was calculated by conventional pulsed wave Doppler as the following: $Tei\ index = a - b/b$ where *a* is the sum of IVCT (isovolumic contraction time) and IVRT (isovolumic relaxation time) and *b* is ET (ejection time). **Pulsed tissue** velocity imaging measures systolic myocardial velocities at the basal segments of the lateral LV wall for calculation of the E/E' ratio (the ratio between Transmitral flow velocity in early diastole and Left Ventricular averaged basal septal and lateral tissue velocity).

2D speckle Tracking was performed as follows: based on echocardiographic speckle tracking algorithm, apical four-chamber, two-chamber and threechamber views were analyzed in each subject. In each cardiac apical view, three points at the endocardial border were placed including two annular points at the base and one point at the apex. After that, the system calculates global longitudinal strain (GLS). To assess GCS, the endocardial border was traced automatically in end diastole in each short-axis view, with entire myocardium inside the region of interest for optimal tracking. Mid- and basal-short-axis views were divided in 6 segments while apical short-axis view was divided to 4 segments. After approving of border tracing, the system calculates global circumferential strain.

3D Echocardiography: full-volume acquisition of the LV was obtained by harmonic imaging from the apical approach. Six ECG-gated consecutive beats were acquired during end-expiratory breath-hold to LV full volume. All data sets were analyzed off-line using a commercially available software (4D Auto LVQ, GE-Vingmed, Horten, Norway). Papillary muscles were included within the LV chamber. After the adjustments software provided the LV volumes, EF. Subsequently, an automatic trace of the epicardial border was displayed to set the region of interest required for LV mass and 3D myocardial deformation parameters. The 3D GLS and

GCS from the 17 myocardial segments at end-systole was calculated.

Statistical Analysis: Data were statistically described in terms of mean ± standard deviation (± SD), median and range, or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using Student *t* test for independent samples in comparing 2 groups when normally distributed and Mann Whitney *U* test for independent samples when not normally distributed. Comparison of numerical variables between more than two groups was done using one-way analysis of variance (ANOVA) test with posthoc multiple 2-group comparisons. For comparing categorical data, Chi square (χ^2) test was performed. Exact test was used instead when the expected frequency is less than 5. Correlation between various variables was done using Pearson moment correlation equation. P values less than 0.05 was considered statistically significant. The Receiver Operating Characteristic (ROC) curve analysis was performed to determine the best Echocardiographic predictor of subtle myocardial affection in Duchenne Muscular Dystrophy. All statistical calculations were done using computer programs SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

Results

This current study included 28 asymptomatic patients with DMD as well as 28 age and sex matched healthy controls. Their age ranged from 9 to 16 years and they were all males among DMD patients. They were all free of cardiac symptoms.

Demographic and conventional echocardiographic data of the studied population: No significant difference between the DMD patients and the controls as regards the demographic data [table 1].

By comparison of the conventional echocardiographic measurements and Doppler and tissue Doppler derived parameters, there was no significant statistical difference between the controls and DMD group in all parameters apart from LV E/E' ratio which was significantly higher in cases than controls [table 2].

2D and 3D derived speckle tracking (strain data) showed significant difference between cases and controls as shown in table 3 as well as 3D derived EF which was significantly lower in DMD patients. [table 3]

Table 4 represents a **ROC curve analysis of the echocardiographic parameters** that proved statistically significant between cases and controls, it shows that the 3 D derived parameters have recorded the highest sensitivities and specificities in distinctions between DMD patients and controls (100%).

Table 1: Demographic and Clinical data of Cases vs. Controls

	DMD Group (n=28)	Control Group (n=28)	P-Value
Variable	Mean ± SD	Mean ±SD	
Age (Years)	10.2±1.2	10.1±1.05	NS
BSA	1.1±0.05	1.1±0.04	NS
Heart Rate (BPM)	86±11	87.1±12	NS

BPM (Beats per minute), BSA (Body surface area), DMD (Duchenne muscular Dystrophy) n (number), NS (Non-significant).

Table (2): Comparison of M-Mode and Conventional and Tissue Doppler Parameters of LV functions in Cases vs. Controls:

	DMD Group (n=28)	Control Group (n=28)	P-value
Variable	Mean ± SD	Mean ± SD	
EDV (ml)	71.68±23.77	76.96±27.54	NS
ESV (ml)	22.42±11.50	25.53±10.37	NS
EF (%)	69.63±6.89	66.92±4.98	NS
FS (%)	37.24±4.22	35.43±3.14	NS
MV E/A	1.41±0.18	1.42±0.21	NS
LV Tei	0.36±0.05	0.37±0.03	NS
LV E/E'	8.81±1.89	5.21±1.23	<0.001

DMD (Duchenne muscular Dystrophy), EF (Ejection fraction), EDV (end diastolic volume indexed to body surface area), FS (fractional shortening), Mitral E/A (Early to late diastolic filling velocity across mitral valve ratio), mL (milliliter), n (number), NS(Non-significant) LV E/E' (Early diastolic filling velocity across mitral valve to mean of the peak early diastolic tissue velocities at the septum and mitral annulus ratio)

Table (3) 2D and 3D speckle tracking of LV functions in cases vs. control

	DMD Group (n=28)	Control Group (n=28)	P-value
Variable	Mean ± SD	Mean ± SD	
2D GLS	-18.28±1.20	-23.80±1.44	<0.001
2D GCS	- 12.94±2.10	-19.67±1.11	<0.001
3D GLS	-16.45±1.2	-24.2±3.1	<0.001
3D GCS	- 7.1±0.96	-18.9±2.1	<0.001
3D EF	54.2±4.5	70.2±6.1	<0.001

DMD (Duchenne muscular Dystrophy), EF (Ejection Fraction), GCS (Global circumferential strain), GLS (Global longitudinal strain), 2D (2 Dimensional), 3D (3 Dimensional), n (number)

Table (4): (ROC) curve analysis for discrimination between cases with DMD and normal controls using relevant echocardiographic measures

	LV E/E'	2D-GCS	2D-GLS	3D-GCS	3D-GLS	3D-EF
Cut-off	>6.89	≤-13.58 (%)	≤-19.40 (%)	≤-14.6(%)	≤-13.20 (%)	≤58.4 (%)
Sensitivity	89.3	96.4	96.4	100.0	100.0	100.0
Specificity	96.4	100.0	100.0	100.0	100.0	100.0

DMD (Duchenne muscular Dystrophy), EF (Ejection Fraction), GCS (Global circumferential strain), GLS (Global longitudinal strain), ROC: Receiver operating curve, 2D (2 Dimensional), 3D (3 Dimensional), n (number)

Discussion

Cardiac disease is a major cause of death in patients with muscular dystrophies accounting for a total of 40% of all DMD deaths. In view of this high percentage developing tool for early detection of myocardial affection in DMD patients is crucial as myocardial damage after the symptom onset with overt LV dysfunction may be irreversible and progressive, ending in death.

In our study, the examined DMD patients, who were free of cardiac symptoms, had normal EF and FS as compared to normal controls. Similarly, Mertens et al., described normal systolic function (EF and FS) in young patients (aged <12 years) with DMD. (9)

Diastole is an active myocardial process that is influenced by alterations in cytosolic calcium concentration and flux. The lack of dystrophin in patients

with DMD disrupts the sarcolemma membrane integrity resulting in altered intracellular calcium haemostasis and impaired ventricular relaxation. Diastolic dysfunction is often present in the absence of significant symptoms of identifiable systolic abnormalities.(10)

Left ventricular E/E' ratio is the ratio between Transmitral flow velocity in early diastole and Left Ventricular averaged basal septal and lateral tissue velocity. In diastolic dysfunction tissue velocity is reduced before flow velocity is affected, this makes the ratio higher in patients with diastolic dysfunction.(11)

In our study, the E/E' ratio was significantly increased in cases compared to controls denoting subtle diastolic dysfunction in DMD patients. This is in concordance with Markham et al., who found abnormal diastolic indices in DMD patients with normal systolic function compared with controls.(5)

Similar studies concluded that echocardiographic evidence of diastolic dysfunction precedes the development of dilated cardiomyopathy and applies to other dystrophinopathies and female carriers.(12)

Compared to normal controls, our patients had a statistically significant reduction of LV (GLS) with p-value <0.001 and LV (GCS) with p-value <0.001 by 2D STE. This is in concordance with a recent study done by Spurney et al., in 2015 where Speckle-tracking echocardiography demonstrated subclinical myocardial dysfunction with decreased average circumferential and longitudinal strain in DMD patients with normal EF. ⁽¹³⁾

Hor et al. evaluated the natural history of occult cardiac dysfunction in DMD and found that DMD patients with normal EF had reduced LV GCS at an early age (<10 years) compared with control subjects. The DMD patients age >10 years with normal EF had further decline in left ventricular myocardial peak circumferential strain compared with younger DMD patients. They concluded that myocardial strain abnormalities are prevalent in young DMD patients despite normal EF, and these strain values continue to decline with advancing age. ⁽⁴⁾

According to Kalam et al., the advantage of GLS is its superior ability to predict major adverse cardiac events, including hospital readmission and mortality, particularly when the ejection fraction is normal or near normal. ⁽¹⁴⁾

To our knowledge this study is the first to involve the use of 3D derived strain in assessment of systolic functions of DMD patients. 3D derived GLS and GCS were significantly lower in DMD patients than in controls. Also 3D derived EF was significantly lower in cases compared to controls which may render 3D echocardiography a promising tool in substituting CMR in patients with DMD for accurate assessment of EF in DMD patients as it provides real volumetric assessment of left ventricle compared to the Teicholtz derived assessment in M-Motion Echocardiography. ⁽¹⁵⁾

To our knowledge, there were not relevant studies that discussed the sensitivity and specificity of different echocardiographic parameters in detecting subtle myocardial affection in DMD patients.

Through analysis of the (ROC) curve, the parameters with the highest sensitivity and specificity to detect preclinical cardiomyopathy in asymptomatic Duchenne patients, in our study, were in order: 3D derived EF, GLS, GCS (sensitivity and specificity of 100%) followed by 2D derived GLC and GCS with sensitivity 96.4% and specificity 100%.

This may prompt the use of 3D echocardiography as a promising bedside method for patients with DMD

Conclusion

Young patients with DMD may suffer from asymptomatic cardiomyopathy that may not manifest until very late, when treatment would be less effective in combating the remodelling that occurred in cardiac muscle. In this aspect conventional Echocardiography is delayed in diagnosis and cannot be relied upon for early detection. The combination of conventional pulsed Doppler and tissue Doppler showed early diastolic affection in asymptomatic DMD patients. 2D derived GCS and GLS have showed great accuracy in detection of early systolic dysfunction. However, 3D derived parameters revealed superior to all the above mentioned parameters in early detection of subtle myocardial affection, offering a good substitute to CMR in DMD patients.

Conflict of Interest: No

Financial Support: No

Ethical Clearance: The aim and nature of the study was explained for each parent before inclusion. An informed consent was obtained from parents/surrogates before enrolment. The study design was confirmed to the requirements of Revised Helsinki Declaration of Bioethics (2008). The study protocol was presented to and approved by the scientific ethical committee of Paediatric Department, faculty of medicine, Cairo University.

References

1. Ogata H, Nakatani S, Ishikawa Y, Negishi A, Kobayashi M, Ishikawa Y, et al. Myocardial strain changes in Duchenne muscular dystrophy without overt cardiomyopathy. *Int J Cardiol.* 2007;115(2):190–5.
2. Nolan MA, Jones ODH, Pedersen RL, Johnston HM. Cardiac assessment in childhood carriers of Duchenne and Becker muscular dystrophies. *Neuromuscul Disord.* 2003;13(2):129–32.
3. Towbin JA. A noninvasive means of detecting preclinical cardiomyopathy in Duchenne muscular dystrophy? Vol. 42, *Journal of the American College of Cardiology.* 2003. p. 317–8.
4. Hor KN, Wansapura J, Markham LW, Mazur W, Cripe LH, Fleck R, et al. Circumferential Strain

- Analysis Identifies Strata of Cardiomyopathy in Duchenne Muscular Dystrophy. A Cardiac Magnetic Resonance Tagging Study. *J Am Coll Cardiol*. 2009;53(14):1204–10.
5. Markham LW, Michelfelder EC, Border WL, Khoury PR, Spicer RL, Wong BL, et al. Abnormalities of Diastolic Function Precede Dilated Cardiomyopathy Associated with Duchenne Muscular Dystrophy. *J Am Soc Echocardiogr*. 2006;19(7):865–71.
 6. Hor KN, Kissoon N, Mazur W, Gupta R, Ittenbach RF, Al-Khalidi HR, et al. Regional circumferential strain is a biomarker for disease severity in duchenne muscular dystrophy heart disease: A cross-sectional study. *Pediatr Cardiol*. 2014;36(1):111–9.
 7. Cheitlin MD, Armstrong WF, Aurigemma GP, Beller GA, Bierman FZ, Davis JL, et al. ACC/AHA/ASE 2003 guideline update for the clinical application of echocardiography: Summary article. Vol. 16, *Journal of the American Society of Echocardiography*. 2003. p. 1091–110.
 8. Teichholz LE, Kreulen T, Herman M V., Gorlin R. Problems in echocardiographic volume determinations: Echocardiographic-angiographic correlations in the presence or absence of asynergy. *Am J Cardiol*. 1976;37(1):7–11.
 9. Mertens L, Ganame J, Claus P, Goemans N, Thijs D, Eyskens B, et al. Early Regional Myocardial Dysfunction in Young Patients With Duchenne Muscular Dystrophy. *Journal of the American Society of Echocardiography*. 2008;21(9):1049–1054.
 10. Ashwath ML, Jacobs IB, Crowe C a, Ashwath RC, Super DM, Bahler RC. Left ventricular dysfunction in duchenne muscular dystrophy and genotype. *Am J Cardiol [Internet]*. 2014;114(2):284–9. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24878125>
 11. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF, Dokainish H, Edvardsen T, et al. Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr [Internet]*. 2016;29(4):277–314. Available from: <http://dx.doi.org/10.1016/j.echo.2016.01.011>
 12. Wang M, Yip G, Yu CM, Zhang Q, Zhang Y, Tse D, et al. Independent and incremental prognostic value of early mitral annulus velocity in patients with impaired left ventricular systolic function. *J Am Coll Cardiol [Internet]*. 2005;45(2):272–7. Available from: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve & db=PubMed & dopt=Citation & list_uids=15653027
 13. Spurney CF, McCaffrey FM, Cnaan A, Morgenroth LP, Ghelani SJ, Gordish-Dressman H, et al. Feasibility and Reproducibility of Echocardiographic Measures in Children with Muscular Dystrophies. *J Am Soc Echocardiogr*. 2015;28(8):999–1008.
 14. Kalam K, Otahal P, Marwick TH. Prognostic implications of global LV dysfunction: a systematic review and meta-analysis of global longitudinal strain and ejection fraction. *Heart [Internet]*. 2014;100(21):1673–80. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24860005>
 15. Wood PW, Choy JB, Nanda NC, Becher H. Left ventricular ejection fraction and volumes: It depends on the imaging method. *Echocardiography*. 2014;31(1):87–100.

The Association of Glutathion Peroxydase-1 Serum and Sensorineural Hearing Loss in MDR TB Patients with Kanamycin Therapy

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Abstract

Introduction: Kanamycin therapy in Multi-Drug Resistance Tuberculosis (MDR-TB) patients increases the possibility of sensorineural hearing loss through increasing the level of Reactive Oxygen Species (ROS) production in cochlea, particularly in hair cells. In normal state, ROS is detoxicated by numerous antioxidant enzymes, including glutathione peroxidase-1 (GPx-1). Imbalance of antioxidant enzymes and ROS production leads to death of hair cells and eventually sensorineural hearing loss. **Objective:** This study aimed to observe the association of GPx-1 level and sensorineural hearing loss in MDR-TB patients with Kanamycin therapy.

Method: This study was a prospective observational study conducted at Dr. Hasan Sadikin General Hospital, Bandung, Indonesia, between February to April 2017. 17 patients were included into the study with pre- and post-kanamycin therapy examination within 3 weeks duration using pure tone audiometry and serum level of GPx-1. Statistic analysis was done using Mann Whitney test with significant level of $p < 0.05$.

Result: A significant reduction of GPx-1 level in 3 weeks period after the initial Kanamycin administration was found in the study; $p < 0.001$. Furthermore, there was a significant alteration in the hearing threshold on frequency of 500-800 Hz after Kanamycin administration; $p < 0.05$. There was a significant association between GPx-1 level and sensorineural hearing loss in Kanamycin therapy; $p < 0.05$.

Conclusion: Sensorineural hearing loss in patient with history of Kanamycin therapy was associated with level of GPx-1 degradation.

Keywords: GPx-1, Kanamycin, MDR TB, Sensorineural hearing loss.

Introduction

Tuberculosis (TB) remains a concern among global health problem with a high mortality and morbidity rate.¹ WHO also stated that Indonesia had approximately 6,800 new Multi Drug Resistance TB (MDR TB) annually with approximately 2% of new cases and 12% of re-treatment TB were MDR TB.^{2,3,4} Among all injection drugs for MDR TB, Kanamycin is widely used as stated in WHO's recent MDR TB guideline due to its wide distribution area and affordable price.^{5,6,7,8}

In general, three types of antioxidant present in human body.¹⁴ Among all GPx, Glutathione peroxidase-1 (GPx-1) is the main glutathione peroxidase enzyme family; mainly found in erythrocyte, liver, lungs, kidney, and

almost in all cells' organ (cytosol, mitochondria, and peroxisome).^{15,16} Furthermore, in cochlea, GPx-1 has a higher enzymatic activity in organ of corti, spiral ganglion, stria vascularis, spiral ligament, and another supporting cell.^{17,18,19} Higher activity of SOD and CAT are also found in stria vascularis and organ of corti. GSH and GPx are the main antioxidants in those areas.¹⁴

Study conducted by Alli, et al. in 2014 on 83 MDR TB patients showed that there was a significant degradation of antioxidant enzyme activity, including glutathione transferase and glutathione peroxide.²⁰ It was strengthened by Madebo et al who also showed a significant decrease in glutathione peroxide level in TB MDR patients.^{20,22}

Rakhmawati in her study found sensorineural hearing loss, particularly in high frequencies, 4000-8000 Hz, in MDR TB patient treated using Kanamycin within the 19th to 22nd day of therapy, affecting high frequency hearing ability to lower frequency.⁵ Study conducted by Jiang et al in 2006 found that there was a shift in auditory brain stem response (ABR) by 45-50 dB in the 14th day that was remained for 5 weeks also showed that the death of hair cells happened in the 11th day and 30% of the superficial hair cells died after 14 days.²⁴ It is proposed that hearing loss due to Kanamycin's toxicity mostly started on higher frequency tone as it is located on the basal of cochlea; this progressivity happens due to difference of survival ability among the hair cells on basal and apex cochlea; as explained by the lower level of GPx-1 in basal hair cell in comparison with apex of cochlea.²⁵

This study aims to observe the association between GPx-1 level and SNHL in MDR TB patients treated using Kanamycin.

Material and Method

This study was an analytic prospective observational study with pre- and post- intervention examination for association between variables, which had been ethically legalized before. Participants. Patients with MDR TB at MDR TB Polyclinic of Internal Medicine Department of Dr. Hasan Sadikin General Hospital, Bandung between February to April 2017. The inclusion criteria for the study were patients with MDR TB with plan for Kanamycin therapy, aged 20-50 years old, had intact tympanic membrane in both ears, had type A result on tympanometry examination, normal hearing threshold on

DPOAE examination and audiometry. Exclusion criteria for the study were patient with history of treatment using ototoxic drugs except TB-MDR treatment, had a history of another diseases, including renal failure, diabetes mellitus, liver diseases, systemic lupus erythematosus (SLE), and cardiovascular diseases. Intervention. Data was collected from physical examination and laboratories data of already diagnosed MDR TB patients and planned for kanamycin therapy. Data before and 3 weeks after treatment consist of personal data collection, physical exam of ENT, tympanometry, pure tone audiometry, DPOAE, and blood sample collection for glutation peroksidase-1 (GPx-1) serum. Outcome. The data then analyzed for comparison of subject group characteristic using paired t-test if the data is normally distribute, and using Wilcoxon if the data is abnormally distribute. The data is also analyzed for GPx-1 level correlation with SNHL using Mann-Whitney test. The result is statistically significant if $p \leq 0,05$.

Findings: This study was held from February 2017 to April 2017, using 17 subject that fulfill the inclusion criteria. All subject received same test for pre and post Kanamycin therapy, which includes tympanometry, pure tone audiometry, DPOAE, and GPx-1 level.

Table 1: Subject Characteristic

Characteristics	n=17
Gender, n (%)	
Male	7 (41,2)
Female	10 (58,8)
Age (years)	
Mean ± SD	36 ± 8
Range	23 – 46

Table 2: GPx-1 Level Before and After Kanamycin Therapy

	Measurement		Decendants (%)	p-value
	Before therapy (u/l)	After 3 weeks therapy (u/l)		
GPx-1				
Mean ± SD	4,49 ± 3,12	1,2 ± 1,0	70.42 ± 20,94	<0,001*
Range	1,01 – 14,01	0,07 – 5,15	18.81 – 98,54	

Analysis using paired-t test. *significant if $p \leq 0.05$

Based on these table GPx-1 level before therapy with range 1,01-14,01 ($4,49 \pm 3,12$) and GPx-1 level after therapy ($1,2 \pm 1,0$) with range 0,07 – 5,15.

Table 3: Correlation between GPx-1 level and DPOAE value

	DPOAE test (Dp-NF)		p-value
	Pass n=4 (23,5%)	Refer n=13 (76,5%)	
GPx-1			
Mean ± SD	66,60 ± 21,02	84,59 ± 14,86	0,062*
Range	18,81 – 92,36	64,40 – 98,54	

Analysis using paired-t test. *significant if $p \leq 0.05$

From the analysis above, GPx-1 median value at ear that having DPOAE test a “refer” value is higher (84,59 ± 14,86) compared to those who have DPOAE test a “pass” value (66,60 ± 21,02), but it’s not significant statistically ($p=0,062$).

Table 4: Audiometry examination before and after Kanamycin therapy

Frequency	Ear	Threshold (dB)		p-value
		Before Therapy Mean ± SD	After Therapy Mean ± SD	
500 Hz	AD	20,6 ± 5,6	23,7 ± 5,3	0,002
	AS	21,2 ± 4,5	24,7 ± 4,1	0,020
1.000 Hz	AD	18,8 ± 3,3	19,4 ± 5,0	0,041
	AS	18,2 ± 5,0	21,8 ± 3,5	0,048
2.000 Hz	AD	14,4 ± 3,6	17,7 ± 3,3	0,045
	AS	14,4 ± 3,9	18,5 ± 5,8	0,016
4.000 Hz	AD	16,8 ± 5,6	20,9 ± 4,4	0,050
	AS	15,3 ± 6,0	21,8 ± 6,4	0,020
8.000 Hz	AD	19,1 ± 7,3	24,4 ± 6,6	0,003
	AS	18,0 ± 7,7	25,9 ± 10,3	0,004

Analysis using paired-t test. *significant if $p \leq 0.05$

There’s a significant increase in hearing threshold on both ear from pre to post Kanamycin therapy using audiometry each frequency.

Table 5: Correlation between GPx-1 Level and Sensorineural Hearing Loss

	SNHL		P value
	Yes n=13 (76,5%)	No n=4 (23,5%)	
GPx-1 Pre Therapy			
Mean ± SD	3,68 ± 1,99	7,13 ± 4,88	0,049
Median	3,73	5,88	
Range	1,01 – 6,32	2,75 – 14,01	
GPx-1 Post Therapy			
Mean ± SD	0,95 ± 0,71	1,99 ± 2,17	0,013
Median	0,82	1,30	
Range	0,07 – 2,59	0,21 – 5,15	

Analysis using Mann-Whitney test. *significant if $p \leq 0.05$

There’s a significant correlation between GPx-1 level and SNHL condition.

Discussions

This study conclude MDR TB is mostly suffered by female (58.2%) compared with male (41,8%). Liu et.al hypothesized that female mostly spend their day taking care of their family who has MDR TB, compared to male, so the risk of bacterial infection transmission is higher in female.²⁸ This result also found in Pelaquin et.al study and WHO data survey on 2015.^{2,29} Pelaquin study stated that gender does not affect the ototoxic effect of Kanamycin in MDR TB therapy and there is no direct correlation between MDR TB incidence and gender.²⁹

Based on age group, this study conclude that MDR TB cases occur mostly on productive age (23 – 46 years old). This result was supported by Rakhmawati and Reviono et.al study that also found that MDR TB cases most likely occur on age 20 – 50 years.^{5,8} Medical record data at Dr. Hasan Sadikin General Hospital, Bandung, Indonesia on 2016 stated that MDR TB mostly happen in age group 25-54 years.⁴ Productive age have higher working time than other age group, which may affect the obedience for taking medicine, which then lead to drug resistance. Productive age also has more contact to different people in work, school, or other activity, so the risk of bacterial transmission is higher and could influence the incidence of MDR TB.²⁸

Kanamycin is known for its side effect damaging outer hair cell of cochlea. This study used DPOAE on frequency ranged 1,500 Hz to 8,000 Hz which was tested prior and 3 weeks after the therapy begin. The result was most of the study subject exhibit “refer” value, which indicates damage at cochlear cell hair. Other study by Mustikaningtyas also exhibit the same result.^{25,29} DPOAE test could provide initial data of hearing condition and early detection of ototoxicity. Reavis et.al stated that DPOAE could detect around 78% of hearing problem cases, which then confirmed using HFA. Other study also stated that DPOAE test is sensitive in monitoring of ototoxicity caused by drugs.²⁸

MDR TB infection is a chronic infection, marked by a decrease in one of antioxidant enzyme. Study of Alli et.al and Madebo stated that the antioxidant enzyme known to be decreased by chronic infection is GPx-1.^{16,17} This study found that GPx-1 level is significantly decrease after 3 weeks therapy of Kanamycin. ROS production happens continuously inside the cell, together with a decrease in antioxidant production, which results an imbalance level of antioxidant and ROS. This imbalance leads to DNA, cell membrane, cell

protein and kinase protein damage. DNA damage can be repaired by Base Excision Repair (BER) mechanism, but if the damage exceeded BER capability, the cell will activate protein P53 and result in apoptosis.²⁷ GPx-1 level is determined by many factor, such as inflammation process, inadequate nutritional intake, and low social economy condition.²⁰

Pure tone audiometry testing is used to monitor the change of hearing threshold due to Kanamycin therapy. A study conducted by Rakhmawati also shows a decrease on sensorineural hearing function from frequency 4.000 Hz to 8.000 Hz.⁵ Other study conducted by Mustikaningtyas shows that SNHL after Kanamycin therapy happens in several level (48% mild, 24% moderate, 4% moderate-severe, 1% severe and 15% very severe).²⁹

Baseline data, consist of HFA, tympanometry, speech audiometry, and OAE, should be recorded before administration of ototoxic therapy to determine the hearing threshold. Pure tone audiometry is the only exam that still used before administering ototoxic therapy.²⁶

Early stage of Kanamycin therapy does not exhibit hearing problem on speech frequency (500 – 4.000 Hz), so not many patient realized that hearing problem is already happened. HFA exam can be useful for early detection of hearing problem, so further and more severe condition can be prevented.¹⁴

Table 3 showed a tendency of diminishing level of GPx-1 level after Kanamycin therapy, although it is not statistically significant. This may result from a minimal number of samples. On this study, decreasing level of GPx-1 level is more likely to be lower on “refer” value ear compared to “pass” value ear after therapy, whereas GPx-1 level is higher on “refer” value ear compared to “pass” value ear before therapy. This may result from higher exposure of ROS on “refer” value ear cochlea as an effect of intracellular defense, which then lead to an increase in GPx-1 level at the beginning to balance ROS level. This mechanism will end at some point due to maximal compensatory effect of GPx-1 enzyme, so the imbalance of ROS and antioxidant enzyme is no more tolerable, which lead to the damage of cochlear hair cell.^{14,23}

Table 5 shows that GPx-1 level is significantly related to SNHL. Low GPx-1 level decreasing the capability of this enzyme to eliminate ROS, especially in basal area of cochlea.³¹ This phenomenon is because GPx-1 level in basal area of cochlea is lower than in

apex area, causing basal area to be more vulnerable.¹⁵ Study conducted by Sharma et.al showed that 18 MDR TB patient that is given Kanamycin therapy for 6 weeks, develop sensorineural hearing problem, 2% on the first week and 12% after 6th week. Mostly having bilateral hearing problem.²⁵

The limitations of this study were the fact that GPx-1 examination performed with ELISA which only saw serum levels or amount of the enzyme, but not the activity of the enzyme.

Conclusion

There is a significant correlation between GPx-1 level and SNHL condition proceeding Kanamycin therapy on MDR TB patient, characterized by a decrease in GPx-1 level and an increase in hearing threshold on subjects after administration of Kanamycin therapy.

Conflict of Interest: There was no conflict of interest in this study.

Ethical Clearance: The ethical clearance is granted from KEPK, Dr Hasan Sadikin General Hospital, Bandung no.LB.04.01/A05/EC/033/II/2017.

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References

1. Sharma R, Yadav R, Sharma M, Saini V. Quality of Life of Multi Drug Resistant Tuberculosis Patients : a Study Of North India. *Acta Medica Iranica*. 2014 ;52:448–53.
2. World Health Organization. Global Tuberculosis Report. Geneva. WHO. Switzerland.2015.
3. Pusat Data dan Informasi Kementerian Kesehatan RI. Tuberculosis. 2015. Jakarta. Kemenkes RI. 2015.
4. Unit Rawat Jalan Rumah Sakit Hasan Sadikin. 2016.Data Rekam Medis. RS.Hasan Sadikin Bandung.RSHS.
5. Rakhmawati L, Agustian R.A, Wijana. Peluang Kejadian ototoksitas pada penggunaan kanamisin dalam pengobatan tuberkulosis resisten obat ganda selama 1 bulan. *MKB*. 2015;47(4):224–30.
6. Sub Direktorat Tuberculosis Direktorat Jenderal Pengendalian Penyakit dan Penyehatan Lingkungan. Pengendalian TB resisten Obat. Jakarta. Depkes RI.2011.
7. Caminero J, Sotgiu G, Zumla A, Migliori G. 2010. Best-drug Treatment for multidrug-resistant and extensively drug-resistant tuberculosis. *Lancet Infect Dis*. 2010;10:621–9.
8. Shim Ts, Jo Kw. Medical treatment of pulmonary multidrugs-resistant tuberculosis. *Infect Chemoter*. 2013; 45(4):367–74.
9. Liu H, Ding D, Jiang H, Wu X, Salvi R. Ototoxic destruction by Co-administration of Kanamisin and Ethacrynic acid In Rats. *Jzus*. 2011;12:853–61.
10. Huth ME, Ricci AJ, Cheng AG. Mechanism of Aminoglycoside Ototoxicity and Targets of Hair Cell Protection. *Int J Otolaryngol*. 2011;14:314–55.
11. Lubos E, Loscalzo J, Handy D. Glutathione Peroxidase-1 in Health and disease: From Molecular to Therapeutic Opportunities. *Antioxid Redox Signal*. 2011;15:1957–69.
12. Margis R, Dunand C, Texeira FK, Pinheiro MM. Glutathione peroxidase family - an evolutionary overview. *FEBS J*. 2008;275:3959–70.
13. Ohlemiller K, Macfaden S, Ding D. Targeted Mutation Gene for Glutathione Peroxidase Increase Noise Induced Hearing Loss in Mice. *JARO*. 2000;1:243–54.
14. McFadden SI, Ohlemiller K. The influence of Superoxide Dismutase & Glutathione Peroxidase Deficiency on Noise induce Hearing Loss in Mice. *Noice Health*. 2001;3:49–64.
15. Kil J, Pierce C, Tran H, Gu R. Ebselen treatment reduces noise induced hearing loss via the mimicry and induction of glutathione peroxidase. *Hear Res*. 2006;44–51.
16. Alli J, Kehinde A, Kosoko A, Adenowo O. Oxidative Stress and reduced vitamin C and E level associated with Multi drugs Resistant Tuberculosis. *JTR*. 2014;2:52–8.
17. Madebo T. 2003. Circulating antioxidants and lipid peroxidation product in untreated tuberculosis in Ethiopia. *Am J Clin Nutr*;78:117–22
18. Le Prell C. G DC, Rudnick E.W, Nelson M.A, Deremer J.S, Prieskorn DM, Miller J.M. Assessment of Nutrient Supplement to Reduce Gentamisin – Induced Ototoxicity. *JARO*. 2014;15:375–93.
19. Jiang H, Sha S, Forge A, Schact J. Caspase-Independent Pathway of Hair cell death induced by Kanamycin In vivo. *cell death differ*. 2006;13:20–30.

20. Dugal P, Sarkar M. Audiologic monitoring of Multi Drug Resistant Tuberculosis Patients on Aminoglycoside Treatment with Long Term Follow Up. *BMC ENT Dis.* 2007;7:1-7.
21. Erlinda E, Purnami N, Supriyadi. Correlation between superoxide dismutase serum and sensoryneural hearing disorder in patient with multi drug resistance tuberculosis. *Folia Medica Indonesiana.* 2013;49:42-50.
22. Sagwa E, Ruswa N, Mavhunga F, Renie T, Leufkens H. Comparing amikacin and kanamycin-induced hearing loss in multidrug-resistant tuberculosis treatment under programmatic conditions in Namibian retrospective cohort. *BMC Pharmacol Toxicol.* 2015;16:36-45.
23. Sharma V, Bhagat S, Verma B, Singh R. Audiological Evaluation of Patients Taking Kanamycin for Multidrug Resistant Tuberculosis. *Iran J Otol.* 2016;28(3):203-8.
24. Durrant JD, Campbel K. Ototoxicity monitoring. *J Am Acad Audiol.* 2009:1-25.
25. American Academy of Audiology. Position Statement and Clinical Practice Guidelines: Ototoxicity monitoring. *Am Ad Audiol.* 2009:1-25.
26. Deaval G, Martin E, Horner J, Roberts R. Drug-induced Oxidative Stress and Toxicity. *J Toxicol.* 2012;12:1-13.
27. Liu Q, Shao Y, Song H, Li G. 2013. Rates and risk factors for drug resistance tuberculosis in Northern China. *BMC pub health.* 2013;13:1-7.
28. Peloquin C BS, Nitta A, Simone P, Goble M. Aminoglycoside Toxicity: daily versus Thrice Weekly Dosing for Treatment of Mycobacterial Disease. *Clin Infect Dis.* 2004;11:1538-44.
29. Mustikaningtyas E, Purnami N. Hearing disorder in multidrug-resistant tuberculosis patients at the outpatients unit, pulmonary department, DR Soetomo Hospital Surabaya. *Folia Medica Indonesiana.* 2013;49(4):263-7.
30. Klemens J M, Hughes LF, Somani S, Campbel K. Antioxidant Enzyme Levels Inversely Covary with Hearing Loss after Amikacin treatment. *J Am Acad Audiol.* 2006;43:134-42.
31. Kohza S. Ototoxicity in Tuberculosis treatment in South Africa: Exploring the current status. *Afr J Pharm Pharmacol.* 2013;7:2140-5.

Risk Factors of Osteoporosis in Postmenopausal Women in Karbala Governorate–Iraq 2019

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Abstract

Background: Osteoporosis is a major public health problem because it leads to weakness of skeleton, increase risk of fractures particularly of the spine and hip, increases morbidity and mortality which are a huge burden on the health system.

Objectives:

1. To evaluate bone mineral density (BMD) of postmenopausal women by dual energy x-ray absorptiometry.
2. To explore the association between bone density at lumber spine and investigated risk factors for osteoporosis.

Method: A cross sectional study was carried out from February till the end of June 2019. A purposive sample of (350) women who were referred to DEXA unit in Al-Imam Hussain Medical City in Karbala Province/ Iraq. Data were gathered by direct interview with the patients using a special questionnaire prepared for the purpose of the study.

Results: The overall prevalence of osteoporosis and osteopenia was (48.9% and 27.7%) respectively. The factors such as age, residence, educational level, BMI, history of diabetes, physical activity, sun exposure, age at menarche, duration of menopause, parity and duration of breast feeding showed significant association with bone density. Occupational status, history of hypertension, smoking, menopausal age, personal and family history of minimal trauma fracture showing no significant association with bone density.

Conclusion: The prevalence of osteoporosis in this study was high. Appropriate educational programs and interventions could help to increase the women's peak bone mass therefore reducing their risk of developing osteoporosis.

Keywords: Osteoporosis, Bone mineral density, Dual energy x-ray absorptiometry.

Introduction

Osteoporosis (OP) is known as a “silent global problem”, which is characterized by a decline in the

bone mass and structural deterioration of bone tissue that leads to decrease skeletal strength with increase in bone fragility and vulnerability to fracture⁽¹⁾.

According to World health organization (WHO), osteoporosis is defined by bone mineral density at the hip or lumbar spine that is less than or equal to 2.5 standard deviations(SD) below the mean BMD of a young-adult reference population ⁽²⁾.

Nearly 10% of the world's population and 30%

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of post-menopausal women are suffering from the disease⁽³⁾.

Osteoporosis can be categorized as either primary or secondary. Bone loss associated with primary osteoporosis is a normal part of the aging process, especially following menopause, while secondary osteoporosis is a result of certain medications or medical conditions⁽⁴⁾.

Various risk factors are related with the occurrence of osteoporosis. There are some modifiable risk factors such as sex hormone, dietary intake of calcium and vitamin D, long duration consumption of some medications like steroids and antacids, sedentary life style, smoking and excessive intake of alcohol and caffeine. On the other side gender, age, body size, race and family history are non-modifiable risk factors⁽⁵⁾.

Methodology: Study design, setting and time: A cross sectional study was carried out at DEXA scan unit in Al-Imam Hussain Medical City in Kerbela province/Iraq from January to the end of June 2019.

Sampling method: A non-probability (purposive) sample included (350) females referred to DEXA unit from consultation clinics of Al-Imam Hussain Medical City and other private hospitals in the governorate. All women aged ≥ 40 years with menopausal duration more than one year were eligible to be included in the study. Patients with dementia, malignant tumors, body weight >120 kg, conditions affecting bone metabolism as diseases of the kidney, liver, hyperthyroidism, rheumatoid arthritis, cerebral infarction and patients taking medications affecting bone metabolism such as glucocorticoids, thyroid hormones, thiazide diuretic, anti-seizure, proton pump inhibitors, warfarin, heparin and cancer chemotherapy were excluded.

- Verbal consent was obtained from each participant and ethical approval of Karbala Health Directorate and Al-Imam Hussain Medical City also had taken.
- Data collection method and tools: information's were collected by direct interview with the participants using structured questionnaire consist of sociodemographic data such as: age, residence, occupation, educational level, history of hypertension or diabetes mellitus. Weights and heights were measured without shoes in light clothing by the use of well calibrated digital weight and height scale measuring device. Body mass index (BMI) was calculated by dividing weight in

kilograms by the square of the height in meters as in the equation:

$$\text{Weight (kilograms)} / \text{height (meters)}^2(6):$$

Behavioral risk factors include: smoking habit, sun exposure, level of physical activity.

Patients were also asked about personal and family history of minimal trauma fracture and about reproductive risk factors as: age at menarche, age at menopause, menopausal duration, parity and duration of breast feeding.

Bone mineral density was measured at the lumbar spine L1–L4 by using DEXA machine type (STRATOS, DMS, made in France). The results of measurement categorized according to WHO definition guidelines Normal: T-score (≥ -1.0); Osteopenia: T-score between (-1.0 and -2.5); Osteoporosis: T-score (≤ -2.5)⁽²⁾.

Statistical Analysis: Data analysis was done using SPSS version 24 (statistical package for social sciences). Chi square/Fisher exact test was used to show the association between two categorical variables. P value of ≤ 0.05 was considered as statistically significant.

Results

The mean age of participant was 62.33 (mean \pm SD, 62.33 \pm 8.28).The prevalence of osteoporosis and osteopenia was (48.9% and 27.7%) respectively as shown in (figure 1).

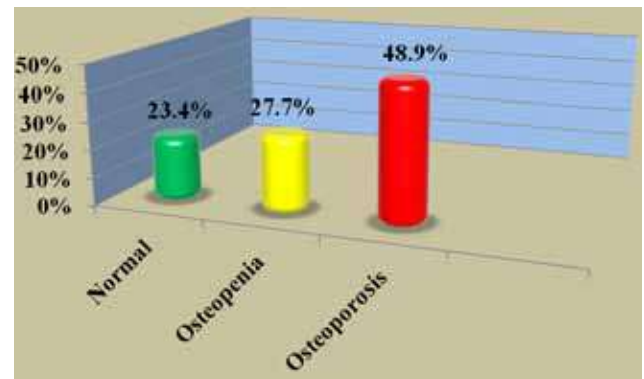


Figure 1: Distribution of women according to the result of DEXA scan

The sociodemographic and behavioral characteristics of the study sample are shown in (Table 1). The majority of women (41.4%) were in the age group (60-69), more than three quarters of them (82.6%) live in urban settings, (53.1%) are illiterate and (85.1%) are housewives. Other characteristics are shown in the following table.

Table 1: Distribution of women according to socio demographic and behavioral variables

Variables	Number (n=350)	Percent %
Current Age		
40-49	17	4.9%
50-59	111	31.7%
60-69	145	41.4%
≥70	77	22%
Residence		
Urban	289	82.6%
Rural	61	17.4%
Educational Level		
Illiterate	186	53.1%
Primary	72	20.6%
Secondary	72	20.6%
University	18	5.1%
Higher education	2	0.6%
Body Mass Index		
Under weight (<18.5)	1	0.3%
Normal (18.5-24.9)	65	18.6%
Over weight (25-29.9)	93	26.5%
Obese (≥ 30)	191	54.6%

Variables	Number (n=350)	Percent %
Smoking		
Non smoker	300	85.7%
Current smoker	21	6.0%
Past smoker	29	8.3%
Exposure to Sun Light		
Never	221	63.1%
< 15 minutes/day	45	12.9%
≥ 15 minutes/day	84	24.0%
Physical Activity		
Sedentary	98	28.0%
Mild intensity	133	38.0%
Moderate intensity	112	32.0%
Vigorous intensity	7	2.0%

Table 2 and table 3 showed that older age group, rural residency, illiterate, low BMI, history of diabetes, physical activity and sun light exposure were significantly associated with osteoporosis. No significant association was found between osteoporosis and each of employment, history of hypertension, smoking, past history and family history of fracture due to minor trauma.

Table 2: Association between result of DEXA scan measurement and women's socio demographic variables

Socio Demographic Variables	Result of DEXA Scan				P-value
	Normal (n=82)	Osteopenia (n=97)	Osteoporosis (n=171)	Total (n=350)	
Age (Year)					<0.001*
40-49	9(52.9%)	6(35.3%)	2(11.8%)	17(100.0%)	
50-59	37(33.3%)	34(30.7%)	40(36.0%)	111(100.0%)	
60-69	32(22.1%)	41(28.2%)	72(49.7%)	145(100.0%)	
≥ 70	4(5.2%)	16(20.8%)	57(74.0%)	77(100.0%)	
Residence					<0.001*
Urban	72(24.9%)	90(31.2%)	127(43.9%)	289(100.0%)	
Rural	10(16.4%)	7(11.5%)	44(72.1%)	61(100.0%)	
Educational Level					<0.001* ^F
Illiterate	27(14.5%)	45(24.2%)	114(61.3%)	186(100.0%)	
Primary	23(31.9%)	16(22.3%)	33(45.8%)	72(100.0%)	
Secondary	25(34.7%)	30(41.7%)	17(23.6%)	72(100.0%)	
University	6(33.3%)	6(33.3%)	6(33.3%)	18(100.0%)	
Higher education	1(50.0%)	0(0.0%)	1(50.0%)	2(100.0%)	
Body Mass Index					<0.001* ^F
Under weight (<18.5)	0(0.0%)	1(100.0%)	0(0.0%)	1(100.0%)	
Normal (18.5-24.9)	7(10.8%)	12(18.4%)	46(70.8%)	65(100.0%)	
Over weight (25-29.9)	19(20.4%)	24(25.8%)	50(53.8%)	93(100.0%)	
Obese (≥ 30)	56(29.3%)	60(31.4%)	75(39.3%)	191(100.0%)	

Socio Demographic Variables	Result of DEXA Scan			Total (n=350)	P-value
	Normal (n=82)	Osteopenia (n=97)	Osteoporosis (n=171)		
History of Hypertension					
Present	41(24.0%)	47(27.5%)	83(48.5%)	171(100.0%)	0.972
Absent	41(22.9%)	50(27.9%)	88(49.2%)	179(100.0%)	
History of Diabetes					
Present	30(32.6%)	34(37.0%)	28(30.4%)	92(100.0%)	<0.001*
Absent	52(20.2%)	63(24.4%)	143(55.4%)	258(100.0%)	

*P value ≤ 0.05 was significant. F: Fisher-exact test.

Table 3: Association between result of DEXA scan and behavioral risk factors.

Variables	Result of DEXA scan			Total	P-value
	Normal	Osteopenia	Osteoporosis		
Physical Activity					
Sedentary	5(5.1%)	22(22.5%)	71(72.4%)	98(100.0%)	<0.001*F
Mild intensity	19(14.3%)	40(30.1%)	74(55.6%)	133(100.0%)	
Moderate intensity	53(47.3%)	33(29.5%)	26(23.2%)	112(100.0%)	
Vigorous intensity	5(7.4%)	2(2.6%)	0(0.0%)	7(100.0%)	
Smoking					
None smoker	74(24.7%)	86(28.6%)	140(46.7%)	300(100.0%)	0.134
Current smoker	2(9.5%)	3(14.3%)	16(76.2%)	21(100.0%)	
Past smoker	6(20.7%)	8(27.6%)	15(51.7%)	29(100.0%)	
Exposure to Sun					
Never	43(19.5%)	67(30.3%)	111(50.2%)	221(100.0%)	<0.001*
< 15 minutes/day	2(4.4%)	11(24.5%)	32(71.1%)	45(100.0%)	
≥ 15 minutes/day	37(44.0%)	19(22.7%)	28(33.3%)	84(100.0%)	
History of Fracture Due to Minor Trauma					
Yes	9(18.8%)	8(16.6%)	31(64.6%)	48(100.0%)	0.055
No	73(24.2%)	89(29.4%)	140(46.4%)	302(100.0%)	
Family History of Fracture Due to Minor Trauma					
Yes	8(36.4%)	4(18.1%)	10(45.5%)	22(100.0%)	0.607
No	69(22.7%)	85(28.1%)	149(49.2%)	303(100.0%)	
Don't know	5(20.0%)	8(32.0%)	12(48.0%)	25(100.0%)	

The association between osteoporosis and reproductive variables are shown in table 4

Table 4: Association between result of DEXA scan and reproductive variables

Variables	Result of DEXA scan			Total	P-value
	Normal	Osteopenia	Osteoporosis		
Age of menarche (year)					
≤11	40(52.7%)	15(19.7%)	21(27.6%)	76(100.0%)	<0.001*
12-14	42(23.3%)	72(40.0%)	66(36.7%)	180(100.0%)	
≥15	0(0.0%)	10(10.6%)	84(89.4%)	94(100.0%)	
Age at menopause (years)					
<45	8(17.8%)	9(20.0%)	28(62.2%)	45(100.0%)	0.164
45-49	26(25.7%)	23(22.8%)	52(51.5%)	101(100.0%)	
≥ 50	48(23.5%)	65(31.9%)	91(44.6%)	204(100.0%)	

Variables	Result of DEXA scan			Total	P-value
	Normal	Osteopenia	Osteoporosis		
Menopausal duration (years)					
≤5	44(51.2%)	27(31.4%)	15(17.4%)	86(100.0%)	<0.001*
6-10	21(24.7%)	34(40.0%)	30(35.3%)	85(100.0%)	
≥11	17(9.5%)	36(20.1%)	126(70.4%)	179(100.0%)	
Parity					
Nulliparous	4(20.0%)	9(45.0%)	7(35.0%)	20(100.0%)	<0.001*
Prime	5(71.4%)	0(0.0%)	2(28.6%)	7(100.0%)	
Multiparous	30(39.0%)	24(31.1%)	23(29.9%)	77(100.0%)	
Grand multiparous	43(17.5%)	64(26.0%)	139(56.5%)	246(100.0%)	
Duration of breast feeding (month)					
None	15(33.3%)	13(28.9%)	17(37.8%)	45(100.0%)	0.004*
<24	6(37.5%)	4(25.0%)	6(37.5%)	16(100.0%)	
24-59	18(34.7%)	19(36.5%)	15(28.8%)	52(100.0%)	
≥60	43(18.2%)	61(25.7%)	133(56.1%)	237(100.0%)	

Discussion

The prevalence of osteoporosis among participants was (48.9%). This prevalence was higher than a study done in AL- Sulaimani Province 39%⁽⁷⁾, Jordan 37.5%⁽⁸⁾ and 18% in Saudi Arabia⁽⁹⁾, but lower than 50.7% in Iran⁽¹⁰⁾. This inconsistency in the findings is perhaps related to the differences in diagnostic technique used, bone scan site chosen and selection of the patients.

In this study significant association was found between advanced age and the prevalence of osteoporosis. As the age increases, osteoporotic cases increase. This result was similar to other studies done in India and Iran^(11,12). The probable explanation is the alteration of the balance of the cellular activity with ageing process, with a reduced osteoblast response to continued bone resorption, so the resorption cavities are incompletely filled by a new bone formation during the remodeling cycle⁽¹³⁾.

The prevalence of osteoporosis in rural areas was higher than that in urban areas. A recent study reported similar association⁽¹⁴⁾. This might be explained by the rural community had less availability of health services and treatment which leads to lack of early detection of the disease.

Osteoporosis was more prevalent among illiterate women which is in line with other studies^(15,16).

High prevalence of osteoporosis in those with normal BMI in comparison with obese patients.

This difference was supported by other studies^(17,18). High BMI is responsible for the ability to endure larger mechanical loads thereby reducing bone resorption and stimulating bone formation. Besides, large body weight and BMI reflect the nutritional status, and malnutrition directly affects bone remodeling⁽¹⁹⁾.

No significant association was found between history of hypertension and the risk of osteoporosis. These results disagreed with the other studies^(20,21). This difference can be explained by many hypertensive patients were not enrolled in the study because of exclusion criteria.

The study showed that osteoporosis was more prevalent among non-diabetic women in comparison with type 2 diabetic patient. This finding was agree with the findings of one study⁽²²⁾ but disagree with other⁽²³⁾.

Osteoporosis is more prevalent among women who not exposed to sun compared to women who exposed for ≥ 15 minutes. Similar study done in India stated that poor sunlight exposure is one of the factors contributing to bone loss in women above 40 years of age⁽²⁴⁾.

The current study failed to demonstrate a significant association between family history of fracture and risk of developing osteoporosis. This was inconsistent with Buttros et al., who reported that maternal history of fracture was clinical indicator of risk for osteoporosis⁽²⁵⁾. This could possibly be explained by recall bias of family history of prior fracture.

Our study showed an association between the increase in age at menarche and risk of developing osteoporosis. Early menarche may have a protective effect on the development of osteoporosis since it is associated with higher circulating estrogen during and after menarche. This result agrees with the results of other study that reported associations between earlier menarche and increased BMD⁽²⁶⁾.

The results showed that the risk of osteoporosis increase with the increase in duration of menopause. This was in concordance with research literatures^(12, 27).

Results of the current study demonstrated that parity and duration of lactation were significantly higher in the osteoporosis group than in the normal group. An association between parity and bone loss was reported by other study.⁽²⁸⁾

Conclusion

Osteoporosis in this study appear to be associated with several risk factors include (older age, rural residence, low BMI, illiteracy, sedentary life, no sun exposure, age at menarche, menopausal duration, parity and duration of lactation).

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References

1. Kanis JA, Burlet N, Cooper C, Delmas PD, Reginster JY, Borgstrom F, et al. European guidance for the diagnosis and management of osteoporosis in postmenopausal women. *Osteoporosis International*. 2008;19(4):399-428.
2. Cosman F, de Beur SJ, LeBoff MS, Lewiecki EM, Tanner B, Randall S, et al. Clinician's Guide to Prevention and Treatment of Osteoporosis. *Osteoporosis International*. 2014;25(10):2359-81.
3. Bijelic R, Milicevic S, Balaban J. Risk Factors for Osteoporosis in Postmenopausal Women. *Medical archives (Sarajevo, Bosnia and Herzegovina)*. 2017;71(1):25-8.
4. Sözen T, Özışık L, Başaran NÇ. An overview and management of osteoporosis. *European journal of rheumatology*. 2017;4(1):46-56.
5. Singh P. Epidemiology of Osteoporosis and Impact of Nutritional Awareness among Pre and Post Menopausal Women of Allahabad District: Department of Food Nutrition and Public Health Ethelind Collage of Home Science Faculty of Agriculture 2017.
6. Labban L. Nutritional knowledge assessment of syrian university students. *Journal of the Scientific Society*. 2015;42(2):71-7.
7. Qaradakh TA, Mahmood TA, Ahmed RA. Bone Mineral Density value among Postmenopausal Women and it's correlation with body mass index in Sulaimani Governorate. *Journal of Dental and Medical Sciences* 2015;14(12): 110-4
8. Hyassat D, Alyan T, Jaddou H, Ajlouni KM. Prevalence and Risk Factors of Osteoporosis Among Jordanian Postmenopausal Women Attending the National Center for Diabetes, Endocrinology and Genetics in Jordan. *BioResearch Open Access*. 2017;6(1):85-93.
9. Anitha Oommen IA. Prevalence of osteoporosis and factors associated with osteoporosis in women above 40 years in the Northern Part of Saudi Arabia. *International Journal of Research in Medical Sciences*. 2014;Vol 2, No 1 (2014).
10. Saei Ghare Naz M, Ozgoli G, Aghdashi MA, Salmani F. Prevalence and Risk Factors of Osteoporosis in Women Referring to the Bone Densitometry Academic Center in Urmia, Iran. *Global journal of health science*. 2015;8(7):135-45.
11. Aggarwal N, Raveendran A, Khandelwal N, Sen RK, Thakur JS, Dhaliwal LK, et al. Prevalence and related risk factors of osteoporosis in peri- and postmenopausal Indian women. *J Midlife Health*. 2011;2(2):81-5.
12. Sharmai SH, Millani F, Alizadeh A, Ranjbar ZA, Shakiba M, Mohammadi A. Risk Factors of Osteoporosis in Women Over 50 years of Age: A Population Based Study in the North of Iran. *Journal of the Turkish-German Gynecological Association*. 2008;9(1).
13. Baccaro LF, Machado VdSS, Costa-Paiva L, Sousa MH, Osis MJ, Pinto-Neto AM. Factors associated with osteoporosis in Brazilian women: a population-based household survey. *Archives of osteoporosis*. 2013;8(1-2):138.
14. Kim J, Lee J, Shin JY, Park BJ. Socioeconomic disparities in osteoporosis prevalence: different results in the overall Korean adult population and single-person households. *J Prev Med Public Health*. 2015;48(2):84-93.

15. Mai B. Estimation of 10-year probability bone fracture using WHO Fracture Risk Assessment Tool (FRAX), published in An-Najah National University. Nablus, Palestine. 2013.
16. Allali F, Rostom S, Bennani L, Abouqal R, Hajjaj-Hassouni N. Educational level and osteoporosis risk in postmenopausal Moroccan women: a classification tree analysis. *Clinical rheumatology*. 2010;29(11):1269-75.
17. El Maghraoui A, Ghazi M, Gassim S, Ghozlani I, Mounach A, Rezqi A, et al. Risk factors of osteoporosis in healthy Moroccan men. *BMC musculoskeletal disorders*. 2010;11(1):148.
18. Lloyd JT, Alley DE, Hawkes WG, Hochberg MC, Waldstein SR, Orwig DL. Body mass index is positively associated with bone mineral density in US older adults. *Archives of osteoporosis*. 2014;9(1):175.
19. Wu S-F, Du X-J. Body mass index may positively correlate with bone mineral density of lumbar vertebra and femoral neck in postmenopausal females. *Medical science monitor: international medical journal of experimental and clinical research*. 2016;22:145.
20. Popović¹ MR, Tasić I. Association between hypertension and osteoporosis in postmenopausal women. 2009.
21. Zhang J, Zhang K, Shi H, Tang Z. A cross-sectional study to evaluate the associations between hypertension and osteoporosis in Chinese postmenopausal women. *Int J Clin Exp Med*. 2015;8(11):21194-200.
22. Anaforoglu I, Nar-Demirer A, Bascil-Tutuncu N, Ertorer ME. Prevalence of osteoporosis and factors affecting bone mineral density among postmenopausal Turkish women with type 2 diabetes. *Journal of Diabetes and its Complications*. 2009;23(1):12-7.
23. Moghimi N, Rahimi E, Derakhshan S, Farhadifar F. Osteoporosis in postmenopausal diabetic women; prevalence and related factors. *Iranian Journal of Nuclear Medicine*. 2008;16(30):28-33.
24. Kadam N, Chiplonkar S, Khadilkar A, Divate U, Khadilkar V. Low bone mass in urban Indian women above 40 years of age: prevalence and risk factors. *Gynecological Endocrinology*. 2010;26(12):909-17.
25. Buttros DdAB, Nahas-Neto J, Nahas EAP, Cangussu LM, Barral ABCR, Kawakami MS. Fatores de risco para osteoporose em mulheres na pós-menopausa do sudeste brasileiro. *Revista Brasileira de Ginecologia e Obstetrícia*. 2011;33:295-302.
26. Parker SE, Troisi R, Wise LA, Palmer JR, Titus-Ernstoff L, Strohsnitter WC, et al. Menarche, menopause, years of menstruation, and the incidence of osteoporosis: the influence of prenatal exposure to diethylstilbestrol. *The Journal of clinical endocrinology and metabolism*. 2014;99(2):594-601.
27. D'Amelio P, Spertino E, Martino F, Isaia GC. Prevalence of postmenopausal osteoporosis in Italy and validation of decision rules for referring women for bone densitometry. *Calcified tissue international*. 2013;92(5):437-43.
28. Sharma N, Natung T, Barooah R, Ahanthem SS. Effect of Multiparity and Prolonged Lactation on Bone Mineral Density. *J Menopausal Med*. 2016;22(3):161-6.

Identification of Some Dermatophytes Isolated by PCR Technique in Misan Province/Iraq

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Abstract

Dermatophytes are a complex group of fungi, which include three genera *Trichophyton*, *Epidermophyton* and *Microsporum*. These fungi have the ability to degrade the keratin layer resulting in dermatophytosis, also known as Tinea or Ringworm. Because conventional method used to diagnose dermatophytes are slow and unspecialized, there is a need to use improved diagnostic method. Specialized primers were used OPAA11, OPD18, OPAA17 and OPU15 and the DNA sequence of the nuclear ribosome regions ITS1 and ITS4 were used. DNA was extracted for 14 isolates from dermatophytes (were isolated from patients in Misan province/southern Iraq Misan province/southern Iraq) and amplified by PCR for identify at species level by sequencing from the ribosomes using the MEGA program of mapping of the studied fungi to know the evolutionary relationships where the results of the genetic tree showed the existence of complex relationships between dermatophytes. The aim of this study was to identify different types of skin fungi as quickly and accurately as possible.

Keywords: Dermatophytes, dermatophytosis, Tinea, Trichophyton, AP-PCR.

Introduction

The fungal infections caused by skin fungi Dermatophytes, also known as ringworm, dermatophytosis, ringworm. Dermatophytosis or Tinea, a highly infectious skin disease of humans and animals^[1]. Dermatophytosis is one of the most common infections worldwide and is estimated at 20-25%^[2]. Dermatophytes are divided according to the environment Prefer into three types: Zoophilic, Geophilic and Anthrophilic^[3]. These include three species: *Microsporum*, *Trichophyton*, and *Epidermophyton*. Infection by these fungi occur in the skin and accessories such as hair and nails^[4]. The annual cost of treating injuries is estimated at around 500\$ million globally, and these diseases are second only to skin diseases^[5].

Filamentous dermatophytes secrete many metabolic substances that contribute to infection, including enzymes^[6]. The enzymes secreted by dermatophytes can underlie the survival of the fungus on the host and develop^[7,8]. Depending on the efficacy of these enzymes, the fungi races vary in their preference for the type of keratinous tissue, as the genus *Epidermophyton* prefers the tissues of the nails and skin, while the genus *Microsporum* prefers the tissues of the skin and hair, and with respect to the genus *Trichophyton* attacks all keratinized tissues, whether skin, hair or nails^[9].

It is known that the diagnosis of dermatophytes requires a microscopic examination method has been found this method is sometimes inaccurate because it may give false results, especially if the species are close^[9]. In some slow-growing species, such as *T.verruucosum*, a transplant may take several weeks after which several diagnostic tests are required, which usually require different transplant media^[10]. and the phenotypic properties of dermatophytes are altered by many environmental, nutritional and chemical factors, which is why researchers prefer molecular method and genetic characteristics to identify dermatophytes, also thatmolecular method are fast and more specific^[11].

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Materials and Method

Collection of Samples: Clinical samples were collected of infected patients from the dermatological consultant at Al-Sadar General Teaching Hospital and some private clinics in Misan province / Iraq and for the period between December 2018 and June 2019. The study included the collection of samples from the affected areas of the skin, hair and nails for all ages and for both sexes. Part of the clinical specimens were then taken using sterile forceps and cultured on Sabouraud dextrose agar (SDA) medium. Cycloheximide (2.5 g/ml) and chloramphenicol (250 µg/ml) were added to prepare a selective media. The plates were incubated at 28 °C for 2–4 weeks. Dishes were examined for the appearance of any fungal growth^[12].

Extraction of Fungal DNA: DNA extraction of colonies of dermatophytes isolated at the age of 8-10 days after activation on SDA medium containing cycloheximide and chloramphenicol using the Genomic DNA Mini Kit (Plant) supplied by the Taiwanese company Geneaid with a little modification.

Primers and PCR Analysis: Follow the method described by.^[10] To conduct the test, mixing the components of the master mix in 0.2 ml tubes, especially after testing the PCR (Accuower® PCR premix) containing the remaining reactants. Six types of primers used are ITS1 (5'-TCCGTAGGTGAACCTGCGG-3'), ITS4 (5'-TCCTCCGCTTATTGATATGC-3'), OPAA11(5'-ACCCGACCTG-3'), OPAA17(5'-GAGCCCGACT -3'), OPD18(5'-GAGAGCCAAC -3') and OPU15(5'-ACGGGCCAGT -3')^[13], were diluted with 0.5 ml TE in accordance with the company's instructions. The tube components were thoroughly mixed with vortex and all samples were placed in. The PCR thermocycler is operated according to the programs shown in tables 1. After the PCR program was completed, 4µl of DNA Ladder (1000-100 bp) was placed in the first hole of the agarose gel and 5µl of the PCR product in the second hole. The agarose was dissolved in 100 ml of TBE buffer and at a concentration of 1x3µl of ethidium bromide dye was added and the current was fixed at 70 volts for 75 minutes.

Table (1): PCR Amplification Program

a: for ITS1 and ITS4 Primers

PCR Step	Repeat cycle	Temperature	Time
Initial denaturation	1	95 C°	4 min
Denaturation	30	95 C°	1 min
Annealing		58 C°	1 min
Extension		72 C°	2 min
Final extension	1	72 C°	10 min
Hold	-	4 C°	Forever

b: for OPAA11, OPAA17, OPD18 and OPU15 Primers

PCR Step	Repeat cycle	Temperature	Time
Denaturation	3	94 C°	60 sec
Annealing		36 C°	45 sec
Elongation		72 C°	90 sec
Denaturation	32	94 C°	30 sec
Annealing		36 C°	45 sec
Elongation		72 C°	90 sec

Results and Discussion

ITs- PCR: The results obtained using PCR technique showed that the primers ITS1 and ITS4 amplified the genotype of the fungi under study, where the amplified bands ranged from (550 - 750 bp) as shown in Figure 1.

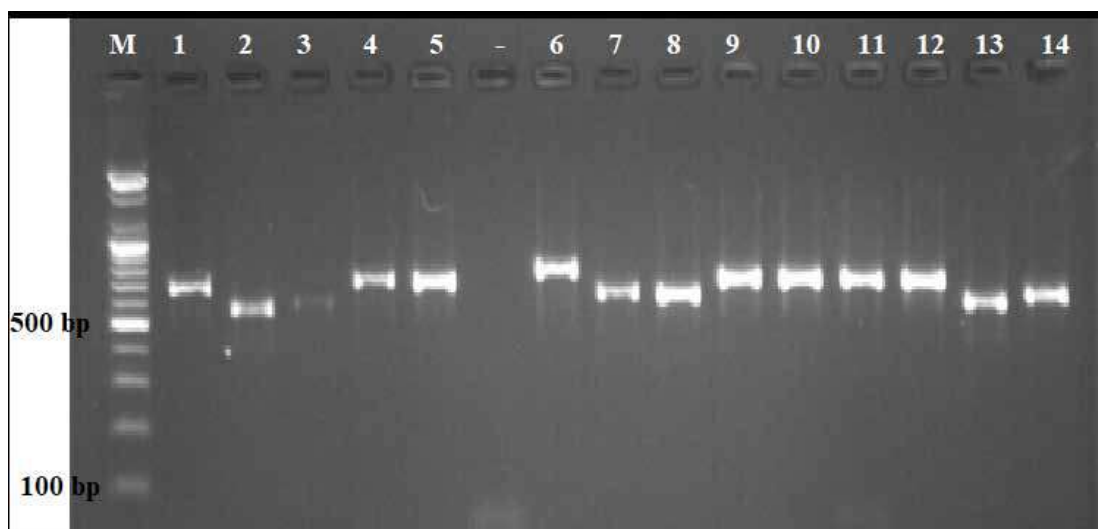


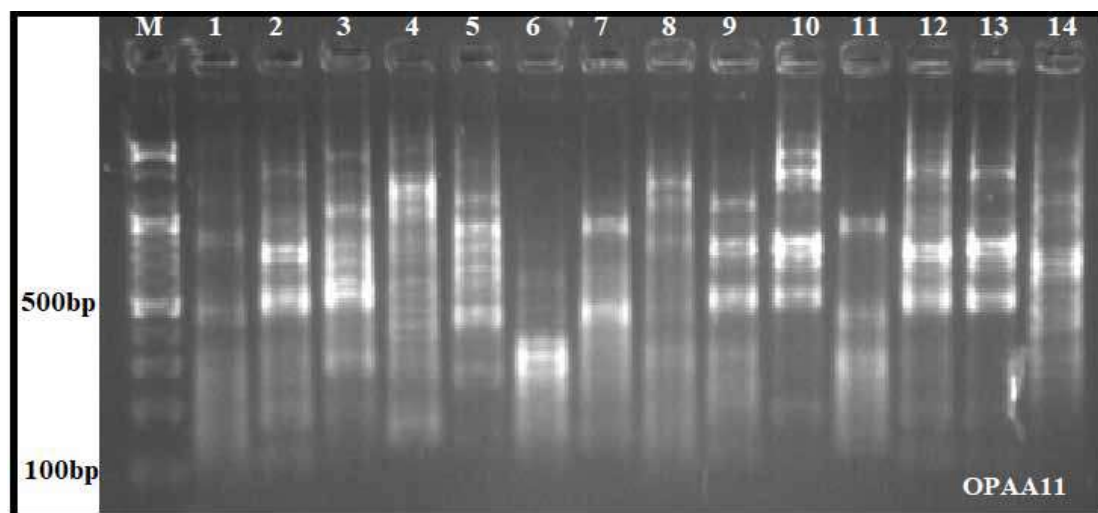
Figure 1: PCR polymers of DNA sequence on the agarose gel using prefixes (ITs1, ITs 4). M:Marker,1: *T. equium*, 2: *T. interdigitale*, 3: *E. floccosum*, 4: *T. mentagrophytes*, 5: *M. persicolor*, 7: *M. audouinii*, 7: *M. canisver. distortum*, 8: *T. erinace*, 9: *M. canisver. equinum*, 10: *M. nanum*, 11: *T. interdigitale*, 12: *T. ajello*, 13: *T. mentagrophytes*, 14: *T. rubrum*.

RAPD-PCR: The study showed that all the RAPD primers used OPAA11, OPU15, OPAA17, and OPD18 amplified the DNA of the fungi under study (Figure 2). The total number of amplified packages was 628

The primer OPAA17 showed 94 bundles and higher Polymorphism 20.2 % While primer showed 200 bundles with less Polymorphism 12% (Table 2).

Table (2): Shows the number of bundles, diversity and genotypes of RAPD prefixes used to amplify the genetic strip

Primers	Total bands	Polymorphic	Monomorphic	Polymorphism %	Diversity
OPAA11	200	24	3	12 %	0.015
OPU15	171	22	6	12.8 %	0.035
OPAA17	94	19	5	20.2 %	0.053
OPD18	163	21	6	12.8 %	0.036
Total	628	86	20	14.45 %	0.034



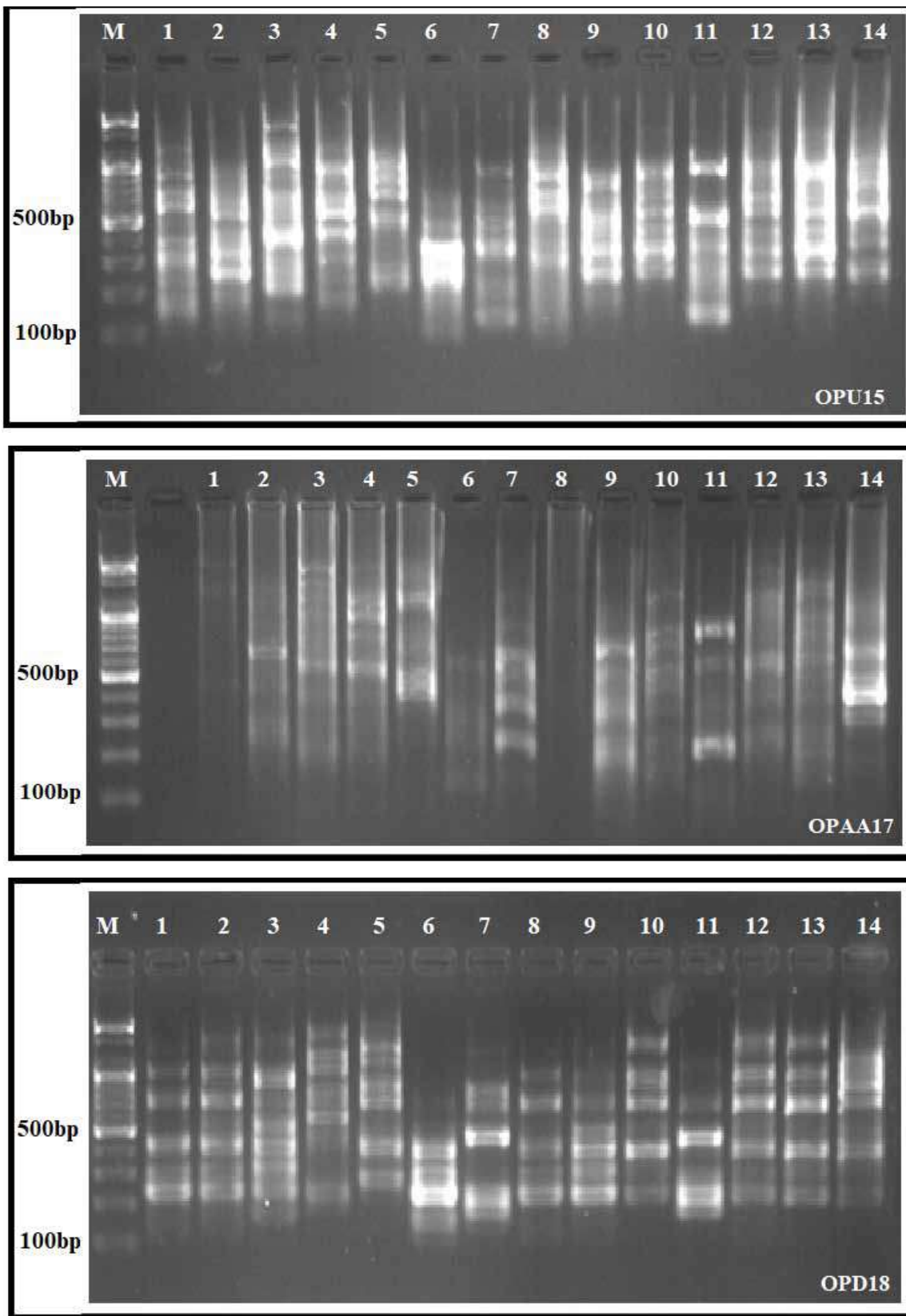


Figure 2 PCR replication DNA sequences on the agarose gel using RAPD technique using primers (OPAA11, OPU15, OPAA17 and OPD 18). M: Marker,1:E.floccosum, 2 M.persicolor, 3: T.mentagrophytes, 4: M.audouinii, 5: T.mentagrophytes, 6: M.canisver.distortum, 7: T.erinace, 8: M .audouinii, 9: T.equium, 10: T.ajello, 11: T.rubrum, 12:M.canisver.equinum, 13: M.nanum, 14: T.interdigitale.

Sequencing: The purified PCR products were sent to Macrogen Lab (Seoul, South Korea). DNA sequences obtained from forward and reverse primer cycle sequences were analyzed by Blast analysis to shrink sequences and align them with previously published sequence data in GenBank.

Genetic tree of studied dermatophytes: The results showed the genetic tree obtained from the application of the MEGA program

It is composed of two main clan groups that included the first clan group *Microsporium audouinii*, the second clan group *Epidermophyton floccosum*, *Trichophyton erinace*, *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Trichophyton interdigitale*, *Microsporium canisver .distortum*, *Microsporium audouinii*, *Trichophyton mentagrophytes*, *Trichophyton equinum*, *Microsporium persicolor*, *Microsporium canisver. equinum*, *Trichophyton ajello* and *Microsporium nanum* (Figure3).

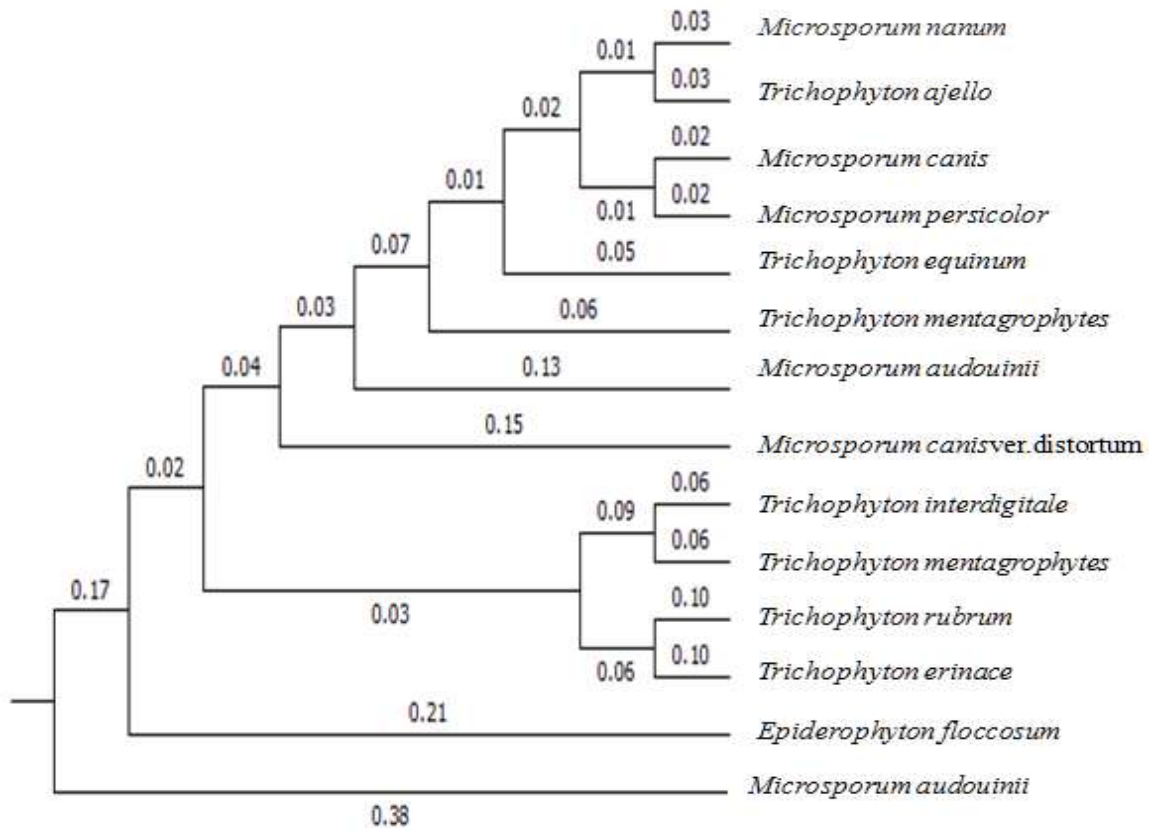


Figure 3: Genetic tree of the studied skin fungi species

PCR technology has become common and indispensable in biological and medical research laboratories for various applications^[14]. The molecular diagnosis of dermatophytes has been able to solve the epidemiology of dermatophytes, such as detecting common sources of infection, infectious method and spreading areas, as well as determining whether re-infection is the original isolation or new strains^[15]. Molecular techniques aim to develop taxonomy, especially for genus, species or strain, and to study the evolutionary correlation between the new taxonomic

orders. These and other studies have distinguished between physiologically similar species, morphologically and also between strains of the same species^[16]. In recent years, specialized region primers have been used for direct detection of fungi in skin and nail samples^[17].

Molecular method provide an appropriate solution to the problems we face in the classification of dermatophytes compared to phenotypic diagnostic method .^[18]It was found that the use of conventional method to identify species takes a long time can not be

sufficiently reliable and in some cases the diagnosis is wrong so molecular method are more rapid, accurate and sensitive than phenotypic method to identify the types of dermatophytes and we can get a result within 24 hours from the samples directly from the extraction DNA. [19]The use of molecular method has also facilitated significant progress in identifying and analyzing the results of the genetic tree of dermatophytes[20].

Traditional and molecular classification method have pros and cons, but traditional method have some advantages over molecular method in estimating differences between fungi. Therefore, we should rely solely on data obtained from molecular method in isolation from other data such as phenotypic traits, as this may lead researchers to Inferring misconceptions from the results of genetic tree analysis[21,22].

The use of PCR in the diagnosis of dermatophytes, where Zarrinet *al.* [18];identification ten species of fungi are *M.gypseum*, *M. canis*, *M. ferrugineum*, *T. rubrum*, *T. mentagrophytes*, *T. tonsurans*, *T. verrucosum*, *T. violaceum*, *T. schoenleinii*, *E. floccosum* while found Wiegand *et al*[23]. *T. violaceum*, the main causative agent of tinea capitis in children, followed by *T. rubrum*, While in Egypt, five types of dermatophytes are identified *T. rubrum*, *T. mentagrophytes*, *T. violaceum*, *E. floccosum*, and *M. canis*[24].

The results of the present study showed that the primers used OPAA11, OPAA17, OPU15 (OPD18) are highly efficient in the diagnosis of dermatophytes by obtaining DNA bundles that appeared visible under ultraviolet radiation and this result is consistent with the findings Liu *et al*[25]-they showed that there is a possibility to diagnose about 25-20 species of dermatophytes using one of these primers. This method is quick and highly efficient for the diagnosis of dermatophytes since the diagnosis based on genetic characteristics is more accurate than depending on phenotypic characteristics[13].have used a number of Researchers used this technique in the diagnosis of pathogenic fungi, including dermatophytes[26].The number of bundles of dermatophytes studied varied when using these primers Figure (4 a). This may be due to genetic mutations and new traits or may be due to differences in time periods obtained which can lead to genetic variation between isolates[27]. Obtained in this study as in Figure 4b.

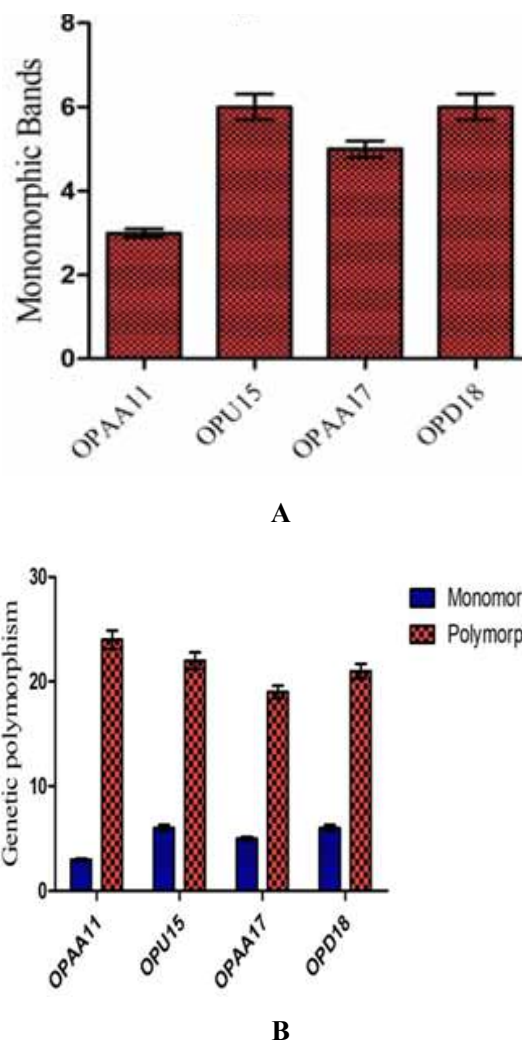


Figure 4 A: The number of packets configured for each primer using PCR-RAPD technology. B. Single and multiple genotypes

Conclusions

PCR technology provides a solution to the problems we face in diagnosing skin fungi by conventional method. In addition, PCR technology is quick, easy and high accuracy.

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Conflict of Interest: There are no conflict of interest.

Source of Funding: Self source funding

Ethical Clearance: Permission to conduct this study was issued by the Health institutional; AL-Sadar Teaching Hospital, and the Swabbing from patients was carried out by a public health technician.

References

1. Pal M. Dermatophytosis in an Adult Cattle due to *Trichophyton verrucosum*. *Animal Husbandry, Dairy and Veterinary Science* 2017; 1(1): 1-3.
2. Sahoo A K, Mahajan R. Management of tinea corporis, tinea cruris, and tinea pedis: A comprehensive review . *Indian dermatology online journal* 2016; 7(2):77]
3. Ziolkowska G, Nowakiewicz A, Gnat S, Troscianczyk A, Zieba P, Majer D B. Molecular identification and classification of *Trichophyton mentagrophytes* complex strains isolated from humans and selected animal species. *Mycoses* 2015; 58(3): 119-126]
4. Reddy K R. Fungal Infections (Mycoses): Dermatophytoses (Tinea, Ringworm). *Journal of Gandaki Medical College-Nepal* 2017; 10(1)]
5. El-Diasty E M, Ahmed M A, Okasha N A G W. A, Mansour S F, El-Dek S I, El-Khalek H M A, Youssif M H. Antifungal activity of zinc oxide nanoparticles against dermatophytic lesions of cattle. *Romanian j. biophys* 2013; 23: 191-202]
6. Mohammed S J, Noaimi A A, Sharquie K E, Karhoot J M, Jebur M S, Abood J R, Al-Hamadani A. A Survey Of Dermatophytes Isolated From Iraqi Patients In Baghdad City. *AL-QADISIYAH MEDICAL JOURNAL* 2015; 11(19): 10-15]
7. Elavarashi E, Kindo A J, Rangarajan S. Enzymatic and non-enzymatic virulence activities of dermatophytes on solid media. *Journal of Clinical and Diagnostic Research J Clin Diagn Res* 2017; 11: 23-25.
8. Gnat S, Lagowski D, Nowakiewicz A, Zięba P. Phenotypic characterization of enzymatic activity of clinical dermatophyte isolates from animals with and without skin lesions and humans. *Journal of applied microbiology* 2018; 125(3): 700-709.
9. Rippon J W. *Medical mycology; the pathogenic fungi and the pathogenic actinomycetes*. Eastbourne, UK; 1982]
10. Liu D, Coloe S, Baird R, Pedersen J. PCR identification of *Trichophyton mentagrophytes* var. *interdigitale* and *T. mentagrophytes* var. *mentagrophytes* dermatophytes with a random primer. *Journal of medical microbiology* 1997; 46(12): 1043-1046]
11. Faggi E, Pini G, Campisi E, Bertellini C, Difonzo E, Mancianti F. Application of PCR to distinguish common species of dermatophytes. *Journal of clinical microbiology* 2001; 39(9): 3382-3385]
12. Kannan P, Janaki C, Selvi G S. Prevalence of dermatophytes and other fungal agents isolated from clinical samples. *Indian journal of medical microbiology* 2006; 24(3): 212.
13. Mitchell T G, Sandin R L, Bowman B H, Meyer W, Merz, W G. Molecular mycology: DNA probes and applications of PCR technology. *Journal of medical and veterinary mycology* 1994; 32(1): 351-366]
14. Wellinghausen N, Wirths B, Franz A R, Karolyi L, Marre R, Reischl U. Algorithm for the identification of bacterial pathogens in positive blood cultures by real-time LightCycler polymerase chain reaction (PCR) with sequence-specific probes. *Diagnostic microbiology and infectious disease* 2004; 48(4): 229-241]
15. Baeza LC, Matsumoto M T, Almeida A M F, Mendes- Giannini M J S. Strain differentiation of *Trichophyton rubrum* by randomly amplified polymorphic DNA and analysis of rDNA nontranscribed spacer. *J. Medical Microbio* 2006; 55: 429-436.
16. Putignani L D, Arezzo S, Paglia M G, Visca P. DNA-based detection of human pathogenic fungi: dermatophytes, opportunists, and causative agents of deep mycoses. In *Molecular identification of Fungi* 2010; 357-415.
17. Kim J Y, Choe Y B, Ahn K J, Lee Y W. Identification of dermatophytes using multiplex polymerase chain reaction. *Annals of dermatology* 2011; 23(3): 304-312]
18. Zarrin M, Salehi Z, Mahmoudabadi A Z. Identification of dermatophytes by arbitrarily primed PCR. *Asian Biomedicine* 2015; 9(3): 291-298.
19. Didehdar M, Shokohi T, Khansarinejad B, Sefidgar SA A, Abastabar M, Haghani I, Mondanizadeh M. Characterization of clinically important dermatophytes in North of Iran using PCR-RFLP on ITS region. *Journal de mycologiemedicale* 2016; 26(4): 345-350]
20. Graser Y, Czaika V, Ohst T. Diagnostic PCR of

- dermatophytes—an overview. *JDDG:Journal der DeutschenDermatologischen Gesellschaft* 2012; 10(10): 721-725.
21. Li J, Hyde K D, Zhang K Q. Methodology for Studying Nematophagous Fungi. In *Nematode-Trapping Fungi* 2014 ; 13-40.
 22. Lafta AA. Taxonomical and Molecular Study of the Nematode-Trapping fungi and their antagonistic relationship with the *Trichoderma harzianum* and *Pseudomonas fluorescens*. Master thesis, University of Misan, Iraq 2019; 72.
 23. Wiegand C, Mugisha P, Mulyowa G K, Elsner P, Hipler U C, Graser Y, Nenoff P. Identification of the causative dermatophyte of tinea capitis in children attending Mbarara Regional Referral Hospital in Uganda by PCR-ELISA and comparison with conventional mycological diagnostic method. *Medical mycology* 2016; 55(6): 660-668.
 24. Taha M, Elfangary M, Essa S, Younes A. Species identification of dermatophytes isolated from human superficial fungal infections by conventional and molecular method. *Journal of the Egyptian Women's Dermatologic Society* 2017; 14(2): 76-84.
 25. Liu D, Coloe S, Baird R, Pedersen J. Application of PCR to the identification of dermatophyte fungi. *Journal of medical microbiology* 2000; 49(6): 493-497.
 26. Kano R, Nakamura Y, Watari T, Watanabe S, Takahashi H, Tsujimoto H, Hasegawa A. Molecular analysis of chitin synthase 1 (CHS1) gene sequences of *Trichophyton mentagrophytes* complex and *T. rubrum*. *Current microbiology* 1998; 37(4):236-239.
 27. Ibrahim S A. Isolation and diagnosis of some of the causes of the effect of heat. PhD Thesis, University of Basra, Iraq 2013; 170-169.

Studying the Influence of Nano ZnO and Nano ZrO₂ Additives on Properties of PMMA Denture Base

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Abstract

The aim of this study was to prepare materials that use to manufacture a denture by using a composite material, also studying their properties. Poly methyl methacrylate (PMMA) resin is widely utilized in dental applications. Two types of additives (Nano zinc oxide and Nano zirconium oxide) with different weight percentages (1%, 2%, 3%, 4% and 5%) were added to PMMA resin to improve its properties. The mixture was chosen experimentally to obtain the optimum properties also to avoid cracks formation. The ratio of PMMA and dichloromethane were (20% wt) and (80% wt) respectively for pure specimens. The result showed that there was an increasing in thermal conductivity, completion strength and a decreasing in roughness.

Keywords: PMMA, biomaterial Dental Materials, Prosthetic dentistry.

Introduction

Biomaterials are defined as natural or synthetic origin materials that are used as treatment, supplement or replacing any part of a living tissues or to do function in close contact with living tissue. Therefore two important criteria which biomaterial must fulfill are biocompatibility and bio-functionality⁽¹⁾. The developments in artificial bone and tooth field seem to solve most of the hard tissue problems. On the other hand artificial bone and tooth may cause an improvement in their properties⁽²⁾.

Dental Materials, it is the science which deals with the materials used in the dentistry, their physical, chemical, mechanical properties and with their manipulation as such properties are related to the proper selection and use by the dentist. The study of dental material enables the dentist to understand the behavior of these materials, proper selection for appliance in patient and how to use them to their best advantage⁽³⁾. Prosthetic dentistry is the replacement of missing teeth, which may have been lost for a variety of reasons, with either fixed or removable dentures, that using depending upon a many factors of these replacements.



Figure (1-1): Images of Prosthetic Denture⁽⁴⁾

Denture base material represents one type of biomaterial that must be have good properties, compatibility, performance, color stability and dimensional stability, in addition to esthetical pleasing and use in the oral cavity the part of denture that rests on the basis tissue and to which teeth are tied. Acrylic prosthetic resins are utilized in a number of kinds of dental prostheses, including removable partial or complete dentures, implant-supported prostheses and transitional prostheses. Poly methyl methacrylate (PMMA) material has been widely utilized as a denture based material because of its desirable characteristics

Poly (methyl methacrylate), more often called PMMA, is a commonly used low cost thermoplastic

polymer with boundless applications to everyday life. PMMA is the most commercially important acrylic polymer and is sold under several trade names including Plexiglas and Acrylate. High transparency makes PMMA an ideal replacement for glass where impact or weight is a serious concern. PMMA is compatible with human tissue making it an important material for transplants and prosthetics, especially in the field of ophthalmology because of its transparent properties⁽⁵⁾.

PMMA has high mechanical strength, high Young's modulus and low elongation at break. It does not shatter on rupture. It is one of the hardest thermoplastics and is also highly scratch resistant. It exhibits low moisture and water absorbing capacity, due to which products made have good dimensional stability. Both of these characteristics increase as the temperature rises⁽⁶⁾.

Many researchers study denture base, in 2013 Shyang and his coworkers⁽⁷⁾, studied the effect of the incorporation of hydroxyapatite (HA) particles on the flexural properties of denture based. The results showed that the addition of (HA) particles increases the flexural modulus of PMMA denture base. Furthermore, flexural strain and flexural strength of PMMA/HA composite materials were decreased with the addition of (HA) particles⁽⁷⁾. In 2014 Mohamed and his coworkers⁽⁸⁾, A. A., et al., (2014), studied the effect of the addition of zirconium oxide (ZrO_2) Nano fillers powder with different weight fraction. The results showed that the addition of zirconium oxide (ZrO_2) Nano fillers powder into heat-cured acrylic resin (PMMA) significantly increases the fracture toughness, hardness and flexural strength of heat-polymerized acrylic resin⁽⁸⁾. In 2015 Sama and her coworkers⁽⁹⁾, study the effect of the addition titanium oxide Nano filler (TiO_2) on some mechanical and physical characteristics of denture base material The results showed that titanium oxide Nano filler (TiO_2) into heat cured acrylic denture base material will highly increase the impact strength and transverse strength, and a significant increase in surface Prosthetic dentistry hardness sand surface roughness. Also, the water sorption and decrease when compared with the control group (pure)⁽⁹⁾. In 2016 Eman and her coworkers⁽¹⁰⁾, investigated the effect of the addition of zirconium oxide Nano particles (ZrO_2) on the fracture resistance of mandibular implant retain over denture base material and transmitted of stresses to the implants⁽¹⁰⁾.

In this study, the results showed that the addition of zirconium oxide Nano particles significantly increase the fracture resistance of mandibular implant retain over denture base material and decrease the problem of repeated fracture of denture base material.

Experimental Work:

Used Materials:

1. Poly (methyl methacrylate) (PMMA).
2. Chloride methylene (CH_2Cl_2).
3. Nano- zinc oxide (ZnO).
4. Nano- zirconium oxide (ZrO_2).

Mould Preparation: The mould which used in this study was made from plastic has a circular shape with height (2.5cm) and diameter (4 cm).

Proportioning and Mixing of PMMA: The mixture was chosen experimentally to obtain the optimum properties also to avoid cracks formation. The ratio of PMMA and dichloromethane were (20%) and (80%) respectively for pure specimens. The ratios of Nano ZrO_2 and ZnO were (0.02%, 0.04%, 0.06%, 0.08% and 1%) from the percentage of the PMMA ratio.

The liquid dichloromethane was poured in a dry and clean beaker then the PMMA particles slowly added to the liquid. A magnetic stirrer was used to homogenize the mixture. The beaker must seal very well to prevent the formation of any bubbles and placed in an electric stirrer for 90 minutes until the solution is totally homogenized. After that the homogenized solution was poured into the mould and left for two days at room temperature to be casted. The mold was previously lubricated with paraffin to prevent adhesion and to easily extracting of the specimens from the mold.

1. Thermal Conductivity: Thermal conductivity (K) is the intrinsic property of a material which relates its ability to conduct heat. Thermal conductivity coefficient can be calculated according to (Fourier's Law).

The thermal conductivity depends on the many factors include (degree of crystallization, molecular weight, porosity). All polymer material have low thermal conductivity between (0.17-0.25 W/m.K), therefore most of polymer using as insulated material for this reason. This property represented the disadvantage of poly methyl methacrylate when used as denture base

materials; because of the high thermal conductivity of denture bases lead to ⁽¹¹⁾:

1. Improved tissue.
 2. Better appreciation of taste.
 3. Reduces feeling of dentures to the foreign body.
- 2. Compression Test:** Compression test (Brazilian) was determined according to ASTM (D664) by using cylindrical specimens. The specimens were placed with its horizontal axis between platens of the testing machine. Diametrical strength was calculated by

$$\text{Compression } (\sigma) = \frac{2F}{\pi DL} \dots \dots \dots (1)$$

Where (σ) compression (MPa), (F) Maximum applied load (N). (D) Diameter of

Specimens (mm), and (L) length of the specimens (mm).

- 3. Roughness:** The surface roughness of product is very important surface properties and surface finish design requirements for many reasons and consideration which include Corrosion resistance. Such as, Cost consideration, Electrical and thermal contact resistance, Fatigue and notch sensitivity, and subsequent processing such as painting and coating appearance. Frictional wear, and lubrication consideration.

Results and Discussion

- 1. Thermal conductivity Test:** The values of thermal conductivity for pure PMMA, for all specimens that were prepared in the current work are illustrated in the figure (1). The effect of the addition of various types of nanoparticles (zinc oxide (ZnO) and zirconium oxide (ZrO₂)) showed an increasing in the thermal conductivity values because of the ceramic nanoparticles which serve as physical cross-linking centers between the PMMA molecules for the phonon conduction, have thermal conductivity insulating PMMA polymer ⁽¹²⁾.

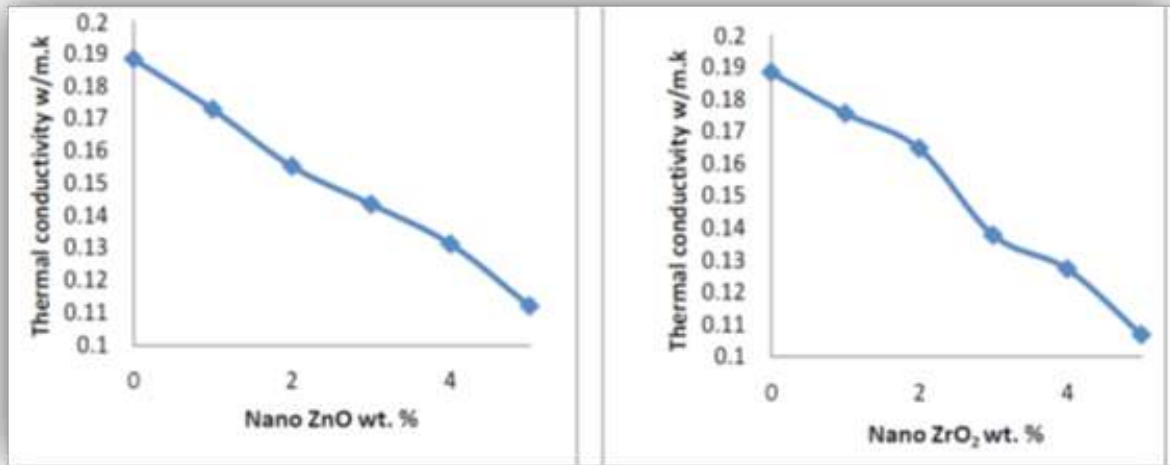


Figure 1: Thermal conductivity for Nano ZnO and ZrO₂ reinforced Specimen and Pure PMMA specimen

- 2. Compression Test:** The values of compression for pure PMMA, for all specimens that were prepared in the current work are illustrated in the figure (2). The effect of the addition of various types of nanoparticles (zinc oxide (ZnO) and zirconium oxide (ZrO₂)) showed an increasing in the compression values because of the formation

of strong physical cross-links (supra molecular) bonding which covers (shield) the nanoparticles, and this in turn leads to prevent the cracks propagation within the PMMA material, as well as, the good bonding between the nanoparticles and PMMA matrix leads to change the propagation of cracks ^(13, 14).

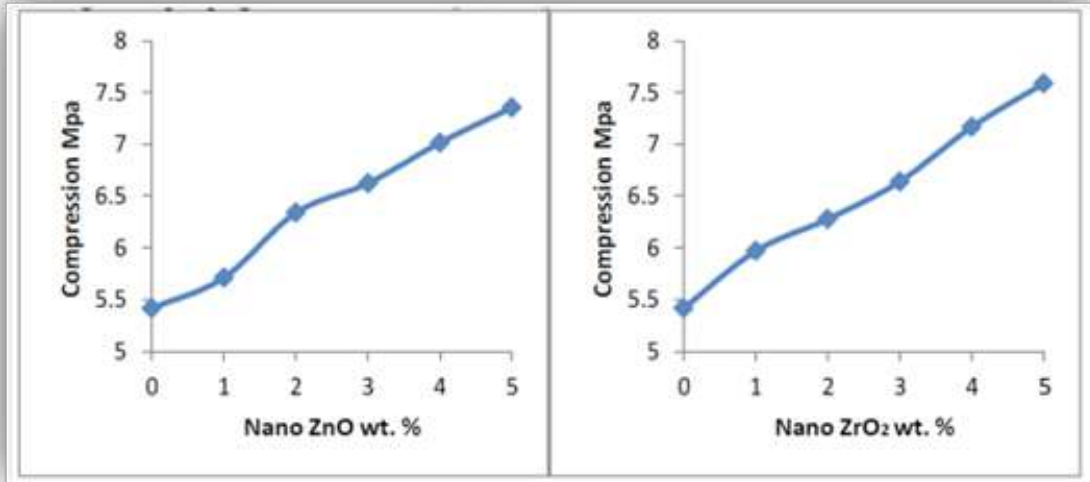


Figure 2: Compression strength for nano ZnO & ZrO₂ reinforced specimen and pure PMMA specimen

3. **Roughness Test:** The values of Roughness for pure PMMA, for all specimens that were prepared in the current work are illustrated in the figure (3). The effect of the addition of various types of nanoparticles zinc oxide (ZnO) and zirconium oxide (ZrO₂) It can be noticed that the values of surface roughness decreased with increasing of the volume fraction of all types of particles for all groups. This

is related to the surface roughness test is concerned with outer surface and not with inner surface of composite specimens. Furthermore, the number of particles that will be involved with in surface of the composite specimens increased when increasing the volume fraction of these particles in PMMA composite⁽¹⁵⁾.

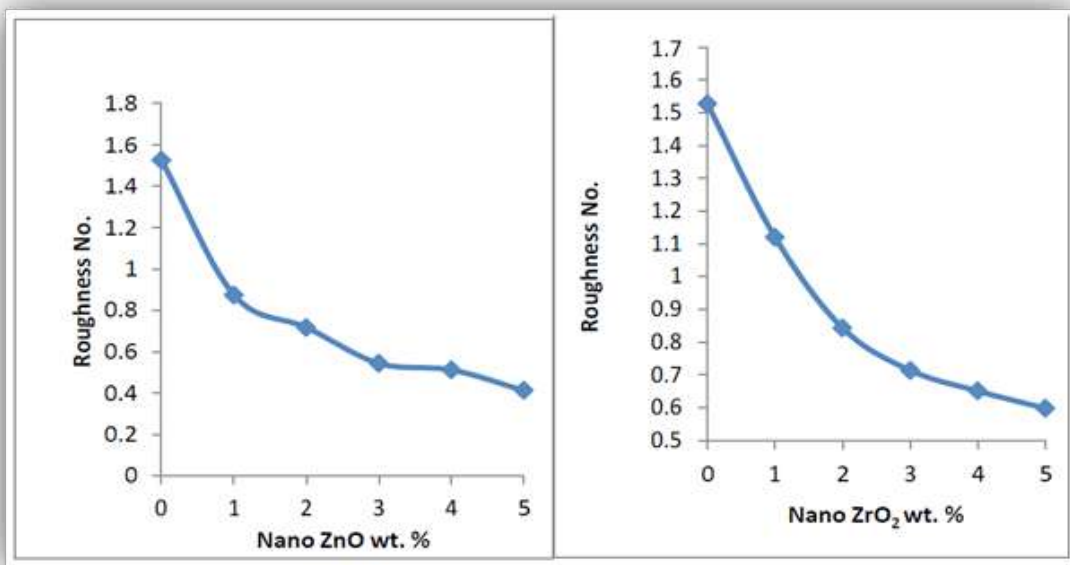


Figure 3: Roughness for nano ZnO & ZrO₂ reinforced specimen and pure PMMA specimen

Conflict of Interests: The authors declare that they have no conflict of interest.

Source of Funding: Self-funding.

Ethical Clearance: The researchers already have ethical clearance from College of Science, Mustansiriyah University, Iraq.

References

- Ramakrishna S, Mayer J, Winter-mantel E, Leong KW, "Biomedical Applications of Polymer-Composite Materials: A Review", *Composit Sci Technol.* 2001; 61: 1189- 1224.
- Hench LL, "Biomaterials: A forecast for the Future", *Biomaterials.* 2002; 19: 1429-1423.
- Anusavice KJ. "Phillips' Science of Dental Materials", 10th Ed., WB. Saunders Co. Philadelphia, PP. (237-271), (1996).
- Qahtan AH. " Study the Effect of Nano-Al₂O₃ and Fiber Glass on Mechanical and Physical Properties of PMMA Composites for Prosthetic Denture", *Engin Technol J.* 2018; 36: Part A, No. 7.
- Campo EA. *The Complete Part Design Handbook*, Hanser, 2006.
- Harper CA. *Handbook of Plastic Processes*, John Wiley & Sons, 2005.
- Shyang CW, Tay, H. K., Azlan, A. and Mohd I. Z. A., " Flexural Properties of Hydroxyapatite Reinforced Poly (methylmethacrylate) Composites". *J Reinforced Plastics and Composites* 2008; 27(9):945-952.
- Mohamed AA, Mohamed IE. "Effect of Zirconium Oxide Nano Fillers Addition on the Flexural Strength, Fracture Toughness and Hardness of Heat-Polymerized Acrylic Resin", *World J Nano Sci Engin.* 2014; 4(2): 50-57.
- Sama AA, Shatha SA. "The Effect of the Addition of Silanized Nano Titania Fillers on Some Physical and Mechanical Properties of Heat Cured Acrylic Denture Base Materials", *J. Bagh. Coll. Dentistry.* 2015; 27(1): 86-91.
- Eman MR, Amani RA, Asmaa NE. "Effect of Nano-Zirconia Reinforcement on Stresses and Fracture Resistance of Lower Implant Retained Over Denture", *Res. J Pharmac Biolog Chem Sci.* 2016; 7(3): 897-903.
- Phillips RM. *Skinner's Science of Dental Materials*, 8 Thed. W.B. Saunders, company. Philadelphia, New York, USA, (1982}.
- Vishal M, Kananbala S. "Evaluation of Morphological Effect on Thermal and Mechanical Performance of PS/PMMA/CdS Nanocomposite Systems", *Adv Nanoparticles.* 2013; 2(3): 205-216.
- Majid S, Nabi MK, Abbas R., " An Experimental Investigation of HA/AL₂O₃ Nano Particles on Mechanical Properties of Restoration Materials ", *Engin Solid Mechan.* 2014; 2(3): 173-182.
- Suryasarathi B, Mahanwar PA. "Effect of Fly Ash on the Mechanical, Thermal, Dielectric, Rheological and Morphological Properties of Filled Nylon 6". *J Minerals & Materials Charact Engin.* 2014; 3(2): 65-72.
- Al-Momen MM. "Effect of Reinforcement on Strength and Radio-opacity of Acrylic Denture Base Materials". M. Sc. Thesis., College of Dentistry, University of Baghdad, Iraq, (2000).

Association of Osteoarthritis and Periodontitis in Sample of Iraqi Patients with Knee Osteoarthritis

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Abstract

Background : Osteoarthritis (OA and Periodontitis (PD) share physiopathological characteristics ,and many previous studies show association of PD with other chronic musculoskeletal and bone diseases such as rheumatoid arthritis and Osteoporosis.

Objectives: To investigate the association between OA and PD in a sample of Iraqi patientswith knee OA.

Patients and Method: A case-control study included 150 patients with OA and 150 healthy controls. The WHO community periodontal index was used to assess periodontitis, Periodontitis was defined as a CPI greater than or equal to “code 3”. Binary regression analysis used to assess the predictors of periodontitis among OA patients

Results: OA patients were about 2.3 folds more likely to have Periodontitis, (odds ratio = 2.29, P. value < 0.05). In OA group only smoking showed a significant correlation with Periodontitis; where out of the 38 cases with periodontitis 7 (18.4%) were smokers compared to only 6 (5.4%) of 112 with no Periodontitis, (P. value = 0.013), Other variables showed no significant correlations, (P. value > 0.05).No statistically significant correlation had been found between prevalence of Periodontitis and severity of OA represented by KL score, (P. value > 0.05).

Conclusions: Patients with knee OA were about 2.3 folds more likely to have Periodontitis compared to healthy controls. Presence of Periodontitis was not affected by age, gender, Occupation, Alcohol consumption, BMI or severity of disease in knee OA patients.

Keywords: Osteoarthritis , Periodontitis, physiopathological characteristics

Introduction

Osteoarthritis is a degenerative joint disease, occurring primarily in older people and characterized by erosion of the articular cartilage, hypertrophy of bone at the margins (i.e., osteophytes), subchondral sclerosis, and

a range of biochemical and morphologic alterations of the synovial membrane and joint capsule¹ OA is the most prevalent form of arthritis and a major cause of pain and disability . The exact pathophysiology of the condition has not been well understood yet^{2,3}. Periodontal disease is broadly classified as either gingivitis or periodontitis; these conditions are distinguished by the presence of alveolar bone involvement that occurs with periodontitis and not with gingivitis⁴⁻⁶

Both Osteoarthritis and Periodontitis are common chronic diseases that have major impact on public health and quality of life. Periodontitis is an inflammatory

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disease that its most important consequence is the loss of bone supporting the teeth. OA patients also suffer from an important inflammatory component in the soft tissue and bone structural modifications, so that OA and PD share pathophysiological characteristics.⁷ Many previous studies show association of PD with RA, of which an important local Iraqi study⁸. Also the association between PD and bone diseases with other systemic diseases also had been found^{9,10}. However, the relationship between OA and PD remains unclear.

Patients and Method:

This was a case-control study conducted at the Rheumatology Unit of Baghdad Teaching Hospital in Medical City and Al-Furat Al-Awsat hospital (Najaf) from October 2017 till July 2018. A total of 150 patients with knee OA were included in the study and 150 age and sex matched healthy controls were included. Patients with rheumatoid or other inflammatory arthritis, Chronic disease, Malignancy, users of some medications (bisphosphonates, CCB, phenytoin, cyclosporine) and pregnant women were excluded. Radiographic severity of OA calculated using Kellgren and Lawrence system. The oral examination and diagnosis of periodontitis were performed by specialized dentists at Rheumatology unit in Baghdad teaching hospital and Dental Clinic in Al-Furat Al-Awsat hospital (Najaf). The oral examination was explained to each participant beforehand. The WHO community periodontal index (CPI) was used to assess periodontitis (table 1)¹¹, and the mouth was divided into sextants, the index tooth numbers were 11, 16, 17, 26, 27, 31, 36, 37, 46, and 47. An approximately 20 g probing force was applied to each tooth by a specially designed, lightweight CPI metallic probe with a 0.5-mm ball tip, with a black band between 3.5 and 5.5 mm (figure 1), and the highest CPI code for each subject was recorded. Periodontitis was defined as a CPI greater than or equal to ‘‘code 3’’,¹²⁻¹⁴

The WHO community periodontal index (CPI) was used to assess periodontitis¹¹. Statistical analysis was performed using the statistical package for social sciences version 25, and appropriate statistical tests and procedures were applied accordingly with a level of significance of < 0.05.

Results

No statistically significant differences had been found between both groups in their baseline characteristics (P. value > 0.05). Periodontitis was reported in 38 (25.3%) OA patients and 18 (12%) controls. The OA patients were about 2.3 folds more likely to have Periodontitis, (odds ratio = 2.29, P. value < 0.05). (Table 1). Out of the 150 OA patients 46 (30.7%) had KL score of 2, 63(42%) had a score of 3 and 41 (27.3%), had KL score of 4, (Figure 1). Among the demographic variables of the OA group only smoking showed a significant correlation with Periodontitis; where out of the 38 cases with periodontitis, 7 (18.4%) were smokers compared to only 6 (5.4%) of 112 with no Periodontitis, (P. value = 0.013), Other demographic variables, BMI and KL score showed no significant correlations with the prevalence of Periodontitis, (P. value > 0.05), (Table 2). Binary regression analysis revealed that smoking still significantly associated with Periodontitis in OA group after adjustment for other variables with an odds ratio of 4.83 indicated that smoker OA patients were about 4.8 folds more likely to have Periodontitis than nonsmokers, (P. value = 0.04), (Table 3).

Table 1: Distribution of Periodontitis among the studied groups

Periodontitis	OA group		Control group		OR (95% CI)	P. value
	No.	%	No.	%		
Yes	38	25.3	18	12.0	2.29 (1.35-4.60)	0.003
No	112	74.7	132	88.0		
Total	150	100.0	150	100.0		

OR: odds ratio .CI: confidence interval of OR

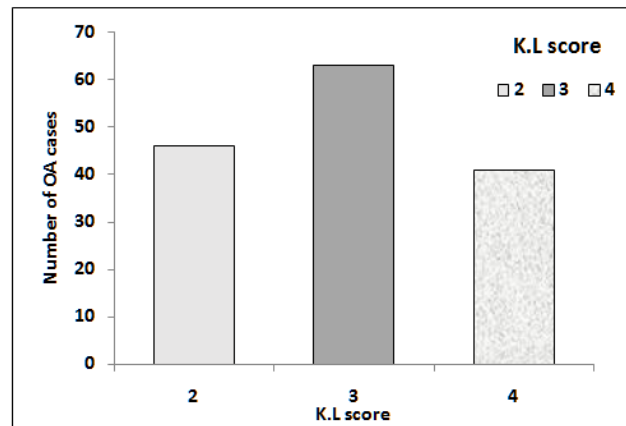


Figure 1. Distribution of OA patients according to KL score

Table 2: Relationship between Periodontitis and demographic variables of OA patients

Variable		Periodontitis		No Periodontitis		P. value
		No.	%	No.	%	
Age (year)	≤ 55	15	39.5	56	50.0	0.253
	56 - 60	9	23.7	30	26.8	
	> 60	14	36.8	26	23.2	
Gender	Female	28	73.7	89	79.5	0.46
	Male	10	26.3	23	20.5	
Occupation	Employee	18	47.4	47	42.0	0.93
	Housewife	12	31.6	39	34.8	
	Retired	6	15.8	21	18.8	
	Other	2	5.3	5	4.5	
Smoking	Yes	7	18.4	6	5.4	0.013
	No	31	81.6	106	94.6	
Alcohol	Yes	0	0.0	1	.9	0.56
	No	38	100.0%	111	99.1%	
BMI	Normal	16	42.1	26	23.2	0.079
	Overweight	13	34.2	48	42.9	
	Obese	9	23.7	38	33.9	
K.L. score	2	11	28.9	35	31.3	0.952
	3	16	42.1	47	42.0	
	4	11	28.9	30	26.8	

Table 3: Results of binary regression analysis for the predictors of periodontitis among OA patients

Variables	B	OR	95% C.I. for OR	P. value
Age	0.07	0.93	0.85 – 1.01	0.08
Gender	0.21	0.81	0.25 – 2.68	0.73
Occupation	0.31	1.36	0.82 – 2.25	0.24
Smoking	1.57	4.83	1.09 – 21.41	0.04
Alcohol	0.04	1.04	0.07 – 15.77	0.98
BMI	0.08	1.08	0.97 – 1.20	0.14
K.L. Score	0.06	0.94	0.56 – 1.60	0.82

Discussion

The current study found that PD were more frequent in OA group than controls, where OA patients were about 2.3 folds more likely to have Periodontitis,

Chronic inflammation is thought to play a role in the pathogenesis of both (PD) and (OA), and increased blood levels of pro-inflammatory mediators such as IL-6, TNF alpha, and C-reactive protein have been documented in adults with OA and PD.¹⁵Mobility limitation resulting from osteoarthritis, particularly in the lower extremities, makes it difficult for those affected to visit dental offices for both routine hygiene

and treatment. A large national survey in Australia found that persons who had osteoarthritis were less likely to have visited a dental professional within the past 2 years.¹⁶ Also certain medications used to treat osteoarthritis, including corticosteroids and non-steroidal anti-inflammatory drugs, may suppress the immune system, thus potentially affecting the tissues of the oral cavity by increasing the risk of delayed wound healing, prolonged bleeding time, and fungal infections.¹⁷Finally , many patients with KOA also may have hand OA and the severity of osteoarthritis in the hands is correlated with impaired functional ability.¹⁸Hence, many people with osteoarthritis in their hands are unable to maintain proper oral hygiene, resulting in accumulation of plaque and calculus, which increases the likelihood of dental caries and periodontal disease.¹⁹However ,this finding disagree with Chung et al. which provided that OA and PD showed no significant association in overall analysis.²⁰Also this finding is inconsistent with Kandati et al. which reported that OA was not significantly associated with any PD category (P-value =0.28).¹⁵

The current study revealed No statistically significant correlation between prevalence of PD and the severity of OA and this finding is inconsistent with Chung et al. that reported that patients with severe

OA were more likely to have PD ($P=0.0316$)²⁰. In the present study no statistically significant relationship was found between PD and demographic variables except for smoking, where OA smokers were more likely to have PD compared to non-smokers on univariate analysis. Furthermore binary regression analysis revealed that smoking still significant after adjustments for other variables and that smoker OA patients were about 4.8 folds more likely to have Periodontitis than nonsmokers, (P .value = 0.04). These results are similar to those reported by Dina Al- Tayeb¹⁹, Gautam DK et al.²¹ and Haffajee.²² All of these studies have shown that compared to non-smokers, adult smokers have a higher prevalence and severity of periodontitis. However, in the present study smoking is a risk factor to get PD and have a synergistic effect with OA.²²

It is well known that tobacco smoke contains many cytotoxic substances such as nicotine, which can penetrate the soft tissue of oral cavity, adhere to the tooth surface or enter to the blood stream. Potential molecular and cellular mechanisms in the pathogenesis of smoking associated periodontal diseases has been reported and these include, immuno-suppression, exaggerated inflammatory cell responses, and impaired stromal cell functions of oral tissues^{19,21,22}.

A potential importance of this study is that it is the first study performed in Iraq, Middle East and Arabic region that studied this concept, so it may be useful for other researchers as a baseline for subsequent future studies.

Conclusions

Periodontitis was more frequent in patients with knee OA compared to healthy controls Smoking was independent risk factor of Periodontitis

Ethical Clearance: Ethical approval was taken from Medical department, College of Medicine, University of Baghdad. Verbal consent was obtained from all participants

Conflict of Interest: None

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References

1. Paul E. Di Cesare, Dominik R. Haudenschild, Jonathan Samuels, Steven B. Abramson. Pathogenesis of Osteoarthritis. In; Kelley and Firestein's text book of rheumatology, tenth edition. Philadelphia, PA: Elsevier; 2017: 1685
2. Hunter DJ, Felson DT. Osteoarthritis. *BMJ*2006;332:639–42. phic area.
3. Burkitt HG, Stevens A, Lowe JS. Skeletal system. In: Basic Histopathology. 3rd ed. New York, NY: Churchill Livingstone; 1996:260.
4. Williams RC. Periodontal disease. *N Engl J Med* 1990; 322:373.
5. Laudenbach JM, Simon Z. Common dental and periodontal diseases: evaluation and management. *Med Clin North Am* 2014; 98:1239.
6. Armitage GC. Development of a classification system for periodontal diseases and conditions. *Ann Periodontol* 1999; 4:1.
7. Gurt, C. López, M.J. Sales, L. Tio et al. Periodontitis disease as a model of inflammation and bone remodelling to study osteoarthritis drug effects. Results from a pilot study in OA patients treated with chondroitin sulfate. *Joca*.2014.02.552
8. Alosami Mohammed. Association of Porphyromonus gingivalis with Rheumatoid arthritis. *Iraqi JMS*. 2016;14:231-236.
9. YH Lee, JO Choi, SH Nam. Relationship between periodontal diseases and bone diseases in some bone disease patients. *Biomed Res* 2018 Volume 29 Issue 13.
10. Marcelo R. Marques, Marco A.D. da Silva, Silvana P. Barros. Periodontal disease and osteoporosis association and mechanisms: A review of the literature. *Braz J Oral Sci*. 2003; 2(4): 137-140.
11. World Health Organization. Oral Health Surveys Basic Method. Geneva; 1997:36-38.
12. Kingman, A., Albandar, J. M. Methodological aspects of epidemiological studies of periodontal diseases. *Periodontology* 2002 29, 11–30
13. Kwon YE, Ha JE, Paik DI et al. The relationship between periodontitis and metabolic syndrome among a Korean nationally representative sample of adults. *Journal of clinical periodontology* 2011; 38(9): 781–6.
14. M Preshaw, Philip. Detection and diagnosis of periodontal conditions amenable to prevention. *BMC oral health* 2015. 15. S5. 10.1186/1472-6831-15-S1-S5.
15. Kandati, Sahiti, Sambamoorthy et al. Osteoarthritis and Periodontal disease - Is there an association?.

- 142nd APHA Annual Meeting and Exposition 2014;3 (1):118.
16. Pokrajac-Zirojevic V, Slack-Smith LM, Booth D. Arthritis and use of dental services: a population based study. *Aust Dent J.* 2002;47:208–213.
17. Kelsey JL, Lamster IB. Influence of musculoskeletal conditions on oral health among older adults. *Am J Public Health* 2008;98:1177–1183.
18. El-Sherif HE, Kamal R, Moawyah O. Hand osteoarthritis and bone mineral density in postmenopausal women; clinical relevance to hand function, pain and disability. *Osteoarthritis Cartilage.* 2008;16:12–17
19. Dina Al-Tayeb. The effects of smoking on the periodontal condition of young adult saudi population. *Egypt Dent J.* 2008;54:1–11.
20. Chung M, Koo N, Lee B. Association of osteoarthritis and periodontitis based on the korea national health and nutrition examination survey *Annals of the Rheumatic Diseases* 2017;76:977-978.
21. Gautam DK, Jindal V, Gupta SC et al. Effect of cigarette smoking on the periodontal health status: A comparative, cross sectional study. *J Indian Soc Periodontol.* 2011;15(4):383-7.
22. Haffajee AD, Socransky SS. Relationship of cigarette smoking to attachment level profiles. *J Clin Periodontol.* 2011;28:283–95.

The Effectiveness of Special Exercises with the Black Bean in Improving the Lactic Endurance and the Digital Achievement of Runners 800 m Youth

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Abstract

The aim of this study was to prepare exercises using the black bean and in the form of doses based on studied scientific basis. The sample of the research was for Karbala players in 800 m activity for the youth group of 7 players. The experimental method was used for one group by tribal and remote testing. The black bean was given in capsules the results of the study showed that there was a significant effect of the black pill dose and the sports training, which was demonstrated by the emergence of significant differences in the post-test in running 800 meters for the benefit of Dimensional test.

Keywords: *Improving, Lactic, Endurance.*

Introduction

Human societies at this stage witness a scientific renaissance in a wide range and in various fields and it is based on the foundations of scientific research and the objective study. Physical education is one of these areas that have been progressed. Arena is one of the games that have developed as they occupy a good place among games and events Sports as a result of the high potential of players and the pursuit of serious and continuous in the teaching process¹, which led to the high level and the breadth of popularity in all countries of the world. In order to keep pace with the progress of the game, many researchers have tried to find ways to help improve the player's physical and functional efficiency. Some of these medicinal plants ² have been used and given the global trend of expanding the use of plant raw materials in the manufacture of pharmaceuticals instead of chemicals ³ with harmful side effects (7: 7) and the importance of the black bean increased after the mention of the Prophet Muhammad (peace and blessings of God be upon him), which God Almighty said, the importance of research lies in the recognition of the effect of anaerobic exercises in the development of lactic endurance and the achievement of a hostile 800 meters youth. The problem

of research is that⁴ most players of effective 800 meters for the youth class are characterized by a clear drop, especially in the final distance of the race, which is a critical distance and concentrated fatigue in the athlete and through the directions of researchers in the field of sports training physiology and by the knowledge of many references of medicinal plants and found that black seed plant has a great benefit, especially for athletes working under the Lactic energy system⁵ and through our observations on the^{6,7} level of players and physical ability, we try to contribute to the development of players physically and functionally, using some plant Black pill so as to raise the efficiency of the players less expensive and without collateral damage. Research's Goals: Preparation of exercises with anaerobic effort to take the black bean in the development of the tactical endurance and achievement of runners 800 meters youth. Identifying the effect of exercise with the treatment of the black bean in the development of lactic resistance and achievement of runners 800 meters young.

Research Hypotheses: There is a positive effect of the exercise in the treatment of black bean in the development of Lactic endurance for young runners of 800 meters.

Research’s Areas:

1. **Human area:** Players of Karbala province clubs athletics 800 meters youth for the training season 2018-2019.
2. **Time:** for the period from 5/9/2018 to 5/11/2018.
3. **Place:** Karbala International Stadium

Methodology: The researchers used the experimental method of a one-group method of pre and post measurement that suit to problem type.

Sample of the Study: The sample of the study was 7 players of Karbala province clubs for the activity 800 meters youth for the training season 2018 -2019.

Homogeneity of the sample: The researchers conducted homogeneity between the sample members in order to start with a single line of origin. This was done by finding homogeneity of the dependent variables as well as the anthropometric measurements as shown in Table (1):

Table (1). Homogeneity of the dependent variables as well as the anthropometric measurements

No.	Variable	Measuring unit	Test value (Leven)		Indication level	
			Calculated	Standard error		
1	Age	Year	1,246	0,322	Not significant	matching
2	Training age	Year	0,372	0,429	Not significant	matching
3	mass	Kg	0,088	0,871	Not significant	matching
4	Length	Cm	1,270	0,320	Not significant	matching
5	Lactic endurance	Minute	2,347	0,228	Not significant	matching
6	The completion time is 800 meters	Degree	1.873	0.231	Not significant	matching

Collecting information means:

1. Observation.
2. Tests and measurements.
3. Registration and unloading form of test’s results.

Instruments and tools used in research:

1. Height and weight measuring device.
2. Athletics track
3. Leather measuring machine 20 meters.
4. Boundary (7)
5. Three electronic timer (Caslo)
6. Treadmill

Lactic Endurance Test (Abu El-Ula Ahmad, 1997, 3):

- The purpose of the test: Measurement of tactical endurance
- Machine speed: 14 km/h
- Inclination angle: 11 Degree, 20%
- Test time: till the player is tired
- The Procedure: after the player finishes warm up

for 5-10 minutes The player is start playing on Treadmill as shown in Figure (4) The machine starts at the specified speed (14 km/h) The device starts to increase the speed gradually up to the prescribed speed This gives the experimenter Sufficient opportunity to work on the device in a suitable and consistent manner and after reaching the prescribed speed, two electronic timers will begin switch on by the arbitrators The player has to work on the treadmill until he reaches the extreme fatigue so that he cannot run on the treadmill then the two timers are stopped.

- Registration: the experimenter’s time is recorded from the beginning of the test the arrival of the device to a speed of (14 km/h) until the end of work (fatigue).
- Measuring the digital completion time of 800 meters: The digital achievement of the s of the research sample is based on the results obtained in the Iraqi clubs championship which is held annually in Baghdad.
- The exploratory experiment: The researchers conducted an exploratory experiment on a sample of (5) players on Tuesday 5/9/2018 at 3:00 pm at

the Karbala International Stadium. The exploratory experiment helped the researchers in identifying: the validity of the equipment and tools used in the research.

- **Pre-tests:** The researchers conducted pre-tests on Sunday, 10/9/2018 at 3 pm and in Karbala International Stadium.

Specific Exercises: The proposed exercises started on 15/9/2018. The training period is set at 8 weeks. The total number of training units is 24 training units. Number of weekly training units: (3) units. Weekly training days: (Sunday - Tuesday - Thursday). Total module time: (90) minutes. The main section of the module is: (30-45) minutes. Training method used: high intensity training and repetitive training. Training intensity used: (85 - 95%) of the extreme intensity of the player’s performance.

- **Procedures of using the black bean:** The researchers used scientific sources to know how to

give the prescribed doses and discover that (1 g/day) capsules before and after exercise in two hours is the best dose to give good results (4: 13).

- **Post-tests:** on 13/11/2019 at 3:00 pm at Karbala International Stadium the post-test are made.
- **Statistical method used in the research:** The researchers used the statistical bag (SPSS) to find the appropriate statistical processes.
- **Presenting, analyze, and discuss results:** Presenting the results’ differences between pre-test and post-tests of the research sample of research’s variables and their analysis. Table (2) show The difference in the computation and its standard deviation and the value of (t) and the significance of the differences between the results of the pre-test and the post- tests of the research sample in the variables .

Table (2). The difference in the computation and its standard deviation and the value of (t).

Assessments		Pre-test		Post-test		(t) value	Standard error	Differences indications
Lactic endurance	Minute	1.510	0.101	2.81	0.29	4.698	0.003	Significant
Digital achievement	Second	1.590	0.231	1.539	0.211	8.543	0.000	Significant

*Significant at the level of significance (0.05) if the error level is less than (0.05)

Results Discussion

The results showed a significant difference between pre-tests and post- tests of the research sample to test the digital achievement and the non-tactical endurance test and for the post-test. The researchers attribute this difference to the effectiveness of the anaerobic exercise, especially if it is built on a systematic scientific basis through the use of appropriate and gradual stress and taking into consideration individual differences. Individual’s physical ability is reflected in the results of the variables of study. This is what Essam Abdul Khaliqsaid: “Skill performance is related to physical and motor abilities of the individual” . Practitioners can attribute this result to the effectiveness of anaerobic exercise, which lasted (12) weeks with (3) weekly training modules and in the form of high-intensity infant training are important method that also aim to improve

the overall endurance, The training method is one of the method used in the training of mid-range sprinters, including an enemy of 800 meters, through which the development of the aerodynamics needed by the athlete in the distance The researchers explained that the reason for the development of the non-tactical endurance is the result of a number of things, foremost of which is the type of exercise offered to the players during 24 doses Which resulted in the ability to resist the fatigue caused by the accumulation of lactic acid as a result of the exercises performed, as well as the insufficient rest to remove the accumulated acid. This means that the players repeat work with the presence of quantities of lactic acid as well as low blood pH, As This has positively affected the work of the internal organs of the body, especially in the work of the vital organizations that delay the decline of PH blood quickly by reducing the acidity caused by acid

lactic acid and converted from strong acid to weak acid, which contributed to delay the decline of blood pH And then increase physical effort. Jabbar Rahimah, asserts that the improvement of the capacity of the production of energy in lactic acid system requires the guidance of the training load, which makes the rate of accumulation of lactic acid in the muscles and blood is greater than the rate of disposal to ensure that the threshold exceeded the laconic difference.

Conclusion

There is significant effect of the black bean in the improvement of lactic stress and time of digital achievement. There is a significant effect of the dose of black bean and proposed exercises to improve the search variables and for the benefit of the post-test.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the College of physical education & sport science/Wasit University, Iraq and all experiments were carried out in accordance with approved guidelines.

References

1. AbuEl-UlaA. Physiology and Morphology of Sports and Measurement Method, Cairo, Dar Al-Fikr Al-Arabi, 1997; 4: 26-31.
2. El Bastawisy A. Foundations and theories of sports training, Dar Al-Qalam, Cairo. 1999; 5.
3. BahaaE. The Biology of Sport and Motor Performance, Dar Al-Fikr Al-Arabi, Cairo. 1992; 1(3).
4. JabbarR. Physiological and Chemical Foundations of Sports Training, Doha, Qatar Book House.2007; 7(5).
5. EssamA. athletic training theories and applications, 9 Edition, Cairo, Dar Alfiker Al- Arabi, 1999.
6. Ali A. Encyclopedia of Medicinal and Aromatic Plants Production, Cairo, Atlas Press, 1996.
7. Mohsen A. The Illustrated Dictionary of the grasses, 1 Edition, Al-Alami Institute of Publications, Beirut. 2003; 188.
8. Mohsen AM. The Prophetic Medicine, Edition, Dar al-Mujtaba, 2006; 1: 123-127.

Urinary Tract Infection in Spontaneous Urticaria among Thi-Qar Patients

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Abstract

Urticaria is a common worldwide disease characterized by local transient skin or mucosal edema (wheal), deeper tissues involvement (angioedema), or both. It is classified into acute (initially) and chronic (after 6 weeks' duration); and into spontaneous (symptoms occur spontaneously) or inducible (in response to specific stimuli). Occasionally, infections are blamed as an underlying cause; of them are urinary tract infections (UTIs). An equal number (465) of urticaria patients and their age-sex matched controls were evaluated for presence of UTIs in a case-control observational study. Pyuria was found in (19.8%) of urticaria patients and (7.7%) of controls; while urine culture was positive in (8.2%) of urticaria patients and (2.4%) of controls. Association of urticaria with both pyuria and positive culture results were highly significant (p value < 0.001).

Keywords: *spontaneous urticaria, urinary tract infections, urinalysis, pyuria, case-control study.*

Introduction

Urticaria is characterized by local transient skin or mucosal edema (wheal), deeper tissues involvement (angioedema) or both^(1,2).

It is a common worldwide disease with lifetime prevalence ranging from around 8% to 22%^(1,3,4), with detrimental effect on quality of life measures (both objective functioning and subjective well-being).²

Different classification schemes of urticaria exist.

According to duration, urticaria is classified into acute and chronic^(2,4). Acute urticaria last less than 6 weeks while episodes of daily or almost daily wheals or angioedema lasting for 6 weeks or more are designated as chronic urticarial⁽²⁻⁴⁾. There is no qualitative difference between acute and chronic spontaneous urticaria, but acute forms tend to be more severe¹. However, we

should notice that all urticarias are acute initially with some (about 20% to 45%) become chronic after a period of time (i.e. 6 weeks)³. According to clinical behavior, urticaria can be classified into spontaneous (symptoms occur spontaneously) or inducible (in response to specific stimuli such as physical stimuli)^(1,3-5). This classification (rather than etiology based) is regarded the most practical when defining groups of patients, since etiology of urticaria at time of first consultation is often unknown^(2,3). Spontaneous urticaria (ordinary urticaria) include acute, intermittent (episodic), and chronic (idiopathic) subtypes, while inducible urticaria encompass physical and contact urticarias^(3,5). Urinary tract infections (UTIs) refer to growth of microorganisms (mostly bacteria) within the urinary tract. They are considered the commonest bacterial infection, though incidence is difficult to be accurately assessed since they are not reportable diseases⁶. The gold standard for the diagnosis of a UTI is the detection of the pathogen, in the presence of clinical symptoms, by urine culture (using midstream urine)⁷. Pyuria is the presence of an increased number of polymorphonuclear leukocytes in the urine (generally >10 WBC/HPF)^(8,9). It is evidence for genitourinary tract inflammation, not necessarily UTI, and being just present is not an indication for

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treatment. Lack of pyuria, however, is strong evidence UTI is absent^(8,9,14).

Methodology

Patients and Method: An age and sex-matched case-control observational analytic study arranged over a period of 2 years (since January 2017 till March 2019) to evaluate the association between urticaria and urinary tract infections.

Patients with clinical diagnosis of spontaneous urticaria was recruited from those with various types of urticaria attended specialist day clinics in 2 general hospitals and 4 specialist private dermatology clinics at Thi-Qar province in south of Iraq.

Each patient was evaluated by dermatologist to exclude patients with inducible urticaria, urticariavasculitis, and known urticarial drug reactions. All patients diagnosed as spontaneous “ordinary” urticaria, who agreed to be involved in study, were included. Repeated cases taken once.

Control group was selected randomly from patient attending these clinics who were not complaining from urticaria nor presented primarily for genitourinary complaints. Care was performed in this selection to match, whenever possible, proportions of study group regarding age, sex, and known influential factors such as pregnancy and diabetes mellitus.

Verbal consent was taken from each in both groups and extra cost was added on regarding investigation.

Data regarding age, sex, marital status, pregnancy, diabetes mellitus, were recorded and, whenever applicable, every patient was interrogated about symptoms of urinary tract infection i.e. urinary frequency, urgency, dysuria, new onset hematuria, suprapubic pain). They were examined for suprapubic and/or costovertebral tenderness, and for fever.

After carefully instructing patient regarding washing the area with soap and water and passing first part of voided urine, a clean mid-stream urine sample was collected using the commercially available sterile wide mouth leak proof 5 ml container and submitted directly (as early as possible) to the laboratory for analysis.

Initial rapid urine leucocyte esterase test was done using a test strip (Dipstick), and pyuria was regarded positive when leucocyte esterase test was positive.

Ten ml of urine sample was centrifuged for 5 minutes at 1500 rpm, 9.5 ml of supernatant was decanted, deposit was suspended and examined microscopically for presence of RBC, WBC, epithelial cells, cast, crystals, and bacteria.

White blood cell was expressed as cells per high power field (WBC/HPF), and pyuria was considered positive when number exceeds 10 (WBC/HPF).

Urine samples revealing high count of squamous epithelial cells (> 20/HPF) were regarded contaminated and urine sampling repeated with extra careful instructions regarding methodology.

Urine specimens with pyuria were inoculated on blood agar and MaConckey agar plates and incubated at 37C° for 24hours. The single pure isolated colony, when present, was transferred to nutrient agar medium for preservation and to carry out other tests. Positive cultures were recorded.

All data were tabulated, cleaned, edited and entered “IBM SPSS Statistics” program version 25 for analysis. Pearson Chi-Square Independence test (χ^2) was employed to assess the association. *P* value <0.01 were considered statistically significant.

Results

A total of 465 patients with clinical diagnosis of urticaria, which was regarded as non-inducible (i.e. spontaneous), was recruited for study.

Their age ranged from 3 to 77 years with a mean age of 35.74 (\pm SD 17.450) years. Regarding the control group (No.=465) their age ranged from 3 to 75 years with a mean age of 35.21 (\pm SD 17.234) years. Distributions, regarding the age group, were comparable. (Table 1).

Table 1: Distribution of both urticaria and control groups according to age.

Age (Year)	Urticaria Group		Control Group	
	No.	Percent	No.	Percent
1-10	57	12.3	59	12.7
11-20	29	6.2	30	6.5
21-30	70	15.1	70	15.1
31-40	117	25.2	116	24.9
41-50	98	21.1	101	21.7
51-60	52	11.2	50	10.8
61-70	33	7.1	32	6.9
71-	9	1.9	7	1.5
Total	465	100.0	465	100.0

Females constituted majority with 322 (69.2%) patients in the study group leaving males with 143 (30.8%) patients. Comparable figures are found in control group: 324 (69.7%) patients and 141 (30.3) patients for females and males respectively.

Pyuria was regarded positive in 92 (19.8%) patients of the urticaria group, while it was found only in 36 (7.7%) of the control group. (Figure 1).

A highly significant association between urticaria and pyuria was observed, ($\chi^2(1) = 28.410, p < 0.001$). (Table 2).

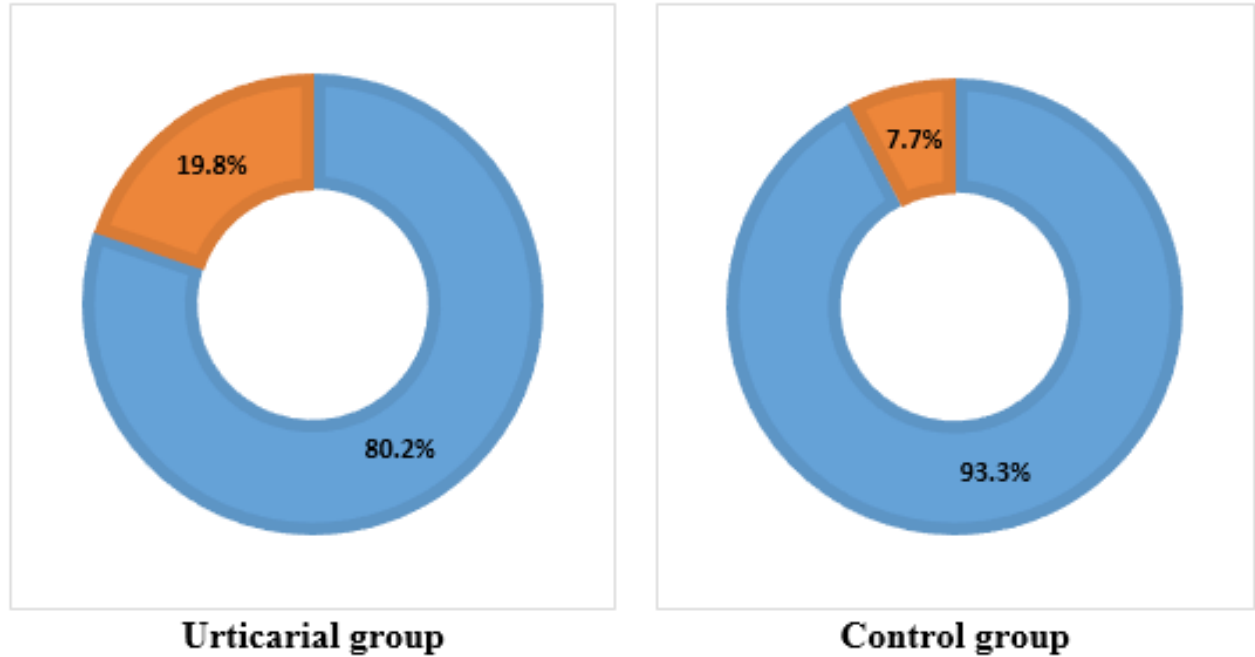


Figure 1: Pyuria distribution in both groups

Table 2: Association between urticaria and pyuria (Chi-Square Tests)

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	28.410	1	.000		
Continuity Correction	27.405	1	.000		
Likelihood Ratio	29.262	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	28.380	1	.000		
N of Valid Cases	930				

Positive urine culture results were obtained from 38 (8.2%) patient in the urticaria group, while such results were found in 11 (2.4%) urine samples from the control group. (Figure 2).

The association between urticaria and positive urine culture was a highly significant association, ($\chi^2(1) = 15.705, p < 0.001$). (Table 3).

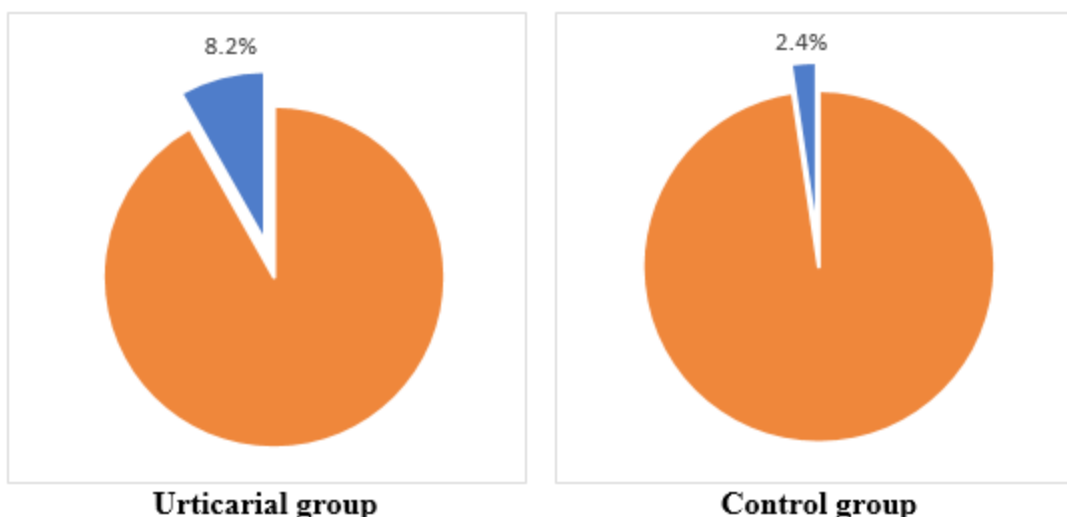


Figure 2: Positive urine culture distribution in both groups

Table 3: Association between urticaria and positive urine culture (Chi-Square Tests)

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	15.705	1	.000		
Continuity Correction	14.563	1	.000		
Likelihood Ratio	16.568	1	.000		
Fisher’s Exact Test				.000	.000
Linear-by-Linear Association	15.688	1	.000		
N of Valid Cases	930				

Regarding symptoms attributed to urinary tract infections: out of 92 urticaria patients with pyuria, 30 (32.6%) patients denied any such symptom. Out of 38 patients with positive urine culture, 11 (28.9%) revealed same negative symptomatic history.

Pregnant females constituted 12 from those 30 asymptomatic pyuria, and 5 of the 11 asymptomatic positive urine culture subgroups.

Regarding the isolated pathogens in positive culture results, these were dominated, in the urticaria group, by *Escherichia coli* which found in 20 (52.6%), followed by *Staphylococcus aureus* In 9 (23.6%), *Pseudomonas Spp.* In 5 (13.1%), *Klebsiella Spp.* In 3 (7.8%), then *Proteus* in 1(2.6%). In the control group, *Escherichia coli* was found in 7 (63.6%), followed by *Staphylococcus aureus* In 4 (36.6%), and *Pseudomonas Spp.* In 2 (18.1%).

Discussion

Association between infections (bacterial, viral, parasitic, or fungal) and ordinary (spontaneous) urticaria

(acute or chronic) has been noted long before, as early as in the 1920ies^(3,10,11). Their role had been discussed and included in most reviews¹¹, Never the less, proving a cause and effect relationship is often difficult, and inappropriate “blaming” a condition for causing urticaria may occur³.

Nearly all of the numerous studies reporting evidence for infectious agents triggering urticaria are case reports or retrospective observational studies without appropriate controls.¹² The relevance and frequency of infectious diseases varies between different patient groups and different geographical regions^(1,4,6). Urinary tract infection has been reported in number of publications as a cause in both acute and in chronic spontaneous (less in inducible) urticaria and angioedema¹⁰. As far as there is no possibility to challenge the patient with the suspected pathogen, thus making definitive recommendations regarding the role of infection in urticaria needs more research^(2,10).

Urinary tract infection, remarked initially by pyuria

and positive leukocyte esterase test was frequently noted to be found in cases of urticaria attending our clinics. The current study was arranged to test the substantial role and the “weight” of this association which, as we thought, did not receive the deserved attention in available studies.

Over period of 2 years we were able to collect a cohort of 465 patients with acute and chronic urticaria, which could be regarded as a reasonable sample of patient that get over many epidemiologic studies^(2,6,10,12) and enable studying the demographic characters of urticaria among our community.

Females (322 patients) outnumber males (143 patients) with a ratio of 2.2:1. Most epidemiologic studies reported similar predominance of females with variable ratios⁽¹⁻⁶⁾, though some excludes acute urticaria and extremes of age from this female predominance³.

Age groups affected were dominated by third to fifth decade, this may in part be due to more tendency to consult earlier in those age groups. So that many cases of urticaria that develop on just a single or a few occasions diminish within a week may be overlooked and not included. Most studies reported such peak age between 20 and 40 in chronic spontaneous urticarial^(1,6). When all types of urticaria were surveyed, a bimodal age distribution in patients aged birth to 9 years and 30 to 40 years was revealed^(1,3). acute spontaneous urticaria (along with urticarial reactions) may represent the first peak¹.

The term pyuria literally means “pus in the urine” but, in common usage, the focus is not on the presence of pus but on the number of white blood cells (WBCs) or amount of leukocyte esterase (LE) that exceeds a threshold and suggests a urinary tract infection (UTI)^(8,9).

Pyuria was detected (both by urine microscopy and by leukocyte esterase test) in 92 (19.8%) patients of the urticaria group, while it was found only in 36 (7.7%) of the control group. Statistical analysis of the two rate values revealed a highly significant association (with a p value < 0.001) between urticaria and pyuria.

Using evidence of inflammation (pyuria) in the urine to screen for who needs a culture seems justified on the basis of practicality at point of care and likelihood of UTI^(9,13). The absence of pyuria is a strong indicator that a UTI is not present and is useful in ruling out a UTI^(8,9,14).

Also If there are, in fact, some true UTIs without evidence of inflammation from the urinalysis, are they as harmful as those with “pyuria”? Animal data demonstrate it is the inflammatory response, not the presence of organisms, that causes the harmful effects and renal damage⁹.

Adding to that asymptomatic bacteriuria (positive urine cultures, with or without pyuria, without accompanying genitourinary symptoms attributable to infection) is regarded as harmless and is not an indication for treatment^(8,14).

Available data about prevalence of pyuria in general community is scare, but in our study it was found in (7.7%) of the randomly selected control group (465 patients) who were seeking medical advice for conditions not related to genitourinary complaints.

Culture: Despite availability of molecular diagnostic approaches for diagnosis of many infections, UTI are still generally diagnosed, as they have been for decades, by urine culture results⁽⁷⁻⁹⁾. However, urine culture may not be necessary as part of the evaluation of outpatients with uncomplicated UTIs^(13,14).

Positive urine culture results were obtained from 38 (8.2%) patient in the urticaria group, while such results were found in 11 (2.4%) urine samples from the control group. When these figures were statistically tested, the association between urticaria and positive urine culture was found to be a highly significant association, (with a p value < 0.001).

Comparison of these results with data obtained from other studies is impeded by variable differences between study designs¹⁵.

Prevalence of community-associated UTI was reported to be 0.7%, However frequency of UTIs vary according to geographical setting and location, and providing exact figures is challenging^(6,16). Positive culture results were found in 11 (2.4%) urine samples from the control group, those were assumed to be asymptomatic since they were attending clinics for complaints not primarily related to genitourinary complaints. However, when those with positive culture results were carefully questioned about symptoms related to UTIs, positive and negative replies were obtained and thus constituting a hybrid between UTIs and asymptomatic bacteriuria.

Pyuria has multiple causes¹⁷, and we concentrate in current study on UTIs but others should be considered in cases where culture is Negative

The exact mechanism of how infectious agents cause urticaria is not known^(10,11). It is accepted that hives are caused by “friendly fire” from the human body’s own defenses rather than caused directly by the infectious agents. It has been postulated that these agents trigger release of histamine and leukotrienes from the mast cells and basophils by IgE antigen complex; or through anaphylotoxin C3a, C4a generated through activation of complement system or through the kinins, e.g., bradykinin^(11,18).

Conclusion

Though establishing a causal relationship through experimental study is difficult, this study showed a highly significant association between bacterial UTI and spontaneous urticaria.

Further prospective studies to elucidate effect of eradicating UTIs on course of urticaria is advisable.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the College of Medicine, University of Thi-Qar, Iraq and all experiments were carried out in accordance with approved guidelines.

References

1. Michihiro H, Shunsuke T, Takaaki H. Urticaria and Angioedema. In: (eds.) Fitzpatrick’s Dermatology. 9th edition. New York. McGraw-Hill Education; 2019; 684-709.
2. Zuberbier T, Aberer W, Asero R. The EAACI/GA2LEN/EDF/WAO Guideline for the definition, classification, diagnosis, and management of urticaria. *Allergy* 2014; 69: 868–887.
3. Clive EH, Sarbjit S. Urticaria, Angioedema In: Jean L Bologna, Julie V Schaffer, Lorenzo Cerroni (eds.) *Dermatology*. 4th edition. China. Elsevier Limited; 2018; 304-319.
4. Camila A, Katherine B, Abraham K. Urticaria: A comprehensive review: Epidemiology, diagnosis, and work-up. *J Am Acad Dermatol*. 2018; 79(4):599-614.
5. Clive EH, Alexander M. Urticaria In: Christopher EM. Griffiths, Jonathan Barker, Tanya Bleiker, et al. (eds.) *Rook’s Textbook of Dermatology*. 9th edition. John Wiley & Sons, Ltd; 2016; 42:1–18.
6. Betsy Foxman. Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. *The American Journal of Medicine* 2002; 113(1): 5-13.
7. Michael L, Loretta G. Laboratory Diagnosis of Urinary Tract Infections in Adult Patients. *Clinical Infectious Diseases* 2004; 38(8):1150–8.
8. Brittany N. Interpretation of Urinalysis and Urine Culture for UTI Treatment. *US Pharm* 2013; 38(11):65-68.
9. Kenneth B. The Diagnosis of UTI: Concentrating on Pyuria. *PEDIATRICS* 2016; 138(5): e 20162877.
10. Bettina W, Ulrike R. Urticaria and infections. *Allergy, Asthma & Clinical Immunology*. 2009; 5:10
11. Pawel L, Magdalena S, Magdalena P. The role of focal infections in the pathogenesis of psoriasis and chronic urticaria. *PostepDermAlergol* 2013; 2: 77–84
12. Mareri A, Adler SP, Nigro G. Herpesvirus-associated acute urticaria: an age matched case-control study. *PLoS One*. 2013; 8(12):e85378.
13. Walter E, S Ragnar N. Urinary Tract Infections: Disease Panorama and Challenges. *The Journal of Infectious Diseases* 2001; 183(1): S1–S4.
14. Andrea G, Mark E, Trevor C. Urinary Tract Infection and Asymptomatic Bacteriuria Guidance. 2019.
15. Cansin S, Bulent E, Fazil O. The Etiology of Different Forms of Urticaria in Childhood. 2000.
16. Tandogdu Z, Wagenlehner FM. Global epidemiology of urinary tract infections. *Curr Opin Infect Dis*. 2016; 29(1):73-9.
17. Dieter RS. Sterile pyuria: a differential diagnosis. *Compr Ther* 2000; 26(3): 150–152.
18. Sharma AD. Role of Nasal Carriage of Staphylococcus aureus in Chronic Urticaria. *Indian J Dermatol*. 2012; 57(3):233-6.

Antimicrobial Peptides AMPs Produced by *Bacillus* spp.

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Abstract

Bacillus species are one of the most interesting Gram-positive bacteria, forming endospore which are usually capable to produce variety of secondary metabolite compound such as antibiotic, enzymes which playing important roles In pharmaceutical industry, subtilin, bacilysin, gramicidin, tyrocidine, bacitracine, polymyxin, etc. The *Bacillus* species have a wide range of antimicrobial activisms since they are used as antibacterial, antifungal, antiviral, antimycoplasma and anti amebocytic agents .The production of this active compounds involve orangutans peptides, that divided into two class first class ribosomally generated and post-translationally altered which include (lantibiotics and lantibiotic-like peptides),second class non-ribosomally procreated, besides a various number of non-peptidicsubestansis like polyketides, an amino - sugar, and a phospholipid. In this review abridge the structures of antimicrobial peptide produced from *Bacillus*, the genetics encoded and analysis their generative and the current finding of antimicrobial activity for each peptide.

Keywords: *Antimicrobial, Peptides, AMPs, Bacillus spp.*

Introduction

The excessive uses of antibiotics have led to the appearance of highly reactance species of athogenic bacteria as well as, these strains could Easley rapidly gained extra resistance to the newcomer synthetic antibiotics¹. The distinguished of new active compound is the most obvious curriculum to fighter this excesses antibiotics resistance^{2,3} the Rhizosphere region of plant root is the source of Most important of microorganisms found, it had determined significant consideration due to the ability to produced secondary metabolites like antibiotics and enzymes which played important role in plant and human life⁴ the important of the bacillus as genus is attribioted to forming spores and to the great part playing in agricultural, indesterialand pharmacy aspect. *Bacillus* spp. consider one of the most complicated bacteria at the diversity in genetics, structural, activity, sorting, and environmental level, allowing them to be very consequential in various habitat, notably in soil (5).antibiotics such as subtilin, bacilysin, gramicidin, tyrocidine, bacitracine, polymyxin, could produced by *Bacillus* species and exhibition antibacterial, antifungal, antihelmenthic and phytotoxic activity. ⁶sequence of genomic have expressed that *Bacillus spp* have highly

numerous of genes associated in the accumulative of different metabolites such as antibiotic ^{7,8}. According to their structural form and biosynthetic mechanism, this compound could be classified include dominantly ribosomally producing peptide involving bacteriocins,or non-ribosomally synthesized comprises small microbial peptides synthesized enzymatically, besides numerous of non peptdes compounds for example polyketides, an amino sugar, and a phospholipid ⁹. The aims of this review is to describe the synthesis and chemical structural of various antimicrobial peptides produced from different species of *Bacillus* . Peptide antibiotics exempld the prevailing class. They showed highly rigid, hydrophobic and cyclic structures with extraordinary constituents such as D-amino acids and are commonly resistant to hydrolysis by enzymes like peptidases and proteases (10). Moreover, amino acid cysteine residues could oxidized to disulphides or could be amended to property intermolecular C–S (thioether) bonds, and consequently the peptide compound non-sensitive to oxidation. Basically, two varied pathways for synthesis allows the founding of an extraordinary substances 1- the ribosomal synthesis of linear precursor peptides that are subjected to post-translational modification and

proteolytic processing . 2- the non-ribosomal synthesis of peptides by large megaenzymes, the non-ribosomal peptide synthetases (NRPSs) .⁷

Ribosomal Peptide Antibiotics: Ribosomally synthesized peptide antibiotics are extensively circulation in natures, include among 12 and 50 amino acid residues. They are customarily cationic and displayed great structural variety ¹¹. Bacteriocins are ribosomally synthesized AMPs that are produced by bacteria and are usually active against strains of bacteria that are closely related to the producer strains ^{12,13}.

Bacteriocins had specific characteristic made it suitable alternate to antibiotics and prevent the growth of bacteria, even against certain multidrug resistant bacteria in the same related species or wide spectrum of effectiveness . They are usually heat-stable, small peptides made of short chains almost about 20-60 amino acid residues; as well as long chains can also be found. Most bacteriocins are products from Gram-positive

bacteria, whoever, Some bacteriocins could produced from Gram-negative bacteria.^{14,15}. There is no effect of bacteriocins on mankind due this cells do not have a receptor recognized it ^{16,17}. That's make bacillus be ideal and perfect as stotred for new and effectively bacteriocins. Based on discriminated structural and functional particularity, Bacteriocins are categorize into two category, category 1 and 2 ¹⁶. Mostly of the bacteriocins generative from *Bacillus* spp resources to the category 1, dubbed lantibiotics¹⁸ Lantibiotics are peptide-derived antimicrobial agents that are ribosomally synthesized and post translationally modified to biological form of activity . Lantibiotics was abbreviator of lanthionine-containing antibiotic peptides.¹ Lanthionines consist of two alanine residues of amino acid that are linked at the β-carbons by a thioether bon . ¹⁹ (Figure 1) . production of bacteriocins controlled by regulatory system consisting of a histidineprotein kinase (HPK) and a response regulator (RR) in the presence of the specific autoinducer peptide (AIP).

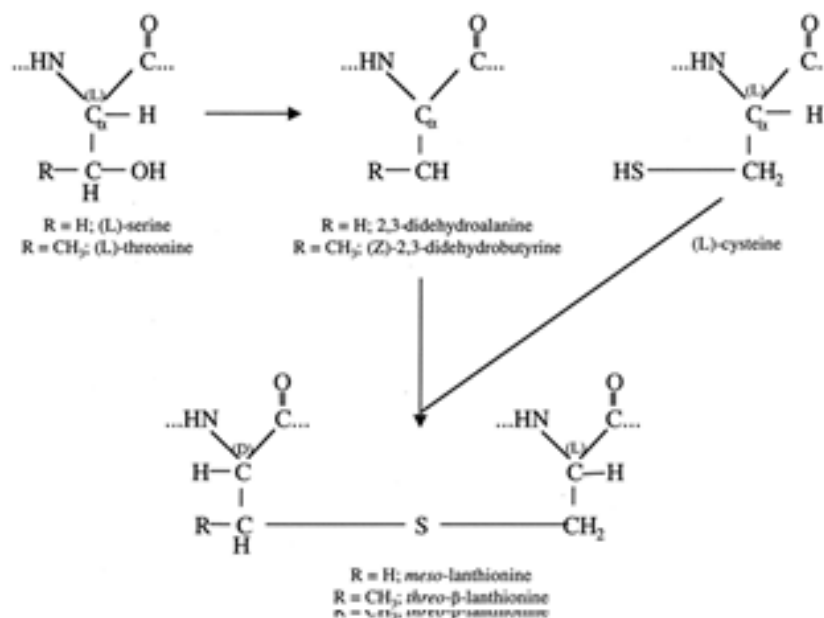


Figure 1: Chemical structure of lantibiotics

The class II bacteriocins could be further divided into four subclasses, class a : (active against *Listeria* and pediocin-like), class b consist of two peptide, class c (cyclic), and class d (nonpediocin single linear).¹⁶lantibiotics can be additionally divided in to two sub division A and B for their commonality structure,

molecular weighing and biologic activism . sub division A lantibiotic (molecular weight 2100 – 3500 Dalton; almost 20 – 37 a.a residue) exhibit a more linearity the secondary structure with net charge be positive compare with sub division B includes globular broadly uncharged lantibiotics²⁰.

Subtilin: Subtilin is synthesized by *B.subtilis* ATTC 6633, considered very important adverting and focusing antibiotics. Subtilin is a small peptide antibiotic (figure 2), its chemical structure consists of 32 amino acid of pentacyclic²³. Subtilin is settled to acid and temperature manipulating above to 121°C for one hour, and showed activity against various number of Gram positive bacteria consisting bacillus spp.. The mechanism of subtilin action appeared very complex, including the associating to a appointed target cell as well as lipid

II which is targeted by vancomycin antibiotic, which is structure belongs to kind glycopeptide²¹ numerous genetic studies reveal that clump of ten genes *spa* BTCSIFEGRK controlled Subtilin generation and its locus the chromosome, transcription occurs with 2 promoters. Subtilin regulates/activates its own biosynthesis via a two component regulatory system. The aggregation of the genes domination the production of various proteins developable in the processes of maturation as well as production of such compound²⁴⁻²⁷,

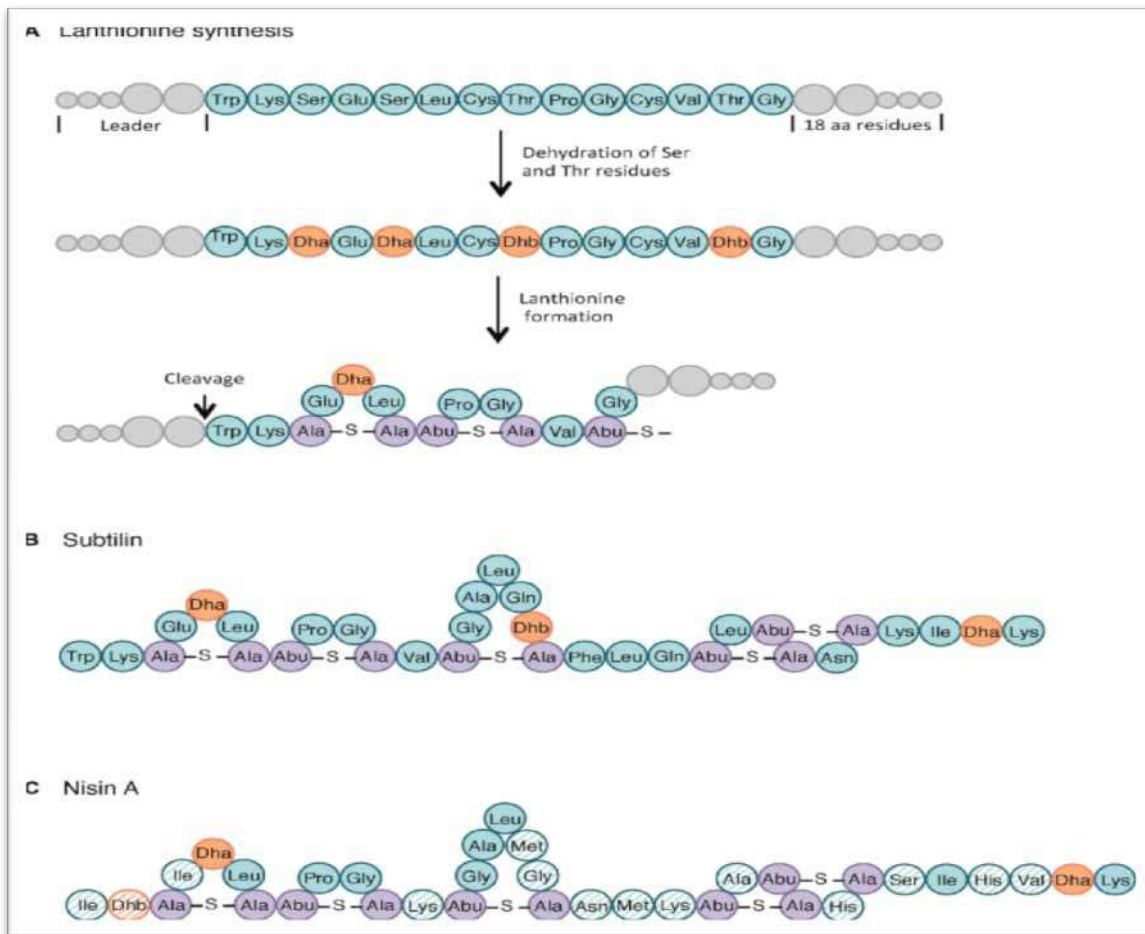


Fig 2 :generated of Lanthionine. (A) Commonality pathway of the lanthionine production. (B) the chemical structure of subtilin (C) the chemical structure of nisin A . Adopted from ^{27,28}.

Ericin: Ericin S and ericin A are two lantibiotic belong to type A its synthesized by Strain of *B. subtilis* A 1/3 with sturdy resembles to subtilin . The genetic studies reveals that the gens encoded ericin gene is clump consist of two structural gene *eri S* and *eri A* (29). Purified ericin (mainly ericin S) have antimicrobial

activity athwart a different species of bacteria, particularity against athwart *Clavibactermichiganensis*, the causative assignee of tomato bacterial sore³⁰.

Mersacidin: Mersacidin is a tetracyclic peptide,output by *Bacillus* sp. strain HIL Y-85,54728

this lantibiotic is the one of the most smaller of lantibiotic known so far, the M.W is (1825 Dalton). It is an uncharged molecule of twenty amino acids constituting four intra molecular thioether bridges, which impart a globular structure to the molecule³¹

It enumerates to the lantibiotics family group of peptides containing lanthionine- with antimicrobial activities³². Group type B lantibiotics include Mersacidin, actagardine, and the cinnamycin., which consist of flatter globular peptides without net charge or a net negative charge. In contrast, type A lantibiotics are flexible, elongated peptides that act by constituting pores in the bacterial membrane. As well as, lanthionine lantibiotics encompass a number of uncommon amino acids,

such as didehydroalanine, didehydrobutyrine, methylanthionine, *S*-aminovinylcysteine, etc^{33,34}. The mersacidin gene cluster involved of the structural gene *mrsA* (figure 3), besides genes implicated in beyond translational alteration (*mrsD* with *mrsM*), regulation (*mrsR1*, *mrsR2*, *mrsK2*), transport (*mrsT*) and immunity (*mrsFEG*)³⁵. Mersacidin produced its activism on bacterial cell through prevention the synthesized of cell wall; mersacidin could configure the complex with lipid II as previously shown for subtilin. Numerous studies declared the importance of mersacidin in prevention the growth of Gram positive bacteria ones enterococci expressing the V and A vancomycin resistance phenotype, besides MRSA, strain of *Staphylococcus aureus* which resistant to methicillin.

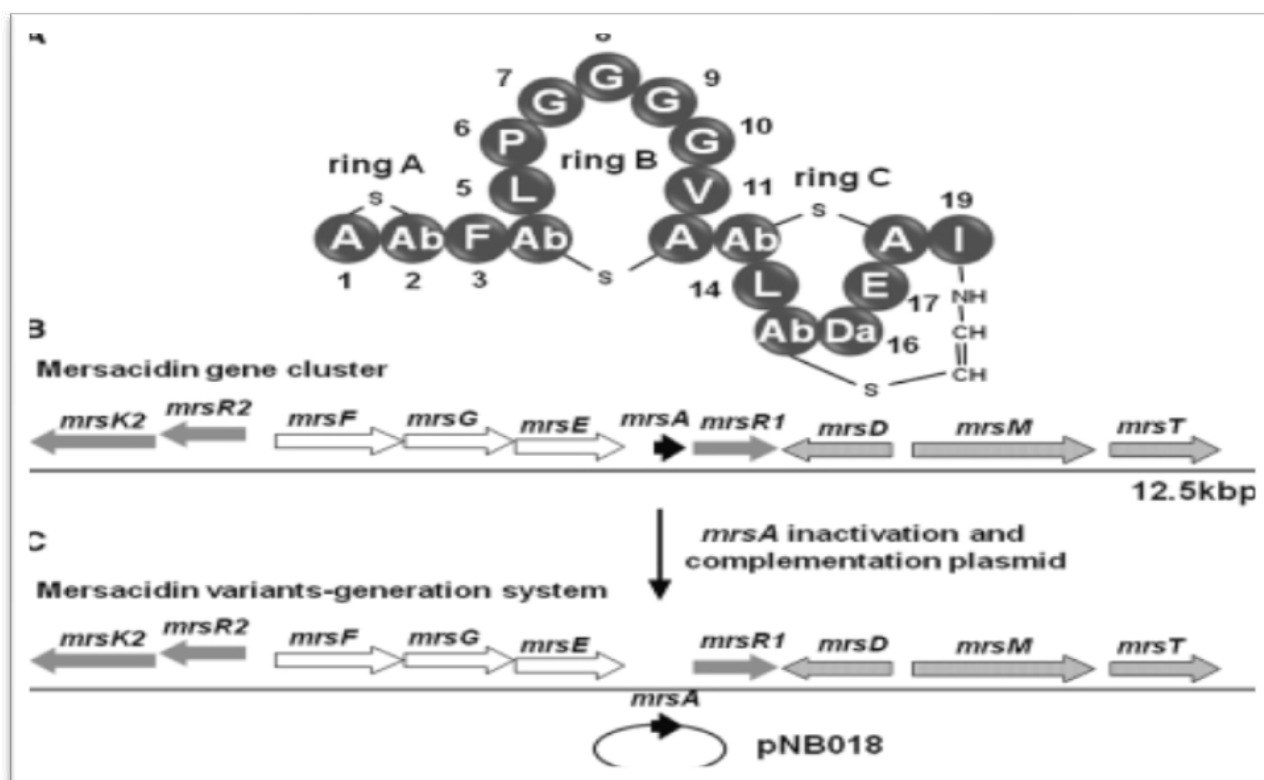


Figure 3. The Structure of Mersacidin and the Gene Cluster: (A) Primary structure of mersacidin (B) Organization of the mersacidin biosynthetic gene clump. (C) Engineered system for generating mersacidin mutants. Da, dehydroalanine; Ab, 2-aminobutyrate

Subtilosin A: Subtilosin A is unusual lantibiotic composed of number of amino acid almost 35 inherently produced from *Bacillus subtilis* and from *Bacillus atrophaeus* and isolated from *Bacillus amyloliquefaciens*. Structure of Subtilosin A is peptide contain macrocyclic,

and there is no found lanthionine and methylanthionine residues, Subtilosin A is configurative from its precursor by proteolytic splitting of the N-terminal leader peptide and cyclization through covalently bond between the N-terminal asparagine and the C-terminal glycine.

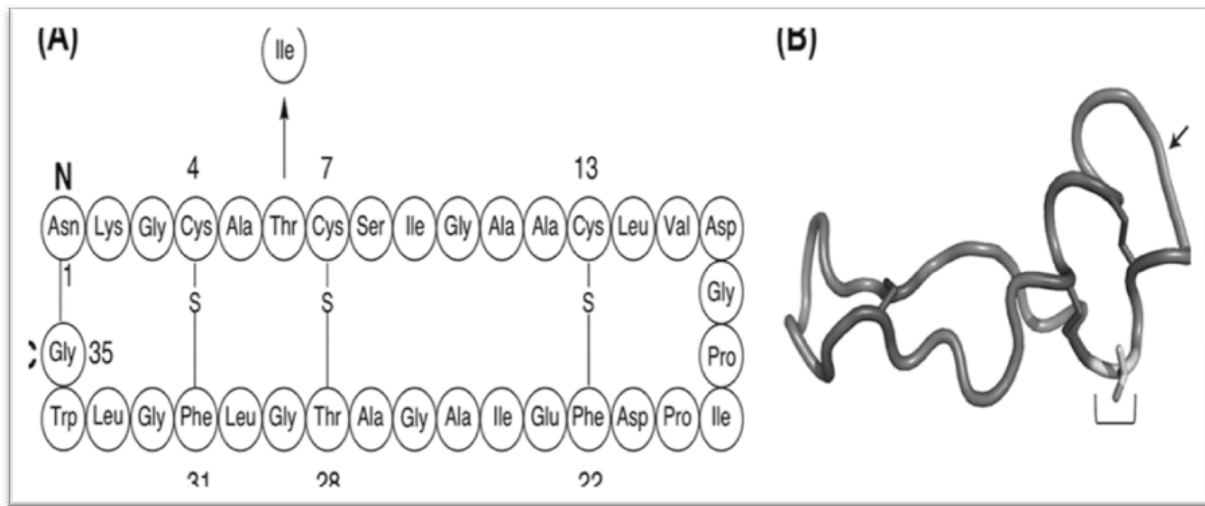


Figure 4: Structures of subtilisin A. (A) Amino acid concatenation of subtilisin A. The backbone cyclization of the peptide via an amide bond between the N and C limit. (B) Backbone involuted hulk of subtilisin A .

Sublancin 168: Sublancin 168 is an unusual lantibiotic secreted by the strain *B. subtilis* 168, incorporates singular lanthionine bond and two extraordinary disulfide bonds. Sublancin 168 is a novel and distinctively S-linked bacteriocin glycopeptide comprising of 37 amino acids (45). Using NMR declared that Sublancin 168 comprises of two α -helices and ring well-defined inter helices. The two helices span residues 5–16 and 24–34, and the ring region comprises

residues 17–25 amino acid. The 9 amino-acid loop region comprises a β -S-linked glucose moiety attached to Cys22. The three-dimensional structure provides unusual high stability of sublancin 168. This lantibiotic had good antimicrobial activity against some species of Gram positive bacteria, involving *B. megaterium*, *B. subtilis* 6633, and *S. pyogenes*, and *S. aureus*, this activity of this compound would be very important in different applications, in agronomic and industrial field.

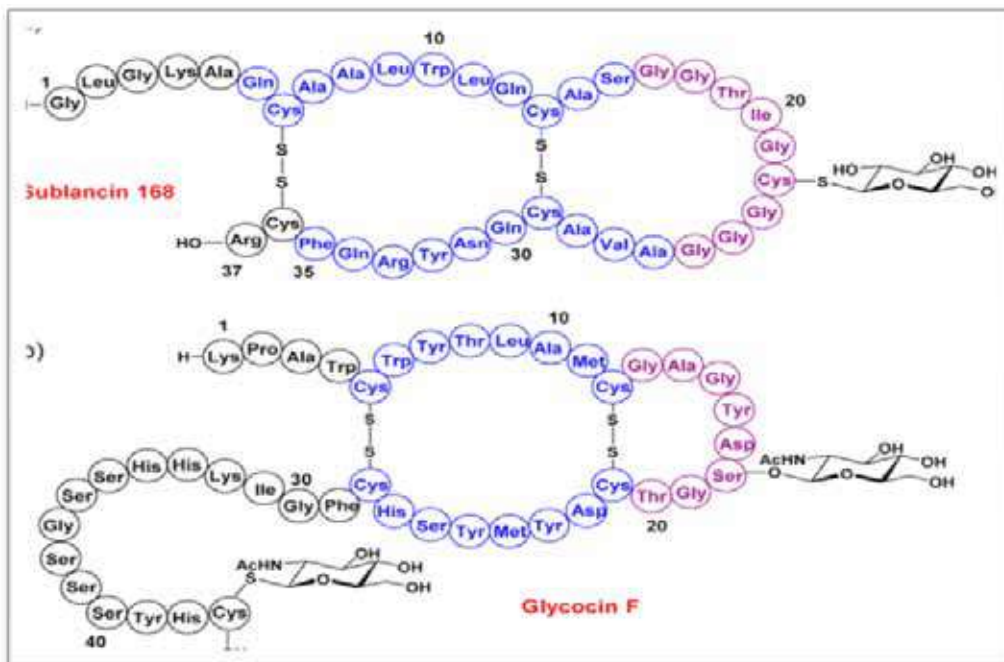


Figure 4: Chemical structures of Glycocin. (a) Sublancin 168. (b) Glycocin F.

Some species of bacillus could produced proteins with antimicrobial activity, it is characterized and identified insufficiently, its known as bacteriocin – like inhibitory compound (BLIS). One of this substances is from *B. cereus* is able to produce BLIS which have interested ascribe to the probable implementation as ordinary food preservatives. *B. licheniformis*, also produced BLIS this bacteria dissociated from water buffalo rumen, lichenin synthesis by this bacteria under anaerobically requirement, the activism of this peptide athwart wide variety of microbes found in buffalo rumen attributed to the ability to tolerant abroad range of pH and high temperature. Gene sequences of *B. thuringiensis* is identical to *B. cereus*, to chitin and thuricins family include H, S and 17, is BLIS generated from *B. thuringiensis* with abroad inhibitory spectrum. The effect of Thuricin H on variety species belong to Gram positive bacteria include *Staph. aureus* and *Listeria spp.* Thuricin S is heat stable, prevent the accretion of bacteria belong to gram positive, involving *Salmonella enterica*, *Listeria monocytogenes* and *Pseudomonas aeruginosa*; while thuricin 17 it's activity athwart other species of *Bacillus*.

Non – Ribosomal Peptide Antibiotics:

Nonribosomal peptides (NRP) are a class of peptide, ordinary synthesized by bacteria and fungi. Non ribosomal peptide synthetases (NRPSs) are involved in the biosynthesis of numerous peptide and peptide-like natural products that have been utilized in medicine, agriculture, and biotechnology, besides other fields.

Numerous Strains of *Bacillus* spp generative NRP thru serial steps mechanism consisting the choosing the amino acid and adsorption of residues such as macrolactones (surfactins and fengycins) and cyclic lipopeptidides (iturin group).

Cyclolipopeptides (CLPs): Cyclic lipopeptides (CLPs) are one of the significant type of biosurfactants which possess special surface-active as well as activity against fungal. CLPs are produced through non-ribosomal peptide synthetases (NRPs), and produced particular variety of CLP products differentiated according to the sequences of amino acid, length ramified chain of fatty acids and the kind of bonds which bind the amino acids.

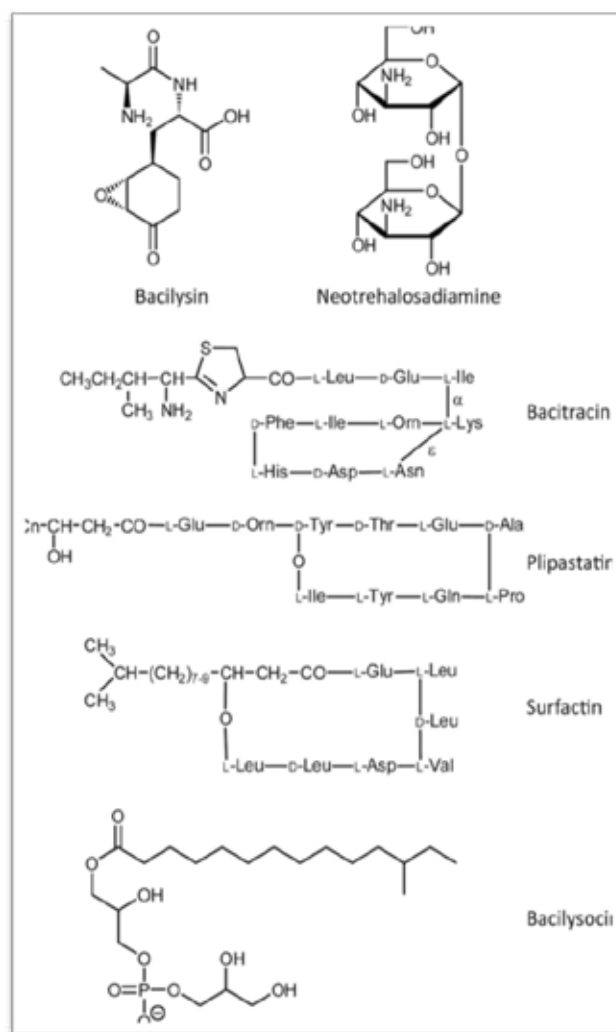


Figure 5. chemical Structures of some non-ribosomal peptides synthesis by variable strains of *B. subtilis* . adopted from(86)

Conclusion

The *Bacillus* species have a wide range of antimicrobial activisms since they are used as antibacterial, antifungal, antiviral, antimycoplasma and antiamebocytic agents. The production of this active compounds involve orangutans peptides, that divided into two class. first class ribosomally generated and post-translationally altered which include (lantibiotics and lantibiotic-like peptides), second class non-ribosomally procreated, besides a various number of non-peptidic substants like polyketides, an amino - sugar, and a phospholipid. In this review abridge the structures of antimicrobial peptide produced from *Bacillus*, the genetics encoded and analysis their generative and the current finding of antimicrobial activity for each peptide.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Department of Microbiology/ College of Science/Al-Mustansiriyah University, Iraq and all experiments were carried out in accordance with approved guidelines.

References

- Mondol MA, Shin HJ. Diversity of Secondary Metabolites from Marine Bacillus Species: Chemistry and Biological Activity. *Mar. Drugs*.2013; 11: 2846-2872.
- Islam MT, Hossain MM. Biological Control of Peronosporomycete Phytopathogens by Antagonistic Bacteria. In *Bacteria in Agrobiolgy: Plant Disease Management*; Maheshwari, D.K., Ed.; Springer-Verlag: Berlin/Heidelberg, Germany, 2013; 167–218.
- Li J, Vederas JC. Drug discovery and natural products: End of an era or an endless frontier? *Science*.2009;325: 161–165.
- Mussa A, Majid R. Study the effect of Purified Pyoluteorin Produced from *P. Aeruginosa*, Isolated from Rhizospheric Plant Wheat on some UTI Bacteria Biofilm Formation . *Research J. Pharm. and Tech*. 2018; 11(12).
- Mansour A, Zeinab R. Isolation and identification of Bacillus species from soil and evaluation of their antibacterial properties .*Clin. Microb. infec*. 2015; 2 (1): 23233.
- Hmidet N, H Ayed, Jacques P, Nasri M.Enhancement of Surfactin and Fengycin Production by *Bacillus mojavensis* A21: Application for Diesel Biodegradation.*BioMed Research International*.2017.
- Stein T. Bacillus subtilis antibiotics structure, syntheses and specific functions. *Mol. Microbiol*.2005; 56: 860 – 867.
- Abrioel H, Franz C. Diversity and applications of Bacillus bacteriocin . *FEMS Microbiol Rev*.2011; 35: 201 – 232.
- Singh, P. K., Chittputna, Ashish, Sharma, V., Patil, P. B., and Korpole, S. Identification, purification and characterization of Laterosporulin, a Novel bacteriocin produced by *Brevibacillus* sp. Strain GI-9. *PLoS One*.2012; 7:e31498.
- Katz E, Demain A. The peptide antibiotics of Bacillus: chemistry, biogenesis, and possible functions. *Bacteriol Rev*.1977; 41: 449–474.
- Marx R, Stein T, Entian K-D & Glaser SJ Structure of the Bacillus subtilis peptide antibiotic subtilisin A determined by 1H-NMR and matrix assisted laser desorption/ionization time-of-flight mass spectrometry. *J Protein Chem*.2001; 20: 501–506.
- Motta A, Flores F, Souto A. Antibacterial activity of a bacteriocin-like substance produced by Bacillus sp. P34 that targets the bacterial cell envelope. *Antonie Van Leeuwenhoek*.2008; 93(3): 275–284.
- Chandra DS, Byng WY. Antimicrobial peptides of the genus Bacillus: a new era for antibiotics .*Canad .J .ofMicrobiol* . 2015; 61 (2): 93 – 103.
- Dischinger J, Chipalu S. Lantibiotics: promising candidates for future applications in health care. *Int. J. Med. Microbiol*. 2014; 304: 51–62.
- Garneau S, Martin NI. Two-peptide bacteriocins produced by lactic acid bacteria. *Biochimie*.2002; 84: 577–592.
- Qin Y, Wang Y, He Y, Zhang Y, She Q. Characterization of Subtilin L-Q11, a Novel Class I Bacteriocin Synthesized by Bacillus subtilis L-Q11 Isolated From Orchard Soil . *Frontiers in Microbiology*.2019; 10: 484.
- Yang S, Lin C, Sung, C, Fang JY. Antibacterial activities of bacteriocins: application in foods and pharmaceuticals. *Front. Microbiol*. 2014; 5:241.
- Asaduzzaman SM, Sonomoto K.Lantibiotics: diverse activities and unique modes of action. *J BiosciBioeng*.2009; 107: 475–487.
- McAuliffe O. Lantibiotics: structure, biosynthesis and mode of action.2001; 25:285-308.
- Lee H, Kim HY. Lantibiotics, Class I bacteriocins from the genes Bacillus . *J MicrobiolBiotechnic*.2011; 21: 229 – 235.
- Parisot J, Carey S, Breukink E, Chan W. Molecular mechanism of target recognition by subtilin a Class I lanthionine antibiotic . *Antimicrobiol Agents Ch*. 2008; 52 : 612 – 618.
- Dhas JB, Hena BV. Bacteriocin from Bacillus subtilis a novel drug against diabetic foot ulcer bacterial pathogens.*Asian Pac J Trop Biomed*.2013; 3(12): 942-946.
- Galvez A, Abriouel H, Lopez RL, Omar NB.

- Bacteriocin – based strategies for food bio – preservation . *International Journal of food Microbiology*.2007; 120 : 51 – 70.
24. Burkard M, Entian K, Stein T. Development and application of a microtiter plate – based auto induction bio assay for detection of the lantibioticsubtilin . *J Microbiol Meth*. 2007; 70 : 179 – 185 .
 25. Entian KD, de Vos WM. Genetics of subtilin and nisinbiosyntheses: biosynthesis of lantibiotics. . *technolLett*. 2005; 27(21): 1641-8.
 26. KleinC, EntianKD. Genes Involved in Self-Protection against the LantibioticSubtilin Produced by *Bacillus subtilis* ATCC 6633..*appl and environ microbiology*.1994; 60: 2793-2801.
 27. Cotter P, Hill C, Ross RP. Bacteriocins: developing innate immunity for food. *Nat. Rev. Microbiol*.2000; 3: 777–788.

Effect of Infliximab and Methotrexate on Bone Mineral Density in Rheumatoid Arthritis Patients

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Abstract

Background: Osteoporosis is an extra-articular complication of rheumatoid arthritis that results in increased risk of fractures and associated morbidity, mortality, and healthcare costs. The study aims at evaluation of changes in bone mineral density in a Rheumatoid arthritis patients on infliximab and methotrexate.

Patients and Method: A cross sectional study enrolled 60 RA patients diagnosed according to the ACR 1987/2010 revised criteria for the classification of RA. Thirty patient were on infliximab and other (30 patient) on methotrexate. Dermatographic and clinical data were collected (disease duration, disease activity score index of 28 joints (DAS 28) and (CDI), functional class, body mass index and treatment history. Patients with histories of chronic disease and smokers were excluded. Complete blood count, erythrocyte sedimentation rate serum calcium, phosphorous, alkaline phosphatase, vitamin D level were measured in both groups. Bone mineral density was measured by dual energy x-ray absorptiometry of hip and lumber spines for patients. Tor Z-score equal or less than (-2.5 standard deviation) of healthy young adults was taken as osteoporotic, and scores between (-1 to -2.5 standard deviation) was taken as osteopenic. Informed consent was obtained from individuals.

Results: The analysis of Dual energy x-ray absorptiometry of hips and lumber spines revealed that the number of RA patients on Infliximab having osteoporosis was 1 (3%) and 12 (40%) were osteopenic, compared to patients on MTX osteoporosis was present in 8 (26%) and osteopenia in 13 (43%), which is a significant difference, p-value (0.019). Vitamin D level in patient on Infliximab was low in 24 (80%) and normal in 6 (20%) patients. While in MTX it was low in 13 (43.3%) and normal in 17 (56.7%) of patients, p-value (0.003).

Conclusions: There was significant decrease in bone mineral density in RA patients on MTX while infliximab had a role in arrest in bone loss.

Keywords: RA, MTX, Infliximab, Methotrexate.

Introduction

Rheumatoid arthritis (RA) is a symmetric chronic autoimmune inflammatory poly arthritis of unknown etiology primarily affecting the small joints of hands and feet. Larger joints can be involved such as the ankles,

shoulder, and knees. It is progressive disease that can lead to joint destruction, deformity, and disability, with heterogeneous manifestations^[1,2]. In Iraqi patients, the prevalence is 1%.^[3] The exact cause remains unknown, but the genetic, environmental and immunological factors that play a role.^[4] The American Rheumatism Association 1987 revised criteria for the diagnosis of RA.^[5] American college of rheumatology/European league against rheumatism collaborative initiative classification criteria (2010 ACR/EULAR) and Score for RA.^[6] Two of commonly used drugs for treatment are the followings; 1st; Methotrexate-A dihydrofolatereductase

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inhibitor originally used for its anti-proliferative effects in the treatment of cancer, methotrexate is now an anchor drug among DMARDs and a gold standard against which all emerging therapies are compared.

An oral drug administered on a weekly basis, its anti-inflammatory mechanisms of action and are largely related to its induction of adenosine release to the inflammatory. The 2nd drug is (Infliximab) is a chimeric monoclonal antibody, infliximab is also cytotoxic for TNF-expressing cells. Infliximab is administered as an intravenous infusion every 8 weeks (after an initial loading regimen). Infliximab standard dose (3mg/kg), can be titrated up to 10 mg/kg, if needed and/or the dosing interval can be decreased (to every 6 or every 4 weeks). Infliximab is recommended to be administered concurrently with methotrexate (at least 7.5 mg/week) to prevent neutralizing antibodies development.^[7] Osteoporosis (OP) is a common complication of RA. OP mechanisms in RA are not fully understood, but it is thought that osteoclast dysfunction with cytokines that mediated them are the principal pathogenesis factors of this bone disease.^[8] RA bone loss is of multifactorial nature, but the inflammation has a major role in its development. Bone loss progression in RA patients is more severe, & are associated with greater risk of bone loss. So, the presence of initial radiographic damage, antibodies to cyclic citrullinated peptide (anti-CCP), C-reactive protein (CRP) levels, and other inflammatory markers are used to identify patients at greatest risk for developing progressive joint damage.^[9,10]

Heidari B et al & Dolan L et al found that^[10,11] treatment of RA patients with DMARDs for two years will decreased the levels of bone resorption markers like deoxypyridinoidine (D-PYR) significantly. However, decreasing disease activity by suppression of inflammatory process in RA is expected to preserve further bone mass. TNF has profound effects on bone. TNF Over-expression cause local & generalized bone erosion. Therefore, TNF is an important link between chronic inflammation and bone loss. TNF is also act as central inflammatory mediator of RA and its therapeutic inhibition leads to dramatic improvement in RA signs and symptoms.^[12,13] OP is an early and common feature in RA and occurs in two forms during the course of the disease:^[14] 1st; Periarticular osteopenia^[15], 2nd

Generalized OP: is an extra-articular RA complication which affects the axial and appendicular bones that cause an increased risk of fractures and related morbidity, mortality, and healthcare costs.^[16]

Patients and Method: A cross sectional study was conducted on 60 RA patients at rheumatology outpatients clinic, in Baghdad Teaching Hospital from July 2013-July 2014. Thirty RA patient were treated by biological agent (infliximab) and 30 patient on non biological DMARD (methotrexate). RA patients diagnosed according to American College of Rheumatology 1987, 2010^(5,6) criteria. All female patients were of 50-years-old (premenopausal) and male of under 55. All RA patients were subjected to the following: detailed history and clinical examination, calculation of body mass index, bone mineral density measurement of lumbar spine (L1-4) (L2-4) and right proximal femur (femoral neck, greater trochanter and total). Osteoporosis was diagnosed according to WHO guidelines criteria for osteoporosis diagnosis⁽¹⁷⁾, and DEXA machine (Dexxum) 3, Korean company (osteosys) was used.

Laboratory investigation: the following investigation done for all patients; 1. complete blood count (CBC), 2. Erythrocyte sedimentation rate (ESR), 3. Total serum calcium (N=8.4-10.2 mg/dl), 4. Total serum phosphorus (N=2.3-4.7mg/dl), 5.Total serum alkaline phosphatase (N=40-150 IU/L), 6.Total serum 25-hydroxyvitamin D was measured by ELIZA The kit was derived from Euroimmun Medizinische Labordiagnostika AG (Germany), Serum vitamin D level (N=22-42 ng/ml) while level of less than 22 ng/ml consider low. Statistical analysis was carried out using SPSS version 20. A *p*-value of ≤ 0.05 was considered as significant

Results

Table 1 shows the distribution of RA patients by vitamin D, Calcium, phosphorous as well as alkaline phosphatase. Vitamin D mean was (20.92±3.95) mg/dl and (61.7%) of patients had low vitamin D. Serum calcium mean was (8.25±1.12) mg/dl and (58.3%) of patients had normal serum calcium. Serum phosphorous mean was (3.54±0.78) mg/dl and (96.7%) of patients had normal phosphorous. ALP mean was (78.57±31.82) mg/dl and (88.3%) of patients had normal ALP.

Table 1: RA Patients distribution by Vitamin D, Calcium, Phosphorous and Alkaline Phosphatase

Variable	Mean±SD	Frequency (%)
Vitamin D ng/ml		
Normal	20.92±3.95	23 (38.3%)
Low		37 (61.7%)
Serum Calcium mg/dl		
Normal	8.25±1.12	35 (58.3%)
Low		25 (41.7%)
Serum Phosphorous mg/dl		
Normal	3.54±0.78	58 (96.7%)
High		2 (3.3%)
Alkaline Phosphatase IU/L		
Normal	78.57±31.82	53 (88.3%)
High		7 (11.7%)

SD = Standard deviation

Table 2 shows the association of types of therapy with BMI. There was no significant association between types of therapy with BMI.

Table 2: Association of types of therapy with BMI

Variable	Types of Therapy		X ²	P value
	Biologic (%)	DMARD (%)		
BMI			0.725	0.867
< 18.5 kg/m ²	1 (3.3)	2 (6.7)		
18.5-24.9 kg/m ²	7 (23.3)	5 (16.7)		
25-29.9 kg/m ²	8 (26.7)	9 (30.0)		
≥ 30 kg/m ²	14 (46.7)	14 (46.7)		

*p value ≤ 0.05 is significant, BMI= body mass index, DMARD=disease modify antirheumatic drugs

Table 3 shows the association of types of therapy with vitamin D, serum calcium and phosphorous as well as ALP.

A significant association was found between types of therapy with vitamin D

Table 3: Types of therapy against vitamin D, serum calcium, phosphorous and ALP

Variable	Types of Therapy		X ²	P value
	Biologic (%)	DMARD (%)		
Vitamin D ng/ml			8.531	0.003
Normal	6(20.0)	17(56.7)		
Low	24(80.0)	13(43.3)		
Serum Calcium mg/dl			1.714	0.190
Normal	15(50.0)	20(66.7)		
High	15(50.0)	10(33.3)		
Serum Phosphorous mg/dl			2.069	0.150
Normal	28(93.3)	30(100.0)		
Low	2(6.7)	0(0.0)		
ALP IU/L			1.456	0.228
Normal	28(93.3)	25(83.3)		
High	2(6.7)	5(16.7)		

*p value ≤ 0.05 is significant

Table 4 shows the association of types of therapy with T-L2L4, T-L1L4, T- neck, T- torch, T- total hip. A significant relation between types of therapy with T total.

Table 4: Types of therapy against T-L2L4, T-L1L4, T-Neck, T- Torch, T-Total hip.

Variable	Types of Therapy		X ²	P value
	Biologic (%)	DMARD (%)		
TL2L4			0.902	0.637
Normal	13 (43.3)	11 (36.7)		
Osteopenia	12 (40.0)	11 (36.7)		
Osteoporosis	5 (16.7)	8 (26.8)		
TL1L4			3.355	0.187
Normal	16 (53.4)	10 (33.3)		
Osteopenia	10 (33.3)	11 (36.7)		
Osteoporosis	4 (13.3)	9 (30.0)		
T neck			3.333	0.189
Normal	18 (60.0)	11 (36.7)		
Osteopenia	9 (30.0)	15 (50.0)		
Osteoporosis	3 (10.0)	4 (13.3)		

Variable	Types of Therapy		X ²	P value
	Biologic (%)	DMARD (%)		
T troch				
Normal	13 (43.3)	14 (46.7)	3.760	0.153
Osteopenia	13 (43.3)	7 (23.3)		
Osteoporosis	4 (13.4)	9 (30.0)		
T total				
Normal	17 (56.7)	9 (30.0)	7.946	0.019*
Osteopenia	12 (40.0)	13 (43.3)		
Osteoporosis	1 (3.3)	8 (26.7)		

*p value \leq 0.05 is significant

Table 5 shows the association of types of therapy with Z-L2L4, Z-L1L4, Z- neck, Z- torch, Z- total hip. There was significant association between types of therapy with Z- total.

Table 5. Types of therapy against Z-L2L4, Z-L1L4, Z- Neck, Z- Torch, Z- Total

Variable	Types of Therapy		X ²	P value
	Biologic (%)	DMARD (%)		
ZL2L4				
Normal	14 (46.7)	10(33.3)	2.889	0.236
Osteopenia	10 (33.3)	8 (26.7)		
Osteoporosis	6 (20.0)	12 (40.0)		
ZL1L4				
Normal	15 (50.0)	7 (23.3)	4.719	0.094
Osteopenia	10 (33.3)	14 (46.7)		
Osteoporosis	5 (16.7)	9 (30.0)		
Z neck				
Normal	15 (50.0)	11 (36.7)	1.098	0.578
Osteopenia	10 (33.3)	13 (43.3)		
Osteoporosis	5 (16.7)	6 (20.0)		
Z troch				
Normal	11 (36.7)	11 (36.7)	1.689	0.430
Osteopenia	11 (36.7)	7 (23.3)		
Osteoporosis	8 (26.6)	12 (40.0)		
Z total				
Normal	11 (36.7)	9 (30.0)	6.819	0.033*
Osteopenia	17 (56.7)	11 (36.7)		
Osteoporosis	2 (6.6)	10 (33.3)		

Discussion

This study showed that patients with rheumatoid arthritis on biological agents (anti TNF alpha) had arrest bone loss while in non biological (DMARD) showed decrease in bone mineral density. In this study the mean age of RA patients was (40.70+9.09)years. and female: male ratio was 3:1 similar to O.Dell's T.R,etal that show RA is more common in women (female:male ratio was 3:1) and RA occurs at any age but typically late child bearing years .^[18] The bone mineral density was significantly associated with types of therapy, which

showed non significant decrease in bone loss in RA patients on biological agents (anti TNF alpha). this finding is in agreement with that of Wijbrandts CA et al who found TNF blockade may result in an arrest of general bone loss in patients used infliximab in combination with methotrexate, lumbar spine and femoral BMD remained unchanged.^[19] Also Large UJ et al showed significant BMD increase in femoral neck and on ameliorating trend in the spine in patients with rheumatoid arthritis on infliximab.^[20] Hougeberg G, et al found strong evidence of causal link between inflammation and bone loss in

RA patients, anti-inflammatory effects of infliximab was potent enough to arrest inflammatory bone loss at hip but not at the spine and hand.^[21] The current study found significant association between RA patients on DMARDs (MTX) and decrease in BMD, this finding agrees with Cranney AB et al who found that BMD of femoral neck did not differ significantly between MTX treated group and RA patients without treatment.^[22]

Morgan SL et al found in their study that BMD significantly higher in RA patient who did not receive MTX versus those who received MTX.^[23] The current study showed that body mass index showed non statistically significant difference with types of therapy used and 46% of patients with biological and non biological DMARD were obese this finding is consistent with the recent finding of Senturk T et al that anti TNF alpha treatment may have indirect positive effect on lean mass, throughout the general health improvement of patients leading to increase appetite.^[24] and Briot K et al who found that Anti TNF agents in inflammatory rheumatic diseases are associated with increase in BMI which result from decrease bone resorption and increase in body weight and lean mass which is observed in parallel with increase in IGF-1.^[25] and also found high BMI in MTX treated group attributed to reduction of disease activity.^[26] The current study found significant association between anti TNF alpha and decrease vitamin D level, this result disagrees with Vacca A et al who found that in inflammatory rheumatic disease anti TNF alpha agents seem to improve vitamin D level as well as disease activity but it remains controversial.^[27]

Low vitamin D in patient with anti TNF alpha in the current study may be due to decrease sun exposure (majority of the female patients are veiled) and may be part of disease activity and long duration RA which leads to deformity and immobility. Other explanation was most of patients used NSAIDs that influenced liver metabolism of vitamin D.^[28] and recent study show absence of overall decrease in bone mineral density associated with low vitamin D level.^[29] This study results revealed statistically non-significant decrease in vitamin D level in RA patients on non biological (DMARD), which agrees with Raczkiewicz A et al who found adequate DMARD therapy (without steroid) seem to have beneficial effect on vitamin D level.^[30] In this study there is non-significant changes in calcium, phosphorous, and alkaline phosphatase level in RA patients on biological and non biological agent, which is similar to Lange U et al findings.^[20]

Conclusion

There was significant decrease in bone mineral density in RA patients on MTX while infliximab had a role in arrest in bone loss.

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Mirjan Medical City, Iraq and all experiments were carried out in accordance with approved guidelines.

References

- Harris Jr. ED, Firestein GS. Clinical Features of Rheumatoid Arthritis. In: Harris ED, Ruddy S, Budd RC, editors. Kelley's textbook of rheumatology. 1. 8th ed. Philadelphia: WB Saunders Company; 2008; 321–33.
- Lehmann KA, Maijer KI, Gerlag DM, et al. The Clinical Picture of Rheumatoid Arthritis According to the 2010 American College of Rheumatology/ European League Against Rheumatism Criteria: Is This Still the Same Disease?. *Arthritis & Rheumatism* 2012; 64:389-93.
- Al-Rawi ZS, Alazzawi AJ, Alajili FM et al. Rheumatoid arthritis in population samples in Iraq. *Ann Rheum Dis* 1978; 37(1): 73–75.
- Myo M, Philip A, Ling L, et al. Does Anti-TNF Therapy Cause a Less Significant Fall in Bone Mineral Density in Patients With Rheumatoid Arthritis? *The Internet Journal of Rheumatology*. 2011; 6 (2): 1528-8412.
- Arnett FC, Edworthy SM, Bloch DA, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. *Arthritis Rheum* 1988; 31:315.
- Giles J T and Bathon J M. Management of Rheumatoid arthritis: Hochbery MC, Silman AJ, Smolen JS, et al. *Rheumatology*, 5th edition. USA; 2010; 955-63
- Xu S, Wang Y, Lu J, et al. Osteoprotegerin and RANKL in the pathogenesis of rheumatoid arthritis-induced osteoporosis. *Rheumatol Int*. 2011; 32(11):3397-403.
- Zhang J, Redden D, McGwin JG, et al. Generalized Bone Loss as a Predictor of 3-Year Radiographic Damage in African American Patients with

- Recent-Onset Rheumatoid Arthritis. *Arthritis Rheum.* 2010;62(8): 2219–26.
9. Heidari B, Monadi M, Mirsaed M. Bone mineral density changes during treatment of rheumatoid arthritis with disease-modifying-anti-rheumatic drugs. *Caspian J Intern Med.* 2012; 3(1): 354-58.
 10. Dolan L, Moniz C, AbrahaH,etal. Does active treatment of rheumatoid arthritis limits disease-associated bone loss? *Rheumatology (oxford).* 2002;41:1047-51.
 11. Schett G, RedlichK,HayerS,etal. Osteoprotegerin protects from generalized bone loss in TNF-transgenic mice. *ArthritisRheum.* 2003;48:2042–51.
 12. Redlich K, Hayer S, Zwerina J, etal. Repair of Local Bone Erosions and Reversal of Systemic Bone Loss Upon Therapy with Anti-Tumor Necrosis Factor in Combination with Osteoprotegerin or Parathyroid Hormone in Tumor Necrosis Factor-Mediated Arthritis *American Journal of Pathology.* 2004; 164(2): 543–55.
 13. Böttcher J and Pfeil P. Diagnosis of periarticular osteoporosis in rheumatoid arthritis using digital X-ray radiogrammetry *Arthritis. Research & Therapy.* 2008; 10:103.
 14. Hoff M, Haugeberg G, Odegård S, etal. Cortical hand bone loss after 1 year in early rheumatoid arthritis predicts radiographic hand joint damage at 5-year and 10-year follow-up. *Ann Rheum Dis.* 2009; 68:324-29.
 15. Sarkis K, Salvador M, Pinheiro M, etal. Association between osteoporosis and rheumatoid arthritis in women: a cross-sectional study. *Sao Paulo Med J.* 2009;127(4):216-22.
 16. Hameed k, Akil M. Osteoporosis in: McCloskey E, Peel N, Eastell R. *ABC of Rheumatology* 4th ed. UK: A John Wiley & sons, Ltd. 2010;65-70
 17. O’Dell JR, Imboden JB and Miller LD. *Rheumatoid arthritis in: Imboden JB, Hellmann DB, Stone J H. Current Diagnosis & treatment.* 3rd ed. New York Chicago San Francisco Lisbon London Madrid Mexico City Milan New Delhi San Juan Seoul Singapore Sydney Toronto;2013:139-55
 18. Wijnbrandts CA, kalassen R, Dijkgraaf MGW, etal. Bone mineral density in rheumatoid arthritis patients 1 year after adalimumab therapy: arrest of bone loss. *Ann Rheum Dis* 2009;68:373-376.
 19. Lange U, Teichmann J, Muller-Ladner U,etal. Increase in bone mineral density of patients with rheumatoid arthritis treated with anti TNF alpha antibody: a prospective open –label pilot study. *Rheumatology* 2005;44:1546-1548.
 20. Haugeberg G, ConaghanPG,QuinnM,etal. Bone loss in patients with active early rheumatoid arthritis: infliximab and methotrexate compared with methotrexate treatment alone. *Ann Rheum Dis* 2009;68:1898-1901.
 21. Cranney AB, Mckendry RJ, Wells GA, etal. The effect of low dose methotrexate on bone density. *The Journal of Rheumatology* 2001; vol. 28 no. 11: 2395-2399.
 22. Morgan SL, Chen DT, Carlee J,etal. Effect of methotrexate therapy on bone mineral density and body composition in rat adjuvant arthritis. *The Journal of Rheumatology* 2004; vol. 31 no. 9: 1693-1697.
 23. Senturk T, CildagS,Akdam I. Effect of anti-tumor necrosis factor- α therapies on weight and body mass index in patients with rheumatoid arthritis and ankylosing spondylitis. *Ann Rheum Dis* 2013;72:A875-A876.
 24. BriotK,GameroP,LeHenanffA,etal. Body weight, body composition, and bone turnover changes in patients with spondyloarthritis receiving anti-tumour necrosis factor α treatment. *Ann Rheum Dis* 2005;64:1137-1140.
 25. JurgensMS,Jacobs JW, GeenenMM,etal. Increase of body mass index in a tight controlled methotrexate-based strategy with prednisone in early rheumatoid arthritis. *Ann Rheum Dis* 2013;71:660.
 26. VaccaA, Porru G, DessoleG,etal. Vitamin D Insufficiency and Deficiency in Two European Cohorts of Patients with Inflammatory Rheumatic Disorders. *Ann Rheum Dis* 2014;73:197.
 27. Soesbergen RM, Lips P, EndeA,etal. Bone metabolism in rheumatoid arthritis compared with postmenopausal osteoporosis. *Ann Rheum Dis* 1986;45:149-155.
 28. Vagadia V, Bartholomeul P, Kelly M, etal. Osteoporosis and metabolic bone disease. *Rheumatology* (2011) 50 (suppl 3): 69-74.
 29. Raczkiewicz A, Bachtta M, Kulig M, etal. Vitamin d status and its relation with disease activity, disability, treatment schedule, mood and quality of life in polish rheumatoid arthritis patients. *Ann Rheum Dis* 2013;72: 849-1136.

Effects of Infliximab on Rheumatoid Factor & Anti-cyclic Citrullinated Peptide Antibodies in Patients with Rheumatoid Arthritis

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Abstract

Background: Anti-cyclic citrullinated peptide antibodies (ACPA) and rheumatoid factor (RF) are two important investigations that help in confirming the diagnosis and may help deciding strategies for the treatment. This study's aim is to investigate the effect of infliximab, a tumor necrosis factor inhibitor on ACPA and RF in patients with rheumatoid arthritis.

Patients and Method: Thirty five Iraqi patients with established RA, enrolled in this study during September 2013-May 2014. They received 3 mg/kg infliximab intravenously at weeks 0, 2, 6, and every 8 weeks thereafter in combination with methotrexate (15-20) mg. At baseline, week 24, CRP and ESR were determined and the disease activity score (DAS28) was calculated. Serum samples collected at the same time points were used to measure ACPA, and IgM-RF (ELISA).

Results: RF mean at the first visit was (106.1±25.2) IU/ml and at the second visit it reduced to (60.1±14.6) IU/ml and the difference was statistically significant, (P=0.038). ACPA mean was (466.5±61.4) U/ml at the first visit reduced significantly to reach (241.9±36.6) U/ml at the second visit (P<0.001). A dramatic and significant change had been found in the disease activity; (P<0.001) mean DAS 28 was (5.7±1.1) at the first visit with a range of (2.7– 8.6), at the second visit the mean was (4.5±1) and the range was (2.04–6.4).

Conclusions: Anti-TNF a treatment in RA cause decrease in serum titers of RF and ACPA in patients with clinical improvement.

Keywords: *Anti-TNF a treatment, RF, ACPA.*

Introduction

Today, a much more aggressive treatment approach is advocated for people with rheumatoid arthritis (RA), with prescription of non-biologic DMARDs within three months of diagnosis to reduce disease activity and prevent joint deformity^[1]. The 2012 revision updated the 2008 ACR recommendations, the 2012 update addressed

use of DMARDs and biologic agents, switching between therapies, the use of biologic agents in high-risk patients, TB screening with the use of biologic agents, and vaccination in patients with RA receiving DMARDs or biologic agents^[2].

Infliximab: is a chimeric monoclonal antibody, specifically binds to both soluble and membrane-bound TNF α with high affinity forming stable non disassociating immune complexes. Infliximab was approved by the U.S. Food and Drug Administration for the treatment of (RA). Treatment regime consists of intravenous infusions at 0, 2 and 6 weeks. Subsequent infusions are given 6 or 8 weeks thereafter, depending on clinical response. Infliximab dose is usually 3mg/kg iv (dose range 3-10mg/kg)^[3].

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RF: In established (RA), RF has sensitivity on the order of 70%. A positive RF assay, far from specific for RA, can be found in many other autoimmune diseases, and a small percentage of healthy people. IgA isotype has been linked to erosive disease and to rheumatoid vasculitis, but its precise clinical utility remains unclear. Higher titers of RF are associated with more severe disease, but as a longitudinal measure of disease activity RF fares poorly [4]. Anti-citrullinated protein antibodies (ACPA) are autoantibodies that are present in the majority of patients with RA. Clinically, cyclic citrullinated peptides (CCP) are frequently used to detect these antibodies with high sensitivity in patient serum or plasma. [5]. Effect of therapy on ACPA & RF status; TNF- α -inhibiting agents like infliximab can reduce disease activity and delay radiographic progression of RA [6]. Determination of ACPA, RF levels during treatment course may give clues regarding effectiveness of treatment and role of these antibodies in disease process. Several papers have reported effects on ACPA, in patients treated with [DMARDs mainly methotrexate MTX] with [7-11] or without [12, 13] infliximab. The DAS28 score is widely used to assess disease activity, the response to treatment and the need for biological therapy. The higher the value, the more active the disease. Interpretation: DAS28 provides the physician with a number on a scale from 0-10 indicating current RA disease activity.

- Remission: DAS28 \leq 2.6
- Low Disease activity: DAS28 (2.6 -3.2)
- Moderate Disease Activity: DAS28 (3.2-5.1)
- High Disease Activity: DAS28 $>$ 5 [14].

Patients and Method

The trial was conducted at rheumatic diseases center in Baghdad Teaching Hospital, Iraq. Thirty five Iraqi patients, with refractory RA who diagnosed according to the American College of Rheumatology Revised 1987ACR criteria +2010 ACR/EULAR, were enrolled in this study between September 2013-May 2014. All candidates: 1st had failed treatment with methotrexate and another DMARD course. 2nd No biological agents had been used previously in these patients. They received 3 mg/kg infliximab intravenously at weeks 0, 2, 6, and every 8 weeks thereafter in combination

with methotrexate (15-20) mg/wk. Serum samples were collected before infusion at baseline and at week 24, and stored At -20°C until further analysis. These variables were recorded at baseline and after 24 weeks of infliximab therapy: tender and swollen joint counts, patient assessments of general health on visual analogue scale, erythrocyte sedimentation rate (ESR), serum CRP level and DAS28 score. ESR normal value for men (15-20mm/hr) and for women (20-30mm/hr), CRP normal value less than 10mg/L. DAS28 parameter was used to evaluate clinical activity & response to treatment. Functional class using was assessed at baseline & after 24 wks of infliximab therapy. ACPA was measured by ELISA and titers greater than 25 IU/ml were considered positive.

Results

There were 35 patients enrolled in this study, with a mean age of (48.9 \pm 11.7) years (range: 27–77) age. Interval distribution of the studied group revealed that 8 patients (22.9%) aged 39 years or less, 11 patients (31.4%) aged 40-49 years, 11 patients (31.4%) aged 50–59 years and 5 patients (14.3%) aged more than 60 years and above. Females were the dominant; they were 27 represented (77.1%) of the studied group compared to only 8 males (22.9%). The female to male ratio was (3.4:1). The disease duration of the patients ranged (2 – 20) years with a mean of (7.2 \pm 4.5) years, 9 patients (25.7%) had a disease duration of less than 5 years, 18 patients (51.4%) had their disease for 5–9 years and 8 patients (22.9%) had the disease for 10 years or more as in (Table 1).

All patients received infliximab in a dose of (3 mg/kg infliximab intravenously at weeks 0, 2, 6, and every 8 weeks), Methotrexate (MTX) was received by 20 patients (57.1%), 15 patients received combination of 2 or more treatment; 11 patients (31.4%) received MTX + Prednisolone (PND), 4 patients (10.5%) received other Disease Modifying Drug (HCQ 400 mg, azathioprine and sulfasalazine) in addition to MTX and PND. Non-steroidal anti-inflammatory drugs (NSAIDs) received by all patients; Diclofenac (100 mg) received by 20 patients (57.1%) and Ibuprofen by 15 (42.9%). On the other hand, none of the patients received biological treatment prior to the study and use of PND was stopped in 4 patients (10.5%) as in (Table 2).

Table 1: Demographic characteristics of the studied group (N=35).

Characteristics	No. of patients	%
Age (years)		
≤ 40	8	22.9
41 – 50	11	31.4
51 – 60	11	31.4
> 60	5	14.3
Mean±SD*	48.9±11.7	-
Range	27 – 77	-
Sex		
Male	8	22.9
Female	27	77.1
Disease duration (years)		
< 5	9	25.7
5 – 9	18	51.4
≥ 10	8	22.9
Mean±SD	7.2±4.5	-
Range	2 – 20	-

*SD: standard deviation

Table 2. Distribution of types of treatment received by the patients (N=35)

Treatment type	No. of patients	%
MTX*	20	57.1
MTX + PND	11	31.4
MTX + PND + other DMARD**	4	10.5
NSAIDs		
Diclofenac 100 mg	20	57.1
Ibuprofen 800 mg	15	42.9

* MTX median dose was 15 mg, median dose of PND was 5 mg/day** Other DMARDs include (HCQ 400 mg, azathioprine, and sulfasalazine).

Out of the 35 patients enrolled in this study, 7 patients were missed at the second visit, so they were excluded from the following comparison. As it shown in table 3, the mean RF at the first visit was (106.1±25.2) and at the second visit it was reduced to (60.1±14.6) and the difference was statistically significant, (P=0.038). Regarding the ACPA, the mean was (466.5±61.4) at the first visit reduced significantly to reach (241.9±36.6) at the second visit (P<0.001). A dramatic and significant change had been found in the disease activity; the mean DAS28 was (5.7±1.1) at the first visit with a range of (2.7-8.6), at the second visit the mean was (4.5±1) and the range was (2.04-6.4). Furthermore, according to DAS28 values, at the first visit only one patient (3.6%) had low disease activity, 5 patients (17.9%) had moderate, and 22 (78.6%) had high disease activity. At the second visit these figures were significantly changed; 3 patients (10.7%) had remission, only one patient (3.6%) had low disease activity without remission, 16 patients (57.1%) had moderate disease activity and only 8 patients (28.6%) still had high disease activity these findings indicated a trend of change in disease activity from high toward the moderate and low disease activity, table 3, 4. Regarding the other parameters, it had been significantly found that the mean number of tender joints of the patients reduced from 14.1±1.4 at the first visit to 9.3±1.2, (P=0.005), similarly, the mean number of swollen joints reduced from 7.9±0.8 Dropped to 5.5±0.7 at the second visit (P=0.021). The mean values of Visual Analogue Scale (VAS) by doctor and by Patient were slightly reduced and the mean difference between the mean values at the first and second visits was only 0.5 and 0.4 respectively which did not reach the statistical significance, (P>0.05). Also, at the second visit, a statistically significant reductions in mean values of ESR (P<0.001), CRP (P<0.001), table 3.

Table 3. Comparison of mean clinical and laboratory values of in 28 patients completed the study at first and second visit. (7 patients were missed at the 2nd visit)

Finding	First visit	Second visit	Difference Mean±SE*	P.value
	Mean±SE*	Mean±SE*		
RF	106.1±25.2	60.1±14.6	46.0±21.1	0.038 sig
ACPA	466.5±61.4	241.9±36.6	224.6±47.4	< 0.001 sig
DAS28	5.7±1.1	4.6±1.0	1.1±0.27	< 0.001 sig
No. of tender joints	14.1±1.4	9.3±1.2	4.8±1.6	0.005 sig
No. of swelling joints	7.9±0.8	5.5±0.7	2.4±0.9	0.021 sig
VAS by doctor	5.8±0.3	5.3±0.4	0.5±0.4	0.27 NS
VAS by patient	5.7±0.3	5.3±0.3	0.40±0.2	0.33 NS
ESR	67.2±4.7	42.1±4.4	25.1±5.6	< 0.001 sig
CRP	31.7±3.4	14.6±2.5	17.1±3.8	< 0.001 sig

Sig: Significant, NS: Not Significant and SE: Standard Error of mean

Table 4. Changes in disease activity according to DAS28 categories of the 28 patients completed the second visit.

DAS28 category	Disease activity			
	1 st visit		2 nd visit	
	No.	%	No.	%
Remission	0	0.0	3	10.7
Low	1	3.6	1	3.6
Moderate	5	17.9	16	57.1
High	22	78.6	8	28.6
Total	28	100.0	28	100.0

Chi square = 15.3, P. value = 0.0016 (sig)

The distribution of the functional classes reported at the first visit showed that 3 patients (10.7%) had class I, 13 (46.4%) had class II, 7 (25%) had class III and 5 patients (17.9%) had class IV, at the second visit there was an increase in the number of patients who had the first three classes and a decrease in the number of patients with class IV; 5 patients (17.9%) had class I, 14 patients (50%) had class II, 8 patients (28.6%) had class III and only one patients remain with class IV, this indicated an improvement in the patients function, however, these differences in the functional classes didn't reach the statistically significance despite the clinical significant, (P>0.05), Table 5.

Table 5. Comparison of functional class at first and second visit (N=28)

Functional class	No. of patients	%	No. of patients	%
I	3	10.7	5	17.9
II	13	46.4	14	50.0
III	7	25.0	8	28.6
IV	5	17.9	1	3.6
Total	28	100.0	28	100.0

Chi square = 3.27, P. value =0.38 NS

Discussion

Although none of the patients who were positive for RF and ACPA at baseline became negative during follow up, a significant RF and ACPA decrease in patients treated with infliximab after 24 wks. A significant decrease in ACPA levels found at week 24 of treatment (p<0,001) & significant decrease in RF level (P=0.038) at week 24 of treatment.

Regarding clinical measures of disease activity there was significant change in DAS28 (P<0.001), but

the functional assessment failed to reach the significant value (p>0.05). Other laboratory parameters showed significant reduction in the ESR (P<0.001) and CRP (P<0.001). *Alessandri et al.* showed that a small but significant decrease in ACPA levels at week 24 of treatment in the patients with clinical improvement. This effect, also observed for RF, was dependent on infliximab, since reductions in ACPA levels were not observed after treatment with MTX alone[9]. Nevertheless, DMARD-only therapy can result in a significant (>25%) reduction in both ACPA and RF in about 50% of patients [11]. *Rönnelid et al.* showed that treatment with sulphasalazine, but not other DMARDs, resulted in a drop in ACPA levels, but this decrease occurred only in the first year of follow-up and did not correlate with clinical indicators [13]. *Nissinen et al.* showed that ACPA (measured by CCP1 assay) did not change during 6 weeks of follow-up, though 60% of the patients had a significant clinical response. IgM-RF levels were somewhat decreased in the first weeks of therapy [8]. *Bobbio-Pallavicini et al.* studied autoantibody profiles during long-term (78weeks), combination treatment with infliximab and MTX. Though treatment resulted in a significant decrease in disease activity scores, no changes in the percentages of patients who were positive for ACPA or IgM-RF were observed. Titers of RF, on the other hand, were significantly reduced, unlike those of ACPA [7]. *Caramaschi et al.* showed that RF levels decrease but ACPA remain stable in RA patients treated with infliximab for 22, wks[11]. *De Rycke et al.* showed that RF levels but not ACPA is modulated by infliximab treatment in rheumatoid arthritis, with follow-up period of 30 weeks [10]. An explanation of the discrepancies could be that the end-point may be different in the different series (from 14 weeks to 12 months or 18 months), At these later time points, clinical parameters may not reflect primary response to treatment but also secondary loss of response, which can be influenced by development of antibodies to infliximab [15]. And the ELISA test differed from one study to another. Our results showed significant reduction in both auto antibodies after 24weeks of infliximab treatment in association of clinical improvement, these results were supported by the previous result of *Alessandri et al* [9].

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols

were approved under the Al Karama Teaching Hospital, Iraq and all experiments were carried out in accordance with approved guidelines.

References

1. Singh JA, Furst DE, Bharat A et al. 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. *Arthritis Care Res (Hoboken)* 2012;64:625–39
2. Knight DM, Trinh H, Le J, Siegel S, et al : Construction and initial characterization of a mouse-human chimeric anti-TNF antibody. *Mol Immunol* 1993, 30:1443-53.
3. Witherington RH, Teitsson I, Valdimarsson H, et al. Prospective study of early rheumatoid arthritis. II Association of rheumatoid factor isotypes with fluctuations in disease activity. *Ann Rheum Dis* 1984;43:679–85
4. Young BJ, Mallya RK, Leslie RD, et al”Anti-keratin antibodies in rheumatoid arthritis”. *Br Med J* 1979;2(6182):97-9
5. Lipsky PE, van der Heijde DM, St Clair EW et al. Infliximab and methotrexate in the treatment of rheumatoid arthritis. Anti-tumor necrosis factor trial in rheumatoid arthritis with concomitant therapy study group. *N Engl J Med* 2000;343:1594–602.
6. Bobbio-Pallavicini F, Alpini C, Caporali R et al. Autoantibody profile in rheumatoid arthritis during long-term infliximab treatment. *Arthritis Res Ther* 2004;6:R264–72 .
7. Nissinen R, Leirisalo-Repo M, Peltomaa R et al. Cytokine and chemokine receptor profile of peripheral blood mononuclear cells during treatment with infliximab in patients with active rheumatoid arthritis. *Ann Rheum Dis* 2004;63:681–7.
8. Alessandri C, Bombardieri M, Papa N et al. Decrease of anti-cyclic citrullinated peptide antibodies and rheumatoid factor following anti-TNFalpha therapy (infliximab) in rheumatoid arthritis is associated with clinical improvement. *Ann Rheum Dis* 2004;63:1218–21.
9. deRycke L, Verhelst X, Kruithof E et al. Rheumatoid factor, but not anti-citrullinated protein antibodies, is modulated by infliximab treatment in rheumatoid arthritis. *Ann Rheum Dis* 2004;64:299–302.
10. Caramaschi P, Biasi D, Tonolli E et al. Antibodies against cyclic citrullinated peptides in patients affected by rheumatoid arthritis before and after infliximab treatment. *Rheumatol Int* 2005;26(1):58-62.
11. Mikuls TR, O’Dell JR, Stoner JA et al. Association of rheumatoid arthritis treatment response and disease duration with declines in serum levels of IgM rheumatoid factor and anti-cyclic citrullinated peptide antibody. *Arthritis Rheum* 2004;50:3776–82.
12. Rönnelid J, Wick MC, Lampa J et al. Longitudinal analysis of anti-citrullinated protein/peptide antibodies (anti-CP) during 5 year follow-up in early rheumatoid arthritis: anti-CP status is a stable phenotype that predicts worse disease activity and greater radiological progression. *Ann Rheum Dis* 2005;64:1744-49
13. A. M. Van Gestel, C. J. Haagsma, and P. L. C. M. Van Riel, “Validation of rheumatoid arthritis improvement criteria that include simplified joint counts,” *Arthritis and Rheumatism*, 1998; 10:1845-50.
14. Wolbink GJ, Vis M, Lems W et al. Development of anti infliximab antibodies and relationship to clinical response in patients with rheumatoid arthritis. *Arthritis Rheum* 2006;54:711-5.

Study the Influence of Aqueous and Organic Extracts of *Conocarpus erectus* on the Growth of Some Pathogenic Bacteria

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Abstract

The aim of this study was to detect the effect of active compound in fruit, leave and stem of *Conocarpus* (which extracted by cold and hot water, and by methanol and ethanol alcohol) on the growth of *Staphylococcus aureus*, *Streptococcus agalactiae*, *E.coli*, *Klebsiellapneumonia*, *Enterobacter*, *Proteus mirabilis*, *Salmonellatyphi* and *Pseudomonas aeruginosa*. Also, this study aimed to determine the MIC value of methanol and hot aqueous extracts. The present study detected the methanol extract was the higher effect on bacterial growth and the inhibition zone diameter was 19mm, while the hot aqueous extract, ethanol extract and cold extract were 15, 12 and 7.8 mm respectively. The present study detected the least value of MIC for methanol and hot aqueous extracts were 6.25 mg/ml against *Staphylococcus aureus* and *Streptococcus aglatial*.

Keywords: *Conocarpus*, antibacterial, MIC, extract, bacteria.

Introduction

Antimicrobial resistant is the resistance of a microorganism to an antimicrobial drug that originally effective for the treatment of infection caused by it¹. Resistant microbes are increasingly difficult to treat, requiring alternative medications or higher doses—which may be more costly or more toxic. Microbes resistant to multiple antimicrobials are called multidrug-resistant (MDR); or sometimes superbugs². A few infections are now completely untreatable due to resistance³. For this reason, we must begin to research on a new source for antibiotic or research on source produce new antibiotic, medical plants good source for production antimicrobial agent. natural products are considered a valuable source of drugs development against various diseases⁴. According to the World Health Organization (WHO) medicinal plants would be the best source to obtain a variety of drugs. About 80% of individuals from developed countries use traditional medicines which have compounds derived from the medicinal plants⁵. *Conocarpus erectus* one of medicinal plants is a low branching evergreen shrub or tree with a typical height of up to 40 feet. It contains phenols such as flavonoids and tannins as major constituents,

these phenolic compounds have antimicrobial activity against different types of bacteria, thus consider a good alternative in treated multidrug-resistant bacteria⁶.

Different parts of *Conocarpus erectus* as leaves, stem and fruits have antioxidant, anticancer and antimicrobial properties, In folk medicine, it was reported to astringent, styptic and tonic preventing anemia, catarrh, conjunctivitis, diabetes, diarrhea, fever, gonorrhea, headache, hemorrhage, orchitis, prickly heat, swellings and syphilis⁷.

Material and Method

Samples Collection: The Leaves, stem and fruit of *Conocarpus* collected during November and December from the garden of the college of sciences, University of Kufa. Washing with tap water and once with sterile water and dried at room temperature and pulverized into powder with an electric blender.

Preparation of extracts:

- Hot aqueous extract:** The hot aqueous extract was prepared by mixing of 30 gm of plant powder with 300 ml of distilled water and putting in the water bath for 30 min. Then, the mixed filtered and dried

at laboratory temperature. The crude extract was collected and kept in a laboratory until uses⁸.

- Cool aqueous extract:** The cool aqueous extract was prepared by mixing of 30 gm of plant powder with 300 ml of distilled water for 48 h. with shaking. Then, the mixed filtered and dried at laboratory temperature. The crude extract was collected and kept in a laboratory until uses⁸.

Preparation of Methanol and ethanol Extracts:

The plant powder (30 g) of each part was steeped in 150 ml methanol for 7 days at room temperature with vibrating day by day followed by filtration. Each extraction concentration at 40 C to remove the organic solvent affording the known weight of each crude methanol and ethanol extract. The defatted crude extracts were ready for bioassay⁹.

Study the influence of aqueous and organic extracts of Conocarpus on the growth of bacteria: Used the method of agar diffusion by well¹⁰ in susceptibility test for the active components of plant by make four equal well in Muller Hinton with diameter 6mm by cork borer and added 0.1ml from each extraction, before this stapes spreading 0.1 ml from bacterial suspension on surface of media,after then incubation the plate over night in 37 C and then measured the diameter of inhibition zone to detect the effect of test plant on growth of bacteria .

Determining the MIC: Used the broth dilution method to determine the MIC value by used nine sterile tube and added 0.5ml of sterile broth for each tube,added

0.5ml from active compound for the first tube,mix the active compound and broth thoroughly and transfer 0.5ml from this tube into the second tube,repeatd this step to seventh tube and discard 0.5ml of broth from final tube . the eighth and ninth tube remain without antibiotic, inoculation the tubes from first to eighth tube with 0.1ml from bacterial suspension (which comparison with MacFarland tube 0.5) and the ninth tube content on broth only without bacteria after then incubation all tube at 37C for 24h, after then examine each tube if it was clear or turbid to determine the MIC¹¹.

Antibiotic sensitivity test: Tested the sensitivity of bacteria to some of the antibiotic by cultured each genus of bacteria on Muller Hinton agar by spreading 0.1ml from bacterial suspension(which comparison with MacFrland tube 0.5) on agar surface and put the antibiotic disc in each plate after then incubator all plate at 37 C for 24 h. and measured the inhibition zone¹².

Result and Discussion

This study showed the methanol extract was higher effect on bacterial growth and the inhibition zone diameter was 19mm and this agree with¹³,while the hot aqueous extract,ethanol extract and cold extract were 14.5,12 and 7.8 mm respectively (fig. 1), the antibacterial activity of Conocarpus attributed to phenols such as flavonoids and tannins as major constituents,this phenolic compounds have antimicrobial activity against different types of bacteria⁶.

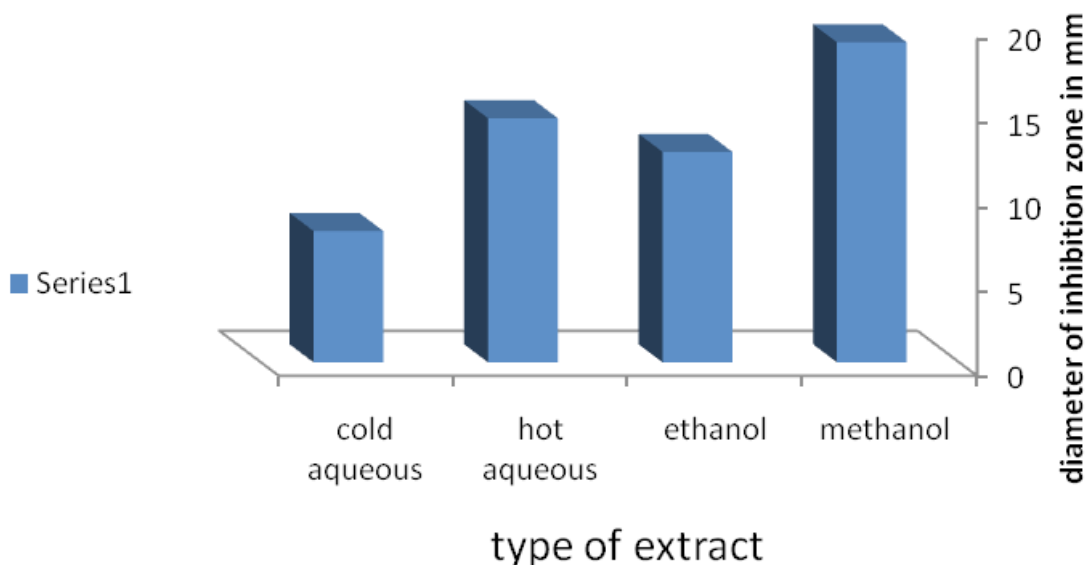


Fig. 1: Effect the active compound of methanol extract on bacterial growth

This study showed the methanol extract of leaves gave higher effect against *Streptococcus* and the inhibition zone diameter was 27mm and the least effect against *Enterobacter* and *Salmonella* the inhibition zone diameter was 17 mm the antibacterial activity of methanol extract for leave attributed to high containing from phenolic compounds¹⁴,for the methanol extract of fruit gave higher effect against *Streptococcus* and the inhibition zone diameter was 25mm and the least effect against *Enterobacter* and *Proteus* the inhibition zone diameter was 12 mm,while the methanol extract of stem gave higher effect against *Streptococcus* and the inhibition zone diameter was 23 mm and the least effect against *Salmonella* and the inhibition zone diameter was 8 mm (table 1).

Table 1: Effect the active compound of methanol extract on bacterial growth

Bacteria \ Extract	Leave	Fruit	Stem
Staph. aureus	24 mm	21mm	16mm
Streptococcus	27mm	25mm	23mm
E.coli	20mm	14mm	12mm
Klebsiella	20mm	18mm	16mm
Proteus	22mm	12mm	14mm
Enterobacter	17mm	12mm	11mm
Salmonella	17mm	16mm	8mm
Pseudomonas	19mm	15mm	11mm

This study showed the ethanol extract of leaves gave higher effect against *Streptococcus* and the inhibition zone diameter was 24 mm and the least effect against *Salmonella* and *Enterobacter* the inhibition zone diameter was 8 mm and this result was near to ¹⁵,for the ethanol extract of fruit gave higher effect against *Streptococcus* and the inhibition zone diameter was 23 mm and the least effect against *Pseudomonas* which was resistance to it,while the ethanol extract of stem gave higher effect against *Streptococcus* and the inhibition zone diameter was 22 mm and the least effect against *Enterobacter*, *Salmonella* and *Pseudomonas* which were resistance to it (table 2).

Table 2: Effect the active compound of ethanol extract on bacterial growth

Bacteria \ Extract	Leave	Fruit	Stem
Staph. aureus	17mm	15mm	13mm
Streptococcus	24mm	23mm	22mm

Bacteria \ Extract	Leave	Fruit	Stem
E.coli	13mm	10mm	9mm
Klebsiella	13mm	13mm	9mm
Proteus	12mm	11mm	8
Enterobacter	8mm	8mm	0
Salmonella	8mm	8mm	0
Pseudomonas	9mm	0	0

This study showed the hot aqueous extract of leaves gave higher effect against *Staph. aureus* and the inhibition zone diameter was 22 mm and the least effect against *Salmonella* and the inhibition zone diameter was to 10 mm,for the hot aqueous extract of fruit gave higher effect against *Staph.aureus* and the inhibition zone diameter was 20 mm and the least effect against *Klebsiella*, *Proteus* and *Enterobacter* the inhibition zone diameter was 9 mm, while the hot aqueous extract of stem gave higher effect against *Staph. aureus* and the inhibition zone diameter was 18 mm and the least effect against *Salmonella* which was resistance to it (table 3).

Table 3: effect the active compound of hot aqueous extract on bacterial growth

Bacteria \ Extract	Leave	Fruit	Stem
Staph. aureus	22mm	20mm	18mm
Streptococcus	20mm	18mm	15mm
E.coli	13mm	10mm	8mm
Klebsiella	13mm	9mm	8mm
Proteus	14mm	9mm	11mm
Enterobacter	11mm	9mm	9mm
Salmonella	10mm	11mm	0
Pseudomonas	14mm	13mm	8mm

This study showed the cold aqueous extract of leaves gave higher effect against *Staphylococcus* and the inhibition zone diameter was 24 mm and the least effect against *E.coli* which was resistance for it, for the cold aqueous extract of fruit gave higher effect against *Klebsiella*, *Enterobacter* and *Pseudomonas* the inhibition zone diameter was 9mm and the least effect against *E.coli*, *Proteus* and *Salmonella* which were resistance for it,while the hot aqueous extract of stem doesn't have any effect against all bacteria (table 4).

Table 4: Effect the active compound of cold aqueous extract on bacterial growth

Bacteria \ Extract	Leave	Fruit	Stem
Staph. aureus	24mm	8mm	0
Streptococcus	20mm	8mm	0
E.coli	0	0	0
Klebsiella	10mm	9mm	0
Proteus	16mm	0	0
Enterobacter	13mm	9mm	0
Salmonella	13mm	0	0
Pseudomonas	16mm	9mm	0



Fig. 2: Effect the aqueous and organic extract on Streptococcusagalatial 1: cold aqueous extract 2: ethanol extract 3: hot aqueous extract 4: methanol extract

This study showed some isolated bacteria were multi-resistance for most antibiotic (table 5).

Table (5): Antibiotic susceptibility test

Bacteria \ Antibiotic	E. coli	Staph. aureus	Streptococcus	Klebsiella	Enterobacter	Pseudomonas	Salmonella	Proteus
NA	S	R	R	R	S	S	R	R
KF	R	R	R	R	R	R	R	R
TMP	R	R	S	S	S	R	S	R
AM	S	S	R	R	S	R	R	R
CL	S	R	R	R	S	R	R	R
AK	S	S	R	S	S	S	S	R
IPM	S	R	S	S	S	S	S	S
NOR	R	S	S	R	S	S	S	S
CN	S	S	R	S	S	S	R	R
CRO	R	R	R	R	R	R	R	R
CAZ	R	R	R	R	R	R	R	R
PRL	R	R	R	R	S	S	R	S
TE	S	R	R	R	S	R	S	R
APX	R	S	S	R	R	R	R	R
AX	R	R	R	R	R	R	R	R
F	S	R	S	R	R	R	R	R
P	S	R	R	R	R	R	R	R
AZM		S	S					
E		S	S					
VA		R	S					

This study showed the largest MIC value for methanol extract of leaves was 25 mg/ml for *E.coli* and *Salmonella*, and least MIC value was 6.25 mg/ml for *Staph.aureus* and *Streptococcus*. Also, this study showed

the largest MIC value for methanol extract of fruit was 50 mg/ml for *Salmonella* and *Pseudomonas*, and least MIC value was 6.25 mg/ml for *Staph.aureus* and *Streptococcus*. Also, this study showed the largest MIC

value for methanol extract of the stem was 50 mg/ml for *Salmonella*, *Proteus*, and *Pseudomonas*, and least MIC value was 12.5mg/ml for *Staph.aureus*,*Streptococcus* and *Klebsiella* (table6) .

Table 6: MIC values for methanol extraction

Extract Bacteria	Leave (mg/ml)	Fruit (mg/ml)	Stem (mg/ml)
Staph. aureus	6.25	6.25	12.5
Streptococcus	6.25	6.25	12.5
E.coli	25	25	25
Klebsiella	12.5	12.5	12.5
Proteus	12.5	25	50
Enterobacter	12.5	12.5	25
Salmonella	25	50	50
Pseudomonas	12.5	50	50

This study showed the largest MIC value for hot aqueous extract of fruit was 100 mg/ml for *Enterobacter*, and least MIC value was 12.5 mg/ml for *Staph.aureus*. Also, this study showed the largest MIC value for hot aqueous extract of leaves was 25 mg/ml for *Salmonella*, *Pseudomonas*, *Proteus*, *Enterobacter*, *E. coli* and *Klebsiella*, and least MIC value was 6.25 mg/ml for *Staph.aureus* and *Streptococcus* . Also, this study showed the largest MIC value for hot aqueous extract of the stem was 100 mg/ml for *Salmonella*, *Proteus*, and *Pseudomonas*, and least MIC value was 12.5mg/ml for *Staph.aureus* and *Streptococcus* (table 7).

Table 7: MIC values for hot aqueous extract

Extract Bacteria	Leave (mg/ml)	Fruit (mg/ml)	Stem (mg/ml)
Staph. aureus	6.25	12.5	12.5
Streptococcus	6.25	25	12.5
E.coli	25	25	25
Klebsiella	25	50	25
Proteus	25	50	100
Enterobacter	25	100	50
Salmonella	25	50	100
Pseudomonas	25	25	100

Conclusion

The active compounds which extracted by methanol were the higher effect on bacterial growth. the least value of MIC for methanol and hot aqueous extracts were 6.25 mg/ml and were against *Staphylococcus aureus* and *Streptococcus agalactiae*

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Department of Biology, Faculty of science, Kufa University, Iraq and all experiments were carried out in accordance with approved guidelines.

References

- Bonjar, S.G.H., and Nik, K.M. Antibacterial activity of some medicinal plants of Iran against *Pseudomonas aeruginosa* and *P. fluorescence*. *Asian Journal of Plant Sciences*, 2004; 3(1): 61-64.
- Jan Hudzicki, A.S.M. Kirby-Bauer Disk Diffusion Susceptibility Test Protocol Archived 2011-06-26 at the Wayback Machine, 2011.
- Goossens, H.; Ferech, M.; Vander Stichele, R. and Elseviers M. "Outpatient antibiotic use in Europe and association with resistance: a cross-national database study". *Lancet*, 2005; 365 (9459): 579–87.
- Chaudhary, G., Goyal, S. and Poonia, P. *Lawsonia inermis* L: A phytopharmacological review. *IJPSDR*, 2010; 2: 91-98.
- Nagarajan, M., Rajasekaran, S. and Ganesh, S. K. Antibacterial activity of *Lawsonia inermis* L. *Int. J. Modern Biol. Med.*, 2013; 4: 169-175.
- Maryam Bashir, Muhammad Uzair and Bashir Ahmad Chaudhry. A review of phytochemical and biological studies on *Conocarpus erectus* (Combretaceae). *Pakistan Journal Pharmaceutical Research*, 2015; 1(1): 1-8.
- Abdel -Hameed ES, Abdel SAB and Sabra NA. Protective Effect of *Conocarpus erectus* Extracts on CCl 4-Induced Chronic Liver Injury in Mice. *Global J Pharm.*, 2013; 7: 52-60.
- Mohammed, H.Y. The effect of leaves extract of (*Conocarpus erectus* L.) plant on *Ulocladium botrytis* and *Alternaria solani* fungi that isolated from *Ulocladium botrytis*, *Journal of College of Education for Pure Science*, 2012; 2(1): 120-129.
- El-Sayed, S. Abdel-Hameed; Salih, A. Bazaid; Mohamed, M. Shohayeb; Mortada, M. El-Sayed and Eman, A. El-Wakil. Phytochemical Studies and Evaluation of Antioxidant, Anticancer and Antimicrobial Properties of *Conocarpus erectus* L.

- Growing in Taif, Saudi Arabia. *European Journal of Medicinal Plants*,2012; 2(2): 93-112.
10. Egorove, N. S. *Antibiotics Scientific Approach*. Mirpublishers .Moscow,1985.
 11. Josiphine, A.M.; Helen, K.M. and Paul,A.G. *Laboratory manual and workbook in Microbiology*, 2006;8th, p :98.
 12. Sharma K.D., Karki S., Thakur N.S., Attri S. Chemical composition, functional properties and processing of carrot. *Journal of Food Science and Technology*, 2012; 49: 22-32, doi: 10.1007/s13197-011-0310-7.
 13. Yasir, M. H. The effect of leaves extract of (*Conocarpus erectus* L.) plant on *Ulocladium botrytis* and *Alternariasolani* fungi that isolated from. *Journal of College of Education for Pure Science of thiqr*,2012; 2(1): 120-129.
 14. Ahmed, K., Rehman, H. A., Aziz, A. A., Meraj, S., andAhmed,N. Environment friendly (green) method for the synthesis of zinc nanoparticles by using *Conocarpus erectus* leaves extract. *International Journal of Biology and Biotechnology*,2016; 13 (3): 341- 345.
 15. Dayane Kelly Dias do Nascimento Santos, Wesley Henrique de Oliveira Melo, Anastássia Mariáh Nunes de Oliveira Lima and et.al.*Conocarpus erectus* L., a plant with a high content of structural sugars, ions and phenolic compounds, shows antioxidant and antimicrobial properties promoted by different organic fractions. *Asian Pacific Journal of Tropical Biomedicine*,2018;8:463-470.

Antibacterial and Antibiofilm Activity of Aqueous Extract and Essential Oil of *Origanum majorana* and their Activity on Some Physiological Parameters of Blood in the Male of White Rats

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Abstract

The aim of this study was to detect the influence (aqueous extract and essential oil) of *Origanum majorana* on the growth of *Staphylococcus aureus*, *Enterococcus*, *E.coli*, *Klebsiella pneumonia*, *Proteus mirabilis*, *Salmonellatyphi*, *Enterobacter*, *Acinetobacterbaumannii* and *Pseudomonas aeruginosa*. Also, this study aimed to detection the influence of essential oil of *Origanummajorana* (which gave a higher influence on bacterial growth) on biofilm information. Also this study aimed to detection the influence of essential oil of *Origanummajorana* on some physiological parameters of blood in a male of white rats.

This study showed the essential oil *Origanummajorana* was a higher effect than aqueous extract. This study showed the ability of bacteria to formation of biofilm and biofilm inhibitors by essential oil of *Origanummajorana* . The results of the antibiotic sensitivity test showed some of the *bacteria* isolates were highly resistant to the antibiotic; therefore, it is considered multidrug-resistance (MDR). The results of the effect essential oil of *Origanummajorana* in vivo showed variation in values in some physiological parameters of blood in the male of rats

Keywords: *Origanummajorana*, essential oil, antibacterial, antibiofilm, bacteria, physiological parameters of blood.

Introduction

Discover the antibiotic in the last century contributed in treated many infection diseases which causes by many microorganism, used this antibiotic continue for a long time in treated diseases but in the last years some of the bacteria became resistance to many antibiotic and this antibiotic became unable to treated diseases, resistance bacteria to antibiotic begin increasing day after day and the bacteria which sensitive to antibiotic today may become resistance tomorrow so that we most begin to search for alternatives or new source to antibiotic .medical plant consider good source for antibiotic, Sweet marjoram (*Origanummajorana*) one of this plants has been used for centuries both as a culinary and medicinal herb. It has been evidenced in a number of studies that essential oil from sweet marjoram contains mainly terpinene-4-ol, α - and γ -terpinenes, linalool and carvacrol, which are the basis for their antimicrobial properties ^{1,2}. For centuries, marjoram oil has been used

for curing various diseases ³. Marjoram oil is also used in perfumes, soaps, and detergents for its spicy herbaceous notes ⁴. Marjoram is considered among the main crops for increasing Egypt income from foreign currency ⁵. The fresh or dried marjoram leaves and their essential oil are widely used in the food industry as a food ingredient, a herbal tea, flavoring, coloring, nutritional and natural preservatives ⁶.

Marjoram Essential oil from sweet marjoram reduced the growth rate of *Photobacterium phosphoreum* which is the specific organism responsible for spoilage of modified atmosphere packaged fillets of cod ⁷. Whereas other isolates were used rarely in microbiological studies, it has been shown that aqueous and methanolic extracts from sweet marjoram contain multiple compounds with considerable antimicrobial action, e.g. phenolic derivatives (phenolic acids, flavonoids as apigenin, luteolin, quercetin and their glycosides as rutin or isovitexin) ^{8,9}. The antiviral, bactericidal, antiseptic

and antifungal effects of marjoram also attributed to ursolic acid and essential oil and in particular to thymol and carvacrol^{10,11}. Ursolic acid isolated from *O. majorana* appears to be a potent acetylcholinesterase inhibitor in Alzheimer's disease¹².

Material and Method

The plant used in experiment: In this study we used leaves and essential oil of *Origanum majorana*

Which obtain from market the leaves pulverized into powder with an electric blender.

Animals used in the experiment: In this study we used 12 rats (male) their weight between 150-200 g.

Preparation Hot aqueous extract: The hot aqueous extract was prepared by mixing of 30 gm. of plant powder with 300 ml of distilled water and putting in the water bath for 30 min. Then, the mixture filtered and dried at laboratory temperature. The crude extract was collected and kept in a laboratory until uses¹³.

Study the effect of the active compound of *Origanum majorana* on the growth of bacteria in vitro: Used the method of agar diffusion by well¹⁴ in susceptibility test for the extraction and essential oil by make two equal wells in Muller Hinton with diameter 6mm by cork borer and added 0.1 ml from each extraction and essential oil, before this step spreading 0.1 ml from bacterial suspension on surface of media, after then incubation the plate overnight at 37°C and then measured the diameter of inhibition zone to detect the activity of test plant on growth of bacteria.

Antibiotic sensitivity test: Tested the sensitivity of bacteria to some of the antibiotics by cultured each genus of bacteria on Muller Hinton agar by spreading 0.1 ml from bacterial suspension (which comparison with MacFarland tube 0.5) on agar surface and put the antibiotic disc in each plate after then incubator all plate at 37°C for 24 h. and measured the inhibition zone.

Biofilm formation: Tissue culture plate method (TCP) assay (biofilm assay) described by¹⁵ was most widely used and was considered as a standard test for detection of biofilm formation as follows:

1. Isolates from fresh culture were inoculated in TSB containing 1% glucose and incubated for 72 hours at 37°C and then diluted 1:100 with fresh TSB¹⁶.
2. Added 150µl aliquots of the diluted cultures for

each bacterial isolated into individual wells and only broth served as a control to check non-specific binding of media. Each isolate was inoculated in triplicate.

3. The plate was incubated for 24 hours at 37°C. After incubation content of each well was gently removed by tapping the plate. Wells were washed 4 times with phosphate buffer saline (PBS pH 7.2) to remove free-floating 'planktonic' bacteria.
4. Biofilms formed by bacteria in plate was fixed by putting the plate in the oven at 37°C for 30 min.
5. All wells stained with crystal violet (0.1% w/v). Excess stain was removed by thorough washing with deionized water and plates were kept for drying.
6. Added (150 µl) of sodium acetate (20:80, v/v) to dissolve bound crystal violet. The optical density (O.D.) at 630nm was recorded.

Effect of antibacterial agents on Biofilm formation: The same procedure described in (tissue culture plate method for detection biofilm formation) was done with essential oil, 15µl from essential oil added to each bacterial isolated in wells of tissue culture plate. The plate was incubated for 24 hours at 37°C, after fixing with sodium acetate for an hour and all steps done as the same steps that described previously¹⁷.

Study the effect of essential *Origanum majorana* on the growth of bacteria in vivo

In this experiment used 12 rats divided into 4 groups include:

1. Three rats treated with normal saline for a week.
2. Three rats treated with 0.1 bacterial suspension.
3. Three rats treated with 0.1 ml bacteria and after 24h. treated with essential oil of *O. majorana* 0.16 ml/kg which consider safety dose¹⁸ for a week.
4. Three rats treated with essential oil of *O. majorana* 0.16 ml/kg which consider safety dose¹⁸ for a week.

Result and Discussion

Effect the *O. majorana* on bacterial growth: This study showed the essential oil was higher effect than aqueous extract and gave antibacterial activity against all isolated bacteria and this result agree with¹⁹ Thymol and carvacrol, which have been known as major compounds

of these essential oils ^{20,21}, are able to increase the microbial cytoplasm membrane permeability, probably because their capability of dissolving into the phospholipid bilayer aligning between the fatty acid chains and causing a distortion of the membrane physical structure ^{22,23}, while the aqueous extract was least effect and must bacteria were resistance to it. (table 1).

Table 1: Effect the O.majorana on bacterial growth

Bacteria \ Extract	Essential oil (mm)	Aqueous extract (mm)
Staph.aureus	20	13
Staph.aureus	20	15
Staph.aureus	15	10
Staph.aureus	20	13
Enterococcus	25	0
E.coli	24	0
E.coli	25	0
Klebseilla	20	0
Klebseilla	22	0
Klebseilla	22	0
Klebseilla	20	0
Salmonella	20	0
Salmonella	17	0
Salmonella	18	0
Enterobacter	22	0

Bacteria \ Extract	Essential oil (mm)	Aqueous extract (mm)
Pseudomonas	22	10
Acinetobacter	20	12
Proteus	20	0

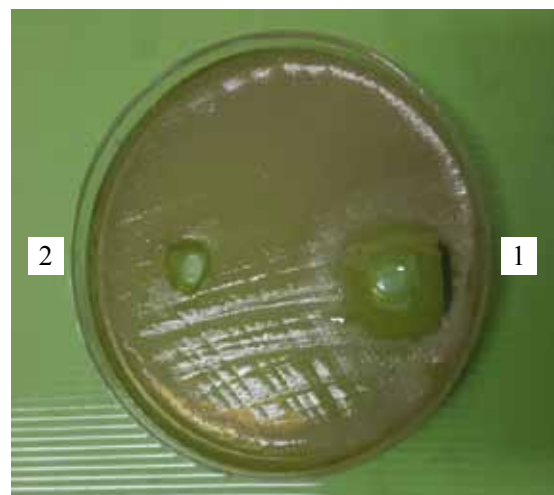


Fig. 1: Effect the O.majorana on Proteus
1: oil, 2: aqueous extract

Antibiotic susceptibility test on gram- positive bacteria

Some isolated bacteria showed multi-resistance for most antibiotic (table 2).

Table (2): Antibiotic susceptibility test

Antibiotic \ Bacteria	Staph.aureus	Staph.aureus	Staph.aureus	Staph.aureus	Enterococcus
NA	R	R	R	R	R
KF	R	S	R	S	R
TMP	R	S	R	S	R
AM	R	S	R	S	R
CL	S	S	R	S	R
AK	S	S	S	S	R
IPM	S	S	R	S	S
AZM	R	S	S	S	S
E	R	S	S	S	S
VA	R	S	R	S	R
NOR	S	S	S	S	S
CN	S	S	S	S	R
CRO	R	R	R	R	R
CAZ	R	R	R	R	R
PRL	R	R	R	R	R
TE	R	S	R	S	R

Antibiotic \ Bacteria	Bacteria				
	Staph.aureus	Staph.aureus	Staph.aureus	Staph.aureus	Enterococcus
APX	S	S	S	S	S
AX	R	S	R	S	R
F	S	S	R	S	S
P	R	S	R	S	R

Antibiotic susceptibility test on gram- negative bacteria

Some isolated bacteria showed multi-resistance for most antibiotic (table3)

Table (3): antibiotic susceptibility test

Antibiotic \ Bacteria	Bacteria													
	E .c	E .c	Kl	Kl	Kl	Kl	Sa	Sa	Sa	En	Ps	Ac	Pr	
NA	S	S	R	R	R	R	S	R	R	S	S	R	R	
KF	R	R	R	R	R	R	R	R	R	R	R	R	R	
TMP	R	R	R	S	S	S	S	S	S	S	R	R	R	
AM	S	S	R	R	R	R	R	R	R	S	R	R	R	
CL	S	S	R	R	R	R	S	R	R	S	R	R	R	
AK	S	S	R	S	S	S	S	R	S	S	S	R	R	
IPM	S	S	S	S	S	S	S	S	S	S	S	S	S	
NOR	R	S	R	R	R	R	S	R	S	S	S	R	S	
CN	S	S	R	S	S	S	S	S	R	S	S	R	R	
CRO	R	S	R	R	R	R	R	S	R	R	R	R	R	
CAZ	R	S	R	R	R	R	R	R	R	R	R	R	R	
PRL	R	S	R	R	R	R	S	R	R	S	R	R	R	
TE	S	S	R	S	R	R	S	R	S	S	R	R	R	
APX	R	R	S	R	R	R	R	R	R	R	R	R	R	
AX	R	R	S	R	R	S	R	R	R	R	R	R	R	
F	S	S	S	R	R	R	R	R	R	R	R	R	R	
P	S	S	S	R	R	R	R	R	R	R	R	R	R	

Biofilm formation and Antibiofilm formation:

The examined isolates gave a positive result and were strong biofilm former according (table4),the essential oil of *O.majorana* showed effects as antibiofilm on bacteria (table 5).

Table (4): Classification of bacterial biofilm formation by tissue culture plate method (TCP)

Mean of OD value at 630nm	Biofilm formation
<0.120	Non
0.120-0.240	Moderate
>0.240	High

Table (5): Biofilm formation and antibiofilm effect of essential oil of *Origanummajorana*

Bacteria	Biofilm Information	Antibiofilm
Staph.aureus	0.295	0.178
Staph.aureus	0.260	0.151
Staph.aureus	0.292	0.158
Staph.aureus	0.392	0.158
Enterococcus	0.563	0.238
E.coli	0.139	0.117
E.coli	0.298	0.126
Klebsiella	0.441	0.165
Klebsiella	0.346	0.175
Klebsiella	0.297	0.145
Klebsiella	0.210	0.131
Salmonella	0.396	0.131

Bacteria	Biofilm Information	Antibiofilm
Salmonella	0.267	0.128
Salmonella	0.326	0.139
Enterobacter	0.144	0.114
Pseudomonas	0.448	0.190
Acinetobacter	0.669	0.236
Proteus	0.485	0.224

Effect the essential oil in vivo:

Physiological Assay: This study showed present variation in total count and differential count of WBCs in different treatment comparison with control group, the total count of WBCs for group which treated with

bacterial suspension reach to 17 ($10^3/\mu\text{L}$) while the control group was 6 ($10^3/\mu\text{L}$) this result attributed to present bacterial infection which led to increasing in WBCs count²⁴, also showed present little increasing in total count of WBCs in group treated with bacteria and oil, only oil which were 7.5 and 7.8 ($10^3/\mu\text{L}$) respectively (table 6), in differential count of WBCs the lymphocyte for group which treated with bacterial suspension reach to 10.3 ($10^3/\mu\text{L}$) while the control group was 3.5 ($10^3/\mu\text{L}$), also showed present little increasing in differential count in group treated with bacteria and oil and only oil comparison with group treated with bacteria which were 6 and 7 ($10^3/\mu\text{L}$) respectively (table 6).

Table 6: Effect the different treatment on total and differential count of WBCs

Parameter Treatment	Total count of WBCs ($10^3/\mu\text{L}$)	Lymphocyte ($10^3/\mu\text{L}$)	Monocyte ($10^3/\mu\text{L}$)
Control group	6	3.5	0.8
Treated with bacteria	17	10.3	0.8
Treated with bacteria +oil	7.5	6	0.6
Treated with oil	7.8	7	0.5

This study showed little variation in RBC count and other parameters associated with it (HGB, MCV, HCT, PLT) in different parameter comparison with the control group except group treated with bacteria showed

decreased in platelet count which were 700 ($10^3/\mu\text{L}$) comparison with the control group which was 1000 ($10^3/\mu\text{L}$) (table 7).

Table 7: Effect different treatment in RBC count and other parameters associated with it (HGB, MCV, HCT, PLT)

Parameter Treatment	RBC ($10^6/\mu\text{L}$)	HGB (g/dl)	HCT (%)	MCV (fL)	PLT ($10^3/\mu\text{L}$)
Control group	7	11	36.8	53	1000
Treated with bacteria	6.5	10.6	35	54	700
Treated with bacteria +oil	7.3	10.8	35	50	1100
Treated with oil	6.5	10	33	53	930

Conclusion

The essential oil of *O. majorana* higher effect on bacterial growth from the aqueous extract. *O. majorana* have antibacterial activity in vivo.

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Faculty of Science, University of Kufa, Iraq and all experiments were carried out in accordance with approved guidelines.

References

1. Vagi, E.; Simandi, B.; Suhajda, A. and Hethelyi E. Essential oil composition and antimicrobial activity of *Origanum majorana* L. Extracts obtained with ethyl alcohol and supercritical carbon dioxide. *Food Res. Int.* 2005; 38: 51–57.
2. Nurzyńska-Wierdak, R. and Dzida, K. Influence of plant density and term of harvest on yield and chemical composition of sweet marjoram (*Origanum majorana* L.). *Acta Sci. Pol. Hortorum Cultus*, 2009; 8 (1): 51–61.
3. Harbi, N.O. Effect of marjoram extract treatment on the cytological and biochemical changes induced by cyclophosphamide in mice. *Journal of Medicinal Plants Research*, 2011; 5(23): 5479-5485.
4. Hazzit, M.; A. Baaliouamer; M. Leonor-Faleiro; M.M. Graca. Composition of the essential oils of *Thymus* and *Origanum* species from Algeria and their antioxidant and antimicrobial activities. *J. Agric. Food Chem.*, 2006; 54(17): 6314-6321.
5. EL-Aeshmawiy, K.H.; H.M. Khidr; M.N. El-sebai and A.M. Saafan . Egyptian Exports of Some Medicinal and Aromatic Plants and Factors Affecting it in the Foreign Markets. *Australian Journal of Basic and Applied Sciences*, 2009; 3(4): 4665-4674.
6. Holley, R.A. and D. Patel. Improvement in shelf-life and safety of perishable foods by plant essential oils and smoke antimicrobials. *Food Microbiol.*, 2005; 22: 273-292.
7. Mejlholm O. and Dalgaard P. Antimicrobial effect of essential oils on the seafood spoilage micro-organism *Photobacterium phosphoreum* in liquid media and fish products. *Let. Appl. Microbiol.*, 2002; 34: 27–31.
8. Janicsak G.; Mathe I.; Miklossy-Vari V. and Blunden G. (1999). Comparative studies of the rosmarinic and caffeic acid contents of *Lamiaceae* species. *Biochem. System Ecol.*, 1999; 27: 733–738.
9. Fecka I. and Turek S. (2008). Determination of polyphenolic compounds in commercial herbal drugs and spices from *Lamiaceae*: thyme, wild thyme and sweet marjoram by chromatographic techniques. *Food Chem.*, 2008; 108: 1039–1053.
10. Roth, L.S. *Mosby's Handbook of herbs and natural supplements*. In: Roth LS (ed). Mosby. A Harcourt Health Sciences Co., St. Louis, MO, 2001; 561–3.
11. Kelly, W.J. *Herbal Medicine Handbook*. Lippincott Williams & Wilkins/A Wolters Kluwer Co., Philadelphia, PA, 2004; 289–90.
12. Chung YK, Heo HJ, Kim EK et al. Inhibitory effect of ursolic acid purified from *Origanum majorana* L. on the acetylcholinesterase. *Mol Cells*, 2001; 11: 137–43.
13. Mohammed, H.Y. (2012). The effect of leaves extract of (*Conocarpus erectus* L.) plant on *Ulocladium botrytis* and *Alternaria solani* fungi that isolated from *Ulocladium botrytis*, *Journal of College of Education for Pure Science*, 2012; 2(1): 120-129.
14. Egorove, N. S. *Antibiotics Scientific Approach*. Mirpublishers . Moscow, 1985.
15. Christensen, G P.; Simpson, W.A.; Younger, J.J.; Baddour, L.M.; Barrett, Melton, D.M. and Beachey, E.H. Adherence of Coagulase – Negative Staphylococci to Plastic . Tissue Culture Plates A quantitative Model for the Adherence of Staphylococci to Medical Devices *J. Clin. Microbiol.*, 1985; 22: 996-1006.
16. Stepanovic, S.; Cirkovic, I.; Ranin, L.; Svabic-Vlahovic, M. Biofilm formation by *Salmonella* spp. And *Listeria monocytogenes* on plastic surface. *Letters in Applied Microbiology*, 2004; 38: 428–432.
17. Al-Saedi, I. A. Isolation and Identification of *Klebsiella pneumoniae* from Various Infections in Hilla Province and Detection of Some Virulence Factors Associated in Their Pathogenicity. M.Sc. Thesis College of Science, Babylon University. Iraq, 2011.
18. El-Ashmawy, I.M.; Amal, S.; Salama, O.M. Acute and long term safety evaluation of *Origanum majorana* essential oil. *Alex J Pharm Sci.*, 2007; 21: 29–35.
19. Jana Luíza, T. M. O.; Margareth, F. M. D.; Edeltrudes, O. L.; Evandro, L. S.; Vinícius, N.T.; Bernadete, H. C.S. Effectiveness of *Origanum vulgare* L. and *Origanum majorana* L. essential oils in inhibiting the growth of bacterial strains isolated from the patients with conjunctivitis. *Braz. Arch. Biol. Technol. J.*, 2009; 52 (1): 45-50.
20. Lambert, R.J.W.; Skandamis, P.N.; Coote, P. and Nychas, G.J.E. A study of the minimum inhibitory concentration and mode of action of oregano essential oil, thymol, and carvacrol. *Journal of Applied Microbiology*, 2001; 91: 453-462

21. Marino, M.; Bersani, C. and Comi, G. Impedance measurements to study the antimicrobial activity of essential oils from Lamiaceae and Compositae. *International Journal of Food Microbiology*,2001; 67: 187-195.
22. Ultee, A.; Slump, R.A.; Stechini, G. and Smid, J. Antimicrobial activity of carvacrol toward *Bacillus cereus* on rice. *Journal of Food Protection*,2000; 63: 620-624.
23. Ultee, A. and Smid, E.J. Influence of carvacrol on growth and toxin production by *Bacillus cereus*. *Journal of Food Microbiology*,2001; 64: 373-378.
24. Iranloye, B.O. Effect of chronic garlic feeding on some hematological parameters. *African Journal of Biomedical Research*.,2002; 5 (12): 81-82.

Psychological Stress among Woman's and it's Health Seeking Behavior towards Breast Examination at Early Detection Centers for Breast Cancer in Hilla Teaching Hospital

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Abstract

Background: Psychological stress as any stimulus, such as fear or pain, which interferes with the natural physiological balance of man, we all experience stress and stress in our daily lives for various reasons, whether due to family life or financial pressures or personal relationships. The study aims to identify the psychological stress among women's and its health seeking behaviors who attending to Early Detection Centers for Breast Cancer. As well as, investigate the relationship between women's their psychological stress and their health seeking behavior.

Methodology: A descriptive study is conducted by a non probability "convenience" sample of (100) woman's who vesting the early detection centers for breast cancer in Hilla City. The questionnaire which are included (40) items. These items are divided into (2) sections which include psychological stress domains which is composed of (23) items; and health seeking behaviors domains which is composed of (17) items. Data are collected through the use of an interview technique by the questionnaire as means for data collection. Data are analyzed through the application of descriptive statistical data analysis approach that includes, frequencies, percentages, mean of scores, standard deviation; and inferential statistical data analysis approach includes, Chi-squared test.

Results: The study results indicate that majority of (65%) of woman's were suffers partial psychological stress, and (54%) of them were never seek health behaviors towards breast examination for detection breast cancer. As well as, there was insignificant association between woman's their psychological stress towards early detection of breast cancer and their health seeking behaviors at p-value >0.05.

Conclusion: Overall woman's with partial psychological stress are never seeks of health and their psychological stress has been not affected their health seeking. Health directorate decision makers need to be employed based on a quality guidelines in order to improve the early detection center for breast cancer. Also, further studies could be undertaken to involve the national level of evaluation woman's knowledge regarding early detection of breast cancer and their health seeking behaviors.

Keywords: *Psychological Stress, Woman's, Health Seeking Behaviors.*

Introduction

Breast cancer is the leading cause of cancer death among women. It can be attributed only about 50% of breast cancer risk to a physiological or behavioral or genetic factor [1]. An increase in the incidence of breast cancer among grief compared with women who suffer from headaches. The relationship between "psycho" and

cancer is still mostly short stories until the end of the nineteenth century [2]. Many reports indicate that 156 of the 200 women with breast cancer have suffered a painful life accident, including psychological aspects and a troubled life, usually like the loss of a loved one [3]. Accumulated knowledge resulted in the twentieth century with regard to tension and its mechanism of

action as well as enthusiasm with regard to the effect of stress hormones in the development of cancer to many research studies. Strong hypotheses have emerged, but experimental cancers maintain stress. But the results of epidemiological studies have been conflicting, ranging from the lack of a relationship between stress and breast cancer [4]. Breast cancer is the most common type of cancer among females worldwide; in the United States alone, it was expected to account for 29% of female cancers [5]. Depression and anxiety are the most common that can be found in patients with breast cancer through their illness starting from diagnosis until the end of the disease disorders [6]. Anxiety ranges between 10% and 30%. Patients suffered from symptoms of anxiety as a result of expected negative results, and a sense of bewilderment about the future, worry about repetition, and the discomfort of the health seeking and consequences of treatment [7]. Regardless of the high frequency of major depressive disorders among cancer patients; often remains detectable; this may result from the fact that the feeling of depression involved in the same physiological effect of cancer [8]. Early detection plays a key role in reducing morbidity and mortality of breast cancer. The American Cancer Society and the Union of Michigan Cancer of the American Medical Association advises that women aged 40 years or older Eger X-ray examination annually. Despite the effectiveness of early detection in reducing breast cancer mortality, these preventive health practices, rates are still low among many minority women [9].

Methodology

Study design: A descriptive study is conducted in order to identify the psychological stress among women’s and its health seeking behaviors who attending to Early Detection Centers for Breast Cancer. As well as, investigate the relationship between women’s their psychological stress and their health seeking behavior.

Study Sample: A non-probability “convenience” of (100) woman’s who vesting the early detection centers for breast cancer in Hilla City.

Study Instrument: A questionnaire which includes which are included in the questionnaire, are (40) items. These items are divided into (2) sections which include psychological stress domains which is composed of (23) items; and health seeking behaviors domains which is composed of (17) items.

Data Collection the Method: Data are collected

through the use of an interview technique by the questionnaire as means for data collection. Data are analyzed through the application of descriptive statistical data analysis approach that includes, frequencies, percentages, mean of scores, standard deviation; and inferential statistical data analysis approach includes, Chi-squared test.

Results

Table (1): Woman’s their Demographic Characteristics

	Rating	No.	%
Age	19-29 years	47	47.0
	30-40 years	29	29.0
	41-51 years	18	18.0
	52+ years	6	6.0
Marital Status	Married	68	68.0
	Unmarried	26	26.0
	Divorced	4	4.0
	Widowed	2	2.0
Education	Unable to read and write	8	8.0
	Able to read and write	11	11.0
	Primary	20	20.0
	Intermediate	11	11.0
	Preparatory	15	15.0
	Diploma and above	35	35.0
Occupation	Housewife	62	62.0
	Employee	32	32.0
	Student	6	6.0
	Retired	0	0
Income	Enough	42	42.0
	Enough and increase	9	9.0
	Enough to certain limit	32	32.0
	Not enough	17	17.0
Residency	Urban	87	87.0
	Rural	13	13.0
No. Children	Not found	66	66.0
	1-2 Childs	25	25.0
	3-4 Childs	8	8.0
	5+ Childs	1	1.0

Out of (100) subject who participated in this study their age ranged from (19-29) years old and constituted (47%) of the study sample. Only (6%) of them their age was over the (52) years and above. It’s obvious among the findings that the highest percent of the study participants were married and constituted (68%) out total number. A thirty five of participants were diploma and above

graduated and works housewife, it constituted (35% and 62%) respectively. The highest proportion of the findings were making sufficiently income, it constituted (42%). Only small percent (9%) were sufficient and

increased income. Most of the study sample residents at urban areas and without children, it composed (87% and 66%) respectively out total number of (100) sample.

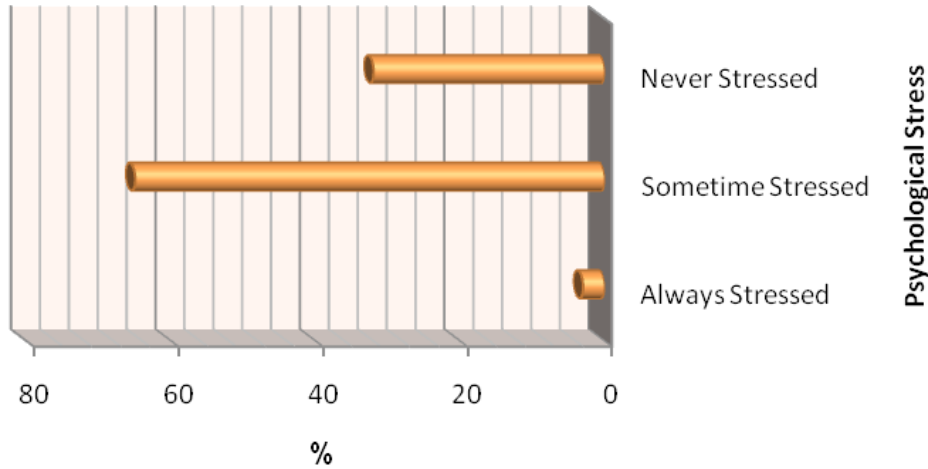


Figure (1): Overall Woman's Psychological Stress

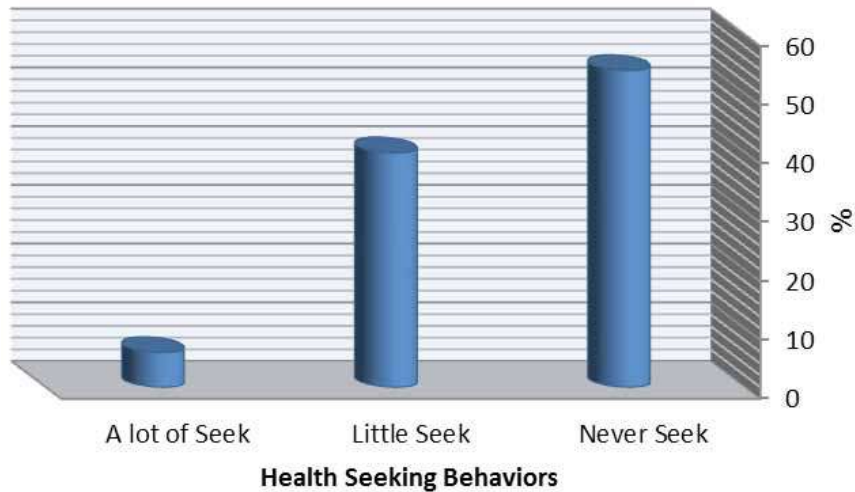


Figure (2): Overall Woman's Health Seeking Behaviors

Table (2): Statistical Relationship between the Woman's their Psychological Stress and their Health Seeking Behaviors

	Scale	Health Seeking Behaviors			Total	d. f	Sig.	
		Never	Little	A lot of				
Psychological Stress	Always	2	0	1	3	4	χ^2 obs.= 6.132 χ^2 crit.= 9.488 P-value=0.190	NS
	Sometime	33	29	3	65			
	Never	19	11	2	32			
	Total	54	40	6	100			

χ^2_{obs} = Chi-square observer, χ^2_{crit} Chi-square critical, Df= Degree of freedom, P-value= Probability value, NS= non significant.

This table depicts there was insignificant association between woman's their psychological stress towards early detection of breast cancer and their health seeking behaviors at p -value >0.05.

Discussions

People with cancer may find physical, emotional and social effects of the disease pressure. Those who are trying to control their stress risky behaviors such as smoking or drinking alcohol or who become more stable may suffer from the poor quality of life after cancer treatment. In contrast, it shows that people who are able to use effective strategies to deal with stress, such as relaxation techniques and stress management, they have low levels of depression, anxiety and symptoms associated with cancer and its treatment. However, there is no evidence that the successful management of psychological stress improves the survival of cancer, it must be health seeking in order to get rid of the psychological and physical negatives. Our findings their age ranged from (19-29) years old and constituted (47%) of the study sample. Only (6%) of them their age was over the (52) years and above. These results come because this age group is the most interested in itself. Results come with study has been measured the quality of breast cancer screening programs. Their results confirmed stress about breast cancer screening can occur especially in women who aged young to adults age groups [20]. It's obvious among the findings that the highest percent of the study participants were married and constituted (68%) out total number. This results come because most of the study participants in our society is considered the age of marriage. Expectations and experience in breast imaging study find that the most of those woman's were married^[21]. Also, when assessed the transferred women's their knowledge and practices about breast cancer affiliated to Ahvaz' University. The results showed that the majority of the patients were married^[22]. A thirty five of participants were diploma and above graduated and works housewife, it constituted (35% and 62%) respectively. While in a descriptive study has been assessed the depression and anxiety among women with breast cancer in Sohag University. Find that the most woman's works at homes and with low level of education [23]. The highest proportion of the findings were making sufficiently income, it constituted (42%). Only small percent (9%) were sufficient and increased income. As is common, women depend on their husbands for their monthly income. Most of the study sample residents at urban areas and without children, it composed (87% and 66%) respectively out total number of (100) sample. Because the population density is one of the residents of the urban and this is what confirmed our results. Our findings represented the majority of (65%) of woman's were suffers partial psychological stress when reviews

the early detection of breast cancer center in Hilla City. This results come as being the many reviews of the center has become so is normal with a partial stress. The our results come with a systematic review cross-sectional study was conducted in Iran, deals with psychological side in women with breast cancer. Their findings reveals that mild levels of depression for women with breast cancer were present to serious levels. There is an increase in the risk of depression in women with breast cancer. Therefore, it seems necessary to plan preventive and therapeutic measures in order to improve mental health and quality of life of patients ²⁴. Cancer is the first cause of death among American women and Asian American women have the lowest for Asian detection of cancer among all ethnic groups in the United States rates. The American Cancer Society reported that the incidence of breast cancer rate was 81.6/100,000 and the mortality rate of 12.5% among American women Asian. Breast cancer is the leading cancer among Chinese women, Korean and Vietnamese women and Cambodian. Epidemiological studies have indicated an increase in the risk of breast cancer among Asian women and their descendants after emigrating to the United States ²⁵. Our findings demonstrated the majority of (54%) of woman's were never seek health behaviors during towards breast examination for detection breast cancer in Hilla City. In our society the lack of follow-up health awareness through publications and mast media as well as, the attend health seminars that was shot by those non-existent women only after they are sick and be forced to correct the illness. In early detection for cues to expanded control and care for breast cancer among women from Western Kenya. Its confirmed that it's need to be creating breast cancer awareness alongside clear guidelines on accessing screening and treatment because of the lack of follow-up health awareness about the early detection of breast cancer.

Conclusions

Woman's with partial psychological stress are never seeks of health and their psychological stress has been not affected their health seeking. Health directorate decision makers need to be employed based on a quality guidelines in order to improve the early detection center for breast cancer. Also, further studies could be undertaken to involve the national level of evaluation woman's knowledge regarding early detection of breast cancer and their health seeking behaviors.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Collage of Nursing/Babylon University, Iraq and all experiments were carried out in accordance with approved guidelines.

References

1. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S., Cancer Incidence and Mortality Worldwide. Lyon, International Agency for Research on Cancer. IARC CancerBase. 2013; 11.
2. Antonova L, Aronson K, Mueller CR. Stress and breast cancer: from epidemiology to molecular biology. *Breast Cancer Res.* 2011;13:208.
3. Bleiker EM, van der Ploeg HM. Psychosocial factors in the etiology of breast cancer: review of a popular link. *Patient Educ Couns.* 2009;37(3):201-214.
4. Roberts FD, Newcomb PA, Trentham A, Storer BE. Self-reported stress and risk of breast cancer. *Cancer.* 2011;77:1089–1093.
5. Hassan MR, Shah SA, Ghazi HF, Mujar NMM, Samsuri MF. Anxiety and Depression among Breast Cancer Patients in an Urban Setting in Malaysia. *Asian Pac J Cancer Prev.* 2015; 16:4031-4035.
6. Härter M, Reuter K, Aschenbrenner A, Schretzmann B, Marschner N, Hasenburg A, et al. Psychiatric disorders and associated factors in cancer: results of an interview study with patients in inpatient, rehabilitation and outpatient treatment. *Eur J Cancer.* 2001; 37: 1385-1393.
7. Mohamed S, Kaur K, Sulaiman AH, Zainal NZ, Taib NA, MyBCC Study group. Perceived distress and its association with depression and anxiety in breast cancer patients. *PLoS One.* 2017; 12: e0172975.
8. Pasquini M, Biondi M, Costantini A, Cairolì F, Ferrarese G, Picardi A, Sternberg C. Detection and treatment of depressive and anxiety disorders among cancer patients: feasibility and preliminary findings from a liaison service in an oncology division. *Depress Anxiety.* 2006; 23: 441-448.
9. Su X, Ma GX, Seals B, Tan Y, Hausman A. Breast cancer early detection among Chinese women in the Philadelphia area. *J Womens Health (Larchmt)* 2006;15(5):507–519.
10. Fan T, Mao Y, Sun Q, Liu F, Lin J. Branched rolling circle amplification method for measuring serum circulating microRNA levels for early breast cancer detection. *Cancer science.*2018; 109(9): 2897.
11. EL-Saghir NS, Khalil MK, Eid T, El Kinge AR, Charafeddine M, Geara F. Trends in epidemiology and management of breast cancer in developing Arab countries: a literature and registry analysis. *Int J Surg.* 2007; 5: 225-233.
12. Massie MJ, Holland JC. *Overview of Normal Reactions and Prevalence of Psychiatric Disorders*. New York: Oxford University Press. Pp.273–282.
13. Yu MY, Hong OS, Seetoo AD. Uncovering factors contributing to under-utilization of breast cancer screening by Chinese and Korean women living in the United States. *Ethn Dis.* 2003;13(2):213–219.
14. Anderson O. Breast healthcare and cancer control in limited-resource countries: a framework for change. *Nat Clin Pract Oncol.*2006; 3: 4-5.
15. Morse EP, Maegga B, Joseph G, Miesfeldt S. Breast cancer knowledge, beliefs, and screening practices among women seeking care at district hospitals in Dar Es Salaam, Tanzania. *Breast Cancer.*2014; 8: 73.
16. Dündar P, Erbay O, Dilek O. The knowledge and attitudes of breast self-examination and mammography in a group of women in a rural area in western Turkey. *BMC Cancer.*2006; 6: 43.
17. Khaleghnezhad N, Khaleghnezhad A. The assessment of knowledge, attitude and behavior towards breast cancer screening method among female teachers in Tehran. *Iran J Surg.*2008; 16: 46-54.
18. Khani H, Moslemizadeh N, Montazeri A, Godazandeh Ga, Ghorbani A. Breast cancer prevention: knowledge, attitudes and practices among iranian health workers in southern coastwise of the caspian sea in 2006: a multi center study. *Iran Quart J Breast Dis.*2008; 2: 28-37
19. Abbaszadeh A, Taebi M, Simin K, Haghdoost A. The relationship of health beliefs of Kermanian women and participation in mammography. *J Qual Res Health Sci.*2011; 10: 9-17.
20. Rauscher GH, Murphy AM, Orsi JM. Beyond the mammography quality standards act: measuring the quality of breast cancer screening programs. *AJR* 2014;202: 145–151.
21. Susan H, Aimee M, Martha N. Listening to Women:

- Expectations and Experiences in Breast Imaging. *J Womens Health (Larchmt)*. 2015; 24(9): 777–783.
22. Afsaneh A, Abdolhassan D, Saeed Z. The Knowledge and Practice of Women Referred to the Health Centers Affiliated to Ahvaz' University of Medical Sciences on Breast Cancer and its Screening Method. *JMDH*. 2016; 4 (4): 757-763.
23. Hanan Yousif Aly1, Asmaa Abd ElGhany Abd ElLateef2 and Ahmed El Sayed Mohamed.: Depression and Anxiety among Females with Breast Cancer in Sohag University: Results of an Interview Study. *Remedy Open Access – Psychiatry*. 2017; 2(21): 1-7.
24. Azar J, Amir H, Masoumeh B. Depression in Women with Breast Cancer: A Systematic Review of Cross-Sectional Studies in Iran. *Asian Pac J Cancer Prev*, 2018; 19 (1): 1-7
25. Miller BA, Chu KC, Hankey BF, Ries LA. Cancer incidence and mortality patterns among specific Asian and Pacific Islander populations in the US. *Cancer Causes Control*. 2008;19(3):227–256.

The Effect of Bacterial Infections on the Immune States in Eczematic Patients

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Abstract

Background: Eczema is one of most important global diseases that affects both genders at all age groups, the relationship between bacteria and allergy in Eczematic patients is still as a great need of studies to show more of the microbial role in eczema.

Objective: This study has been investigating the main common bacterial secondary infections associated with Eczema lesion and estimation the serum levels of immunoglobulin types and cytokines in both patients and control groups.

Material and Method: Swabs samples were taken from infected eczema lesions in patients consulting in Dermatology Consultation Unit in Medical Marjan City in Al-Hilla Province. Microbiology investigation for swabs were done with antibiotic sensitivity test. Blood was collected for measuring the concentrations of serum IgG, IgA, IgM by single radial immunodiffusion assay, IgE, IL-1 β , IL-4, and IL-10 were measured using ELISA kits.

Results: The noted profile of bacteria associated with cases of pyogenic eczema were *Staphylococcus aureus* (81.08%), *Streptococcus pyogenes* (5.1%) and *Pseudomonas aeruginosa* (8.1%). Several skin areas were affected, such as Hands (35.13%), Thighs (18.9%) and Feet (18.9%). The relation between pyogenic Eczema lesions and Occupation, Season and Geography were studied. At the immunological level, we found a significant increased ($p \leq 0.05$) in the concentrations of IgM, IgG, IgA and IgE compared with control groups with a significantly increased ($p \leq 0.05$) in the concentrations of cytokines (IL-1 β , IL-4, and IL-10) that stimulated the Th2 antibody production.

Conclusion: We concluded that the bacterial infections played an important role in systemic humoral and cellular immunity in eczematic patients.

Keywords: Bacterial infections; immunoglobulin; cytokine & Eczematic patients.

Introduction

Eczema (atopic dermatitis) is a type of skin inflammation and common skin diseases that can cause a variety of symptoms, from an itchy red rash to patchy sores. ... However, are not all people with eczema will experience infections^(31,25) The infections of the skin and soft tissues of most Common infections, may lead to local and dangerous Systemic complications. These infections can be Potentially life-threatening has been progressing

rapidly; Therefore, early recognition and appropriate medical²². Eczema is a specific inflammatory reaction of the skin which includes a range of highly etiologically heterogeneous clinical conditions⁹

Surgical management task *Staphylococcus aureus* and *Streptococcus pyogenes* plays an important role in skin and soft tissue infections and contributes of most complex skin disorders such as atopic dermatitis and other skin lesions²⁴. (*S. aureus*) colonization/

infection is a very common and important factor in the pathophysiology of a topic dermatitis⁷.

Bacterial resistance against commonly used antibiotics has increased considerably in the last decades. The most common causes of secondary bacterial infections of the skin are staphylococci and. Secondary infections to skin lesions can be potentially life threatening and may progress rapidly^(20,23).

Systemic immune response had been altered when foreign bacterial antigen enter the body through skin with suppression it's immunological barrier, Related pathological changes Includes intracellular edema of the skin and skin Inflammatory infiltration of predominantly lymphocytes

Macrophages²⁶ Eczema is associated with an increased in the serum immunoglobulins (IgG, IgM, IgA and IgE) levels with induction of Th2 cytokine rather than Th1 cytokine through counter balanced between them⁵. Furthermore, the induction of different immunological levels were considered to be antigen-specific mechanisms^(1,10). pro-inflammatory cytokines an increased the migration of inflammatory immune cells into the skin with elevated the IgE levels through down-regulated expression of the anti-microbial peptides necessary for host defense mechanisms^(8,13). The activation of Th2 increased the eosinophilia activity with different types of cytokines (IL-4, IL-5, IL-6, IL-9,

and IL-13) that created a microenvironment suitable for Th2 cell differentiation⁴.

The current work aims at isolation and identification of bacteria causing secondary infection of Eczema, with measurement of serum levels of immunoglobulin types and cytokines at both patients and control groups.

Material and Method

1. Bacteriological Study: Swabs samples were taken from the superlative exudates of infected Eczema lesions in patients consulting in Dermatology Consultation Unit in Medical Marjan City in Al-Hilla Province. was taken by means of sterile disposable swab and inoculated into peptone water as transport medium for aerobic bacteria between the clinic and the bacteriological laboratory

Microbiology investigation for swabs were done according to Cowan and Steel (1985). Gram stain were done and biochemical test according to Collee et al., 1996; Forbes et al., 2010; Leboffe and Pierce, 2011), antibiotic sensitivity test were done as in Brown (2007).

2. Immunological Study: Blood was collected for measuring the concentrations of serum IgG, IgA, IgM by single radial immunodiffusion assay, IgE, IL-1β, IL-4, and IL-10 were measured using ELISA kits. (provided from Ray Bio, USA, Company).

Results and Discussion

Table (1): culture and physiological characters of bacteria isolates from the pyogenic eczema lesion

Characters	S. aureus	S. pyogenes	P. aeruginosa
Gram stain	+	+	-
Shape	Cocci in groups	Cocci in chain	Rods
Growth condition			
Aerobic	+	+	+
Motility	-	-	+
Hemolysis on blood agar	β	β	β
Pigment	Golden yellow endopigment	-	bluish green exopigment
Catalase	+	-	+
Oxidase	-	-	+
Nitrate reductase	-	ND	+
Amylase	ND	ND	-
H ₂ S	ND	ND	-
Lactase	+	ND	-
Mannitol	+	-	ND
Sucrose	+	ND	ND

Patients Profile: The patients were distributed according to the bacterial isolates infections that caused Eczema into 4 groups with one group considered to be control (G5) as in table (2). Bacterial infection was found in some patients, The bacterial infection rates in each type of eczema and dermatitis are summarized in table (2). Staphylococcus aureus is the bacterium that is most commonly responsible for secondary infection of eczema. 55.56%.S. aureus is the predominant bacteria on the uninvolved palms of patients with atopic dermatitis²⁸. in study done by²³ S. aureus was present in eight (35%) of lesions infections and was isolated from all areas. and S. aureus was mixed with group A haemolytic streptococci in one case. Group A haemolytic streptococci were isolated mainly from the extremities. Gram-negative aerobes (P. aeruginosa and E. coli) were isolated from areas on the leg and trunk.

In Singapore mentioned that S.aureus was the commonest organism causing secondary infection of skin lesions and represented 67%, 43.5% and 45% of all positive cultures respectively³⁰.

Staphylococcus aureus is the bacterium that is most commonly responsible for secondary infection

of eczema It is often associated with hair follicle infections (folliculitis), boils and abscesses.¹⁹. Marwa et al. (2007) record that the bacteria S.aureus was the most commonly isolated organism (92.9%), followed by Enterobacteriaceae (35.7%) and Pseudomonas (14.3%) in eczema lesions, S. aureus isolates were obtained from 14 (34%) patients with eczema lesions²³

The S. aureus colonization rate was higher in atopic dermatitis patients, which might be due to the skin barrier defects and imbalance of immune function¹⁶. The result of present study agree with Marwa et al. (2007) showed that Gram-negative bacilli were the second common pathogens causing secondary infection of skin lesions and were found in (21.7%) of all cases. And agree with²⁰ who found that enteric Gram-negative bacilli together with Strept. pyogenes were the second most common causes of secondary infection where each of them represented (23%) the distribution of infections showed in the table (3) the thigh and the hand was the most infected part from the body²⁰ recorded that the most infected part of the body were the finger, scalp, face and neck.

Table (2) Profile of patients according to the bacterial isolates

Groups	Bacterial Isolates	Numbers	(%)
G 1	S. aureus	50	55.56
G 2	S. pyogenes	20	22.22
G 3	P. aeruginosa	12	13.33
G4	S. aureus+ S. pyogenes	8	8.88
G5	Control	20	-

Table (3) Distribution of secondary bacterial infection according to the anatomical site of

Location	No	%
Thighs	13	35.13
Hands	13	35.13
Feet	7	18.7
Ears	3	8.1
Scalp	1	2.7
Total	37	

Testing for the antibiotic sensitivity of staphylococci, Streptococci and Pseudomonas are done

the three isolates were resistance for most of antibiotic use as showed in the figures (1, 2 and 3)

S. aureus isolates had good sensitivity to clindamycin, chloramphenicol, and Methicillin while they were resistant to penicillin, ampicillin, tetracycline and cefotaxime.

Streptococcus pyogenes isolates had good sensitivity to clindamycin, chloramphenicol, and Methicillin while they were resistant to penicillin, ampicillin, tetracycline and cefotaxime. While Pseudomonas aeruginosa isolates were for chloramphenicol and Methicillin

High resistance of S. aureus to ampicillin and penicillin may be indicate with the high incidence of β -lactamase production by staphylococci in the current study, Fusidic acid resistance may be due to the extensive use of topical fusidic acid by patients suffering from secondary skin infections. in the UK the S.aureus isolated from dermatology were high resistance to fusidic acid 50%²⁷.

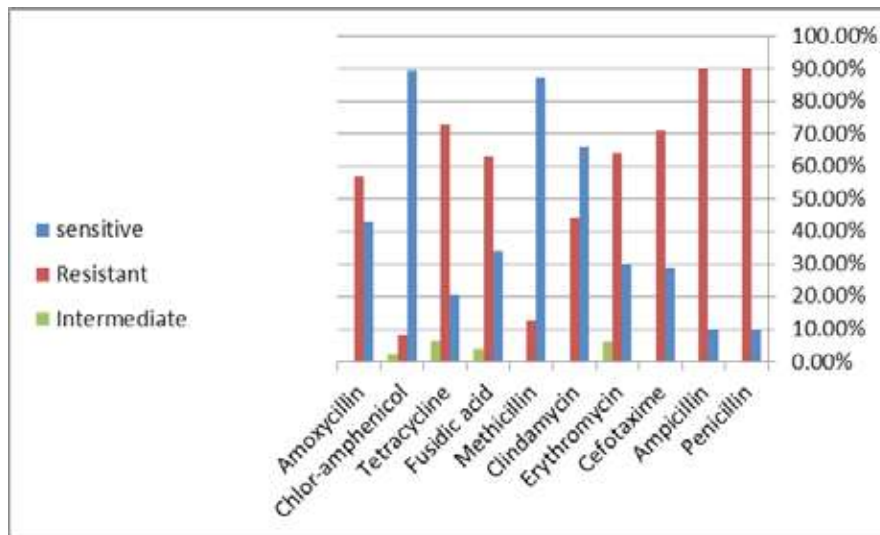


Fig (1) antibiotic sensitivity test of S.aureus

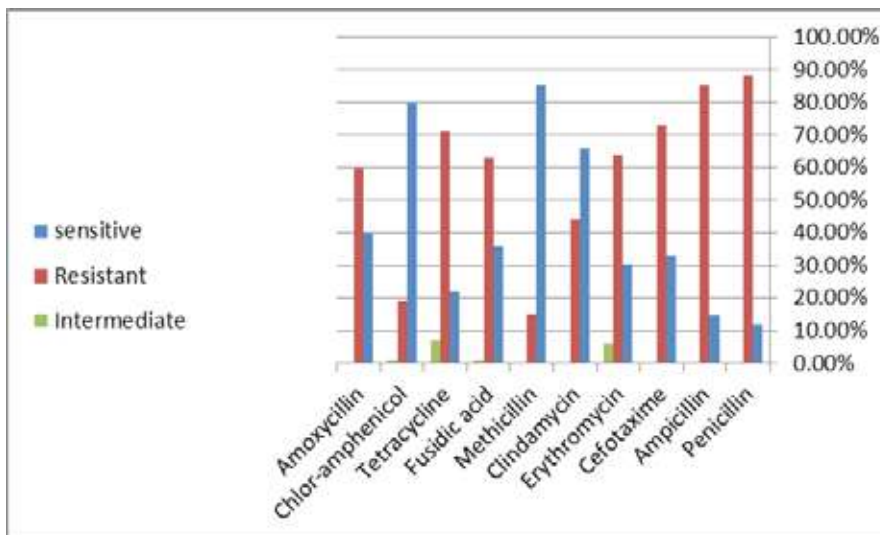


Fig (2) antibiotic sensitivity test of Streptococcus pyogenes

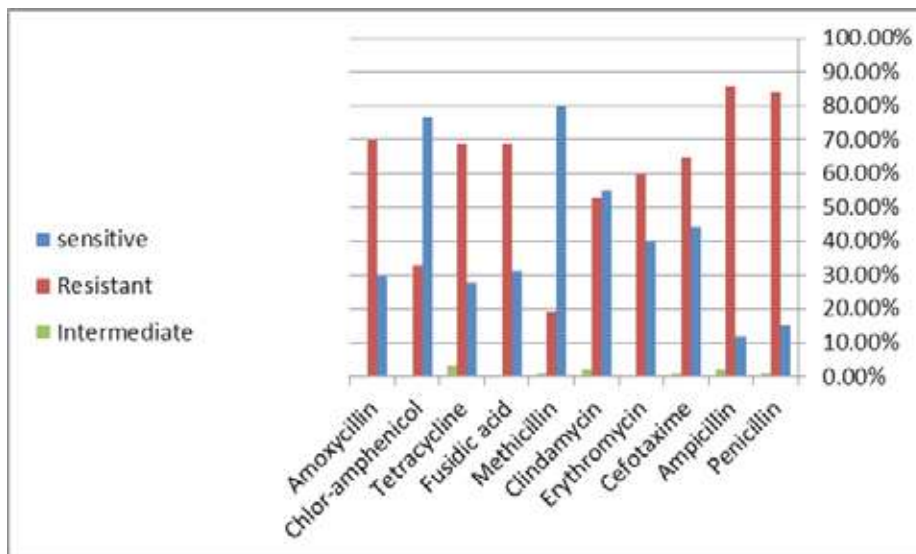


Fig (3) antibiotic sensitivity test of Pseudomonas

At immunological level we found a significant increased ($p \leq 0.05$) in the concentrations of IgM, IgG, IgA and IgE (mg/dl) compared with control groups as in table (3), thus the immunity of Eczematic disease involved mainly humoral immune response associated with a cell-mediated immunity towered many types of exogenous and endogenous factors, or an non specific reaction^(1,14). Increased in IgE concentrations facilitated

the release of different types of inflammatory mediators from mast cells, basophils and immune

Cells involved with Eczema pathogenesis with chemotactic for eosinophils to the site of infections¹². Others studies suggested that the elevated levels of serum antibodies in Eczematic patients may be associated with other pathogens through secondary infections (Roberts).

Table (3): Concentrations of immunoglobulins types in Eczematic patients

Groups	Mean Concentrations (mg/dl)							
	IgG M±S.D.	P- value	IgM M±S.D.	P- value	IgA M±S.D.	P- value	IgE M±S.D.	P- value
(G 1)	1231.42±57.5	0.041 ^a	245.86±36.8	0.021 ^a	223.82±16.7	0.001 ^a	483.18±57.9	0.030 ^a
(G 2)	1197.31±43.8	0.021 ^b	223.74±30.8	0.001 ^a	219.15±14.8	0.000 ^a	367.23±53.9	0.020 ^b
(G 3)	1132.67±23.8	0.100 ^c	137.59±30.4	0.100 ^b	159.70±15.9	0.100 ^b	357.87±36.8	0.120 ^b
(G 4)	1245.38±67.2	0.040 ^a	299.08±40.5	0.101 ^b	220.99±13.8	0.010 ^a	586.63±65.9	0.100 ^c
(G5)*	1115.56±57.4	0.000 ^d	132.53±93.6	0.000 ^c	127.58±91.7	0.000 ^c	190.85±73.2	0.000 ^c

*Control groups

Table (4) showed a significant increased ($p \leq 0.05$) in the concentrations of cytokines that used in this study and this agree with many previous studies had been explained that skin microbial infections inducted the cytokines when penetrated the skin of patients and suppression the skin barrier then bind with IgE on Langerhans' cells, that stimulated TH2CD4 to produce IL-4, which stimulated the IgE production by B lymphocytes^(3,15). IL- 10 had a regulatory role in an inflammatory response and we found the IL-10 polymorphism associated with the elevated the level of IgE in Eczematic and allergic diseases with inhibited

the production of pro- inflammatory cytokines⁶. IL-1 β is a pro- inflammatory cytokines played an important role in the pathogenesis of Eczema that produced from the inflammation of skin and activate Th1CD4 cells proliferation and differentiation². So the bacterial infections affected the systemic immune responses at both humoral and cellular levels that had been seen when the allergic reactions elevated the IgE antibody with increased in numbers of eosinophil because the receptors of this antibody found on the surface of eosinophil and mast cell¹¹.

Table (4): Concentrations of cytokines in Eczematic patients

Patients group	Mean Concentrations (pg/ml)					
	IL-1 β M±S.D.	P- value	IL-4 M±S.D.	P- value	IL-10 M±S.D.	P- value
(G 1)	305.34±34.6	0.004 ^a	91.33±2.31	0.020 ^a	210.63±1.30	0.030 ^a
(G 2)	296.26±32.9	0.200 ^b	76.13±1.22	0.001 ^b	109.57±1.29	0.001 ^b
(G 3)	274.89±24.9	0.010 ^c	70.02±4.01	0.100 ^b	98.39±1.98	0.000 ^c
(G 4)*	79.64±52.2	0.000 ^d	34.82±1.94	0.000 ^c	86.63±6.76	0.000 ^c

*Control groups

Conclusion

From all of the above, we concluded that the bacterial infections played an important role in systemic humoral and cellular immunity in Eczematic patients and both of them produced chronic inflammatory response through stimulated antibody production and secreted of cytokines. Eczema lesions are commonly seen in hand and feet. And lesions were associated with *S. aureus*, *P. aeruginosa* and *S. pyogenes*. From all of the above, we concluded that the bacterial infections played an important role in systemic humoral and cellular immunity in Eczematic patients and both of them produced chronic inflammatory response through stimulated antibody production and secreted of cytokines.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the College of Science for Women, Department of Biology, University of Babylon, Iraq and all experiments were carried out in accordance with approved guidelines.

References

- Al-saimary IE, Bakr SS, Al-Hamdi KE. Serum immunoglobulin and complement component levels in patients with atopic dermatitis. *ABR* 2013;4(1): 111 – 115.
- AL-Musawi MM, Hasan HR, Maluki AH. Relationship between TH1, TH2 immune responses and serum SOD activity in scabies. *Journal of advance Biomedical & Pathology Research*, 2014;4 (1):1-15.
- Bjerke JR. Immunopathogenesis of atopic eczema. *Tidsskr.* 1994;
- Burt TD. Fetal regulatory T cells and peripheral immune tolerance in utero: implications for development and disease. *Am J. Reprod Immunol.* 2013; 69: 346-358.
- Cheng XYH, Liao HG, Li B, Zhang J. TH1/TH2 functional imbalance after AMI: coronary arterial inflammation or myocardial inflammation. *J. Clin. Immunol.*, 2005;25;246 -53.
- EL-Aal AAA, Hassan MA, Gawdat HI, Ali MA, Barakat A. Immunomodulatory impression of anti and pro-inflammatory cytokines in relation to humoral immunity in human scabies. *International journal of Immunopathology and Pharmacology.* 2016;29(2):188-194.
- Hon KL, Tsang YC, Lee VW, et al. Efficacy of sodium hypochlorite
- Howell MD, Novak N, Bieber T, Pastore S, Girolomoni G. Interleukin-10 downregulates antimicrobial peptide expression in atopic dermatitis. *J Invest Dermatol.* 2005;125:738 –745.
- Johansson SG, Bieber T, Dahl R, Revised nomenclature for allergy for global use: report of the Nomenclature Review Committee of the World Allergy Organization, October 2003. *J Allergy Clin Immunol*, 2004;113:832–6.
- Joseph A, Church DG, Kleban B, Joseph AB. Serum immunoglobulin E concentrations and radioallergosorbent tests in children; with Atopic Dermatitis. *Pediat. Res.* 1976;10: 97-99 .
- Kennedy SB. Interleukin-10 suppresses mast cell IgE receptor expression and signaling in vitro and in vivo. MS Thesis. Richmond, VA: Virginia Commonwealth University. 2007.
- Matricardi MP, Rosmini F, Riodino S. Exposure to food born and orofecal microbes versus airborne viruses in relation to atopy and allergic asthma. *Epidemiological study. BMJ.* 2000;320 (12): 412-416.
- Matsuda H, Watanabe N, Geba GP, Sperl J, Tsudzuki M. Development of atopic dermatitis-like skin lesion with IgE hyperproduction in NC/Nga mice. *Int. Immunol.*, 1997;9:461–466
- Okada S, Maeda K, Tanaka Y, Anan S, Yoshida H. Immunoglobulin and their receptors on epidermal Langerhans cells in atopic dermatitis. *J. Dermatol.*, 1996;23: 247-253.
- Ong PY, Leung DY. Bacterial and viral infections in atopic dermatitis: a Comprehensive Review. *Clin. Rev. Allergy Immunol.* 2016;51(3):329-337.
- Park HY, Kim CR, Huh IS, et al. Staphylococcus aureus colonization in acute and chronic skin lesions of patients with atopic dermatitis. *Ann Dermatol* 2013;25:410–6.
- Roberts LJ, Huffam SE, Walton SF. Crusted scabies: Clinical and immunological findings in seventy-eight patients and a review of the literature. *Journal of infection*, 2005;50:375-381.
- (bleach) baths to reduce Staphylococcus aureus

- colonization in childhood onset moderate-to-severe eczema: a randomized, placebocontrolled cross-over trial. *J Dermatol Treat* 2016;27:156–62.
19. Barnes TM, Greive KA .Use of bleach baths for the treatment of infected atopic eczema. *Australas J Dermatol.*2013;54(4):251–8
 20. Brook I, Frazier EH, Yeager JK. Microbiology of infected atopic dermatitis. *Int J Dermatol* 1996; 35: 791–793
 21. Brook I, Frazier EH, Yeager JK. Microbiology of infected poison ivy dermatitis. *Br J Dermatol* 2000; 142: 943–946.
 22. Brook I, Frazier EH, Yeager JK. Microbiology of infected pustular psoriasis lesions. *Int J Dermatol* 1999; 38: 579–581.
 23. Brook I. Secondary bacterial infections complicating skin lesions. *J Med Microbiol*; 2002;51:808-812.
 24. Brüssow H: Turning the inside out: the microbiology of atopic dermatitis. *Environ Microbiol* 2016;18:2089–2102.
 25. Flohr C, Weinmayr G, Weiland SK, et al. How well do questionnaires perform compared with physical examination in detecting flexural eczema? Findings from the International Study of Asthma and Allergies in Childhood (ISAAC) Phase Two. *Br J Dermatol* .2009;161:846–53.
 26. Soter NA. Morphology of atopic eczema. *Allergy* 1989;44:16–9.
 27. Lübbe J. Secondary infection in patients with atopic dermatitis. *Am J Clin Dermatol.*, 2003;4 (9): 642-654. 29. McFadden J.
 28. Nishijima S, Namura S, Kawai S, et al. Staphylococcus aureus on hand surface and nasal carriage in patients with atopic dermatitis. *J Am Acad Dermatol* 1995; 32:677-9
 29. Nor Laegeforen, 114: 1827-8.
 30. Ochsendorf FR, Richter T, Niemczyk UM, Schafer V, Brade V, Milbradt R.: Prospective detection of important pathogens in pyoderma and their invitro antibiotic susceptibility. *Hautz*; 2000; 51(5):319-26.
 31. Pekkarinen PT, von Hertzen L, Laatikainen T, et al. A disparity in the association of asthma, rhinitis, and eczema with allergen-specific IgE between Finnish and Russian Karelia. *Allergy* 2007;62:281-7.

Poultry Resources Multidrug Resistance Bacteria to Human

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Abstract

Chicken was found to be the most reservoirs of resistant *Escherichia. coli* bacteria. Moreover, the high dependence of antibiotics in animal farming is considered the most important factor of the selection and dissemination of antimicrobial resistant microorganisms. Therefore, the current paper aims to search antimicrobial resistance in isolated *E. coli* from chicken feces. The antibiotic disc diffusion technique was used in order to conclude the response of isolated *E.coli* against to antibiotics in sixty isolates collected from chicken's feces.

The isolates *E.coli* were more frequently resistant to Nalidixic acid, Tetracycline, Ampicillin, Sulfamethoxazole, Neomycin and Trimethoprim-sulfamethoxazole respectively. While, Ceftriaxine was recorded lesser resistant in isolated *E. coli* from chicken feces. Both Amoxicillin and Gentamycin have been examined and happen to be similar result of both resistant and sensitivity test.

From this work, we concluded that isolated *E. coli* from locally chicken's intestines are generally resistant to multiple antibiotics thus, should watchful to the public health and veterinary authorities to limit and decrease antimicrobial.

Keyword: *Bacteria, multidrug-resistant, chicken, Antibiotic.*

Introduction

There is a great deal of research and published about the antibiotic-resistant, and the antibiotic did not kill the bacteria as they did. That's for high exposure to antibiotics, food contamination with resistant bacteria or antibiotics presences in addition to its developed immunity against antibiotics.

Previous studies have shown that poultry is one of the significant reservoirs of pathogenic *E.coli*. Antibiotic usage randomly is consider the greatest factor promote the selection, emergence, and dissemination of antimicrobial-resistant bacteria ¹.

E.coli is a general organism in the intestines of people and animals with certain strains that cause cases of gastroenteritis and other systematic diseases as well as blood poisoning². It is also recognized as indicators of antibiotic resistance, because they are part of the natural bacteria of humans, animals also exist in the environment.

The misuse and overuse of these antibiotics lead to accumulation of violative levels of unfit for human consumption poultry tissues and organs, particularly with the lack of knowledge between poultry producers about withdrawal periods of antibiotics, and the occurrence of antibiotic residues in food of animal origin above the maximum residue limits (MRLs) is documented worldwide by numerous public health authorities as being unlawful^(3,4)

The use and misuse of antibiotics have led to the development of resistant or long effective against infections for the treatment and prevention of pathogenic bacterial infections⁵. What happens here may be one of the most severe disasters of our time, and the antibiotics will no longer be useful.

In this study, *E. coli* strains isolated from locally chicken's intestines were collected from Erbil bazaar and analyzed to determine their susceptibilities to antimicrobial as a source of human contamination.

Material and Method

1. Sixty poultry intestines samples from locally chicken’s field were collected after slaughtered in shops within residential units. The intestine placed in a sterile container transferred directly to the diagnostic laboratory. Feces samples were taken out from the gut in a sterile container.
2. The stool samples were supplemented in Tryptone soya broths for pre-enrichment at 37°C for 2 hrs. Then mixed to homogenize and inoculated on Tryptone soya agar, MacConkey agar and incubates at 37° C for 24 hours.
3. All *E.coli* colonies appeared on different media were further identified done by both morphological and by biochemical reactions ⁶.
4. All isolated *E. coli* were examined for sensitivity against thirteen antibiotics depended by antibiotic disk agar diffusion technique according to the clinical laboratory standard^(7,8). The used antibiotics included Ampicillin (10µg), Neomycin (30µg), Amoxicillin (30µg), sulfamethoxazole (300µg), Trimethoprim/sulfamethoxazole (1.25/23.75µg), Ceftriaxine (30µg), Streptomycin (10µg),

Gentamycin (10µg), Amikacin (30µg), Tetracycline (30µg), Nalidixic acid (30µg), Chloramphenicol (30µg) and Nitrofurantoin (300µg).

After incubation at 37° C for 24 hours, the inhibition zone investigated as a response of bacteria to antibiotics. The multidrug-resistant (MDR) strain was identifying as consider resistant of microorganism to three or more different classes of antibiotics⁹.

Results and Discussion

According to table (1) and figure, investigation the prevalence of antibiotic resistance in isolated pathogenic *E. coli* from chicken’s fecesof. The study concluded the different resistance patterns to several antibiotics that have been commonly used in animal’s treatment ¹⁰.

The higher resistance rates were found in Nalidixic acid (90%), Tetracycline (88.33%), Ampicillin (80%), Sulfamethoxazole (75%), Neomycin (70%) and Trimethoprim-sulfamethoxazole (70%) respectively. While Ceftriaxine (66.6%) recorded lower resistant in isolates *E. coli* from chicken feces. Both Amoxicillin and Gentamycin comes out with the similar results of resistant and sensitivity test (50%).

Table (1): Percentage of antimicrobial resistance and sensitivity among isolates E.coli

No.	Antibiotics	Bacterial response to antibiotics	
		Sensitivity	Resistance
1.	Amoxicillin	30 (50%)	30(50%)
2.	Ampicillin	12 (20%)	48 (80%)
3.	Neomycin	18 (30%)	42 (70%)
4.	Gentamycin	30(50%)	30(50%)
5.	Trimethoprim-sulfamethoxazole	18 (30%)	42 (70%)
6.	Nalidixic acid	6 (10%)	54 (90%)
7.	Streptomycin	48(80%)	12 (20%)
8.	Sulfamethoxazole	15 (25%)	45 (75%)
9.	Ceftriaxine	20 (33.3%)	40 (66.66%)
10.	Nitrofurantoin	26(43.3%)	34(56.66%)
11.	Amikacin	48(80%)	12 (20%)
12.	Tetracycline	7(11.66)	53(88.33%)
13.	Chloramphenicol	32(53.33%)	28(46.66%)

The exceeded levels of antibiotic resistance along with the *E. coli* in this study is generally consistent with those reported has previously been taken in the closed area of this topic in countries like China and

Switzerland⁽¹¹⁻¹⁴⁾. That was because Poultry fields where the drug is a widely higher dose of treatment used in treating bacterial disease and promoting feed conversion efficiency ^(12,15).

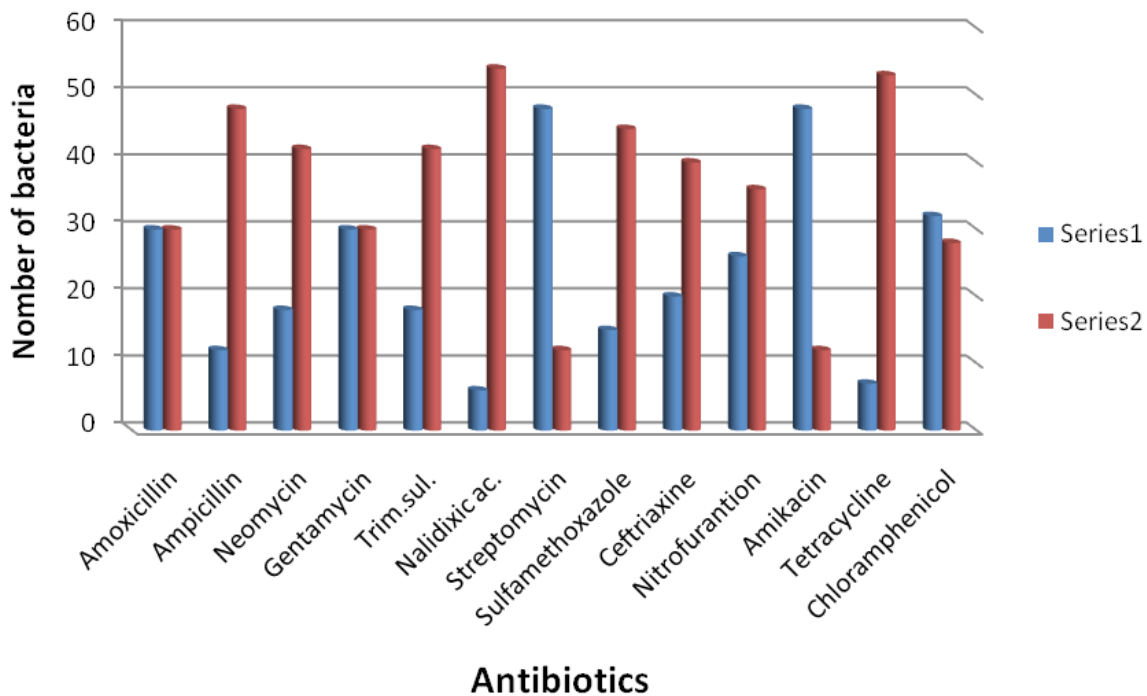


Figure (1): Microbial response to antibiotics

Other factors include incorrect medical diagnosis, prescription of unnecessary medications and the use of antibiotics as additional food for livestock to encourage their growth. In addition, translates into the loss of the economic cost of the cost of medicine.

Paper study results investigated that E.coli being a multidrug-resistant because the strain was defined as one which was resistant to at least three different classes of antimicrobials ¹⁶.

In conclusion, there is growing indication that pathogenic *microbial* infections of individuals are always more becomes hard to treatment and regulations are urgently needed to reduction uses of antimicrobial.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Erbil Polytechnic University-Erbil-Iraq and all experiments were carried out in accordance with approved guidelines.

References

1. Hinton M, Al Chalaby ZAM, Allen V. The persistence of drug-resistant Escherichia coli in the intestinal flora of healthy broiler chicks. Journal of Hygiene, 1982;89:269 –78.
2. Aarestrup FM. Monitoring of antimicrobial resistance among food animals: principles and limitations. J Veterinary Medicine. 2004; 380–388.
3. Salih HIM. RESIDUES OF ANTIBIOTIC IN POULTRY MEAT. M.Sc. thesis,2006, Department of Preventive Medicine and Veterinary Public Health, Faculty of Veterinary Medicine, University of Khartoum.
4. Almashhadany DA. Detection of antibiotic residues among raw beef in Erbil City (Iraq) and impact of temperature on antibiotic remains. Italian Journal of Food Safety 2019; 8:7897. doi:10.4081/ijfs. 2019;7897.
5. Olowe O, Okanlawon B, Olowe R, Olayemi A. The antimicrobial-resistant pattern of Escherichia coli from human clinical samples in Osogbo, southwestern Nigeria. Afr J Microbial Research. 2008;2:8–11.

6. Kamel, Fouad H, Jarjes SF. Essentials of Bacteriology and Immunology. Erbil Polytechnic University, Iraq. 2015.
7. Kamel Fouad H, Chimani HS, Ashti M, Saleem SQ. Development of in-vitro susceptibility testing for pathogenic bacteria. *Al-Qadisiyah Journal of Agriculture Sciences*, 2018; 8(2).
8. Wang N, Guo X, Yan Z, Wang W, Chen B, Ge F, et al. A comprehensive analysis of the spread and distribution characteristic of antibiotic resistance genes in livestock farms of southeastern China. *PLoS One*. 2016; 11.
9. Tenover FC. Mechanisms of antimicrobial resistance in bacteria. *Am J Med*. 2006;119, S3–S10.
10. Gong J, Xu M, Zhu C, Miao J, Liu X, Xu B, et al. Antimicrobial resistance, presence of integrons, and biofilm formation of *Salmonella Pullorum* isolate from Eastern China (1962–2010). *Avian Pathol*. 2013;42: 290–294.
11. Boyen F, Vangroenweghe F, Butaye P, De Graef E, Castryck F, Heylen P, et al. Disk diffusion is a reliable method for testing colistin susceptibility in porcine *E. coli* strains. *Vet Microbiol*. 2010; 144(3-4):359–362.
12. Zhang P, Shen Z, Zhang C, Song L, Wang B, Shang J, et al. Surveillance of antimicrobial resistance among *Escherichia coli* from chicken and swine, China, 2008–2015. *Vet Microbiol*. 2017;203:49–55
13. Yang H, Chen S, White DG, Zhao S, McDermott P, Walker R, et al. Characterization of multiple-antimicrobial-resistant *Escherichia coli* isolates from diseased chickens and swine in China. *J Clin Microbiol*. 2004;42, 3483–3489.
14. Lanz R, Kuhnert P, Boerlin P. Antimicrobial resistance and resistance gene determinants in clinical *Escherichia coli* from different animal species in Switzerland. *Vet Microbiol*. 2003;91:73–84.
15. Chen X, Zhang W, Yin J, Zhang N, Geng S, Zhou X. *Escherichia coli* isolates from sick chickens in China: Changes in antimicrobial resistance between 1993 and 2013. *Vet J*. 2014; 202, 112–115.
16. Tenover FC. Mechanisms of antimicrobial resistance in bacteria. *Am J Med*. 2006;119, S3–S10.

Returnee's Suicide Epidemiology among Internally Displaced Secondary School Students in Tikrit-Iraq

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Abstract

Introduction: One of the severe public health problems among adolescents and adults is suicide and suicidal behaviors. Suicide represent the 3rd leading cause death among adolescents and young adults between the ages of 10-24, accounting for 12% of all reported adolescents deaths in this age. Depression and suicide in a adolescents are not studied well, in spite of its prevalence in Iraqi community. This research aims at studying Returnee's Suicide Epidemiology Among Secondary School Students after Internal displacement in Tikrit-Iraq.

Subjects and Method: A cross sectional, descriptive study with analytic component was carried out on secondary schools students in Tikrit district. Questionnaire were presented to all students in the schools that day, in the classroom, depending on the help and cooperation of the school's administration and teachers during spare time. A screening tool used was the Columbia Depression Scale (CDS), a paper-and-pencil yes/no questionnaire. The DISC can be presented to the adolescents and youths (Ages 11 and over). It consists of a 22 items that are rated as Yes and No scored as (1) & (0) respectively. The total score is calculated as together the score of each of the 22 items. If the result of calculation is 0-6, 7-11, 12-15, 16 and above that mean the chance of depression was very unlikely, moderately likely, likely and highly likely respectively (Appendix -2-A, B)⁽⁶⁰⁾. Group (I) include unlikely and moderately likely considered as low risk for depression and Group (II) include likely and highly likely which considered as high risk for depression. A total of 269 students of returnees after internal displacement were selected randomly from secondary school students.

Results: High depression scores found in 26 (9.7%) while moderate scores found in 64 (23.8%) of Non IDPs of the study sample, which means that 33.5% of students were liable to have depression. High depression scores found in 6 (13.6%) of male Non IDPS students in comparison to 20 (8.9%) of females, while moderate scores found in 4 (9.1%) of males Non IDPs in comparison to 60 (26.7%) of females.

Conclusion: This study results found that 33.5% of students were more likely to have depression. Females more affected by depression and suicide.

Keywords: *Returnee's Suicide Among School Students, Suicide in Returnee's after Internal displacement in Iraq.*

Introduction

One of the common psychiatric disorder is depression, composed of features of the followings;

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loss of interest in usual activities, inability to experience pleasure, & persistent decreasing of mood¹. Depression is usually a disabling disorder which influence affects a individual's job, his study, eating habits & sleeping, wellbeing and feeling of life enjoyment². Depressed patients suffer from sadness, anxiousness, emptiness, worried, hopeless, guilty, helpless, worthless, restless, irritable, hurt. The following are presenting features of depression; lose interest's loss in previously pleasurable

activities, overeating or appetite loss, problems in concentration, remembering details, or decisions making, and there may be suicide contemplate or attempt. Fatigue, loss of energy, insomnia, excessive sleeping, generalized pain or aches, persistent digestive problems³. Depression influence around 7–18% of the people on at least single time in their lives, before the age of forty.⁴ IDPs according to (UNHCR): “persons who are obliged to flee for different reasons (violence, armed conflicts, violation of human rights) without crossing international borders. IDPs legally remain under the protection of their own government-even though that government might be the cause of their flight. As citizens, they retain all of their rights and protection under both human rights and international humanitarian law ⁵. The psychosocial factors that might be influenced by migration, and thereby pose a negative effect on mental health, are social support, social participation and feeling of powerlessness ⁶. This might be the reason that studies dealing with acculturation have reported higher distress and depressive symptoms for those immigrants who migrate to culturally and socially distinct societies and try to adapt to the new social circumstances after migration ⁷. IDPS are of special vulnerability to psychological distress. Researches on displacement and migration state that because displacement include obligatory movement between different societies and cultures put these people at great risk for mental diseases and psychological difficulty in any situations and persons. IDPS usually are held between a miserable present, horrible past and a vague future ⁸. One of the commonest psychological reactions found in IDPS is depression ^(9,10).

Subjects and Method: Formal administrative approval sheet was taken to conduct the study from the ministry of education, department of education in Tikrit Education Directorate. The study was carried out in the secondary schools in Tikrit. This a descriptive study with analytic component carried out on secondary schools students in Tikrit district. Questionnaire were presented to all students in the schools that day, in the classroom, depending on the help and cooperation of the school’s administration and teachers during spare time. The students filled out the questionnaires after explanation of each item by the researcher in about 35 minutes and returned them to researcher at the end of the session. A total of 269 students of returnees after internal displacement were selected randomly from secondary school students. A screening tool used was the Columbia Depression Scale (CDS), a paper-and-

pencil yes/no questionnaire. The DISC can be presented to the adolescents and youths (Ages 11 and over). It consists of a 22 items that are rated as Yes and No scored as (1) & (0) respectively. The total score is calculated as together the score of each of the 22 items. If the result of calculation is 0-6, 7-11, 12-15, 16 and above that mean the chance of depression was very unlikely, moderately likely, likely and highly likely respectively (Appendix -2-A, B) ¹¹. Group (I) include unlikely and moderately likely considered as low risk for depression and Group (II) include likely and highly likely which considered as high risk for depression.

Results

High depression scores found in 26 (9.7%) while moderate scores found in 64 (23.8%) of Non IDPs of the study sample, which means that 33.5% of students were liable to have depression Table 1.

Table 1: Depression Scores in Returnees After Internal Displacement of the sample

Depression score	Non IDPs No. (%)
Weak	86 (32%)
Mild	93 (34.6%)
Moderate	64 (23.8%)
High	26 (9.7%)
Total	269 (100%)

High depression scores found in 6 (13.6%) of male Non IDPS students in comparison to 20 (8.9%) of females, while moderate scores found in 4 (9.1%) of males Non IDPs in comparison to 60 (26.7%) of females Table 2.

Table 2: Depression Scores in Returnees After Internal Displacement against gender

Depression Score	Non IDPs Males No (%)	Non IDPs females No (%)
Weak	27 (61.4%)	59 (26.2%)
Mild	7 (15.9%)	86 (38.2%)
Moderate	4 (9.1%)	60 (26.7%)
High	6 (13.6%)	20 (8.9%)
Total	44 (100%)	225 (100%)

Suicidal attempts found in 142 (52.8%) of returnees after Internal Displacement, while suicidal thoughts found in 34 (12.6%) of returnees after Internal Displacement Table 3.

Table 3: Suicidal thoughts, Suicidal attempts in Non IDPs

Suicide	Non IDPs
Suicidal thoughts	34 (12.6%)
Suicidal attempt	142 (52.8%)
No suicidal factor	93 (34.6%)
Total	269 (100%)

Suicidal attempts found in 135 (60%) of females against 7 (16%) of males of returnees after Internal Displacement. Suicidal thoughts found in 8 (18.2%) of females against 26 (11.6%) of males of returnees after Internal Displacement Table 4.

Table 4: Suicidal thoughts, Suicidal attempts in Non IDPS according to the gender

Suicide	Males Non IDPs No (%)		Female Non IDPs No (%)	
	No	%	No	%
Suicidal thoughts	8	18.2	26	11.6
Suicidal attempt	7	15.9	135	60.0
No suicidal factor	29	65.9	64	28.4
Total	44	100.0	225	100.0

Discussion

Very little information is available concerning suicide epidemiology in Iraqi society. An Iraqi Suicide National Study covered 13 Iraqi (out of 18) governorates, and revealed that 647 cases of suicide were present . Suicide crude rate per 100 000 population in 2015 was 1.09 (1.21 for males, 0.97 for females) & in 2016 1.31 (1.54 for males and 1.07 for females).¹²

This study results (that 33.5% of students were liable to have depression) is supported by Alkhafaji AM et al who found a statistically significant relation in the rate depression rate in IDPS was 34.5% in comparison to 16.4% in their matched group of control¹³. This high figures can be explained by the fact that Psychological disorders frequently take place progressively after multiple causes like: persistent stresses, violence, environmental factors and internal psychogenic factors which include Internalizing Items (fear of new situations, sadness, self underestimation, hopeless, unhappy, worries a lot, seems to have less fun); and Externalizing factors (unnecessary risky behaviors, ignoring rules, misunderstand feelings of others, fights with other children, teases others, blames others for troubles, refuses to share)¹⁴. This high figures is very serious problem because of severe deficiencies in mental

& psychological health care services¹⁵.

For more than 2 decades, Iraqi exposed to sanctions, wars, & displacement which affect all life, & health aspects of women, children, & adolescents. The situation complicated in 2014 by invasion and occupation of a terrorist organization to Iraqi governorates⁽¹⁶⁻¹⁷⁾. In this study, the sample was from returnees secondary school students after internal displacement who their age (12-18 years), this supported by Noori and Janet who found that higher than 1/3 of their sample were aged (18-27 years) and stated that immigrants were young ages (15-24 years old)¹⁸. Also Joseph and Cristina found that (24%) of their study group of immigrants aged between (16-25) years and (33%) were (26-35) years¹⁹. The majority of cases (67.9%) were aged 29 years or below. Rate of suicide in Iraq is below suicide global rate. Young people more commonly affected by suicide, but almost equal gender distribution. Many cultural and social factors have major role in this epidemiology²⁰.

Being a young person, IDP secondary school students are put this group under risk of depression which is supported by Alkhafaji AM et al who found that majority of depressive patients were of high educational level 47%¹³. This was explained by Beiser M who found that young and educated persons was target for violence, terror and experiencing more losing events²¹. High and moderate depression scores were found higher in females 20 (8.9%), 60 (26.7%) respectively than in males 6 (13.6%), & 4 (9.1%) respectively of returnees students from internal displacement. This means that 36.6% of returnees females may affected by depression, in comparison to 22.7% of returnees males. These figures are lower than the prevalence of depression was higher in IDP females (57.9%) than males (42.1%)¹³. This may be explained by the end of internal displacement period will provide a rest and relief after stress of displacement and its related co-morbidities. But predominance of females may explained by the fact the females are more likely than males to ‘internalize’ stress, which put them at higher risk for getting depression. Johnson H found that females are at double risk to develop depression males and the psychological distress level was significantly higher for women than for men²². Piccinelli M suggested that females may be at greater risk of mental distress because of the psychological sequelae of rape, the violent loss of partner and children, and of becoming a single parent or widow²³. This situation complicated by unique Iraqi society, cultural attitudes toward females specially young and unmarried²⁴.

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under Tikrit Medical College, Iraq and all experiments were carried out in accordance with approved guidelines.

References

- Gelder M, Harrison P, Cowen P. shorter oxford textbook of psychiatry, 5th ed. Oxford University press,2006; 11:218
- Rush AJ. The varied clinical presentations of major depressive disorder. *The Journal of clinical psychiatry*, 2007; 68 (8): 4-10.
- Andrews G. Classification of anxiety and depressive disorders: problems and solutions. *Depression & Anxiety* 2008; 25: 274-81.
- Kessler R, Gonagle K, Zhao S. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: results from the National Co morbidity Survey. *Gen Psychiatry* 1994; 11:227.
- KALIN G. "Guiding Principles on Internal Displacement. Annotations." *The American Society of International Law & The Brookings Institute Project on Internal Displacement. Studies in Transnational Legal Policy* 2000;32. *AL-Qadisiya Medical Journal* 2015; 11 (19) .
- Mallett R, Leff J, Bhugra D, Pang D, Zhao JH. Social environment, ethnicity and schizophrenia. A case-control study. *Socio Psychiatry Epidemiol*, 2002; 37:329-35.
- Oppedal B, Roysamb E. Mental health, life stress and social support among young Norwegian adolescents with immigrant and host national background, *Scand Psychology journal*, 2004;45 (10): 131-4.
- Ainslie R.: Cultural mourning, immigration, and engagement: Vignettes from the Mexican Experience. In *Suarez-Orozco Crossings: Mexican Immigration in Interdisciplinary perspective*, 1998;283-300.
- Turner SW, Gorst-Unsworth C. Psychological sequelae of torture. A descriptive model. *Br J Psychiatry*1990; 157: 475–80
- Turner SW, Bowie C, Dunn G, Shapo L, Yule W. Mental health of Kosovan Albanian refugees in the UK. *Br J Psychiatry*2003; 182: 444–8
- Shaffer D, Fisher P, Lucas CP, Dulcan MK, Schwab-Stone ME. NIMH Diagnostic Interview Schedule for Children Version IV (NIMH DISC-IV): description, differences from previous versions, and reliability of some.1996;1.
- National study of suicide: Report on suicide data in Iraq in 2015 and 2016.*J Affect Disord*. 2018 Mar 15;229:56-62.
- Alkhafaji AM, et al. Depression Among Internally Displaced People After February 22,2006 In Al-Diwaniya Governorate. *AL-Qadisiya Medical Journal* 2015; 11 (19): 26-34.
- Nashwan N Hanna, Ashoor R Sarhat, Mohammad KAbdulwahd. Screening of Psychosocial Problems among Secondary School Students in Alhawya City. *Tikrit Medical Journal* 2009; 15 (1): 287-95. Second Scientific Conference
- Sarhat AR, Abdulrahman ZN, Abedalrahman SK, Zardawy Islam AR. A Novel Case Series of Munchausen Syndrome by Proxy Victim.*World Family Medicine/Middle East Journal Of Family Medicine* 2019; 17 (7):17-21.
- Ahmed J Hassen, Ashoor R Sarhat, Nashwan N Hanna. Depression among Secondary Schools Students in Tikrit District. *Indian Journal of Forensic Medicine & Toxicology* 2019;13 (2).
- Faiadh H Faiadh, Ashoor R Sarhat. Screening of Post Traumatic Stress Disorders among Preschools Children in Baijee City.*Diyala Journal For Pure Science* 2010; 6 (3):1-15.
- NooriAK, Janet L. Relation between depression & sociodemographic factors. *International journal of mental health system* 2007; 1 (4). 1-9.
- Joseph D, Cristina Magan. Acculturative Stress, Anxiety, and Depression among Mexican Immigrant Farmworkers in the Midwest United States, *Journal of Immigrant health*; 2000; 2 (3): 119-31.
- Haile F, Ilene H, Samuel N. Determinants of Depression Among Ethiopian Immigrants and Refugees in Toronto, *Journal of research and services*; 2004; 192: 363-72.
- Beiser M, Dion, Gotowiec A, Hyman I. Immigrant and refugee children in Canadian, *Psychiatric Canadian journal* 1995; 40.

22. Johnson H, Thompson A. The development and maintenance of post-traumatic stress disorder (PTSD) in civilian adult survivors of war trauma and torture: A review. *Clinical Psychology Review* 2008; 28(1):36-47.
23. Piccinelli M, Wilkinson G. Gender differences in depression. Critical review. *Br J Psychiatry* 2000;177:486-492.
24. Ashoor R Sarhat. Munchausen's syndrome by proxy in Iraq; case series. *Medical Journal of Tikrit* 2016;21 (1): 271-284.

Clinic-Pathological Characteristics of Breast Cancer among Iraqi Women

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Abstract

Background: Breast cancer is the commonest cancer globally and is the 1st cancer in Iraq among females. Its sequelae and prognosis depend on early diagnosis, this study aimed to identify the clinicopathological characteristics of breast cancer.

Method: Retrospective descriptive study, on 102 breast cancer women, attending the women health center in Al-Elwiyaa Maternity Teaching Hospital department in 2018.

Results: Invasive ductal carcinoma (IDC) was found among 82 (80.4%) of malignant cases, ILC was 14 (13.7%), most of cases diagnosed at stage II 54 (52.9%), followed by stage III 27 (26.5%), and most of lesions detected by the patient 51 (50%). Peak age was 45-54 year 39 (38.2%), followed by 55-64 years in 24 (23.5%), and 10 (9.8%) of breast cancer cases found among of patients aged 25-34 year. Most of the lesions were on the right breast 54(52.9%).

Conclusion: Iraqi women still diagnosed at late stage, and when become symptomatic, this will affect the management, outcome and 5 year survival rate.

Keywords: Breast cancer, clinical characteristics, pathological characteristics. Breast cancer stage.

Introduction

In Iraq, breast cancer is the 1st cancer among females, and the second cause of cancer related deaths.¹ Breast cancer is presented among younger age, late stage, and in aggressive form.^(2,3) Breast cancer management and prognosis depend on early diagnosis, and staging. The aim of cancer staging is to identify the prevalence of the disease, to develop the treatment plan, to provide prognosis information,⁴ and is a good indicator of early detection quality.⁵ In previous study,⁶ the majority of

affected women presented in late stages. Bad prognosis always hand by hand with advanced stages.⁷ In Iraq, usually tumor size at presentation >20 mm.⁸ There is an early detection clinics only and no screening program was applied.^(6,9) This study was aimed to study the changes in presentation of breast cancer within the last 2 decades.

Materials and Method: A total of 102 breast cancer female patients was included in the study. They were recruited from registered patients in the Women Health Centre in Al-Elwiyaa Maternity Teaching Hospital for the period Jan. 2017-Nov. 2017. Information requested was lesion characteristics (histopathology and clinical notes), anatomical staging done according to TNM classification.¹⁰ All patients with full information, histological and radiological reports were included. All information, regarding histopathology was extracted from file records.

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Result: The age distribution of the cases showed that peak age was 45-54 year 39 (38.2%), followed by 55-64 years in 24 (23.5%), and 10 (9.8%) of breast cancer cases found among of patients aged 25-34 year. Half of the cases diagnosed at clinical stage II 54 (52.9%), followed by stage III 27 (26.5%), two cases (1.96%) was at stage zero. The lesion was detected by breast self-examination in 51 (50%), and by clinical breast examination 51 (50%) of breast cancer cases. Lesions were found on the right breast in 54(52.9%), and on the left breast in 47 (46.1%), these findings are shown in table 1.

Table 1. The general and clinical characteristics of breast cancer cases

Patient Characteristics	Frequency	Percent
Age		
25-34 years	10	9.8
35-44 year	16	15.7
45-54 year	39	38.2
55-64 year	24	23.5
65-74 year	7	6.9
> 75 year	6	5.9
Stage		
0	2	1.96
I	18	17.6
II	54	52.9
III	27	26.5
IV	1	0.9
Lesion detected by		
Breast clinical examination	51	50
Breast self-examination	51	50
Site of lesion		
Right	54	52.9
Left	47	46.1
Bilateral	1	0.9
Total	102	100

Table 2. The histological types of diagnosed breast diseases

Histological type	Frequency	Percent
Invasive ductal carcinoma (IDC)	82	80.4
Invasive lobular carcinoma (ILC)	14	13.7
Ductal carcinoma in situ (DCIS)	2	2.0
Others	4	4.0
Total	102	100

Invasive ductal carcinoma (IDC) was found among 82 (80.4%) of malignant cases, Invasive lobular carcinoma (ILC) was 14(13.7%), and Ductal carcinoma in situ (DCIS) found among 2 (2%) (Table 2).

Discussion

The age distribution of cases in this study showed pattern of progressive increased cancer incidence with age, as documented in 2014 Egyptian and Chinese literature.¹¹ The sharp peak of breast cancer cases was at 45-55 years. This finding goes with that reported in Iraq previously (40-49 years),¹² and (35-49 years).¹³ during 1976-1986, the peak was 40-50 year¹⁴ and during 1986-1988 was 45-50 years.¹⁵ The observed peak (40-50 year) is lower than reported in China (55-59 year) and Egypt (60-64 year)¹¹ and in UK (> 65 year).¹³

This difference might be explained by the difference in life expectancy¹⁶. Most of breast cancer women diagnosed at more advanced stages stage II (80.4%). This figure consistent with what reported previously in Iraq (88%).¹³ It is higher than that in UK (39.2%),¹³ and in Turkey (68.6%).¹⁷ This difference might be attributed to the fact that no screening program was implemented in Iraq to detect breast cancer earlier. Early detection clinics were established in 2001. The observed figure (80.4%) is lower than that reported in 2010 (92.4%).¹²

In this study, 50% of the lesions were detected by patient herself (breast self-examination), which is lower than that reported previously in Iraq (90.6%).¹² The finding of decreased percentage of advanced stage at diagnosis about (12%) during the last 12 years, and the decrease in diagnosis by patient herself by (40.6%) than reported in 2010, may be explained by improvement in health services demonstrated by participation of clinical examination, the effectivity of early detection clinics and awareness to breast cancer among the population. Breast clinical examination shared in detection of breast cancer by (50%). The finding reflects the participation of primary health care centers in detection of breast cancer.

Most of breast cancer cases involved the right breast, this was supported by some previous study (55.6%),¹⁸ and another study found that only women born in Asia and middle east countries had higher right sided breast cancer ratio.¹⁹ This finding is opposed by many previous studies which found that breast cancers cases affected left breast more than right side.⁽²⁰⁻²²⁾ Some studies found that patients with right breast tumors are more likely to have familial relative affected with breast cancer²², tend to have more aggressive, and presented at younger age group than those with the left breast tumors.²¹ This study results found that invasive ductal carcinoma found among (80.4%), invasive lobular carcinoma ILC among (13.7%). This figure consistent with previous

findings in Iraq (86.5%), and (8.8%) for IDC and LDC respectively, and in UK (81.5%), (10%), for IDC and LDC respectively.¹³ Here ductal carcinoma in situ was found among (2%) of patients, & this is lower than found in Korea (10.6%) among never screened and (14.1%) among screened women.²³ The high figure among both groups in Korea may be explained by increased awareness among both, population and health staff about breast cancer due to screening program. Screening programs using mammography is widely conducted in many western countries, while is not common in many Asian countries.²⁴ Breast cancer is amenable to preventive strategies by primary and/or secondary prevention, hence a need for effective interventions tackling lifestyle risk factors, break the stigmas and improve awareness about this cancer.²⁵

Conclusion

In Iraq, breast cancer diagnosed in earlier age than western countries, and even other neighboring countries, with high grade stage at diagnosis. There is a need for urgent implementation of screening program.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under Al-Alwiya Maternity Teaching Hospital, Women Health Center and all experiments were carried out in accordance with approved guidelines.

References

1. Annual Statistical Report. Planning Directorate, Ministry of Health/Environment, Republic of Iraq. 2017.
2. Alwan NAS. Breast Cancer Among Iraqi Women: Preliminary Findings From a Regional Comparative Breast Cancer Research Project. *J Glob Oncol* 2016; 2(5): 255-8.
3. Alwan NAS, Tawfeeq F, Maallah M, et al. The Stage of Breast Cancer at the Time of Diagnosis: Correlation with the Clinicopathological Findings among Iraqi Patients. *Journal of Neoplasm* 2017; 2(3:22): 1-10.,
4. Weiss A, Chavez-Mac Gregor M, Lichtensztajn DY et al: Validation study of the American Joint Committee on Cancer 8th edition prognostic stage compared with the anatomic stage in breast cancer. *Jama Oncol*, 2018; 4(2): 203–9.
5. State of Victoria Victorian cancer plan monitoring and evaluation framework Report. State of Victoria, Department of Health and Human Services, June 2018;12.
6. Abedalrahman SK, Al-Khalidy NA, Al-Diwan JK. Advanced Stage at diagnosis among Iraqi breast cancer women. *Sudan Journal of Medical Sciences* 2019;14(2)38-40. DOI 10.18502/sjms.v14i2.4690
7. American cancer society. Breastn Cancer Survival rates. <https://www.cancer.org/cancer/breast-cancer/understanding-a-breast-cancer-diagnosis/breast-cancer-survival-rates.html>
8. Al-Amer HD, Al-Jaberi HK, Al-Hilli M, Al-Diwan J K. Tumor size of breast cancer among attendees to early detection clinic in Iraq. *Int. J. Adv. Res.* 2019; 7(3): 1010-11.
9. Abedalrahman SK, Al-Khalidy NA, Al-Hashimi AS., Al-Diwan JK. Accuracy of FNAB in diagnosis of breast lump. *Indian journal of public health research and development* 2019; 10(1):760-4.
10. Brierley J D, Gospodarowicz M K, Wittekind C, et al. TNM Classification of Malignant Tumours. New York, NY: John Wiley & Sons 2017 UICC.
11. Hamdy A, Aziml, Amal S. Ibrahim. Breast cancer in Egypt, China and Chinese: statistics and beyond. *J Thorac Dis.* 2014; 6(7):864-6.
12. Alwan NAS. Breast cancer: demographic characteristics and clinico-pathological presentation of patients in Iraq. *EMHJ.* 2010; 16 (1):1159-64.
13. Alwan NAS, Kerr D, Al-Okati D, Pezella F, Tawfeeq FN. Comparative Study on the Clinicopathological Profiles of Breast Cancer Among Iraqi and British Patients. *The Open Public Health Journal* 2018; 11:177-91.
14. IMOH/. Results of Iraqi cancer registry 1976-1985. Baghdad 1987;17.
15. IMOH/. Results of Iraqi cancer registry 1986-1988. Baghdad 1990;60.
16. Population Pyramid.net. Population Pyramids of the World from 1950 to 2100. Iraq, 2017. <https://www.populationpyramid.net/iraq/2017/>
17. Ibis K, Ozkurt S, Kucucuk S, et al. Comparison of Pathological Prognostic Stage and Anatomic Stage Groups According to the Updated Version of the American Joint Committee on Cancer (AJCC) Breast Cancer Staging 8th Edition. *Med Sci Monit.* 2018; 24: 3637-43.

18. Zhao Zhi-Fei, Qu BL, Gao LL, et al. Diagnostic accuracy of clinical examination, mammogram, ultrasonogram to detect size of tumor and lymph node in carcinoma of breast. *Biomedical Research* 2016; 27 (4): 1038-44.
19. Melnik Y, Slater PE, Steinitz R, Davies AM. Breast cancer in Israel: laterality and survival. *J Cancer Res Clin Oncol* 1979;95(3):291–3.
20. Hallberg Ö, Johansson O. Sleep on the right side—Get cancer on the left?. *Pathophysiology* 2010; 17(3):157-160.
21. Zeeneldin A A., Ramadan M, Elmashad N, Fakhr I, Diao A, Mosaad E. Breast cancer laterality among Egyptian patients and its association with treatments and survival. *Journal of the Egyptian National Cancer Institute* 2013; 25:199–207.
22. Tulinius H. Ólafsdóttir G. Left and Right Sided Breast Cancer. *Pathology Research and Practice* 1990; 186(1): 92-4.
23. Choi KS, Yoon M, Song SH, Suh M, Park B, Jung KW, Jun JK. Effect of mammography screening on stage at breast cancer diagnosis: results from the Korea National Cancer Screening Program. *Sci Rep.* 2018; 8(1):8882.
24. Bhoo-Pathy N, Yip CH, Hartman M, Uiterwaal CS, Devi BC, Peeters PH et al. Breast cancer research in Asia: adopt or adapt Western knowledge? *Eur J Cancer* 2013; 49: 703–9.
25. Kulhánová I, Bray F, Fadhil I, al-Zahrani AS, el-Basmy A, Anwar WA, et al. Profile of cancer in the Eastern Mediterranean region: the need for action. *Cancer Epidemiol.* 2017; 47:125-32.

Quality of Life among Adolescents Patients with Irritable Bowel Syndrome

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Abstract

Objective(s): The study aims to assess the quality of life for adolescent patients with irritable bowel syndrome in the city of Baghdad and determine the relationship between adolescents' quality of life level and their demographic characteristics.

Methodology: A descriptive study, using the assessment approach was conducted on a purposive "non-probability" sample of (100) patients from both gender aged (12-18) years, attending liver and digestive system diseases teaching hospital in Baghdad city. The instrument of the study was adapted from the World Health Organization quality of life questionnaire (1998) to achieve the purpose of the study, in addition to the participants' demographic characteristics and the some related medical data. The data were collected through direct interview, during the period of the 1st of July to the 16th of August 2018. SPSS program was used in data analysis.

Results: The findings of the study indicated that adolescents' social domain was affected, the finding also showed significant relationships among adolescents' age, gender, marital status, employment status and their quality of life.

Conclusion: Irritable bowel syndrome IBS affected on adolescents quality of life negatively, especially social, psychological, and environmental domains..

Recommendations: The study recommended the need to avoid disease risk factors and additional studies are required to interpret the results of the difference in the quality of life of adolescent patients with irritable bowel syndrome.

Keywords: *Quality of Life, Adolescents, Irritable Bowel Syndrome*

Introduction

Irritable bowel syndrome (IBS) is one of the common digestive system disorder, characterized by chronic abdominal pain, discomfort, bloating, and alteration in the habits of the bowel ¹, IBS can occur at any age, but it start in the early adolescents, the incidence of females more than males ^(2,3).

There's no cure for IBS, but the symptoms can be relieved by changing diet and lifestyle^(4,5). IBS can affects on patients' quality of life due to chronic pain, fatigue, sleep and mood disturbance, and work activities^(6,7). Living with IBS presents daily challenges; IBS may be painful or embarrassing and can seriously affect the quality of life ⁵.

As documented in the previous studies that the impact of IBS on patients' quality of life is serious and similar to other chronic diseases such heart and kidney diseases, IBS has impact on patients' physical, emotional, social and psychological functions^(7, 8, 9).

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Nurses have important role in caring of patients'

with IBS, Iraqi patients with such syndrome need a help for adopted with their health problems, especially the adolescents for their lack of health knowledge ¹⁰. Therefore the researchers bring highlighted on this health problems among adolescents.

Method and Materials

Objective of the study: The study aims to assess the quality of life for adolescent patients with irritable bowel syndrome and to determine the relationship between patients’ quality of life and their demographic characteristics.

Design of the study: A descriptive approach is carried out to achieve the purpose of the study.

Setting of the study: The study was conducted at liver and digestive system diseases teaching hospital in Baghdad city. Data was collected from the period of the 1st of July to the 16th of August 2018.

Sample of the study: a purposive “non-probability” sample of (100) patients from both gender, aged from (11-18) years, with no others chronic diseases.

Instrument of the study and procedure: The data were collected by direct interview; the World Health Organization quality of life questionnaire (1998) was adopted to achieve the goal of the study, this scale consists of 6 domains: physical health, psychological, level of independence, social relationships, environment, and spirituality/religion/personal beliefs. Participants’ sociodemographic characteristics such as (age, sex, marital status, educational level and employment status), and medical information related to IBS also included. The questionnaire was measured on 3 Likert type scale (always, sometimes and never).

Statistical data analysis: Data was analyzed by using the Statistical Package for Social Science (SPSS) version 23. Descriptive and inferential statistics had been used.

Results

This table shows that the majority of sample’s ages (67%) were between 14 and 18years old, more than half (52%) were male. (48%) of them were single and (47%) were married. (50%) of has intermediate school graduates. (50%) of adolescent patients wereEmployee and (68%) of themhaveinsufficient income. (75%) of sample weresmoke, and most of them (77%) with negative family history with IBS.

Table (1): Distribution of samples’ sociodemographic characteristics

No.	Variables	N= 100 F.	100%%
1	Age (years)		
	Early Adolescence (11–13)	33	33
	Middle Adolescence (14–18)	67	67
2	Gender		
	Male	52	52
	Female	48	48
3	Marital status		
	Single	48	48
	Married	47	47
	Widowed	5	5
4	Level of education		
	Read & Write	25	25
	Primary	9	9
	Intermediate	50	50
	Secondary	16	16
5	Employment status		
	Student	11	11
	Employee	50	50
	Don’t employee	39	39
6	Income		
	Sufficient	32	32
	Insufficient	68	68
7	Smoking		
	Yes	75	75
	No	25	25
8	Family history of IBS		
	Positive	23	23
	Negative	77	77

F. = Frequency, %=Percent, IBS = irritable bowel syndrome

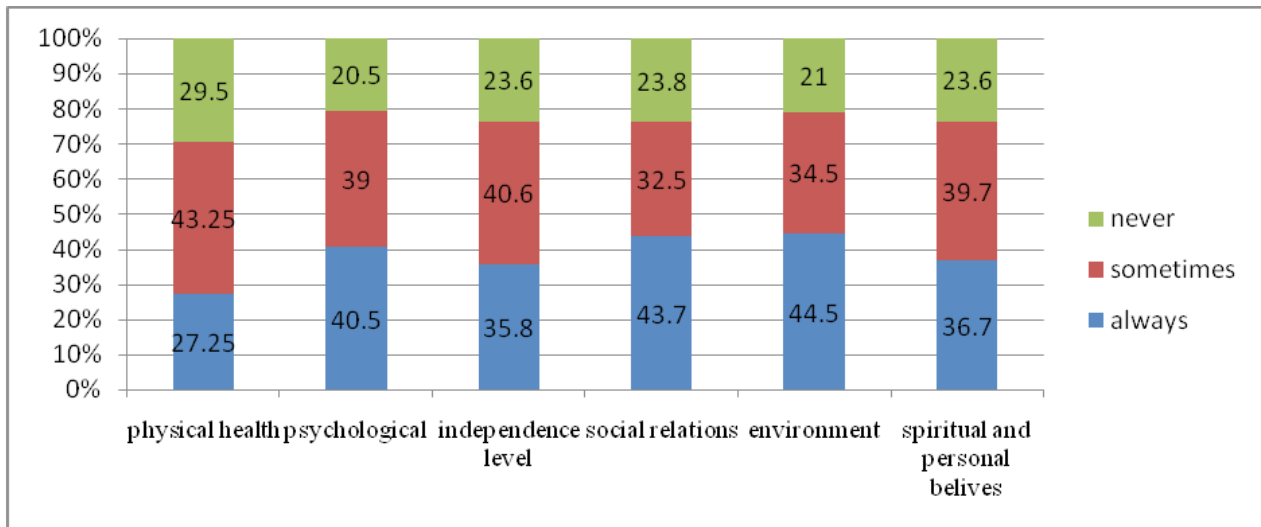


Figure (1): Adolescents' quality of life subdomains percentages

This figure shows that high percentages of adolescent with IBS have sometimes and always score for all subdomains of their quality of life. (43.25%) have sometimes physical health dysfunction, (40.5%) have always psychological dysfunction, (40.6%) have sometimes independence level, (43.7%) have always social relations dysfunction, (44.5%) have always environmental dysfunction, and (39.7%) have sometimes spiritual and personal dysfunction.

This figure reveals that the higher percentage (47%) of adolescent patients with IBS have bad quality of life.

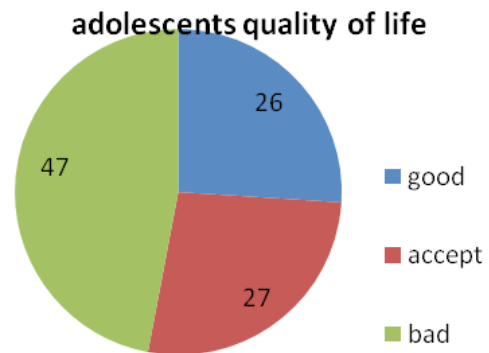


Figure (2): Levels of quality of life for adolescent patients with irritable bowel syndrome

Table (2): Relationship between quality of life level for adolescent with irritable bowel syndrome and their demographic characteristics

Quality of Life	Good	Accept	Bad	Total	χ^2 obs.	Sig.
	F	F	F	F		
Gender					8.324	S
Male	14	20	18	52		
Female	13	7	28	48		
Total	27	27	46	100		
P≤0.05 df=2 χ^2 crit. = 5.99						
Quality of Life	Good	Accept	Bad	Total	χ^2 obs.	Sig.
	F	F	F	F		
Marital Status					22.141	Sig
Single	5	17	26	48		
Married	22	10	15	47		
Widowed	0	0	5	5		
Total	27	27	46	100		
P≤0.05 df= 4 χ^2 crit. = 9.49						

Quality of Life \ Level of Education	Good	Accept	Bad	Total	χ^2 obs.	Sig.
	F	F	F	F		
Read & Write	0	11	14	25	57.501	HS
Primary	0	3	6	9		
Intermediate	11	13	26	50		
Secondary	16	0	0	16		
Total	27	27	46	100		
P≤0.05 df = 6 χ^2 crit. = 12.59						
Quality of Life \ Employment Status	Good	Accept	Bad	Total	χ^2 obs.	Sig.
	F	F	F	F		
Student	0	4	7	11	32.920	HS
Employee	25	14	11	50		
Don't employee	2	9	28	39		
Total	27	27	46	100		
P≤0.05 df =4 χ^2 crit. = 9.49						

df = degree of freedom; f = frequency; P = level of probability; χ^2 crit = critical chi square; χ^2 obs = observed chi square,; sig. = significance; NS = Non significance; HS = High significance

This table shows that there is significant relationship between quality of life level for adolescents with IBS and their gender, marital status, level of education, and employment status.

Discussion

The findings of the present study showed that the majority of sample's ages were between (14- 18) years old who were accounted for (67%). As documented in previous studies irritable bowel syndrome IBS can occur at any age, but mostly at middle adolescents' life, this result supported by similar study about irritable bowel syndrome in the incidence at this age group 11. Relative to their gender, more than half of them were males (52%).According to our society attribute female patients may suffer from health care neglects by their families due to many causes such home duties and health awareness for their families. This result disagreed with a study medication used for patient with IBS that, the incidence more common in female than male 2:112.(48%) of adolescent patients were not married while (47%) of them were married. In Iraqi society some families encouraged the early aged marriage especially in young females due to religious causes and their poor socioeconomic status. This result supported by similar study which showed that the single person more likely to have IBS 13. (50%) of adolescent patients with intermediate school graduates, which indicated low level of education. Their health

disorder or income may affect negatively on their school attendance and may cause school dropout. This result disagreed with another study about patients with IBS that, those patients showed a higher level of education 14. Concerning their employment status, (50%) of adolescent patients was employee. Because their early dropout from school and insufficient income and early marriage affects on demands and encouraged them to have a work in their early life. This result disagreed with a similar study about IBS patients that most of the patients were unemployed due to their health status14. (68%) of adolescent patients have insufficient monthly incomes. This may due to the financial burden of their health disorder and early marriage status. The proportion is similar in a study done by Noorbala, et al.14. (75%) of sample were smoked. Smoking consider as one of the most factors that can trigger IBS, especially early age smoking. This result supported by study done by Greg that indicates that the tobacco is one of the worst factors for digestive system disorders including IBS¹⁵. Most of them (77%) have negative family history for IBS. Most Iraqi families may have negative history or most of such disorder may be not diagnosed in some families so those adolescent did not know about other relatives with such disorder. This result disagreed with a study about patient with IBS that people with first relative degree diagnosed with IBS were at potential risk for such health disorder ¹⁷. Other studies have no serious result that whether genes or the family history is responsible for IBS¹⁸.

Figure (2) indicates that (47%) of adolescents with IBS has bad level quality of life related to their health disorder, while (27%) has accepted level. Unfortunately, this result is indicating low health care services and maladjustment with symptoms of IBS. This result agreed with a study about patients with IBS that those patients showed negative impact of IBS on their health and quality of life⁸.

For more details regarding adolescents quality of life, figure (1) shows the highest percentages of them affected by psychological, social, and environmental domains (40.5%, 43.7%, and 44.5%) respectively, followed by independence level, physical health, and spiritual and personal believes (40.6%, 43.25, and 39.7%). The recurrent pain and alteration in bowel habits affects on their health status and body built and the body mass index negatively, which can cause body image dissatisfaction and isolation from others. IBS symptoms also can cause anxiety and frequent followed up to reduce the uncomfortable symptoms. Many studies showed the adverse effects of IBS on patients' social and psychological status⁸.

The study shows a significant relationship between adolescents' quality of life level and their gender, marital status, education level and employment status. High percentages of males were married and have family responsibilities especially they were less than 18 years, that a burden on their life. Adolescents males when drop out from school they tend to have own work earlier to cover their financial demands in spite of their health status so it can cause adverse outcomes on their quality of life. This result disagreed with a study which showed that patient age, level of education, and employment status haveno relationship with their quality of life level^(11,14). While a study about patients with IBS showed a significant association with their marital status¹³.

Conclusion

The study showed psychological, social and environmental domains more affected on adolescents' quality of lifewho diagnosed with ISB.

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the College of Nursing, University

of Baghdad and all experiments were carried out in accordance with approved guidelines.

References

1. Irritable Bowel Syndromeat Dorland's Medical Dictionary, available from http://en.wikipedia.org/wiki/Dorland%27s_Medical_Dictionary
2. Malagelada JR, Malagelada C. Mechanism-Oriented Therapy of Irritable Bowel Syndrome. *Advances In Therapy*. 2016;33(6):877-893. doi:10.1007/s12325-016-0336-3: P.P. 57–63.
3. Chey WD, Kurlander J, Eswaran S. Irritable bowel syndrome: a clinical review. *JAMA*. 2015; 313(9):949-958. doi: 10.1001/jama. 2015.0954. 2812–9.
4. Talley N: Irritable bowel syndrome. In: Feldman M, Friedman LS, Brandt LJ, eds. *Sleisenger & Fordtran's Gastrointestinal and Liver Disease*. 9th ed. Philadelphia, Pa: Saunders Elsevier; 2010;118.
5. Irritable bowel syndrome, The National Digestive Diseases Information Clearinghouse. <http://digestive.niddk.nih.gov/ddiseases/pubs/ibs/ibs.pdf>. Accessed June 7, 2011.
6. Knowles SR, Austin DW, Sivanesan S, et al. Relations between symptom severity, illness perceptions, visceral sensitivity, coping strategies and well being in irritable bowel syndrome guided by the common sense model of illness. *Psychology, Health & Medicine*.2017;22(5): 524-534. doi:10.1080/13548506.
7. Frequently asked questions, International Foundation for Functional Gastrointestinal Disorders. <http://www.aboutibs.org/site/about-ibs/faq>. Accessed June 7, 2011.
8. Graham DP, Savas L, White D, et al. Irritable bowel syndrome symptoms and health related quality of life in female veterans. *Alimentary Pharmacology & Therapeutics*. 2010;31(2):261-273. doi:10.1111/j.1365-2036. P.P. S3-S11.
9. Penny KI, Smith GD. The use of data-mining to identify indicators of health-related quality of life in patients with irritable bowel syndrome. *Journal of Clinical Nursing*. 2012;21(19-20):2761-2771. doi:10.1111/j. 03897; 119: P.P.654-660.
10. Heitkemper MM. Evidence-based treatments for irritable bowel syndrome with constipation. *Journal of Family Practice*. May 2009;S13-S20. <https://search-ebSCOhost-com.ezproxy.okcu.edu/login>.

- aspxdirect=true & db=pbh & AN=40127253 & site=ehost-live.
11. Irritable bowel syndrome, NIH Publication September 2007;07-693.. The National Digestive Diseases Information Clearinghouse (NDDIC).
 12. RuepertL, et al. Bulking agents, antispasmodics and antidepressants for the treatment of irritable bowel syndrome, Cochrane Database of Systematic Reviews 2011;8.
 13. KajanderK,et al.: A probiotic mixturealleviates symptoms in irritable bowel syndromepatients: a controlled 6-month intervention *Alimentary Pharmacology & Therapeutics*, 2005; 22(5):387-394
 14. Noorbala AA, BagheriYazdi SA, Faghihzadeh S, et al. A Survey on Mental Health Status of Adult Population Aged 15 and above in the Province of East Azarbaijan, Iran. *Archives Of Iranian Medicine*. 2017; 20(11 Suppl. 1):S23-S26.<https://search-ebscohost-com.ezproxy.okcu.edu/login.aspx?direct=true & db=mnh & AN=29481121 & site=e host-live.184:P.P.70-73>.
 15. GregW.: Smoking and Irritable Bowel Syndrome, Posted by HealthStatus/November 17th, 2009.
 16. NicksJ.: Alcohol and Irritable Bowel Syndrome, Buzzle | Privacy Policy, 2012 Buzzle.com.
 17. Wald A.: Pathophysiology of irritable bowel syndrome, Available from <http://www.uptodate.com/home/index.html>. Accessed June 7, 2011.
 18. Spiller R, Ching Lam. An Update on Post-infectious Irritable Bowel Syndrome: Role of Genetics, Immune Activation, Serotonin and Altered Microbiome. *Journal of Neurogastroenterology & Motility*. 2012;18(3): 258-268. doi:10.5056/jnm.18.3.258.:P.P. 13-7.

An Estimation for the Association between the C–RP Tests and RF Tests of Rheumatoid Condition Patients with their Demographic Data. In Maysan Province, Iraq

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Abstract

The present study aims to achieve the following objectives to assessment rheumatic arthritis patients in Maysan Governorate, an influence of the gender and age on the rheumatic arthritis and an effectiveness of the geographical areas (urban,rural) on the incidence of rheumatic. The data were collected between the (January to August 2016)Al-Sadder Teaching hospital in Maysan province and the total number of serum samples were (314).The study's data were analyzed through the use of Statistical processing, with program SPSS 20.0, Sigma Stat 2.03, Sigma Plot 2000, Med Calc and Excel 2010 and the blood samples were collected from patients aged (13–61years) (for both genders) and also from different areas in Maysan governorate, all blood samples were collected from people suspected having arthritis due to they had symptoms of diseases with pain,the rheumatic factor and C–reactive protein (CRP)were evaluated by latex agglutination test. The data analysis revealed that the majority of the patients about 27.4% in the study samples at age group (31-40 year. The chi-squared distribution is applied in hypothesis testing and to a minimum range for confidence intervals for population difference when the underlying distribution is normal.

Keywords: C-reactive protein (CRP), Rheumatoid factors (RF) and chi-squared distribution.

Introduction

Rheumatoid arthritis (RA) is an autoimmune disease in which the immune system of body which generally protects its health by attacking bacteria and viruses and others as foreign substances, attacks the joints via mistakenly. This creates inflammation that causes the tissue that lines the into of joints (the synovium) to be thicken, resulting in pain and swelling around the joints. The lubrication joints and helping them move smoothly by synovium makes a fluid^(2,4,1). The elastic tissue that covers the ends of bones in a joint, as well as the bones themselves have damage when the inflammation goes unchecked. Moreover, there is loss of cartilage and the joint spacing among bones may become smaller, joints can become painful, stable and lose their ability to move. Joint distortion also can occur, the damage of the joint none reversed, doctors recommend early diagnosis and aggressive treatment to control RA because it can occur early^(3,8). Clinical aspects of Rheumatoid arthritis

differ, ordinarily reflecting the severity and stage of the disease. Joint pain, erythema, warmth, swelling, and lack of function are classic⁹. Palpation of the joints appears spongy or boggy tissue. Often fluid can be aspirated from the inflamed joint². Peculiarly, the pattern of joint participation initiate with the small joints in the hands, wrists, and feet. The Rheumatoid arthritis can influence the body beyond the joint, such as blood anemia, blood vessels, eyes, skin, and lungs, the outer lining of the heart muscle (myocardium) and the heart (pericardium), also People with RA are more prone to risk of myocardial infraction (heart attack), atherosclerosis and stroke is markedly increased⁵. The risk factors for RA are inclusive genetic agents which (donate 50% to 60% of the risk of progressing rheumatoid arthritis¹⁰. Age and gender, the rheumatoid arthritis is far more prevalent in women than in men, the female-to-male ratio being (3:1)⁴. Nevertheless, the mechanism by which gender effects the vulnerability to rheumatoid arthritis remains

unclear, infections; several microorganisms have been involved in the expansion of RA based higher titers of the related antibodies in patients with rheumatoid arthritis. One prospect is that these microorganisms excite the expansion of rheumatoid arthritis in persons who carry genetic vulnerability agents to the disease⁵, lifestyle, environmental agents, health and social outcomes^(4, 5). Rheumatoid factor (RF) is the autoantibody that was first set up in rheumatoid arthritis (RA). It is clarifying as an antibody opposed to the Fc portion of IgG and different rheumatoid factors can recognize various portions of the IgG-Fc. RF and IgG join to shape immune complexes that donate to the disease process⁶. Rheumatoid factor can be either monoclonal IgM to polyclonal IgG (type 2) or polyclonal IgM to polyclonal IgG (type 3). Although essentially encountered as IgM, rheumatoid factor (RF) may form of any isotype of immunoglobulins^(7, 6). Rheumatoid factor (RF) is frequently estimated in individual suspected of having any shape of arthritis even though positive outcomes can be due to other reasons, and negative outcomes do not cancel disease. But, in integration with signs and symptoms, it can play a function in both diagnosis and disease prognosis⁴. It is part of the usual disease gauge of rheumatoid arthritis (RF). The presence of (RF) in serum can also mark the appearance of doubtful autoimmune activity detached to rheumatoid arthritis, such as that related with tissue or organ refusal⁷. In such cases, RF can avail as one of diverse serological signs for autoimmunity¹¹. RFs may also be a marker of other autoimmune diseases, such as, definite infections, juvenile arthritis and some types of cancer¹. RF also take place in other deficiency. As a representation, some connective tissue diseases, such as primary Sjögren's syndrome and systemic lupus erythematosus (SLE), may be related with the existence of RF. In addition, RF levels may be raised in individuals with specific infections, such as rubella, malaria and hepatitis C⁸. The grades of RF raise with age, and positive reactions can be found in aged in women^(9,8). Rheumatoid factors are proteins created by the immune system. Typically, the immune system assault disease-causing substances like bacteria and viruses. Rheumatoid factors assault glands, healthy joints or other normal cells by fault. The susceptibility of RF for determined RA is only 60-70% with a specificity of 79%¹¹. C-reactive protein (CRP) is an acute-phase protein that avail as an early sign of infection or inflammation. The

c-reactive protein is synthesized in the organ of liver and is typically establish at concentrations of less than 10 mg/L in the blood. In the course of inflammatory disease states, CRP levels increase quickly within the first 6 to 8 hours and top at levels of up to 345–400 mg/L after 48 hours. A rise or growing levels of CRP submits have an acute infection (inflammation) in the patient¹⁸. The CRP test is not definite sufficient to detect a particular type of arthritis^(5,13).

Materials and Method

The data were collected between the (January to August 2016) and the blood samples were collected from (314) patients age (13 – 61 years) (for both gender) from the serological unite in Al-Sadder teaching hospital. also from different areas in Maysan governorate like AL- Hussein Q, AL- Majddia Q, AL-Ascarry Q, AL-Qadisea Q, Abo Romana Q, Al-Risala Q. RF and CRP were estimated by latex agglutination test, rely on indirect agglutination of latex particles covered with monoclonal anti-CRP antibody and human IgG, respectively. The analysis results were used to detect the findings according to CRP and RF as the follow

C-Reactive Protein: The slide agglutination test (CRP-latex) for the semi- quantitative and qualitative discovery of C - reactive protein in human serum. Particles with goat IgG anti-human are when blended with samples including C - reactive protein; the CRP concentration can increase up to 350 in 12-24 hours. Through tissue necrosis and inflammation arise from microbial infections

Rheumatoid Factor (RF): The slide agglutination test (RF-latex) for the semi quantitative and qualitative discovery of rheumatoid factor (RF) in patient serum. Latex particles covered with human gamma globulin are agglutinated when blended with samples including rheumatoid factor (RF).

Statistical Data Analysis: The study's facts were resolved through the statistical working has been drove out with program SPSS 20.0, MedCalc, Sigma Plot 2000, Sigma Stat 2.03 and Excel 2010. Statistical treatment has assisted us in interpretative analysis, whereas statistical parameters have assisted us to define the range index, standard error, arithmetic median, standard deviation, and confidence interval with precision 95% (95% CI).

Results

Table (1): Association between the C – Reaction Protein tests of individuals.

Criteria	Age Group		C – Reaction Protein				Chi-Square
			Negative	Positive	None Test	Total	
Age	11-20	F	46	15	3	64	$X^2_{\text{observ}} = 35.181$ Critic = 18.13 df = 10 P = 0.000 HS
		%	14.6%	4.8%	1.0%	20.4%	
	21-30	F	38	17	2	57	
		%	12.1%	5.4%	0.6%	18.2%	
	31-40	F	57	19	10	86	
		%	18.2%	6.1%	3.2%	27.4%	
	41-50	F	44	21	15	80	
	%	14.0%	6.7%	4.8%	25.5%		
	51-60	F	10	5	10	25	
	%	3.2%	1.6%	3.2%	8.0%		
	61 and more	F	0	2	0	2	
	%	0.0%	0.6%	0.0%	0.6%		
Total	F	195	79	40	314		
	%	62.1%	25.2%	12.7%	100.0%		
Gender	Male	F	69	22	11	102	$X^2_{\text{observ}} = 1.975$ Critic = 2.920 df = 2 P = 0.372 NS
	%	22.0%	7.0%	3.5%	32.5%		
	Female	F	126	57	29	212	
	%	40.1%	18.2%	9.2%	67.5%		
Total	F	195	79	40	314		
	%	62.1%	25.2%	12.7%	100.0%		
Residency	Urban	F	188	77	38	303	$X^2_{\text{observ}} = 0.490$ Critic = 2.920 df = 2 P = 0.783 NS
	%	59.9%	24.5%	12.1%	96.5%		
	Rural	F	7	2	2	11	
	%	2.2%	0.6%	0.6%	3.5%		
	Total	F	195	79	40	314	
	%	62.1%	25.2%	12.7%	100.0%		

Table (1) indicates there was a high significant relationship between C – Reaction protein of patients with their age at confidence interval ($P < 0.05$), while

show there are no significant relationship between C – Reaction protein with gender and residency at confidence interval ($P > 0.05$) when analyzed by chi-square test.

Table (2): Association between the Rheumatoid Factors tests of individuals.

Criteria	Age Group		Rheumatoid Factors				Chi-Square
			Negative	Positive	None Test	Total	
Age	11-20	F	52	1	11	64	$X^2_{\text{observ}} = 20.717$ Critic=1.812 df= 10 P=0.023 S
		%	16.6%	0.3%	3.5%	20.4%	
	21-30	F	41	5	11	57	
		%	13.1%	1.6%	3.5%	18.2%	
	31-40	F	65	6	15	86	
		%	20.7%	1.9%	4.8%	27.4%	
	41-50	F	61	10	9	80	
		%	19.4%	3.2%	2.9%	25.5%	
	51-60	F	16	6	3	25	
		%	5.1%	1.9%	1.0%	8.0%	
61 and more	F	0	1	1	2		
	%	0.0%	0.3%	0.3%	0.6%		
Total	F	235	29	50	314		
	%	74.8%	9.2%	15.9%	100.0%		
Gender	Male	F	78	6	18	102	$X^2_{\text{observ}} = 2.175$ Critic= 2.920 df= 2 P=0.337 NS
		%	24.8%	1.9%	5.7%	32.5%	
	Female	F	157	23	32	212	
		%	50.0%	7.3%	10.2%	67.5%	
Total	F	235	29	50	314		
	%	74.8%	9.2%	15.9%	100.0%		
Residency	Urban	F	226	28	49	303	$X^2_{\text{observ}} = 0.409$ Critic=2.920 df= 2 P=0.815 NS
		%	72.0%	8.9%	15.6%	96.5%	
	Rural	F	9	1	1	11	
		%	2.9%	0.3%	0.3%	3.5%	
	Total	F	235	29	50	314	
	%	74.8%	9.2%	15.9%	100.0%		

Table (2) indicates there was a significant relationship between rheumatoid factors of the patients with their age at confidence interval ($P < 0.05$), while show there are no significant relationship between rheumatoid factors tests with gender and residency at confidence interval ($P > 0.05$) when analyzed data by chi-square test.

Discussion

This study has been done to summarize and evaluate of rheumatoid arthritis and its distribution according to socio- demographic data with estimate the association between the C-RP tests and RF tests of patients with their demographic information. The level of education of individuals didn't play function in the happening of rheumatoid arthritis. The data analysis revealed the

majority of RA patients are 27.4% at age group (31-40 years), this result agrees with a study conducted by^(18, 16). Also due to the peak age of infected in the universal is between (35 to 45 years) with geographic variances, this agree with study. Most of infected are from females about (67%) more than males which agree with study by¹³, the residence have high effects due to the majority of the patients about 96.5% are from urban regions reverse the rural regions which have agree with study by¹⁵ he have been showed a prevalence of RA among urban Europeans, while rural groups showed much lower prevalence, in our research have dominated patients from urban areas. The study has been showed the majority of patients have C-reaction protein tests presented negative results (62.1%), as well as negative results (74.8%) of

rheumatoid factor which have agree with study by^(16, 17) and the date of incidence distribution of RA diseases annually most occur in June month (27.4%) of the study sample. Table 1 present that the majority of CRP test positive reaction increased in aged (41-50 years) via (6.7%), Also this table indicates there was a high significant correlation between c- reactive protein in the gender with their age at ($P < 0.05$) and the reverse significant correlation between c- reactive protein in the gender with residency ($P > 0.05$) when analyzed by chi-square test. These data have agreement with study by^(12, 13, 18). According to the results in (table 2), which have been revealed the majority of the patients with age (41-50 years) via (3.2%) as positive reaction, this indicates there are a substantial links between rheumatoid factors test in the patients with their age at ($P < 0.05$) but there are no significant relationship between rheumatoid factors test with their gender and residency by ($P > 0.05$), when analyzed by chi-square test. This study is agreement with study by^(14, 11).

Conclusion:

According to the results in tables, the recent study concluded the followings: Most of patient with rheumatoid arthritis (RA) at ages were ranging (31-40) years old with (27.4%), the females are more susceptible for infecting with rheumatoid arthritis (RA) than males by (67.5%). The majority of patients (96.5%) of the study samples were living in urban and therefore they have positive reaction of (CRP) and (RF), also both of reaction have increase with age.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Basic medical science department/Nursing and all experiments were carried out in accordance with approved guidelines.

References

1. ADAMSA, BOJARA W, SCHUNK K. Early Diagnosis and Treatment of Coronary Heart Disease in Asymptomatic Subjects With Advanced Vascular Atherosclerosis of the Carotid Artery (Type III and IV b Findings Using Ultrasound) and Risk Factors. *Cardiology research*, 2018;9:22-27.
2. AJ LB. The first description of rheumatoid arthritis. Unabridged text of the doctoral dissertation presented in 1800. *Joint Bone Spine*, 2001;68:130-143.
3. APPELBOOMT, DE BOELPAEPEC, E EHRlich G, P FAMA EY J. Rubens and the Question of Antiquity of Rheumatoid Arthritis. 1981.
4. BAX D. Rheumatoid Arthritis—Plan to Win. Edited by C. Koehn, T. Palmer and J. Esdaile. £19.99. Oxford University Press, Cary, NC, USA, 2003; 284. ISBN 0-951-3056-1.
5. BUCH M, EMERY P. The aetiology and pathogenesis of rheumatoid arthritis. *HOSPITAL PHARMACIST-LONDON-*, 2002;9:5-10.
6. CUSHJJ, KAVANAUGH A, WEINBLATM E. Rheumatoid arthritis: early diagnosis and treatment, Professional Communications. 2010.
7. DEQUEKER J, RICO H. Rheumatoid Arthritis—like Deformities in an Early 16th-Century Painting of the Flemish-Dutch School. *JAMA*, 1992;268: 249-251.
8. HAYFC, WESTWOOD OMR, NELSONPN. Rheumatoid factors: what’s new? *Rheumatology*, 2006;45: 379-385.
9. KATZRS. Rheumatoid Arthritis: Etiology, Diagnosis, Management. *JAMA*, 1986;255: 3313-3313.
10. KILPATRICKJM, VOLANAKIS JE. Molecular genetics, structure, and function of C-reactive protein. *Immunologic research*, 1991;10:43-53.
11. NATIONAL COLLABORATING CENTRE FOR CHRONIC C. Rheumatoid arthritis: national clinical guideline for management and treatment in adults, Royal College of Physicians of London. 2009.
12. ROTHSCHILDB, ROTHSCHILDC, HELBLING M. Unified theory of the origins of erosive arthritis: Conditioning as a protective/directing mechanism? 2003.
13. SAITOI, SATOS, NAKAMURA M. A low level of C-reactive protein in Japanese adults and its association with cardiovascular risk factors: The Japan NCVC-Collaborative Inflammation Cohort (JNIC) Study. *Atherosclerosis*, 2007;194: 238-244.
14. SCOTT DL. Prognostic factors in early rheumatoid arthritis. 2000.

15. SILMAN AJ. Problems complicating the genetic epidemiology of rheumatoid arthritis. *The Journal of rheumatology*, 1997;24:194-196.
16. VOICEAG. *European Action Towards Better Musculoskeletal Health*. 2005.
17. YOUNGA, DIXEYJ, COX N, DAVIES P. How does functional disability in early rheumatoid arthritis (RA) affect patients and their lives? Results of 5 years of follow-up in 732 patients from the Early RA Study (ERAS). *Rheumatology*, 2000;39:603-611.
18. YOUNG B, GLEESON M, CRIPPS A. *C-Reactive Protein: A Critical Review*. 1991.

The Value of Surfactant Therapy in Preterm Neonates with Respiratory Distress Syndrome

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Abstract

The current study was planned and conducted to evaluate the use of surfactant therapy in preterm neonates with respiratory distress in Al-Diwaniyah Maternity and Children Teaching Hospital. The present cohort study included 186 preterm neonates who were randomly selected from the pool of neonates admitted to Al-Diwaniyah Maternity and children teaching hospital, Al-Diwaniyah province, Iraq. There was no significant association between frequency of other complications and treatment method whether prophylactic, early rescue and late rescue ($P > 0.05$). Morbidity was significantly higher in prophylactic method in comparison to early rescue method ($P = 0.002$); and also it was higher than that seen in association with late rescue method with a borderline significant level ($P = 0.073$). Mortality was also significantly associated with less gestational age ($P < 0.001$). The rate of complications was significantly less in continuous positive air pressure (CPAP) ventilation method in comparison with mask method ($P = 0.006$). Sepsis and BPD were significantly less frequent in CPAP method ($P < 0.05$); whereas, nasal trauma, and air leaks were significantly less in mask method ($P < 0.05$).

Keywords: *Surfactant therapy, preterm neonates, RDS.*

Introduction

In modern obstetric practice, full term newborn is considered when delivery happens after the fetus has completed 37 weeks of gestation. However, a significant number of pregnancies end before this point of gestational period and the condition is going to be labeled as preterm labor⁽¹⁻⁴⁾. Several predisposing factors are frequently associated with preterm labor, such as infection, placenta previa, substance use, placental abruption, inadequate prenatal care, stress, smoking, maternal age < 18 or > 40 , low body mass index, polyhydramnios, oligohydramnios, fetal growth restriction, fetal anomaly, poor nutrition, premature preterm rupture of membranes (PPROM) and other factors⁽⁵⁻¹²⁾. Preterm birth is certainly to be accompanied by the problem of prematurity and respiratory distress (1-5). Other less common complications associated with preterm labor include intraventricular hemorrhage, sepsis and necrotizing enterocolitis^(13, 14). The presence of PPRM may be, in particular, associated with intrauterine inflammation and subsequent neurological

insults^(15, 16), besides, increased risk of accidents due to umbilical cord¹⁷. The principal cause of respiratory failure in preterm infants is respiratory distress syndrome (RDS) which was previously called “hyaline membrane disease”; however, because of its clear association with surfactant deficiency, its new name “RDS” becomes widely accepted in clinical practices¹⁸. The list of causes that are accompanied by respiratory distress in newborn is relatively long, but pulmonary causes, in particular, are often due to some underdevelopment of respiratory system which is a common manifestation of preterm labor (1-4). Indeed, from embryologic perspective, lung passes through five stages of development and preterm labor is often associated with underdevelopment of later stages¹⁹.

The incidence and the associated complications accompanying respiratory distress syndrome have been greatly reduced with the use of antenatal corticosteroids and postnatal surfactant therapy. Lung compliance and oxygenation have been shown to be greatly enhanced following exogenous surfactant administration which

has led to marked reduction in the incidence of pneumothorax and mortality associating RDS^(20, 21). Nevertheless, a clear consensus about the magnitude of benefit of postnatal surfactant use in premature infants is lacking in available published articles. In addition, the rarity of Iraqi literatures disclosing this benefit has justified the conductance of the current study. For those reasons, the currents study was planned and conducted to evaluate the use of surfactant therapy in preterm neonates with respiratory distress in Al-Diwaniyah Maternity and Children Teaching Hospital.

Patients and Method

The present cohort study included 186 preterm neonates who were randomly selected from the pool of neonates admitted to Al-Diwaniyah Maternity and children teaching hospital, Al-Diwaniyah province, Iraq. The study started on January 2018 and ended on June 2019. The main variables included in the study were gestational age, gender, mode of delivery, number of births, time of taking surfactant, neonatal complications and mortality.

Medical intervention was in the form of surfactant administration using prophylactic, early rescue and late rescue method. Verbal consent was obtained from parents and the study was approved by institutional ethical approval committee.

Obtained data were transformed into SPSS (version 23) spread sheet. Categorical data were expressed as number and percentage. Chi-square test and Yates correction were used to study association between categorical variables. The level of significance was considered at $P \leq 0.05$.

Results

The general characteristics of neonates enrolled in the current study are shown in table 1. Complications that have been encountered are demonstrated in table 2. The most common complication was sepsis, followed by nasal trauma, air leak, pulmonary hemorrhage, patent ductus arteriosus and bronchopulmonary dysplasia.

Sepsis was significantly more in prophylactic mode in comparison to early rescue ($P = 0.024$) and to late rescue ($P = 0.005$); however, there was no significant difference in the frequency of sepsis between early and late rescue method ($P = 0.294$), as shown in table 3.

There was no significant association between frequency of other complications, namely nasal trauma, air leak, pulmonary hemorrhage and patent ductus arteriosus, and treatment method whether prophylactic, early rescue and late rescue ($P > 0.05$), as shown in table 3.

Mortality was significantly higher in prophylactic method in comparison to early rescue method ($P = 0.002$); and also it was higher than that seen in association with late rescue method with a borderline significant level ($P = 0.073$); however, there was no significant difference in mortality rate between early and late rescue method ($P = 0.575$), as shown in table 4. Mortality was also significantly associated with less gestational age ($P < 0.001$), as shown in table 5.

In general the rate of complications was significantly less in continuous positive air pressure (CPAP) ventilation method in comparison with mask method ($P = 0.006$). In particular, sepsis and BPD were significantly less frequent in CPAP method ($P < 0.05$); whereas, nasal trauma, and air leaks were significantly less in mask method ($P < 0.05$), as shown in table 6.

Table 1: General characteristics of the study sample

Characteristic	n	%
Total number	186	100.0
Gestational age (weeks)		
24 - 28	44	23.7
28-32	58	31.2
32-37	84	45.2
Gender		
Male	118	63.4
Female	68	36.6
Mode of delivery		
Cesarean section	112	60.2
Normal vaginal delivery	74	39.8
Number of birth		
Single	146	78.5
Twin	39	21.0
Triplets	1	0.5
Time of Taking of Surfactant		
Prophylactic	84	45.2
Early rescue	72	38.7
Laterescue	30	16.1

Table 2: Frequency distribution of neonates according to complications

Complication	n	%
Sepsis	85	45.7
Nasal trauma	38	20.4
Air leaks	25	13.4
Pulmonary hemorrhage	15	8.1
PDA	10	5.4
BPD	8	4.3
No complication	50	26.9

PDA: patent ductus arteriosus; BPD: bronchopulmonary dysplasia

Table 3: Association between method of surfactant administration and complications

Complication	Prophylactic n = 84		Early rescue n = 72		Late rescue n = 30		P1	P2	P3
	n	%	n	%	n	%			
Sepsis	58	68.2	37	51.4	15	50.0	0.024*	0.005**	0.294
Nasal trauma	12	14.1	14	19.4	7	23.3	0.389	0.254	0.658
Air leaks	8	9.4	10	13.9	6	20.0	0.395	0.239	0.635
Pulmonary hemorrhage	6	7.1	5	6.9	2	6.7	0.952	1.000	1.000
PDA	2	2.4	2	2.8	3	10.0	1.000	0.219	0.300

*significant at $P \leq 0.05$; ** highly significant at $P \leq 0.01$

Table 4: Outcome according to method of administration

Outcome	Prophylactic n = 84		Early rescue n = 72		Late rescue n = 30		P1	P2	P3
	n	%	n	%	n	%			
Alive	40	47.6	52	72.2	20	66.7	0.002 **	0.073	0.575
Dead	44	52.4	20	27.8	10	33.3			

** highly significant at $P \leq 0.01$

Table 5: Outcome according to gestational age

Gestational age (week)	Total	Alive		Dead		P
		n	%	n	%	
24-28	44	12	27.3	32	72.7	< 0.001**
28-32	58	36	62.1	22	37.9	
32-37	84	64	76.2	20	23.8	

** highly significant at $P \leq 0.01$

Table 6: Outcome according to ventilation mode

Complication	CPAP n = 54		MV n = 132		P
	n	%	n	%	
Sepsis	25	46.3	92	69.7	0.003 **
Nasal trauma	16	29.6	18	13.6	0.010 **
Air leaks	21	38.9	24	18.2	0.003 **
Pulmonary hg	2	3.7	8	6.1	0.773
PDA	2	3.7	7	5.3	0.932
BPD	4	7.4	1	0.8	0.041 *
No Complication	22	40.7	28	21.2	0.006 **

CPAP; continuous positive air pressure; MV: mask ventilator; PDA: patent ductus arteriosus; BPD: bronchopulmonary dysplasia; *significant at $P \leq 0.05$; ** highly significant at $P \leq 0.01$

Discussion

The current study was conducted to evaluate the role of surfactant in reducing both mortality and morbidity rates in association with preterm infants and RDS. In particular, the main goals were to find which method of surfactant administration is associated with less morbidity and mortality.

We were able to demonstrate that mortality rate was significantly less in association with both early and late rescue method than with prophylactic method. Sepsis was also significantly less frequent in association with both early and late rescue method than with prophylactic method. It has been claimed that the use of prophylactic surfactant may reduce mortality rate in preterm infants; however, the introduction of antenatal steroid strategy and early positive air pressure has changed this claim because of the significant reduction in mortality rate with later two measures²². In one study, it has been found that both prophylactic surfactant and early rescue are equi-effective in reducing mortality and morbidity with no significant variation between both methods²². However, we found, on the contrary, that early rescue is even better than prophylactic surfactant. It is worth to mention that “prophylactic surfactant administration has a disadvantage in that it requires intubation and can lead to over-treatment of preterm infants who may not be prone to developing RDS”²². Moreover, a meta-analysis has shown that prophylactic surfactant is no more superior to early or late rescue method²³, in support for our findings.

In the current study, we found that early rescue is not superior to late rescue method, a finding that is in contrary to the findings of other authors²⁴. Besides, our findings are dissimilar to that of Bahadue and Soll who found that the rate of complications is significantly lower in case of early rescue treatment method²⁵.

The current study also showed that CPAP is preferred to mask method ventilation. In conclusion, late and early rescue method are better than prophylactic method in terms of morbidity and mortality and the use of continuous positive air pressure is preferred to mask method with respect to surfactant administration in preterm infants.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Al-Diwaniyah Maternity and Children Teaching Hospital/Al-Diwaniyah Province, Iraq and all experiments were carried out in accordance with approved guidelines.

References

1. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics. Practice Bulletin No. 171: Management of Preterm Labor. *Obstet Gynecol.* 2016;128(4):e155-64.
2. Quinn JA, Munoz FM, Gonik B, et al. Preterm birth: Case definition & guidelines for data collection, analysis, and presentation of immunisation safety data. *Vaccine.* 2016;34(49):6047–6056.
3. Romero R, Dey SK, Fisher SJ. Preterm labor: one syndrome, many causes. *Science.* 2014;345(6198):760–765.
4. Lawn JE, Davidge R, Paul VK, et al. Born too soon: care for the preterm baby. *Reprod Health.* 2013;10 Suppl 1(Suppl 1):S5.
5. Halimi AA, Safari S, Parvareshi Hamrah M. Epidemiology and Related Risk Factors of Preterm Labor as an obstetrics emergency. *Emerg (Tehran).* 2017;5(1):e3.
6. Ahumada-Barrios ME, Alvarado GF. Risk Factors for premature birth in a hospital. *Rev Lat Am Enfermagem.* 2016;24:e2750.
7. Leal MD, Esteves-Pereira AP, Nakamura-Pereira M, et al. Prevalence and risk factors related to preterm birth in Brazil. *Reprod Health.* 2016;13(Suppl 3):127.
8. Alijahan R, Hazrati S, Mirzarahimi M, Pourfarzi F, Ahmadi Hadi P. Prevalence and risk factors associated with preterm birth in Ardabil, Iran. *Iran J Reprod Med.* 2014;12(1):47–56.
9. Leonard SA, Crespi CM, Gee DC, Zhu Y, Whaley SE. Prepregnancy Risk Factors for Preterm Birth and the Role of Maternal Nativity in a Low-Income, Hispanic Population. *Matern Child Health J.* 2015;19(10):2295–2302. doi:10.1007/s10995-015-1748-4
10. Leneuve-Dorilas M, Favre A, Louis A, Bernard S, Carles G, Nacher M. Risk Factors for Very Preterm Births in French Guiana: The Burden of Induced Preterm Birth. *AJP Rep.* 2019;9(1):e44–e53.
11. Zhang YP, Liu XH, Gao SH, et al. Risk factors for

- preterm birth in five Maternal and Child Health hospitals in Beijing. *PLoS One*. 2012;7(12):e52780.
12. Dekker GA, Lee SY, North RA, McCowan LM, Simpson NA, Roberts CT. Risk factors for preterm birth in an international prospective cohort of nulliparous women. *PLoS One*. 2012;7(7):e39154.
 13. Berekatain B, Saraeian S, Farghadani M, et al. Effect of Vitamin E in Prevention of Intraventricular Hemorrhage in Preterm Neonates. *Int J Prev Med*. 2018;9:97.
 14. Griffin JB, Jobe AH, Rouse D, McClure EM, Goldenberg RL, Kamath-Rayne BD. Evaluating WHO-Recommended Interventions for Preterm Birth: A Mathematical Model of the Potential Reduction of Preterm Mortality in Sub-Saharan Africa. *Glob Health Sci Pract*. 2019;7(2):215–227.
 15. Armstrong-Wells J, Donnelly M, Post MD, Manco-Johnson MJ, Winn VD, Sébire G. Inflammatory predictors of neurologic disability after preterm premature rupture of membranes. *Am J Obstet Gynecol*. 2015;212(2):212.e1–212.e2129.
 16. Menon R, Richardson LS. Preterm prelabor rupture of the membranes: A disease of the fetal membranes. *Semin Perinatol*. 2017;41(7):409–419.
 17. Caughey AB, Robinson JN, Norwitz ER. Contemporary diagnosis and management of preterm premature rupture of membranes. *Rev Obstet Gynecol*. 2008;1(1):11–22.
 18. Dyer J. Neonatal Respiratory Distress Syndrome: Tackling A Worldwide Problem. *P T*. 2019;44(1):12–14.
 19. Schittny JC. Development of the lung. *Cell Tissue Res*. 2017 Mar;367(3):427-444.
 20. Altirkawi K. Surfactant therapy: the current practice and the future trends. *Sudan J Paediatr*. 2013;13(1):11–22.
 21. Niemarkt HJ, Hütten MC, Kramer BW. Surfactant for Respiratory Distress Syndrome: New Ideas on a Familiar Drug with Innovative Applications. *Neonatology*. 2017;111(4):408–414.
 22. Chun J, Sung SI, Ho YH, et al. Prophylactic versus Early Rescue Surfactant Treatment in Preterm Infants Born at Less than 30 Weeks Gestation or with Birth Weight Less than or Equal 1,250 Grams. *J Korean Med Sci*. 2017;32(8):1288–1294.
 23. Rojas-Reyes MX, Morley CJ, Soll R. Prophylactic versus selective use of surfactant in preventing morbidity and mortality in preterm infants. *Cochrane Database Syst Rev*. 2012;CD000510.
 24. Kim SM, Park YJ, Chung SH, Choi YS, Kim CH, Bae CW. Early prophylactic versus late selective use of surfactant for respiratory distress syndrome in very preterm infants: a collaborative study of 53 multi-center trials in Korea. *J Korean Med Sci*. 2014;29:1126–1131.
 25. Bahadue FL, Soll R. Early versus delayed selective surfactant treatment for neonatal respiratory distress syndrome. *Cochrane Database Syst Rev* 2012;11:CD001456.

The Role of Faith Healer Visits in the Management and Prognosis of Mental Illness in Iraq

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Abstract

Background: Mental illnesses denote to disorders generally characterized by abnormalities of mood, thought, and/or behavior. Different attitudes toward mentally ill individuals were found among families, ethnicities and countries, the cultural and religious beliefs often affect the opinions about the nature and the origin of mental illness and even influence the attitude toward those who have mental illness.

Objectives: To investigate and document the rate of mentally ill patients who are visiting the faith healers and the effect of that visit on the management of their condition.

Method: This is a cross sectional study was done in Merjan Teaching Hospital during the period from November 2017 till February 2018 . The sample composed of 187 mentally ill patients (80 males and 107 females). A semi-structured questionnaire was used for information into socio-demographic data and questions about the visit to faith healers (time of the visit, the effect of the visit on the management, source of referral to the faith healer and if the money given or not). Diagnosis of mental illness was made according to DSM-V.

Results: 57.2% of the patients in the present study were females, 61% of the patients were married. 41.2% of our sample completed secondary school and 52.9% of them were unemployed. (74.3%) of patients had history of visit to faith healer. 25.1%, 22.5% and 19.4% were diagnosed as schizophrenia spectrum and other psychotic disorders, anxiety disorders and depressive disorders respectively. The visit to the faith healers was adversely affecting the compliance of mentally ill patients to their medications in about 76.3% of our sample. There was no significant association between history of visit to faith healers and type of psychiatric disease.

Keywords: *Mental illness, faith healers, management.*

Introduction

Mental illnesses denote to disorders generally characterized by abnormalities of mood, thought, and/or behavior, as recognized by the Diagnostic and Statistical Manual, 4th edition, of the American Psychiatric Association (DSM-IV). Mental illness is usually not culturally appropriate. It is associated with disability or distress and not merely a conflict between the individual and culture. Many people have a fear from mental illness and they stigmatize those who are affected by it. The reasons for that view originating from the idea that mentally ill patients cannot control their own behavior and that they may act in strange and possibly aggressive

ways ¹. Stigma can affect the compliance of mentally ill individuals, it prevents him from seeking treatment, finding a job, and living successfully in his culture. To improve the state of mental health around the world, the World Health Organization (WHO) cited advocacy against stigma and discrimination, as it is one of the major barrier to overcome in the community ². Different attitudes toward mentally ill individuals were found among families, ethnicities and countries, the cultural and religious beliefs often affect the opinions about the nature and the origin of mental illness and even influence the attitude toward those who have mental illness, so it is mandatory to understand the cultural beliefs about

mental illness in order to offer effective mental health services³ Many cultures widely believed that mental illness was attributed to the magical forces, Gods anger or the result of supernatural phenomena such as spiritual or evil possession. Treatment of mental illness date back to ancient cultures and was focusing on the method by which they can use to defeat these evil forces or remove the curse. A crude stone instruments was used to made a hole through the skull. It was believed that through this opening the evil spirits thought to be inhabiting patient’s head and causing their psychopathology will leave and the individual would be cured⁴. In ancient Greece, the mental illness was viewed as a sign of guilt and a punishment from the God for both minor and major crimes, and the mentally ill individuals were often abstain by their society and some were even put to death⁵. During this period, the priests were the main therapists, they used the prayers to the God to achieve cure of the patients. Later on, the supernatural or the mystical agents could no longer accepted as the underlying cause of mental diseases. Hippocrates and Aristotle were among the most important and influential figures during this time period⁶.

Patients and Method

This is a cross sectional study was done in Merjan Teaching Hospital during the period from November 2017 till February 2018 . The sample composed of 187 mentally ill patients (80 males and 107 females). Informed consent was obtained from the each patient before data was collected. Patients who did not give the consent were excluded from the study. In case of psychotic patients, the information were obtained from nearby relatives. A semi-structured questionnaire was used for information into socio-demographic data and questions about the visit to faith healers (time of the visit, the effect of the visit on the management, source of referral to the faith healer and if the money given or not). Diagnosis of mental illness was made according to DSM-V. Statistical analysis was carried out using SPSS version 17. Categorical variables were presented as frequencies and percentages. Pearson’s chi square (χ^2) test and fisher exact test were used to find the association between the categorical variables. A *p*-value of ≤ 0.05 was considered as significant.

Result

Figure 1 shows the distribution of patients according to visit to faith healer. Majority (74.3%) of patients had history of visit to faith healer.

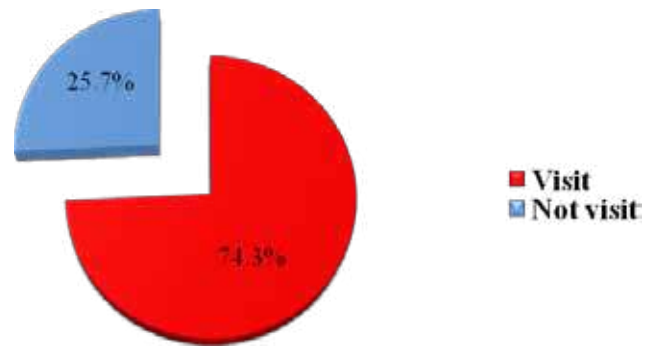


Figure 1: Distribution of patients according to visit to faith healer

Table 1 shows distribution of patients who visit faith healers according to study variables including (time of visit, source of referral to faith healer, money given to faith healer and effect of faith healer on patient compliance with medication). 69.8% of the patients in our study have a visit to faith healers before psychiatric consultation and 67.6% of the patients went to the faith healers with their family members. In most cases (88.5%) money was given to the faith healer. The visit to the faith healers was adversely affecting the compliance of mentally ill patients to their medications in about 76.3% of our sample.

Table 1. Distribution of visitors to faith healer according to study variables

Study Variables	N	%
Time of visit to faith healer		
Before psychiatric consultation	97	69.8%
After psychiatric consultation	31	22.3%
Before and after	11	7.9%
Total	139	100.0%
Source of referral to faith healer		
Himself	45	32.4%
Other	94	67.6%
Total	139	100.0%
Money given to faith healer		
Yes	123	88.5%
No	16	11.5%
Total	139	100.0%
Effect of faith healer on patient compliance with treatment		
Yes	106	76.3%
No	33	23.7%
Total	139	100.0%

Table 2 Shows mean differences of age by history of visit to faith healers. There were no significant differences between means of age by study variable.

Table 2: The mean differences of age by history of visit to faith healers

Variable	History of visit to faith healers	Number	Mean±SD	t-test	P value
Age (Years)	Yes	139	33.92±13.91	0.058	0.954
	No	48	34.06±13.5		

*p value ≤ 0.05 was significant.

Table 3 shows the association between history of visit to faith healers and type of psychiatric disease including (schizophrenia spectrum and other psychotic disorders, depressive disorders, anxiety disorder and

other psychiatric disorders). There was no significant association between history of visit to faith healers and type of psychiatric disease.

Table 3 Association between history of visit to faith healers and type of psychiatric disease

Study Variable	Visit to Faith Healer		X ²	P-value
	Yes (%)	No (%)		
Type of psychiatric disease				
Schizophrenia spectrum	36 (25.9)	11 (22.9)	0.466	0.926
Depressive disorders	26 (18.7)	10 (20.8)		
Anxiety disorders	30 (21.6)	12 (25.0)		
Others	47 (33.8)	15 (31.3)		
Total	139 (100.0)	48 (100.0)		

*p value ≤ 0.05 was significant.

The stigma attached to mental illness and the beliefs that psychiatric disorders was attributed to supernatural forces, had made a significant number of patients in our country to visit the traditional faith healers as shown in the present study which revealed that 74.3% of patients had a visit to faith healer during the course of their disorder. The high number of faith healer visits may also reflects the level of belief & trust in faith healer to manage their illness. The result of this study was higher than the earlier research done in Nepal¹⁶ and this can be explained by many reasons such as the faith healers are easily approachable by the patients in our country. In addition, in the last few years a greater number of such healers appeared in rural areas and even in the urban areas and most of them are using such ways of healing as a job to earn a lot of money from patients and their relatives and to our knowledge there are no legal restrictions to prevent this abusing way of healing. When compared to our results, a minority of patients with mental health problems are choosing the traditional faith healers in India¹⁷. 69.8% of patients in the present study are choosing the faith healers as the first service contact before psychiatric consultation and 67.6% of the

visitors were following the recommendations of relatives and friends to seek help from such persons instead of psychiatrists and most of them gave money to get help from the faith healers. A widely spread wrong ideas about the medical treatment of psychiatric disorders in our culture and most of mentally ill patients and their relatives have a belief that all psychotropic medications are causing addiction and make the mental health more worse, so it is better and more safe at the first time to seek management from the faith healers who are using the Holey Quran and some herbals to treat the mental illness. The effects of mental illness on patient’s ability to take decision about psychiatric consultation along with the effects of other persons (relatives and friends) are the main reasons of the referral to the traditional faith healers not by the patient himself. In most of the cases in our study, the services provided by such healers are no free and money should be given before and sometime after the interview, and this of course has additional burden on the patient and his family. The present study shows that more females approached the traditional healers than males, and this result is nearly similar to other study done in India¹⁹. In our society the cultural

attitudes and limitations that are compelling the mentally ill females to comply and follow the orders of her family and her husband may greatly decreasing the referral rate to psychiatrist. The location of Merjan Teaching Hospital in the center of Hilla city makes most of its attenders from the urban area, thus only 80 patients in our study were from rural area and this may explain the slight increased rate (52.5%) of visitors to the faith healers were from the urban area. It is not easy (in our society) for the mentally ill married patients to visit psychiatrist and administer psychotropic medications because of their belief that psychiatric disorder and its therapeutic measures makes the family life more worse regarding their reputation among relatives and friends, in addition to the economic burden. This may explain why the high rate (64.7%) of the faith healer's clients were married. The level of education among our patients may affect their choice to consult psychiatrist, as 87.8% of visitors to faith healers were of low education level. The higher educated persons have the knowledge about the likely outcome of delay in seeking psychiatric care and they are also more aware of using unhealthy remedies. The inverse relationship between faith healer's visit and level of education is also found in previous studies¹⁸. There was no significant association between history of visit to faith healers and type of psychiatric disease. The present study is of benefit in showing the rate of mentally ill patients who have previous history of faith healers visit and the adverse consequences of following the advice of that healers. The possible factors that contribute to delay in seeking psychiatric care to our patients should be identified and managed in proper way. The active role of media and educational institutions should be directed toward providing adequate information about the common psychiatric symptoms and public education about reducing psychiatric stigma.

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the College of medicine and all experiments were carried out in accordance with approved guidelines.

References

1. M Gelder, P Cowen, P Harrison. Shorter Oxford textbook of psychiatry-5th edition. Classification and Diagnosis.2010; 2: 24.
2. World Health Organization. The World Health Report 2011. Mental Health: New Understanding, New Hope. Geneva: World Health Organization. 2001.
3. Nieuwsma JA, Pepper CM, Maack DJ, Birgenheir D. Indigenous perspectives on depression in rural regions of India and the United States. *Transcultural Psychiatry*. 2011; 48(5): 539-568.
4. Porter R. *Madness: A Brief History*. New York City: Oxford University Press, 2002.
5. Tasman A. *Stigma and mental illness*. Washington, DC, US: American Psychiatric Press, Inc.1992.
6. Millon T. *Masters of the mind*. Hoboken, NJ, US: John Wiley & Sons, Inc. 2004.
7. Rassool G. The crescent and Islam: Healing, nursing, and the spiritual dimension: Some considerations towards an understanding of the Islamic perspectives on caring. *Journal of Advanced Nursing*. 2000; 32: 1476-1484.
8. Cinnirella M, Loewenthal K. Religious and ethnic group influences on beliefs about mental illness: A qualitative interview study. *British Journal of Medical Psychology*. 1999; 72: 505-524.
9. Padela A, Killawi A, Forman J. American Muslim perceptions of healing key agents in healing, and their roles. *Qualitative Health Research*. 2012; 22: 846-858.
10. El-Islam M. Arab culture and mental health care. *Transcultural psychiatry*. 2008; 45: 671-682.
11. Champion J, Bhugra D. Experiences of religious healing in psychiatric patients in south India. *Soc Psychiatry Psychiatr Epidemiology* 1997;32:215.
12. Sorketti E. Pathways to mental healthcare in high-income and low-income countries. *Int Psychiatry*. 2013;10:45-9.
13. Pereira S, Bhui K, Dein S. Making sense of 'possession states': psychopathology and differential diagnosis. *British J Hosp Med* 1995;53:582-6
14. Al-Sabaie A. Psychiatry in Saudi Arabia: cultural perspectives. *Transcult Psychiatry*. 1989;26:245-62.
15. Jacobson L, Merdasa F. Traditional perceptions and treatment of mental disorders in Western Ethiopia before the 1974 revolution. *Acta Psychiatr Scand* 1991;84:475-81
16. Pradhan SN, Sharma SC, Malla DP, Sharma R. A study of help seeking behavior of psychiatric

- patients. ArticleJournal of Kathmandu Medical College, Jan.-Mar., 2013; 2(1): Issue 3,
17. S NAGPAL, N MISHRA, R CHADDA, M SOOD, R GARG. Changing trends of services used as first contact by patients with mental health problems. THE NATIONAL MEDICAL JOURNAL OF INDIA VOL. 2011; 24: 3
 18. Norah A, AshryG. Traditional Healers in Riyadh Region: Reasons and Health Problems for Seeking Their Advice. A Household Survey. The Journal of Alternative and Complementary Medicine. 2010; 2: 199–204
 19. Kapur RL. The role of traditional healers in mental health care in rural India. SocSci Med. 1979;13: 27-31.
 20. Alosaimi FD, Alshehri Y, Alfraih I, Alghamdi A, Aldahash S, Alkhuzayem H. Prevalence of psychiatric disorders among visitors to faith healers in Saudi Arabia. Pak J Med Sci 2014;30(5):1077-1082.

Nurse's of Knowledge toward Newborn Injuries in the Delivery Rooms at AL- Amara City Hospitals

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Abstract

Childbirth wounds are damage to a child before, during or shortly after birth. Childbirth injuries, also known as birth trauma, are known in various forms of severity, but most are mild and these minor injuries become common over time at birth. They are more serious injuries that cause permanent damage. It damages many parts of the body, such as brain damage, nerve damage, bone and muscle damage and, in the worst case, death. Objectives: (i) Assessment knowledge of nurse about Birth injuries. (ii) To identify the relationship between demographic data and knowledge. A survey was conducted in 80 convenient samples with a pre-validated questionnaire . the total period of study are five month 2018/11/20 and ended 2019/6/23 populations of study were the staff in the delivery rooms at AL- Amara city hospitals. The knowledge level is mean in staff nurses who has experience from (5-10) and show the age (20-24) years and have nursing secondary graduate level of education have high level of knowledge and take (1-5) training courses have higher level of knowledge .On comparing these. There is mean nurses knowledge, The study found that there is a relationship between nurses' knowledge and demographic information (training courses).

Keywords: Nurse, Knowledge, Birth injuries.

Introduction

Newborn injury is the damage to the baby during the birth process usually when the child crosses the birth canal¹. It was suggested that trauma associated with childbirth may be caused by difficulty in vaginal delivery especially with childbirth, blood proliferation and shoulder dystocia, and may use sharp tools such as forceps or vacuum during childbirth. The incidence of neonatal injuries ranged from 6-8 cases per 1,000 live births². Neonatal injuries in a child can range from minor injuries to soft tissues at birth, bleeding (pituitary tumor, subchondral bleeding, intracranial bleeding), long bone fractures and bone Broken collarbone, peripheral nerve injuries. On this basis, this study was conducted to determine the incidence, risk factors and outcomes of childbirth injuries. This study aims to provide a comprehensive review of the literature search direction major injuries to newborns³. Twenty of these infections are often categorized according to the etiology, transmission and subsequent outcomes. Whereas, this classification is a strategic first step

towards the development and future progress to know the injury of infants and classify them accurately and correctly. It gives obstetric caregivers a valuable tool to help predict, prevent, or alleviate the severity of childbirth injuries, so we will have long-term results that in turn serve us in the future. Factors responsible for mechanical injury can coexist with the fetus⁴. In 2016, Canker and Carter defined neonatal injury as structural destruction or neonatal dysfunction as a result of a traumatic event at birth. Some of these injuries can be avoided and grandfather ones when appropriate health care is available while others are part of the birth process that can occurs even when health personnel exercise extreme caution. There are also some causes that lead to prenatal injuries such as amniocentesis and intrauterine blood transfusion. However⁵, injuries from fetal scalp electrodes and monitoring of heart rate during childbirth are considered injuries at birth. Over the past 20 years, the number of deaths from childbirth injuries has fallen so that they are no longer included in the 10 most common causes of death in the postpartum period. Birth processes, whether automatic or assisted

another, inherently shocking for newborns. Mechanical events and oxygen ischemia are the causes of birth-related injuries. This review was focused mostly on the mechanical shocks he suffered the newborn due to labor and birth forces experienced by the pregnant mother⁷. To summarize this review, birth-related hypoxia will not be taken separately. Birth-related trauma may affect many neonatal organs (ESM). The incidence of mechanical shock at birth may be somewhat reduced to some extent. The infection rate is 0.82%, and the rate of prevalence of 9.5 per 1,000 live births. Statistics show less than 2% of newborn deaths due to traumatic birth. Birth trauma or perinatal trauma indicates to injuries caused in newborns during childbirth at any stage during the entire birth process. Of course, the incidence of childbirth shocks is high in Western statistics and in reports from developing countries. This increase may coincide with both mortality and morbidity⁶. The total number of maternal injuries was reduced with improvement in obstetric care and prenatal diagnosis. Neonatal trauma in neonatal FD includes minor soft tissue injuries, long or bone clavicle fractures, renal tumor, and peripheral nerve injuries. In the literature, the focus has been highlighted on various risk factors such as infants, active neonates, poor presentations, and labor complications. The study of trauma at birth from an Indian perspective is rare. Thus, this study carefully planned to document the incidence and risk of childbirth trauma with the broader goal of generating income towards reducing neonatal mortality and morbidity⁷. As well as structural or functional deterioration of the newborn in high school known as the birth of the birth of this injury is a tragic event that occurred during the period of labor and delivery, or both. Is not taken into consideration that amniocentesis and move inside the uterus can cause injuries before birth and birth injuries. Injuries under neonatal resuscitation procedures cannot be classified as injuries at birth. When using fetal scalp electrodes and birth within a heart rate monitor, injuries can be described as birth injuries. Where the proportion of newborn injuries previously mentioned and compared with the mortality rate of children, which may occur during the second stage of labor, which occurs during the descent of the fetus through the birth canal⁸⁻¹². The increase in morbidity and mortality of newborn infants occurs as a result of injuries during childbirth. Therefore, there are some measures and guidelines that avoid specific negative results. Acoustic and CT scans and magnetic resonance imaging, where these tests are possible to more accurately predict the abnormalities

that put the fetus at high risk for large injury as this helps to reduce the severity of the injury but does not guarantee that these injuries do not occur. In addition to method that can be used for different conditions there are categories⁹ of birth injuries. Official or professional research tools used in the literature to document or assess the degree of trauma resulting from birth injuries

Sample and sampling techniques Convenient sampling was done for this study; 80 samples collected representing staff nursing. The time it takes to collect the samples were the month. The tools used in this study contains :First part of questionnaire :Demographic data. This theme addresses 5 modules, which include age, educational level, and years of work experience, training session and years of work in the hall of birth. Second part of questionnaire: specific information to sample research, that contains (15) items, which included question regarded injuries of newborn and question about the introduction, causes, signs and symptom, nursing care and treatment of new born injuries. The data collection is formal permission obtained from the authorities for the collection of data. The data was collected from the misan hospital of delivery room. Explained the need and purpose of the study, the knowledge level assessed after obtaining permission from the staff nurses. In order to achieve the above objectives, the study data analysis through the use of the Statistical Package for Social Sciences (SPSS).

Results and Findings

The findings of systematic data analysis in the tables and these correspond to the objectives of the study as follows: The results in this table (1) indicate that the number of participants in the study sample are within the age group (20-24) years was (50%). Also with regard to the level of education topics, and the results showed that more than one level of them has high school graduates (N: 42) was (52.5%). Also in relation to subjects of years of work, the results showed that more than half of them in the age group of the study sample were within (5-10) years (70.0%). In addition, the Number of training courses of nurse involved in the study sample are within group (1-5) was (56.3%). Finally, in the table above, the results showed that the majority of participants more than half of years of experience are within group (5-10) years was (90.0%). And table (2) shows that the majority of participants have a moderate level of knowledge (n = 69, 86.2%), and the results of data analysis, as presented in this table (3), Suggest that there is a statistically

significant relationship among nurses towards their knowledge of their birth injury will their experiment number ($P < 0.05$), when analyzed by chi-square test.

Table (1): Participants' level of knowledge is distributed by mean of questions regarding knowledge nurses towards obstetric injuries.

Level of Knowledge	Frequency	Percent
Low	8	10.0%
Moderate	69	86.2%
High	3	3.8%
Total	80	100.0%

Table (2): Association between the nurses' toward their knowledge about the birth injuries and their no. experience

No. Experience		Knowledge			Total
		Low	Moderate	High	
5-10 yrs	F	8	62	2	72
	%	10.0%	77.5%	2.5%	90.0%
10-15 yrs	F	0	1	1	2
	%	0.0%	1.2%	1.2%	2.5%
15-20 yrs	F	0	3	0	3
	%	0.0%	3.8%	0.0%	3.8%
>20	F	0	3	0	3
	%	0.0%	3.8%	0.0%	3.8%
Total	F	8	69	3	80
	%	10.0%	86.2%	3.8%	100.0%

$\chi^2_{crit.} = 12.592$ $df=6$ $p\text{-value}=0.04P < 0.05$ $\chi^2_{obs.} = 13.140$

Discussion

More than the nurses age group for the study sample was within (20-24) years was (50.0%). This finding is consistent with a study conducted by Hubballi, 2015. This study aims to evaluate demographic characteristics such as (age, educational level of nursing and nurse's experience in the intensive care unit), to assess the quality of nursing care and to reveal the relationship between the quality of nursing care with demographic characteristics. Such as (age, level of education and experience of nursing nurses in the ICU) in Belgaum, Karnataka that show the majority of samples age (20-25) in ratio (66.67%) from study sample.

Also in relation to the level of education subjects the result shows that almost half of them have a secondary nursing graduate (52.5%). this study agrees with study conducted by Rasheid and ali, (2010)⁹, The objectives of this study were to assess nurses' knowledge, provide care for the newborn, meet the requirements of the newly

delivered mother and fetus and monitor progress in their health after delivery.in Al Yarmook Teaching Hospital more sample are nursing secondary graduate in ratio (11%.(The result of this table show that the majority of nurses in years of experience group the study sample were within (5-10)was (90.0%), this agrees with study conducted by Rasheid and ali, (2010)⁹, This study aims : To understanding quality of care have been updated to maintaining high quality of performance in the Al yarmook teaching hospital that show the majority of sample in years of experience. The result show that the majority of the nurses in the number of training courses to the study sample were within(1-5)was (56-3%), this result agrees with the study conducted Rasheid and ali, (2010)⁹, this the study aims : To assess the knowledge of nurses and care of the newborn and meet the requirements of the newly delivered mother and her unborn child and to monitor progress in health after their birth. This table (1) reveals that the majority of participants have moderate level of Knowledge (n=80;

69.2%). This result disagrees with a study conducted by (Hubballi, 2015), which revealed that the majority of nurses had average knowledge.

Conclusion

1. The study shows that the nurses in the age group (20-25) years they (50%) more knowledge about the Birth injuries.
2. The study shows the nurses in Nursing institute graduate have more knowledge about the Birth injuries in ratio (52.5%).
3. The study shows the nurses have (5-10) years of work experience have more knowledge about the Birth injuries in ratio (75.0%).
4. The study shows the nurses which have (1-5) training courses have more knowledge about the Birth injuries (56.2%).
5. The study shows the nurses have moderate level of knowledge through the Mean of questions related to nurses knowledge toward the Birth injuries in average mean of scores (69.2).
6. The study shows that there is a relationship strong between the Demographic characteristics for nurses and knowledge about the Birth injuries.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Pediatric Nursing Department, College of Nursing and all experiments were carried out in accordance with approved guidelines.

References

1. Pressler JL, Hepworth JT. The conceptualization, measurement, and validation of transient mechanical birth trauma. *Clin Nurs Res*. 2000;9(3):317-338.
2. Akangire G, Carter B: Birth injuries in neonates. *Pediatr Rev*. 2016, 37:451-462.
3. Akangire G, Carter B: Birth injuries in neonates. *Pediatr Rev*. 2016, 37:451-462. 10.1542/pir.2015-0125.
4. Chaturvedi A, Stanescu L,² Blickman J,¹ and Meyers S. Mechanical birth-related trauma to the neonate: An imaging perspective. *Insights Imaging*. 2018 Feb; 9(1): 103-118.
5. Hailu D, Worku B. Birth trauma among live born term neonates at a referral hospital in Addis Ababa, Ethiopia. *Ethiop Med J* 2006;44:231-6.
6. Saboo A, Warke C, Malik S, Chokhandre M. Birth Injuries-A Review of Incidence, Perinatal Risk Factors and Outcome. *Bombay Hospital Journal*, Vol. 54, No. 2, 2012.
7. Pressler, Jana L. Classification of Major Newborn Birth Injuries. *J Perinat Neonatal Nurs* 2008; 22(1): 60-67.
8. Hubballi JG. A Descriptive Study to Assess the Knowledge regarding Management of Birth Asphyxia among the Staff Nurses Working in Labour Room and NICU. *Asian J. Nur. Edu. and Research* 5(1): Jan.-March 2015; Page 82-86.
9. Rasheid AM, Ali RM. Assessment of Nurse-Midwives' Knowledge and Practices toward Second Stage of Labor. *Iraqi Sci. J. Nursing*, Vol. 23, Special Issue, 2010.
10. Ojumah N, Ramdhan RC, Wilson C, Loukas M, Oskouian RJ, and Tubbs RS. Neurological Neonatal Birth Injuries. *Cureus*. 2017 Dec; 9(12): e1938.
11. E. M. Mah, P. Foumane, D. H. Ngwanou, S. Nguéfack, A. Chiabi, J. S. Dobit, H. Siyou, J. B. Bogne, E. Mbonda, Fru Angwafo. Birth Injuries in Neonates at a University Teaching Hospital in Cameroon: Epidemiological, Clinical and Therapeutic Aspects. *Open Journal of Pediatrics*, 2017, 7, 51-58.
12. Mondal R, Samanta M, Hazra A, Sabui TK, Debnath A, Chatterjee K, Mukhopadhyay D, Sil A. Prospective Study of Neonatal Birth Trauma: Indian Perspective. *Journal of Clinical Neonatology*. 2016; 5(2).

Measurement Serum Level of Interleukin-34 in Patients with SLE and Healthy Control

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Abstract

Background: Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disease characterized by abnormal function of T-cells and B-cells involving production of autoantibodies and different type of interleukins including complement activation and multiple tissue damage accompanied with different clinical manifestation, all of this happened along with break tolerance. Many researches revealed a key role of interleukins and other biological molecules in SLE patients. Interleukin 34 responsible for increasing differentiation and surviving of autoimmune cells in SLE.

Objective: This study was aimed to estimate the concentration of IL-34 SLEpatients in compare with healthy people.

Materials and Method: This is a case-control study accomplished in the Advisory Clinic for Rheumatic Diseases Center in Al-Najaf city, for the period from December 2018 to August 2019. A total of 60 individuals were included in this study, 30 were diagnosed with SLEby specialist rheumatogy physician, and 30 were healthy controls. Blood sample were collected by venipuncture from 30 patients and 30 healthy controls under sterilized technique and putting in gel tube which then used in sandwich ELISA technique to detect serum level of IL-34.

All data that include age, gender, residence and history of autoimmune diseases were collected from all participants. The data were analyzed by using the statistical package social system (SPSS).

Results: This study show that level of IL-34were significantly higher in SLE patients (49.58±64.03) than in control (0.4±1.25). It is also found that the prevalence of SLE was higher in female in comparewith male26 (86.7%) to 4 (13.3%) respectively.

It also found that SLEwas more frequent in age interval from (31-50) years old.

Conclusion: Elevation of Il-34 concentration may play important role in pathogenesis of SLE, SLE most commonly affectfemales age groups (31-50 years old).

Keywords: SLE, autoimmune disease, IL-34.

Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune and systemic disease recognized by production of antibodies against tissue components especially nucleoprotein and including complement activation and multiple tissue damage involving kidney, nervous system and blood cells¹.

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Different type of cytokines are involved in pathogenesis of SLE and associate with activity of the disease². The causes of SLE is not clearly understood but presence of genetic predisposition and other environmental factors (pregnancy, infections, toxin and Ultraviolet) can lead to exhibit clinical manifestations^{3,4}.

Interleukin 34 is a newly discovered interleukin which is not similar in amino acid sequence in compared to other cytokines. IL-34 share the receptor of colony stimulating factors (CSF-1), its responsible for proliferation and differentiation of white blood cells (Lymphocytes) which lead to increase inflammatory processes and autoimmune activity^{5,6}. The Main tissue that produce IL34 are spleen, thymus, liver, testes, ovaries and brain⁵. Follicular dendritic cells inducing monocyte to proliferate and differentiate by the action of IL-34 producing by this type of dendritic cells⁷.

Interleukin 34 have the ability to enhance production of many types of immune mediators such as interferon gamma, IL-6⁸ and monocyte chemo attractive protein (MCP)⁹.

The current study try to express role of interleukin 34 through measuring serum level of this biomarker in SLE and compared with healthy control.

Subjects and Method

Ethically, data collection and the design of the study groups were accomplished after the approval on the research proposal was done by Research Ethics Committee of AL-Najaf Health Directorate to work in its hospitals.

A case-control study conducted during the period from December 2018 to August 2019 in Al-Najaf city. A total of sixty subjects were included. Thirty SLE patients including 4 male and 26 female, and the female to male ratio was 9:1, those patients were diagnosed by specialist Rheumatology physician according to American college of Rheumatology criteria. However, thirty healthy individuals as control who were attended the Advisory Clinic for Rheumatic Diseases in Al-Najaf city.

Blood sample were collected by venipuncture from 30 patients and 30 healthy controls (five ml/cc of venous were drawing by disposable syringe under sterilized technique in colt activating vacuumed tube). The serum has been collected in Eppendorf tube then stored at -20C to be used for determining the concentration of IL-34 by

ELISA technique.

Quantitative sandwich enzyme immunoassay technique was used, micro ELISA plate had been pre-coated with an antibody to measure IL-34 concentration. The color intensity produced was directly proportional to the amount of IL-34 bound in the initial step. The optical density (OD) was measured spectrophotometrically at a wave length of 450nm. The OD value was proportional to the concentration of IL-34 then, calculate the concentration of substances in the sample by comparing the OD of the samples to the standard curve.

All data that include: age, gender, history of other autoimmune diseases have been collected from all participants, and appropriate statistical and descriptive analysis were performed using IBM SPSS V21.

Results

A total of 60 individuals were included in this study, divided into 30 patients (4 males and 26 females), their ages ranged between (9-55) years, the male to female ratio was 1:9 and 30 as a control group (7 males and 23 females), their ages ranged from (9-55).

Concentration of IL-34 in SLE patients mean±SD (49.58±64.03) was significantly higher than control (0.4±1.25), P value greater than 0.001 Table (2).

frequency of SLE was higher in females than in males each male affected by SLE corresponding with about 7 of females affected by the SLE.

The number of SLE cases was more frequent in age interval (31-50) years old which comprises 16 patients (53.3%) from the total of SLE cases, the lowest number of cases was in the age interval (<=10) which is only 1 case (3.3%) and 3 cases consisted (10%) in age group (11-20) while in control group it include 15 individuals (50%) in (31-55 years) age group, and 8 (26.7%) in age group (11-20 years), while the age group (21-30 years) include 6 individuals (20%) and only 1 (3.3%) was under age of 10 years Table (1).

The mean of ages (mean±SD) for SLE patients were (33.4±12.01) and (31.5±12.59) for healthy control. Variable of age revealed no significant difference between studied group (P value=0.809).

The most affected SLE patients were females (86.7%), whereas male was revealed low percent (13.3%).

Table (1): Demographic information of controls and SLE Patients.

Variables		SLE patients		Healthy control		Statistics	p value
		No.	%	No.	%		
Age	<= 10	1	3.3	1	3.3	F= 0.212	0.809
	11 – 20	3	10.0	8	26.7		
	21 – 30	10	33.3	6	20.0		
	31 and more	16	53.3	15	50.0		
		Mean±SD 33.4±12.01		Mean±SD 31.83±11.56			
Gender	Male	4	13.3	7	23.3	X ² = 3.417	0.181
	Female	26	86.7	23	76.7		
Total		30	100%	30	100%		

Table (2): Show difference in level of interleukin 34 between SLE patients and healthy control by using Chi-square statistical test.

Variable	SLE	Healthy Control	Statistics	p value	Post-hoc Analysis
	Mean±SD	Mean±SD			
IL-34	49.58±64.03	0.4±1.25	X ² = 56.785	<0.001	SLE> C

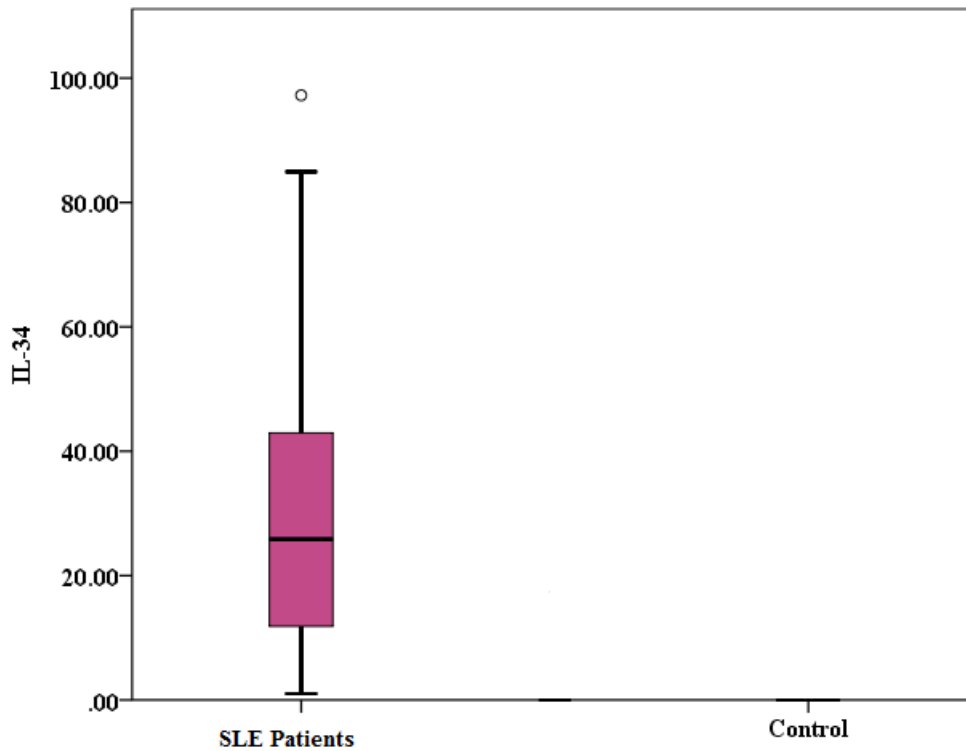


Figure (1): Boxplot of IL-34 levels between studied groups

Regarding to this Figure (1) level of interleukin 34 in SLE patients seems significantly higher than control with range from (1 pg/L) to (80 pg/L) and median fall in approximately (25 pg/L). whereas healthy control show a very low level of interleukin 34 maximally reach to 1pg/L (Mean±SD(0.4±1.25)).

Discussion

Involvement of IL-34 have been shown in different important area such as infection, cancer, transplanted, and autoimmune diseases¹⁰.In this study the concentration of IL-34 in serum of patients with SLE was higher in SLE, while in healthy control was very

low (0.4 ± 1.25)pg/L. This finding is agree with study done by Xie in 2018¹¹ which found that the level of IL-34 was significantly higher in SLE in compare with healthy control and their level directly associate with CRP and anti-ds-DNA and inversely with C3 level, also its level successfully decrease after patients response to treatments. A study revealed that the increasing level of IL-34 led to increase osteoclastogenesis and destroyed bone(erosion arthritis)¹². Over expression of interleukin 34 strongly associate with chronic inflammation and other autoimmune disease such as Rheumatoid arthritis^{13,14}.

In this study, incidence of SLE in females are more than males (86.7% in SLE group were female while just 13.3% of them were males) with male to female ratio about 1:7, results which is almost found in autoimmune diseases reported that SLE is approximately nine times in females more than male¹⁵. Researchers reported that the ratio of females to males ranges from 10:1 to 15:1, and after menopause, the ratio is approximately 8:1¹⁶. Other study done in 1999 revealed the same ratio in 9:1¹⁷.

A lot of factors can explain the different ratio between males and females which include

1. Types of sex hormones in males and females which is already different.
2. Some genes are sex-influenced and sex hormones provoke it to dysregulate immune response¹⁸
3. After all, there is a higher rate of autoimmune diseases among females¹⁹.

Anti-Human leukocyte antigen (HLA) in parous females with SLE increase in compare with males and non-parous females.²⁰

Conclusion

Highest level of IL-34 concentration may play important role in pathogenesis of SLE, SLE most commonly affect females more than males in age groups (31-50 years old).

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Department of Immunology/

Alsader hospital/Najaf city and all experiments were carried out in accordance with approved guidelines.

References

1. Xu WD, Pan HF, Ye DQ. Association of interleukin-18 and systemic lupus erythematosus. *Rheumatology international*. 2013 Dec 1;33(12):3055-7.
2. Elewa EA, Zakaria O, Mohamed EI, Boghdadi G. The role of interleukins 4, 17 and interferon gamma as biomarkers in patients with Systemic Lupus Erythematosus and their correlation with disease activity. *The Egyptian Rheumatologist*. 2014 Jan 1;36(1):21-7.
3. Mak A, Kow NY. The pathology of T cells in systemic lupus erythematosus. *Journal of immunology research*. 2014;2014.
4. Adinolfi A, Valentini E, Calabresi E, Tesi G, Signorini V, Barsotti S, Tani C. One year in review 2016: systemic lupus erythematosus. *Clin Exp Rheumatol*. 2016 Jul 1;34(4):569-74.
5. Lin H, Lee E, Hestir K, Leo C, Huang M, Bosch E, Halenbeck R, Wu G, Zhou A, Behrens D, Hollenbaugh D. Discovery of a cytokine and its receptor by functional screening of the extracellular proteome. *Science*. 2008 May 9;320(5877):807-11.
6. Eda H, Zhang J, Keith RH, Michener M, Beidler DR, Monahan JB. Macrophage-colony stimulating factor and interleukin-34 induce chemokines in human whole blood. *Cytokine*. 2010 Dec 1;52(3):215-20.
7. Ogawa S, Matsuoka Y, Takada M, Matsui K, Yamane F, Kubota E, Yasuhara S, Hieda K, Kanayama N, Hatano N, Tokumitsu H. Interleukin 34 (IL-34) cell-surface localization regulated by the molecular chaperone 78-kDa glucose-regulated protein facilitates the differentiation of monocytic cells. *Journal of Biological Chemistry*. 2019 Feb 15;294(7):2386-96.
8. Cash H, Relle M, Menke J, Brochhausen C, Jones SA, Topley N, Galle PR, Schwarting A. Interleukin 6 (IL-6) deficiency delays lupus nephritis in MRL-Faslpr mice: the IL-6 pathway as a new therapeutic target in treatment of autoimmune kidney disease in systemic lupus erythematosus. *The Journal of rheumatology*. 2010 Jan 1;37(1):60-70.
9. Kim HL, Lee DS, Yang SH, Lim CS, Chung JH, Kim S, Lee JS, Kim YS. The polymorphism of

- monocyte chemoattractant protein-1 is associated with the renal disease of SLE. *American Journal of Kidney Diseases*. 2002 Dec 1;40(6):1146-52.
10. Baghdadi M, Endo H, Tanaka Y, Wada H, Seino KI. Interleukin 34, from pathogenesis to clinical applications. *Cytokine*. 2017 Nov 1;99:139-47.
 11. Xie HH, Shen H, Zhang L, Cui MY, Xia LP, Lu J. Elevated serum interleukin-34 level in patients with systemic lupus erythematosus is associated with disease activity. *Scientific reports*. 2018 Feb 22;8(1):3462.
 12. Chen Z, Buki K, Vääräniemi J, Gu G, Väänänen HK. The critical role of IL-34 in osteoclastogenesis. *PloS one*. 2011 Apr 8;6(4):e18689.
 13. Moon SJ, Hong YS, Ju JH, Kwok SK, Park SH, Min JK. Increased levels of interleukin 34 in serum and synovial fluid are associated with rheumatoid factor and anticyclic citrullinated peptide antibody titers in patients with rheumatoid arthritis. *The Journal of rheumatology*. 2013 Nov 1;40(11):1842-9.
 14. Tian Y, Shen H, Xia L, Lu J. Elevated serum and synovial fluid levels of interleukin-34 in rheumatoid arthritis: possible association with disease progression via interleukin-17 production. *Journal of Interferon & Cytokine Research*. 2013 Jul 1;33(7):398-401.
 15. Peeva E, Zouali M. Spotlight on the role of hormonal factors in the emergence of autoreactive B-lymphocytes. *Immunology letters*. 2005 Nov 15;101(2):123-43.
 16. Ortona E, Pierdominici M, Maselli A, Veroni C, Aloisi F, Shoenfeld Y. Sex-based differences in autoimmune diseases. *Annali dell'Istituto superiore di sanita*. 2016 Jun 28;52(2):205-12.
 17. Mok CC, Lau CS, Chan TM, Wong RW. Clinical characteristics and outcome of southern Chinese males with systemic lupus erythematosus. *Lupus*. 1999 Mar;8(3):188-96.
 18. Christou EA, Banos A, Kosmara D, Bertsiak GK, Boumpas DT. Sexual dimorphism in SLE: above and beyond sex hormones. *Lupus*. 2019 Jan;28(1):3-10.
 19. Dupuis ML, Maselli A, Pagano MT, Pierdominici M, Ortona E. Immune response and autoimmune diseases: a matter of sex. *Italian Journal of Gender-Specific Medicine*. 2019 Jan 1;5(1):11-20.
 20. Jackman RP, Cruz GI, Nititham J, Triulzi DJ, Barcellos LF, Criswell LA, Norris PJ, Busch MP. Increased alloreactive and autoreactive antihuman leucocyte antigen antibodies associated with systemic lupus erythematosus and rheumatoid arthritis. *Lupus science & medicine*. 2018 Sep 1;5(1):e000278.

Detection of Fungi Associated with Some Spices in Local Market in Hilla City (Babylon)

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Abstract

The present study included the isolation and diagnosis of contaminated fungi of some spices sold in the local markets in Hilla city in Babylon Governorate (Iraq) and includes, Black pepper, White pepper, turmeric, mixed spices for meet, Pizza Spices, Beef Shawarma, Pickled Spices, Rosemary ground and others. Results were recorded 346 fungus isolates belonging to 9 different fungal group. The most predominant fungal genera encountered were *Aspergillus spp* (40.17%), *Penicillium spp* (25.14%), *Cladosporium spp* (8.67%) *Alternaria spp*, and *Fusarium spp*. Yeasts were also frequently recovered, but not identified. All fungi were isolated on P.D.A. The study focus on *aspergillus spp* diagnosis by using molecular method to diagnosed it by using sequence techniques. The highest appearance of *Aspergillus flavus* (41.7%) was recorded followed by *Aspergillus niger* (25.9%), *Aspergillus parasiticus* (12.9%).

Keywords: Spice, fungi, identification, P.D.A, Iraq.

Introduction

Spices were described as a natural compound or a combination of natural compounds obtained from seeds, fruits, flowers or trunks (skins, roots, leaves) of several crops of native or exotic origin, aromatic or with a powerful flavor, used in minute amounts and added to food preparing and processing worldwide to provide color, taste, smell or flavor^(3,11,16). Spices are a prominent component of traditional cooking activities and are essential component of millions of people's daily diets around the globe and the majority come from tropical countries and is used to flavoring, coloring or preserving food and beverages¹⁶.

Spices such as pepper, paprika, cumin, ginger, saffron and clove are widely used in the Middle East because they add excellent flavor to products and are

used as medicines because of their preservative and antioxidant properties are extremely important, They are mainly aromatic agents used in tiny quantities if correctly stored and have positive effects as well as antimicrobial characteristics^(4,5). High temperature, moisture and precipitation rates are prevalent in tropical climate. These climate parameters are appropriate for intense microbial development, particularly with regard to fungi. Spices are contaminated in large quantities upon import. Most spices are traded commercially It is in an equipped form, and the drying process is the most important process is used, spices are likely to be exposed to a broad spectrum of microbial contaminants Contamination is likely to happen during the pre- and post-harvest phases during storage, delivery and sale [and/or use]^(23,19). Although spices are present in tiny quantities in foods, they are acknowledged as significant carriers of microbial contamination primarily due to the circumstances under which they were cultivated, harvested and processed. Furthermore, due to possible negligence during sanitation or processing, foods containing spices are more likely to deteriorate and could also have damaging impacts with regard to health¹⁹.

It was observed that most spices contain large

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numbers of molds and bacteria and small numbers of colon bacteria and yeasts. Although spices are present in foods in relatively small amounts. However, they are recognized as important carriers of microbial contaminants mainly due to different stages, The spice passes from planting and harvesting to processing, as well as due to possible neglect during discharge [Or sewage treatment]¹⁹ Food is contaminated with fungi and mycotoxins. and this very serious problems that threaten many developing countries, Especially those that lack the conditions of good food storage and are a source of great concern, which called on these countries to provide healthy food sources to achieve food security²¹. The Food and Agriculture Organization of the United Nations estimates that nearly 32% of the world's food and feed are at risk of contamination with mycotoxins²⁹.

Mycotoxins have significant public health effects. It causes kidney poisoning, immunosuppression, fetal teratogenicity and congenital malformations. These toxins are capable of causing severe acute effects and chronic in human and animal ranging from disorder of the central nervous system, heart, blood vessels, pulmonary systems and death^(9,15). Among the most important Toxins are aflatoxins, which are secondary carcinogenic metabolites produced mainly by *Aspergillus flavus* and *Aspergillus parasiticus*⁽²⁸⁾ Exposure to aflatoxins is known to produce Various diseases like carcinogenic, mutagenic, teratogenic, tremorgenic and hemorrhagic. It also cause damage in the central nervous system, liver or kidneys and effect of male reproductive toxic effects².

Material and Method

Sample Collection: A total of twenty two dried ground samples (Black pepper, White pepper, turmeric, cumin, mixed spices for chicken, mixed spices for meat, Pizza Spices, Rosemary ground, Pickled Spices, Biryani spices, Ginger Spices, cloves, dried Mint, dried Lime, saffron ground, Fenugreek, grill spices, cinnamon ground, Maggi beef, Maggi chicken, Maggi vegetables, Noodles spices) were bought from various locations of local markets Hilla city, depicting distinct kinds of spices. These spice products were selected based on their market accessibility and popular use. Spice samples were generally discovered outside, stored in or on the bare floor in metal or plastic containers, wooden boxes or gunny bags. For each spice 3 replicates were taken from three different places. Each sample (100 g) was put in a new paper bag and transferred immediately to the laboratory and stored in cool place at 4°C for fungal

determination.

Culture of fungal isolate on Potato dextrose agar PDA: Prepare the food medium according to the manufacturer's instructions to dissolve 43 g of the medium in 1 liter of distilled water, then sterilize the sterilizer (autoclave) at 121° C for 15 minutes, then cool the medium and add the antibiotic chloramphenicol at a concentration of 1.2 mg. The fungal samples were cultured on potato dextrose agar (PDA) with three replications for each medium followed by incubated at 25 C° for 7 days, after this period the fungi were investigated²⁶

Identification of the fungal genera:

The fungal isolates were transferred to sterilized plates for purification and identification. Identification of different fungi was done with help of slides prepared by direct mount from the culture. The examined under microscope and identified on the basis of their colony morphology and spore characteristics^(12,27)

Recorded of Results: After incubation and identification percentages of isolated fungi, infection (contamination) in each sample were calculated according to the formula

$$\text{Percentage of appearance} = \frac{\text{Number of isolate that appeared in the same type}}{\text{Total number of samples}} \times 100$$

$$\text{Percentage of frequency} = \frac{\text{Number of isolates per species}}{\text{Total number of isolates of all species}} \times 100$$

Results and Discussion

Three hundred forty six isolates represent 22 species. The results of this study noticed that all samples of spices were infected with fungi Table (1), the fungi belong to 9 fungal genus, the *Aspergillus spp* was (40.17%) followed by *Penicillium spp.* (25.14%) and the *Cladosporium spp.* (8.67%). The results of this study agree with²⁴ were isolated and identified 17 genera. *Aspergillus spp*, *Penicillium spp* and *Rhizopus spp* were the most common genera, *Alternaria* emerged in 40% of samples and *Eurotium spp*, *Fennellia spp* and *Fusarium spp* were detected as moderate contaminating agent where, they were isolated from 26.7% to 33.3% of samples. As well as the results of the present study indicated to occurrence of yeast in some of spice samples but not identified and this result corresponds to what is reached by³¹ When he studied contaminated

fungi for some dried and ground spice samples which indicated *Aspergillus spp*, *Penicillium spp*, *Rhizopus spp*, *Cladosporium spp* and *Trichoderma spp* were the most predominant fungal genera encountered were Yeasts were also frequently recovered. When he studied contaminated fungi for some Relative occurrence values of taxa disclosed ranged between 36.4% for *A. flavus* and 0.6% for *A. parasiticus* and *Absidia spp*.¹⁴ identified fungi in spices like *Acremonium spp*, *Alternaria spp*, *Aspergillus aculeatus*, *A. flavus*, *A. niger*, *A. fumigatus*, *A. terreus*, *Cheatomium spp*, *Choanephora spp*, *Cephalosporium spp*, *Drechslera spp*, *Colletotrichum spp*, *Curvularia spp*, *Fusarium spp*, *Penicillium spp*, *Phoma spp*, *Stemyphylium spp* and *Stachybotrys spp*.¹⁷.¹⁰ show that the predominant mycoflora obtained was distributed in 10 genera. The genus *Aspergillus spp* was the most dominant genus recovered (179 isolates) followed by *Penicillium spp* (44 isolates).

The prevalence of fungi associated with some spices sample appeared in table (2) *Aspergillus spp* was (70.20%) followed by *Penicillium spp* (43.94%) and *Cladosporium spp* (15.15%). In study done by³¹ exhibit the genus *Aspergillus spp* is the most predominant genus encountered, with four species, followed by *Penicillium spp* with two species and all the remaining fungi with one species and the highest percentage relative density was shown by *A. flavus* (36.39), followed by *A. niger* (20.60) and *R. stolonifer* (14.58). The lowest density of occurrence was indicated by *A. parasiticus* and *Absidia corymbifera* (0.60).

²⁴ Record in their research that the *Aspergillus spp* was represented by 10 species and *Penicillium spp* was represented by 7 species, however, *Rhizopus spp* was represented by only 1 species. *A. niger* polluted 93.3% of spices samples and *A. flavus* polluted 60% of them, were the common *Penicillium spp* where, they isolated from 53.3% and 46.7%. of the samples, respectively and *R. stolonifer* contaminated 66.7% of spices. *Aspergillus spp*. and *Penicillium* genera were more frequently detected than other genera of fungi. *Aspergillus niger*. was found in all examined spices samples except Black pill, Caraway, sesame, Black pepper and Cumin while, *Penicillium spp*. were dominant in all samples except Coriander, Ginger, and Caraway¹⁴.

Table (3) showed that the dominant fungal species (percentages of appearance) were *Aspergillus spp* *Penicillium spp*, appeared in all samples of spices such as pepper, paprika, cumin, ginger, saffron and clove

Cladosporium spp. Alternaria spp, Fusarium spp, Mucor spp Rhizopus:¹⁸ isolated 81 species belonging to 38 genera were from different 34 spices in Egypt Where was *the Aspergillus spp* the most prevalent (25) species. This difference in the numbers of isolated species and fungi may be due To the different numbers and types of spices studied in addition to that spices are likely to be vulnerable to the group a wide range of microbial contaminants during the pre- and post-harvest phase, as well as contamination is likely to occur during [Operations of storage, distribution, sale and/or use.⁷ found the *Aspergillus* and *Penicillium spp*. the main components of cardamom, cinnamon, fennel, coriander, cumin, black cumin and white pepper.

The present study recorded the highest appearance of *A. flavus* and *A. niger* in all kinds of spices, And other species of *Aspergillus* appeared in different proportions *A. minisclerotigenes* *A. parvisclerotigenus* *A. oryzae* *A. parasiticus* (table 4) and fig (2).

²² recorded that the most species isolated from different spices were *Aspergillus ruber*, *Aspergillus chevalieri*, *Aspergillus montevidensis*, *Aspergillus pseudoglaucus* and *Aspergillus penicillioides* were the most frequent *Aspergillus* as well, the mycotoxigenic species were *Aspergillus flavus* and *Aspergillus niger*. In other study, *Aspergillus alutaceus*, *Aspergillus fumigatus*, *Chaetomium globosum*, *A. montevidensis*, *A. chevalieri* and *P. chrysogenum* were isolated^{1, 25} isolated 25 species of *Aspergillus* on anise and fennel fruits, of which *A. niger*, *A. flavus*, *A. ochraceus* and *A. flavus var. columnaris* were prevalent in both spices

Table (1): The number and frequency of fungal species isolated from spices

No.	Fungi	Percentage of Frequency	
1	<i>Aspergillus spp</i>	139	40.17
2	<i>Penicillium spp.</i>	87	25.14
3	<i>Cladosporium spp.</i>	30	8.67
4	<i>Alternaria spp</i>	26	7.51
5	<i>Fusarium spp</i>	7	2.02
6	<i>Mucor spp</i>	8	2.31
7	<i>Rhizopus spp.</i>	6	1.73
8	White sterile fungi	16	4.62
9	Yeasts	27	7.80
Total		346	

Table (2): The percentages of fungi isolates appearance associated with spices

No.	Fungi	Percentage of prevalence	
1	Aspergillus spp	139	70.20
2	Penicillium spp.	87	43.94
3	Cladosporium spp.	30	15.15
4	Alternaria spp	26	13.13
5	Fusarium spp	7	3.53
6	Mucor spp	8	4.04
7	Rhizopus spp.	6	3.03
8	White sterile fungi	16	8.08
9	Yeasts	27	13.63

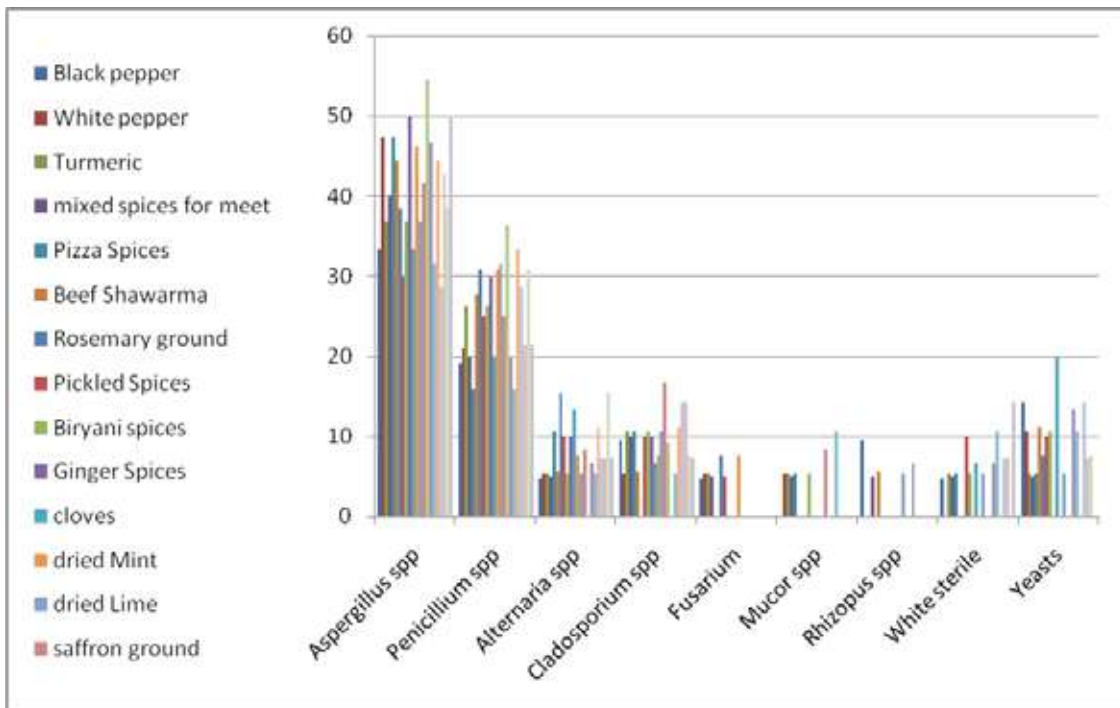


Fig (1): The percentages of appearance of fungi isolated from each samples of spices

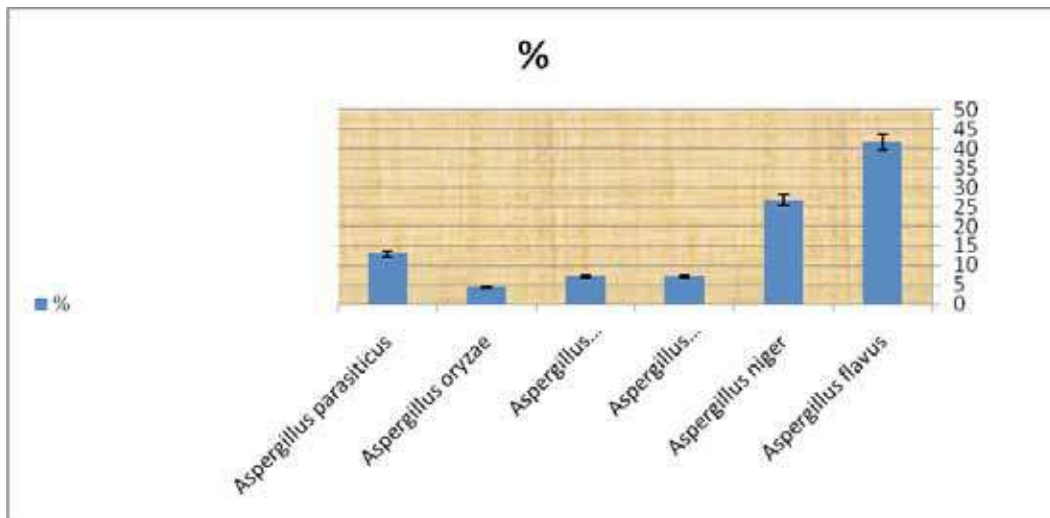


Fig (2): The percentages of appearance Aspergillus spp isolated from each samples of spices

Table (3): The percentages of appearance of Aspergillus spp isolated from each samples of spices

No.	Samples	A.flavus	A. niger	A.minisclerotigenes	A.parvisclerotigenus	A.oryzae	A.parasiticus
1	Black pepper	42.86%	0	14.29%	14.29%	0	28.57%
2	White pepper	33.33%	22.22%	11.11	11.11%	0	22.22%
3	Turmeric	42.86%	28.57%	0	0	14.29%	14.29%
4	mixed spices for meet	37.5%	25%	12.5	12.5%	0	12.5%
5	Pizza Spices	44.44%	22.22%	11.11	11.11%	11.11%	0
6	Beef Shawarma	37.50%	25%	12.50	12.50%	0	12.50%
7	Rosemary ground	40%	20%	0	0	20%	20%
8	Pickled Spices	50%	33.33%	0	0	0	16.66%
9	Biryani spices	42.85%	28.57%	0	0	14.28%	14.28%
10	Ginger Spices	40%	20%	20%	20%	0	0
11	Cloves	60	20	0	0	0	20%
12	dried Mint	33.33%	33.33%	0	0	16.66%	16.66%
13	dried Lime	42.86%	28.57%	14.29%	14.29%	0	0
14	saffron ground	40%	40%	0	0	0	20%
15	Fenugreek	33.33%	33.33%	0	0	0	33.33%
16	grill spices for meet	42.85%	28.57%	14.28%	14.28%	0	0
17	Cumin	33.33%	33.33%			16.66	16.66%
18	cinnamon ground	50%	50%	0	0	0	0
19	Maggi beef	75%	0	0	0	0	25%
20	Maggi chicken	16.66%	33.33%	16.66%	16.66%	0	16.66%
21	Maggi vegetables	60%	40%	0	0	0	0
22	Noodles spices	42.85%	14.28%	14.28%	14.28%	0	14.28%
Total (139)		58	36	10	10	6	18
%		41.7%	25.9%	7.2%	7.2%	4.3%	12.9%

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Department of Biology, Iraq and all experiments were carried out in accordance with approved guidelines.

References

1. Abdel-Hafez SI, El-SaidAHM. Effect of garlic, onion and sodium benzoate on the mycoflora of pepper, cinnamon and rosemary in Egypt. Int. Biodeterior. Biodegrad. 1997;39 (1):61e77.
2. Murad A, Shaima A, Shaima A. Toxicity Effect of Aflatoxin B1 on Reproductive System of Albino Male Rats. Pakistan Journal of Biological Sciences, 2015;18 (3): 107-114.
3. Anonim A. Turkish Food Codex-Spice Paper. Republic of Turkey Ministry of Agriculture and Rural Affairs, Official Gazette, 31.07.2000/24126, 2000;16.
4. Ascenç~aoVL, FilhoVEM. Extraç~ao, caracterizaç~ao química e atividade antifúngica de _oleo essencial Syzygium aromaticum (Cravo da índia). Cad. Pesqui. 2013;20:137e144.
5. Atanda OO, Akpan I and Oluwafemi F. The potential of some spice essential oils in the control of A. parasiticus CFR 223 and aflatoxin production. Elsevier1-7.2006.
6. Ath-HarMA, Prakash HS, ShettyHS. Mycoflora of Indian spices with special reference to aflatoxin producing isolates of Aspergillus flavus. Indian J. Microbiol. 1988;28:125–127.
7. Ayres GI, MundTI, Sondin EW. Microbiology of Food Spices and Condiments. A Series of Books in

- Food and Nutrition. Schmeigert, 1980;249.
8. AyresGI, Mund TI, Sondin EW. Microbiology of Food Spices and Condiments. A Series of Books in Food and Nutrition. Schmeigert, 1980;249.
 9. BhatRV, S Vasanthi .: Food safety in food security and food trade: mycotoxin food safety risk in developing countries. Washington D.C. International Food Policy Research Institute.2003.
 10. Bugno A, Almodovar AB, Pereira TC, Andreoli Pinto TJ, Myrna S. Occurrence of toxigenic fungi in herbal drugs. Braz. J. Microbiol., 2006;37: 47-51.
 11. Bulduk S. Food Technology. 2nd edition, Detay Publishing, Ankara, Turkey.2004.
 12. CMI. "Commonwealth Mycological Institute" . Description of pathogenic fungi and bacteria. Kew, Surry, England.1966.
 13. DimicG, KrinjarS, Dosen-Bogic EvicMV. Dance, a potential producer and sterigmatocystin in spices (Croatian). Tehnol. Mes., 2000;41(4-6):131-137.
 14. El-Gali ZI. Detection Of Fungi Associated With Some Spices In Original Form. Global Journal of Scientific Researches. 31 March,2014;2(3):83-88.
 15. FAO Food and Agriculture Organization of the United Nations. Call for data and experts on microbiological hazard associated with spices and dried aromatic herbs. Avaliable http://www.fao.org/fileadmin/templates/agns/pdf/je_mra/Call_for_data_and_experts_on_spices_Final_20121220.pdf. Accessed:13 mar2013;17.
 16. FAO, Food and Agriculture Organization of the United Nations. Herbs, Spices and Essential Oils: Post -Harvest Operations in Developing Countries. Avaliable at. <http://www.fao.org/3/a-ad420e.pdf>. Accessed: 25 jul,2005;17.
 17. Hashem M, Alamri S. Contamination of common spices in Saudi Arabia markets with potential mycotoxin-producing fungi. Saudi J. Biol. Sci., 2010;17: 167-175.
 18. Kady-EIA, E-Maraghy SS, Mostafa M. Contribution of the Mesophilic fungi of different spicesin Egypt, Mycopathologia, 1992;120:93-101.
 19. Koci-Tanackov SD, Dimi GR, Karali D. Contamination of spices with moulds potential producers of sterigmatocystine. APTEFF, 2007;38: 29-35
 20. Koci-TanackovSD, DimiGR, Karali D. Contamination of spices with moulds potential producers of sterigmatocystine. APTEFF, 2007;38: 29-35.
 21. MakunHA, ST Anjorin, BMoronfoye, FO Adejo, OAAfolabil, G Fagbayibo, B OBalogun, A A Surajudeen .: Fungal and aflatoxin contamination of some human food commodities in Nigeria. African Journal of Food Science, 2010;4: 127-135.
 22. Marcelo Valle Garcia, Gilson Parussolo, Camila Brombilla Moro, Ang_elica Olivier Bernardi, Marina Venturini Copetti. Fungi in spices and mycotoxigenic potential of some Aspergilli isolated. Food Microbiology 2018;73 : 93-98
 23. McKeeLH. Microbial contamination of spices and herbs: a review. lebensm Wiss. Technol.1995;28:1-11.
 24. Mohamed Hashem, Saad Alamri . Contamination of common spices in Saudi Arabia markets with potential mycotoxin-producing fungi. Saudi Journal of Biological Sciences 2010;17: 167–175
 25. MoharramAM, Abdel-Mallek AY, Abdel-HafezAH. Mycoflora of anise and fennel seeds in Egypt. J. Basic. Microbiol. 1989;29(7): 427e435.
 26. NeergaardP. Seed Pathology. 1973;1, JohnVilley, Sons NY.
 27. Nelson PE, Toussoun TA, Marasas WFP. Fusarium spp. An Illustrated Manual of Identification. The State Uni. Press. 1983;203.
 28. Nida'a Shihab Hamed, Abeer Fauzi Murad, Eman Abdul-Wahed Abdul-Rahim. Molecularly Diagnostic of Aflatoxigenic Aspergillus flavus Isolated from Nuts Research Journal of Environmental Toxicology 2016;10 (1): 39-49
 29. Park DL, HNjapau, EBoutrif . Minimizing risks posed by mycotoxins utilizing the HACCP concept {internet}. Nov 17,2009.

Staff's Knowledge and Practices in Environmental Foundation Regarding Prevention from Mobile and Tower Health Risks in Erbil City, Iraq

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Abstract

Mobile phones, at the present time, are an essential part of contemporary communications in every single life. In a lot of countries, above half of the population uses mobile phones and the mobile phone market are rising speedily. Thus, mobile phones, towers and their risks are almost everywhere. This study originally designed to identify the knowledge and practices of 100 staff members in the environmental foundation in Erbil city in Iraq. Accordingly, the standard use of mobile, towers and health risks to identify an association between variables and their knowledge or practices took into consideration. This study was descriptive design began in 01-07-2018 to 01-07-2019. The utilized questionnaire, for data collection, contained three parts. It was viewed by a panel of experts in the nursing field for validity. The outcomes of this study specified that the majority of individuals have not satisfactory knowledge and practices about standard use of mobile phones, towers and health risks. There was a significant association between age, level of education, years of employment and their practical knowledge. Finally, this study recommended preparing a program for training to increase their knowledge, practices, and continue to conducting research regarding mobile phones and other communication facilities.

Keywords: *Health risk, mobile use, mobile towers, practical knowledge, radiation.*

Introduction

Nowadays mobile phones and towers are found every where¹. As billions of human beings utilize mobile phones internationally, a tiny growth in the occurrence of argumentative impacts on health could possess main public health insinuations on extended term foundation. Also the amount of cell phone calls per day, the length of each call and the amount of time people utilize cell phones are vital aspects which improve the health associated danger². Mobile phones, in general, radiate radiofrequency (RF) energy, an arrangement of nonionizing electromagnetic emission, which can be absorbed by tissues close to the phones. The amount of RF energy from mobile phone of the exposed user is depending on many factors. Among these factors; the fountainhead of the phone, the distance between the phone and the user, the extent of the mobile phone and the user's distance from cell phone towers³. Radio frequency emission is a form of electromagnetic radiation. X-rays, radon, and cosmic rays are ionized

electromagnetic radiation, while radio frequency and extremely low frequency, or power frequency are among non-ionized electromagnetic radiation⁴. It can be stated that, the range frequency of RF radiation ranges from 30 kHz to 300 GHz. Thus, cell phones utilize this range for telecommunications. The human body absorbs energy from devices that emit RF⁵. Radio frequency electromagnetic radiation from these devices are risk for health. RF-EMF radio frequency and electro magnetize frequency may be risk for health but absorption of the waves by houses, trees, and other geographical barriers may reduce the exposure level of magnetizing waves. There is controversy about cancer incidence with magnetizing exposure so sometimes testing give negative results for this health problems, while in other in other findings agreed with health problems⁶. There are many studies about health risks as, the study by Meyer⁷ who found no association between mobile phone base station exposure and cancer incidence. The studies done by Eger *et al.*⁸ and Wolf⁹ found a significant association between

mobile phone exposure and increased cancer incidence. Mobile and towers telecommunication systems have developed rapidly, to the point where then a sixth of the world's population use mobile phones more. By the end of 2004, more than a billion subscribers across more than 200 countries were estimated to be using mobile phones¹⁰. The development of mobile communications has increased rapidly. In the 1980s, first-generation mobile phones, using analog technology, allowed the transmission of sound only. The global system for mobile communication has begun in 1991 and includes such new developments as data and image transmission¹¹. The new generation of mobile phones may have many other services in the markets. People have used the new technology for communication globally, but they do not know about potential health hazard from mobile phones. However, concerns the possible effects on health, as a result of the exposure microwave electromagnetic fields, have been expressed for the introduction of mobile phones³. Since the year 2000, several reports have reviewed relevant studies about health risks of a mobile phone to the common and accepted carcinogenic effects of RF and microwave energy¹². Mobile phone use has developed and increased quickly at low prices. Industry sources expected that there will be more and more over billion users worldwide by 2025, far exceeding telephone use via fixed-lines¹³. Thus, even a small impact on health could have a major public health consequence. The aim of this investigation is to identify that the exposure to RF and microwave radiation from mobile phones and their base stations and tower microwaves might affect health and to identify the safety and standard use of these electronic devices. Concern continues about exposure to radiofrequency (RF) fields from sources used for mobile telecommunications, radars, towers, radio and television broadcast, medical and industrial applications. The objectives of this study is identifying staff's knowledge and practices in environmental foundation about health risks, standard mobile use and towers in Erbil City, Kurdistan Region, Iraq. Also, to identify the association between variables of sample study and their knowledge, practices about mobile use and towers.

Methodology

The design of this study is basically a cross-sectional, descriptive study. While, the sample of the study is a non-probability convenient purposive sampling which used to select 100 staff in the environmental foundation in Erbil City, Kurdistan Region, Iraq. The sample

size was calculated by (application the sample size calculator),utilizing the following formula:

$$Sample\ size = \frac{\frac{z^2 \times p(1 - p)}{e^2}}{1 + \left(\frac{z^2 \times p(1 - P)}{e^2 N}\right)}$$

Where N = population size, e = Margin of error (percentage in decimal form), z = z-score and p is the sample proportion. The z-score is the number of standard deviations an assumed amount is further than the mean¹⁴. As we stated the study/the study conducted in the environmental foundation in Erbil city. Time of the study/the study l began in 01-07-2018 to 01-07-2019. The tools of the study was based on the questionnaire that used for data collection, containing three parts (socio-demographic data included (age, address, sex, level of education, years of employment, family status, and type of family) part two included questions related to knowledge depending on the scoring system as followings (1 for I know, 2 for I do not know and 3 for I'm not certain). Part three was included questions about practices, depending on the scoring system as followings (1 for always do, 2 for sometimes do and 3 for never do). The validity of the questionnaire based on the viewingby the panel of experts in the nursing field and according to their comments a questionnaire was corrected and organized. Moreover the environmental foundation and the scientific committee accepted for conducting this study and approval from nursing college and ethical committee While, the inclusion criteria were all staff in the environmental foundation. Furthermore, the exclusion criteria were some staff who are in work with clients.It can be stated that, the data collection was done by interview technique with staff. However, the importance of the study was highlighted in its importance to identify the knowledge and practices of those staff for awareness and prevention. Finally, the data analysis done by using SPSS program version 23 for data analysis.

Results and Discussion

Table 1 below shows the socio-demographic characteristics of study sample as followings: the majority of them were between 22-31 years, most of them from urban, most of them were male, the majority of them were married, most of them graduated from the institute, while most of them had employed about 15-20 years.

Table 1: Socio-demographic characteristic:

Variables	Frequency	Percentage%
1-Age group:		
22-31	55	55%
32-41	27	27%
42-51	18	18%
Total	100	100%
2-Address:		
Urban	83	83%
Suburban	16	16%
others	1	1%
Total	100	100%
3-Sex : Female	40	40%
Male	60	60%
Total	100	100%
4-family status		
Single	28	28%
Married	64	64%
Widow	6	6%
Divorced	2	2%
Total	100	100%
5-tye of family		
Nuclear	38	38%
Extended	62	62%
Total	100	100%
6-Level of education		
Secondary	23	23% ^o
Institute	35	35%
College	34	34%
Others	8	8%
Total	100	100%
7-years of employment		
3-8 years	13	13%
9-14	21	21%
15-20	66	66%
Total	100	100%

Table 2 shows the practice levels of staff so 9% of them can practice mobile use and towers properly, while the majority of them couldn't do practices properly which represented 91% of them.

Table 2: Level of practices for Staff

Type of practice level	Frequency	Percentage %
Practice properly	9	9%
Non-practice properly	91	91%
Total	100	100%

The results of this study agreed with the study done by Meyer⁷ who indicated that some young people practice bodily movements during talking with someone and they have unavailable habit. The outcomes of this investigation also agreed with the study of Savio *et al.*¹⁵ who stated that it is necessary to utilize information system for mobile use in the organizations and another office to work standard and reduce the health risks of mobile and towers.

Table 3 shows the association between variables and practices of staff so there is a significant association between age, address, sex, educational level, years of employment and their practices about mobile and towers, while there was not the significant association between family status, type of family, and their practices. Other findings indicated that there was the significant association between age, address, sex, education level, years of employment and practices of staff regarding utilizing mobile and dealing with towers¹⁶.

Table 3: Association between variables and practices

Variables	Degree of Freedom	P-Value
1-Age	15	0.000
2-Address	2	0.019
3-sex	1	0.041
4-family status	2	0.168
5-type of family	1	0.837
6-education level	3	0.049
7-years of employment	8	0.002

Table 4 shows levels of knowledge among staff regarding mobile and towers, so there are three levels of knowledge as followings (good 9%, fair 76% and bad 15%).

Table 4: Levels of knowledge among staff:

Level of knowledge	Frequency	Percentage %
Good	9	9%
Fair	76	76%
Bad	15	15%
Total	100	100%

Regarding their knowledge about using mobile and dealing with towers, the majority of the participants possess fair knowledge which represented by 76%, while a small number of them have good knowledge which represented by only 9%, and 15% of them have

bad information for that so according to this study there is lack of training course,workshop, symposium and other program in the environmental foundation and other office to increase their knowledge and practice regarding mobile,tower and other communication technology. Patrick et al.¹⁷ in their investigation found similar conclusion to our study. The results found in this study also agreed with the study by Santini and coworkers¹⁸ and Crilly et al.¹⁹.

Table 5 shows the association between variables and level of knowledge of staff regarding mobile and towers, so there is significant association between age, sex, educational level, years of employment and their knowledge about mobile use and towers, while there was no a significant association between address, family status, type of family and their knowledge about mobile use and towers.

Table 5: Association between variables and level of knowledge

Variables	Degree of freedom	P-Value
1-Age	30	0.000
2-Sex	2	0.012
3-Address	4	0.421
4-Family status	4	0.143
5-Type of family	2	0.864
6-Level of education	6	0.000
7-Years of employment	16	0.010

These findings agreed with the study done by Kayyali *et al.*¹¹. In their study they states that in spite of the increasing number of “mHealth Apps” the level of consciousness and using of such APPS by patients, and pharmacist was still somewhat small. Kayyali *et al.* also recommended that awareness and knowledge of these apps should increase both of public and for health professionals. It can be indicated that, the outcome of their study showed that there was lacking sufficient knowledge and practice among staff, clients, patients, and pharmacists in England. Thus, the results found in our investigation are highly agree with the results, perspectives and recommendations found by Kayyali *et al.*¹¹.

Conclusion

The findings of the study revealed that majority of them not practiced with mobile and towers properly and standard which represented nearly about 91%, while small number of staff were practiced properly which

represented about 9% so according to my opinion the cause due to lack of training program for staff in environmental foundation in Erbil City, Kurdistan Region, Iraq, and lack of expert individuals in the office to train and educate other new staff. The other conclusion of this study was there is a significant association between age, address, sex, education level, years of employment and practices of staff regarding using mobile and dealing with towers. Among all these variables the education level and years of employment of staff may effect to increase their practices, knowledge, and experiences. The majority, *i.e.* 76%, of the participants possess bad knowledge with regard to their information about mobile and towers use. Which is a bad indicator and needs to improve by educational programs and workshops. A tiny amount, *i.e.* 9% of them they have good information about dealing with mobile phones and towers. This percentages can be increased by different channels such as; training course,workshop, symposium and other programs in addition to conducting research about mobile and other communication technology. The outcomes of the study, also, indicated that the majority of individuals have not sufficient knowledge and practices about standard use of mobile and towers. Finally, this study recommended that research about magnetic field, mobile, towers should be continued not only to increase the knowledge of the users and workers but also to decrease the hazardous of the mobile and towers radiation .

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the College of Nursing, Hawler Medical University, Erbil, Iraq and all experiments were carried out in accordance with approved guidelines.

References

1. Al-Akhras MA. environmental pollution of cell-phone towers: Detection and analysis using geographic information system. *Jordan Journal of Earth and Environmental Sciences*, 2015;7(2): 77-85.
2. Rööslä M. Systematic review on the health effects of exposure to radiofrequency electromagnetic fields from mobile phone base stations. *Bulletin of the World Health Organization*, 2010;88: 887-896.
3. Repacholi MH., Health risks from the use of mobile

- phones. *Toxicology letters*, 2001;120(1-3): 323-331.
4. Stozhkov YI. Long-term (50 years) measurements of cosmic ray fluxes in the atmosphere. *Advances in Space Research*, 2009;44(10): 1124-1137.
 5. JauchemJR., Effects of low-level radio-frequency (3 kHz to 300 GHz) energy on human cardiovascular, reproductive, immune, and other systems: a review of the recent literature. *International journal of hygiene and environmental health*, 2008;211(1-2):1-29.
 6. KhuranaVG, et al., Epidemiological evidence for a health risk from mobile phone base stations. *International journal of occupational and environmental health*, 2010;16(3): 263-267.
 7. MeyerM, AGartig-Daug, MRadespiel-Troger, Cellular telephone relay stations and cancer incidence. *Umweltmed Forsch Prax*, 2006;11: 89-97.
 8. EgerH, et al, The influence of being physically near to a cell phone transmission mast on the incidence of cancer. *Occupational and Environmental Medicine*, 2006;63(5).
 9. Wolf R, DWolf, Increased incidence of cancer near a cell-phone transmitter station. *International Journal of Cancer*, 2004;1(2): 123-128.
 10. Lester RT, et al., Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (Wel Tel Kenya1): a randomised trial. *The Lancet*, 2010;376(9755): 1838-1845.
 11. Kayyali R, et al., Awareness and use of mHealth apps: a study from England. *Pharmacy*, 2017;5(2): 33.
 12. Krewski D, et al, Recent advances in research on radiofrequency fields and health: 2001–2003. *Journal of Toxicology and Environmental Health, Part B*, 2007;10(4): 287-318.
 13. MillerG. The smartphone psychology manifesto. *Perspectives on psychological science*, 2012;7(3): 221-237.
 14. Daniel W. *Biostatistics: A Foundation for analysis in the health sciences*, 7th edR Wiley. New York, 1999.
 15. Savio PD,R. Gregory, Design Of Next Generation Antenna Mounts In Telecommunication Towers With Low Effective Projected Area. 2015.
 16. Blettner M, et al., Mobile phone base stations and adverse health effects: phase 1 of a population-based, cross-sectional study in Germany. *Occupational and environmental medicine*, 2009;66(2): 118-123.
 17. Patrick K, et al. Health and the mobile phone. *American journal of preventive medicine*, 2008;35(2):177-181.
 18. Santini R, et al., Survey study of people living in the vicinity of cellular phone base stations. *Electromagnetic Biology and Medicine*, 2003;22(1): 41-49.
 19. CrillyP, et al. Community pharmacist perceptions of their role and the use of social media and mobile health applications as tools in public health. *Research in social and administrative pharmacy*, 2019;15(1):23-30.

Mycobiota and Enteric Viruses among Infants with Acute Diarrhea in Iraq

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Abstract

Diarrhea is a disease responsible mortality and morbidity of children under five years of age .The present study revealed that from total of 104 collected stool samples taken from infants with acute diarrhea 55 case of diarrhea recorded in male infants and 49 in female. The finding of our study detected 29 infection with enteric viruses and 75 with non-viral agents. The study recorded 24 infant stool samples were infected with Rotavirus, 5 with Adinovirus and 29 samples with different Mycobiota (fungal community species): *Candida albicans* (24), *C.tropicalis* (1), *C.krusei* (1), *Saccharomyces cereviciae* (1), *Aspergillus niger* (1), *Cladosporium cladosporoides* (1) and *Fusarium verticillioides* (1). Residents of rural community recorded higher rate of viral infection (54) compared with urban residents (15). Control Group revealed 18 infection with Mycobiota only. This study confirmed the interaction of Rotavirus and Mycobiota in the same samples .

Keywords: Diarrhea, Infants, Enteric virus, Mycobiota.

Introduction

Childhood diarrhea is a major public health concern globally, reported to be the second most important disease in the etiology of infant death^(1,2). Acute diarrhea is manifested by a sudden occurrence of three or more watery or loose stools per day lasting for seven to 10 days, 14 days at most, associated with higher mortality cases, correlated to young age, nutritional deficiencies, and inadequate food hygiene practices^(3,4). In developing countries, gastrointestinal disorders are directly associated with higher infant morbidity and mortality among children under five years of age due to different factors associated with occurrence of diarrhea among young children and these differ from place to place and only a few studies have attempted to compare diarrheal disease burden and its contributors in rural and urban communities^(5,6,7).

The clinician encounters acute gastroenteritis in three settings. The first is sporadic gastroenteritis in infants, which is generally caused by Rotavirus. The second is epidemic gastroenteritis, which occurs either in semi-closed communities (e.g. families institutions, on ships, at vacation spots), and the third as a result

of classic food-borne or water-borne pathogens^(8,9,10). Although there are many non-infective factors of diarrhea, the most common causative agents of diarrhea are biotic factors causing infective diarrhea originated from living microorganisms included viruses, bacteria and parasites^(11,12).

The most clinic importance of enteric viruses among infants with acute diarrhea are Rotavirus, Norovirus, Adenovirus and Astrovirus^(13,14). Different groups of viruses have been showed to be causative agents of high incidence of acute viral diarrhea among children during their first years of life¹⁵.

More studies focused on the role of microbiota (bacteria, viruses and parasites) on developing diarrheal cases specially among infants, but Mycobiota (fungal community) such as the causative agents of opportunistic mycoses, has received little attention. However, most studies to date have focused on bacterial colonization events and have left out fungi, a clinically important sub-population of the microbiota. A number of recent findings indicate the importance of host-associated fungi (the mycobiota) in adult and infant disease¹⁶.

Candida is a yeast, part of normal flora in the gastrointestinal tract of healthy individuals can be transmitted from oral cavity to the stomach and intestines leading to diarrheal case. *Candida* species are frequently isolated from stools of children with diarrhea but are not proven as the main causative agent of diarrhea. (17,18). Although *Candida* species not confirmed to be the main causative agent of acute diarrhea among infants, many different species of fungi were isolated from stool samples of diarrheal cases in addition to *Candida* included *Trichosporon* and *Geotrichum* that have been reported to cause diarrhea¹⁹.

The interactions between fungi and bacteria have been reported for a long time, particularly since the introduction of antibiotics in the mid-1900s, whereas the interaction of enteric viruses and mycobiota still unknown²⁰.

The aim of present study is to find the correlation between enteric viruses and Mycobiota among infants with acute diarrhea.

Materials and Method

Sample Collection: Over a period of six months, from October 2018 to March 2019, 104 stool samples were received from infants with acute diarrhea patients admitted to Misan Maternal and Child Hospital in Iraq. Also 52 samples from control group without diarrhea matched for age and selected from patients admitted to the same ward. For processing and testing procedures, samples were transferred to the laboratories of Department of Medical Laboratory Technology at Amarah Technical Institute.

Test of Rotavirus and Adenovirus

Procedure: Test of Rotavirus and Adenovirus from stool was done by using Rota/Adeno kit.

A dropping cap (provided in the kit) was assembled on the sample collection tube. About 4-5 drops (about 100-125 µl) of the mixture from sample collection tube was added into the sample well of the test device. The results were interpreted within 10 minutes.

Negative result: Only one green band (control line) appears in the white central zone of the reaction test (control region).

Rotavirus positive result: In addition to the green control band, a distinguishable red band (Rotavirus result line) also appears in the white central zone of the reaction test (result region).

Adenovirus positive result: In addition to the green control band, a distinguishable blue band (Adenovirus result line) also appears in the white central zone of the reaction test (result region).

Rotavirus–Adenovirus positive result: All the lines above described (a green control band in the control region, a red band and a blue band in the result region) could appear at the same time during the test performance due to a simultaneous infection of Rotavirus and Adenovirus.

Isolation and identification of fungi:

A. Culture Method:

For *Candida* culture, diluting 0.2 g of feces in 1.8 ml of sterile saline solution. A 10 µl aliquot was then plated on Sabouraud's dextrose agar containing 300 µg/ml chloramphenicol and 10 µg/ml gentamicin. Plate cultures for yeasts were incubated in air at 35°C for 48 hours before counting and identified.

By using chrome agar for the identification of *Candida* species, and incubation period 24-48 hours at 35°C. The presumptive identification was made by color and morphology of the colonies; the isolates were further identified microscopically and morphologically.

B. Molecular Method:

For molecular classification of molds, 0.5g of fungal hyphae was carefully removed from petri dishes, transferred to bead tubes for DNA Extraction and Amplification, PCR screening technique. Genomic DNA was extracted from fungal isolates using a Mo-Bio Power DNA extraction kit (Carlsbad CA, USA). Fungal 18S rRNA genes were PCR amplified using NS1 [5'-GTA GTC ATA TGC TTG TCT-3'] and FR-1 [AICCAT TCA ATC GGT AIT]. Process of thermocycling conditions was done. Amplicons were cleaned using a Mo-Bio UltraClean PCR Cleanup Kit and sent for sequencing on an Applied Biosystems 3130xl Genetic Analyzer. The basic local alignment search tool –BLAST was used to classification and identification fungal isolate.

Results

Table 1. Number of diarrheal cases according to age group.

Age (Months)	Diarrheal Cases in Female(%)	Diarrheal Cases in Male (%)	Total No. (%)
< 2	7(6.7)	10(9.6)	17(16.3)
2-6	28(26.9)	14(13.4)	42(40.3)
6-12	10(9.6)	25(24)	35(33.6)
12	4(3.8)	6(5.7)	10(9.6)
Total	49(47.1)	55(52.8)	104(100)

Table 2. Prevalence of enteric pathogens among infants with acute diarrhea according to resident location

Enteric pathogen	No. of infected patients in Rural area	No. of infected patients in City center	Total no. of pathogens (%) n=104
Rotavirus	20	4	24 (23.07)
Adinovirus	3	2	5 (4.80)
Candida albicans	24	0	24 (23.07)
C.tropicalis	1	0	1(0.96)
C.krusei	0	1	1(0.96)
Aspergillus niger	1	0	1(0.96)
Cladosporium cladosporoides	1	0	1(0.96)
Fusarium verticillioides	1	0	1(0.96)

Table 3. Prevalence of enteric pathogens associated with Control Group according to resident location

Enteric pathogen	No. of patients in Rural area	No. of patients in City center	Total no. of pathogens (%) n=52
Rotavirus	0	0	0 (0%)
Adinovirus	0	0	0 (0%)
Candida albicans	4	1	5(9.61)
C.tropicalis	1	1	2 (3.84)
C.krusei	1	0	1(1.92)
Aspergillus niger	0	0	0 (0%)
Cladosporium cladosporoides	0	0	0 (0%)
Fusarium verticillioides	0	0	0 (0%)

Table 4. Single and mixed pathogens associated with stool samples of diarrheal patients

Single Infections	No. of samples infected (%)
Rotavirus	0(0.0)
Adinovirus	5(4.80)
Candida albicans	0(0.0)
C.tropicalis	1(0.96)
C.Krusei	1(0.96)
Aspergillus niger	1(0.96)
Cladosporium cladosporoides	1(0.96)
Fusarium verticillioides	1(0.96)
Total	10(9.61)

Single Infections	No. of samples infected (%)
Mixed Infections	
Rotavirus/Adinovirus	0(0.0)
Rotavirus/Candida albicans	24(23.07)
Total	24(23.07)

Discussion

As shown in table 1. The total of diarrheal cases among infants with acute diarrhea admitted at Misan Maternal and Child Hospital was 104 cases, distributed between male 55 and 49 female . The results of present study revealed that most enteric virus infections were recorded among infants originated from rural community

(Table 2.), which refers to poor hygiene practices, immune status, specially shortage of vaccination campaigns and nutritional deficiencies with an inadequate food hygiene practices²¹. Although the current finding of Rotavirus infection was high, (23.07%), our research recorded lower incidences in comparison with recent studies in neighbor cities in Iraq (Basrah 2018,32.5%, Basrah 2011, 40.5%,mid Iraq 2010,42.2%, Babylon city 2011, 45.7%, and Kurdistan 2005,37%²².

Our results revealed infection of 29 infant with enteric viruses (Rotavirus 24 and Adinivirus 5) and mycobiota (fungal community) infection (Candida albicans 24, non Candida albicans 2, Aspergillus niger1, Cladosporium cladosporoides 1, and Fusarium verticillioides 1) as shown in table 2. Candida albicans among patients with acute diarrhea recorded a high occurrence percentage than Candida albicans associated with control group (9.61%) as shown in table 3. Results revealed 24 mixed infections by two pathogenic microorganisms, Rotavirus and Candida albicans within the same samples (Table 4.). The high rate of Mycobiota infections followed Rotavirus infections may be due to replication process, which induce opportunistic infections such as Candida to be dramatically risk factor and increase the pathogenicity, leads to tissue penetration and inflammation of the mucosa²³. Following the infection with Rotavirus, IgM and IgA responses occur in the small intestine, fecal, serum and salivary antibodies have all been suggested as surrogate markers^(24,25).

Conclusion

Although Candida has clinical and medical importance as a normal resident flora of the gut, Rotavirus is the leading agent of acute diarrhea in infants. Nowadays, Mycobiota will be with an emerged risk factor as opportunistic pathogens, specially under the virulence of viral infection. The role of candida alone or with viral pathogens play important clinical role in developing diarrheal cases among infants as a risk factors like bacteria and other causative agents responsible for mortality and morbidity cases among children under five year age.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols

were approved under the Medical Laboratory Technology Department Amarah Technical Institute and all experiments were carried out in accordance with approved guidelines.

References

1. Nilsson M, Svenungsson B, Hedlund KO, Uhnoo I, Lagergren A, Akre T. Incidence and genetic diversity of group C rotavirus among adults. *J Infect Dis.* 2000;182:678-84.
2. Mathur A, Baghel D, JaatJ, Diwan V, Pathak A. community -Based Participatory Research and Drug Utilization Research to Improve Childhood Diarrhea Case Management in Ujjain, India. A Cross-Sectional Survey. *Int. J. Environ. Res. Public Health*, 2019;16:1646.
3. RadlovićN, Leković Z, VuletićB,V, Simić D. Acute diarrhea in children. *Srpski arhiv za celokupno lekarstvo* 2015;143(11-12):755-762.
4. Gurgel RQ, Cardoso G de S, Silva AM, Santos LN, Oliveira RC. Creche: ambiente expositor ou protetor nas infestações por parasitas intestinais em Aracaju, SE. *Rev. Soc. Bras. Med. Trop.* 2005;38:267-9.
5. Mandomando IM, Macete EV, Ruiz J, Sanz S, Abacassamo F, Vallès X. Etiology of diarrhea in children younger than 5 years of age admitted in a rural hospital of southern Mozambique. *Am J Trop Med Hyg.* 2007;76:522-7.
6. GetachewA, Guadu T,TadieA, GizawZ, GebrehiwotM .Diarrhea Prevalence and Sociodemographic Factors among Under-Five Children in Rural Areas of North Gondar Zone, Northwest Ethiopia. *Hindawi, International Journal of Pediatrics*2018;6031594:8 .
7. Kattula D, Francisi MR, Kulinkina A, Sarkar R .Environmental predictors of diarrhoeal infection for rural and urban communities in south India in children and adults. *Epidemiol. Infect.*, 2015;1-12Cambridge University Press 2015 doi:10.1017/S0950268814003562.
8. Ramani S, Kang G. Viruses causing childhood diarrhea in the developing world. *Curr Opin Infect Dis.* 2009;22(5):477-482.
9. Scarcella C, Carasi S, Cadonia F. An outbreak of viral gastroenteritis linked to municipal water supply, Lombardy, Italy, 2009. *Euro Surveill.* 2009;14 (29):pii. 19274.
10. Kapikian AZ, Chanock RM. Rotaviruses. In: *Fields*

- BN, Knipe DM (eds) *Virology*, 2nd edn, vol 2. New York, Raven Press. 1990;1353-1404.
11. Agustina R, Shankar AV, Ayuningtyas A, Achadi EL, Shankar AH. Maternal agency influences the prevalence of diarrhea and acute respiratory tract infections among young Indonesian children. *Matern Child Health J* 19: 2015; 1033-1046.
 12. Haf erlach T, Bacher U, Kern W, Schnittger S, Haf erlach C. Diagnostic pathways in acute leukemias: a proposal for a multimodal approach. *Ann Hematol*. 2007;86: 311-327.
 13. Giordano MO, Ferreyra LJ, Isa MB, Martinez LC, Yudowsky SI, Nates SV.: The epidemiology of acute viral gastroenteritis in hospitalized children in Cordoba City, Argentina: an insight of disease burden. *Rev. Inst. Med. Trop. Sao Paulo*. 2001;43(4):193-197.
 14. Castello AA, Arguelles MH, Rota RP, Oithoff A, Jiang B, Glass RI. Molecular epidemiology of group A Rotavirus diarrhea among children in Buenos Aires, Argentina, from 1999 to 2003 and emergence of the infrequent genotype G12. *J Clin Microbiol*. 2006; 44(6):2046-2050 .
 15. Wilhelm I, Roman E, Sanchez-Fauquier A. Viruses Causing gastroenteritis. *Clin. Microbiol Infect*. 2003; 93(4): 247-262.
 16. Ward TL, Knights D, Gale CA. Infant fungal communities: current knowledge and research opportunities, *BMC Med*. 2017;15: 30.
 17. Forbes D, L EP Camer-Pesci, P B Ward. Faecal candida and diarrhea. *Arch Dis Child* 2001;84:328-331.
 18. Giordano MO, Ferreyra LJ, Isa MB, Martinez LC, Yudowsky SI, Nates SV. The epidemiology of acute viral gastroenteritis in hospitalized children in Cordoba City, Argentina: an insight of disease burden. *Rev. Inst. Med. Trop. Sao Paulo*. 2001;43(4):193-197.
 19. Talwar O, Chakrabarti A, Chawla A, Mehta S, Walia BNS, Kumar L. Fungal diarrhea: association of different fungi and seasonal variation in their incidence. *Mycopathology*.: 1990;110:101-105.
 20. Dollive S. A tool kit for quantifying eukaryotic rRNA gene sequences from human microbiome samples. *Genome Biol*. 2012;13, R60.
 21. fferrmann JE, Bfacklow NR. Rotavirus. In: Mandell GL, Douglas RG, Bennett JE (eds) . *Principles and practice of infectious diseases*, 3rd edn. New York, Churchill Livingstone. 1990;1234- 1240.
 22. Habash SH, Habeeb SI. Rotavirus Diarrhea in Children Under Five in Basrah: Hospital Based Study. *Pediatric Infectious Diseases*: 2018;3 (2):6
 23. Bishop RF, Barnes GL, Townley RRW. Microbial flora of stomach and small intestine in infantile gastroenteritis. *Acta Paediatr Scand* 1974; 63: 418-22.
 24. Coulson BS, Grimwood K, Hudson IL, Barnes GL, Bishop RF. Role of coproantibody in clinical protection of children during reinfection with rotavirus. *J Clin Microbiol* 1992; 30: 1678-1684.
 25. Grimwood K, Lund JCS, Coulson BS, Hudson IL, Bishop RFB, Barnes GL. Comparison of serum and mucosal antibody responses following severe acute rotavirus gastroenteritis in young children. *J Clin Microbiol* .1988; 26: 732-738.

Epidemiological Study of Toxoplasmosis among Pregnant and non Pregnant in Baghdad City and its Relationship with Blood Groups

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Abstract

This study was conducted during the period from March 2018 to March 2019, and included using of direct hemagglutination method to determine the rate of infection with *Toxoplasma gondii* among women in Baghdad city. Detection of toxoplasmosis was carried out by collecting iso blood samples included 100 samples from pregnant women and 50 samples from non-pregnant women who had previous recurrent abortions due to probable toxoplasmosis at time of pregnancy. The infection rate with *toxoplasma gondii* was higher in non-pregnant women group Higher than the pregnant women group. Study of prevalence of toxoplasmosis among women's age groups revealed that the highest infection rate was in the age group (26-30) years, while the lowest infection rate was in the age groups (15-20) and (>45) years of the pregnant women. The results of abortion frequency demonstrated that two times abortion was most frequent among pregnant women, and three times abortions was most frequent among non-pregnant women. Infection criteria for repeated abortions showed positive results for toxoplasmosis when serological examinations were used. Finally, our results found that the highest infection rate (98.3%) was among the pregnant women with A+ blood group, and (31.25%) among non-pregnant women with O+ blood group.

Keywords: Toxoplasmosis, Pregnant, non-Pregnant.

Introduction

Toxoplasmosis is a zoonotic disease with a broad range of vertebral hosts including types of mammals such as humans, however, the final hosts are domestic cats and other types of cats^(1,2). The causative agent of toxoplasmosis is a protozoan known as *Toxoplasma gondii*, which is an intestinal coccidia. The parasite was first described in a wild rodent (*Ctenodactylus gondii*) in North Africa in 1908, from which the name *gondii* was derived. Serological tests indicate that humans can be infected with toxoplasmosis at any part of the world, but most of these infections are benign in nature, or may be asymptomatic in adults and children after birth³. It is important to study this disease for humans in severe cases which show some symptoms, that in turn affect the infected person and limits or reduces his activity⁴. If the female is infected with toxoplasmosis, very important risk may occur due to fetal intra uterine damage in case of pregnancy, where this parasite causes damage of the fetus during its passage through the placenta and then

causes abortion in most cases, especially in the first trimester of pregnancy or may lead to stillbirth if the infection occurred in the last trimester of pregnancy⁵. Toxoplasmosis caused by *Toxoplasma gondii* parasite is a worldwide spread infection because of the ability of the parasite to cause infection and multiply inside avian and mammal cells⁶. The infection occurs through foods and drinks contaminated with oocysts or ingestion of under cooked meat which contain tissue cysts. The ingestion of one mature oocyst is enough to cause human toxoplasmosis⁷. Blood transfusion is an important source of transmission of acute infection, and transplantation of infected organ and tissue to healthy individuals can also cause infection⁸. It was reported by⁹ that prevalence of *Toxoplasma gondii* in France was due to the wide spread ingestion of undercooked meat. A study conducted by¹⁰ showed that infection rate in Baghdad was (18%), while¹¹ found that the infection rate was (37%) in Basra city, whereas¹² stated that the infection rate in the Northern part of Iraq was (15.26%).

Materials and Method

1. **Collection of Samples:** This study was conducted in the Medical city/Private Nursing Home Hospital, Department of gynecology in Baghdad during the period from March 2018 to March 2019 and included collection iso blood samples from pregnant and non–pregnant women. Also aquestionnaire form was used for data collection including living standard, blood group, number of pregnancies, number of abortions, type of abortion as well as some clinical features which appeared on the infected women.

2. **Laboratory diagnosis of Taxxoplasmosisgondii:** Blood samples (5ml) were collected from 150 women (100 pregnant women) and (50 non-pregnant women) whose medical history indicates the possibility of being infected with previous toxoplasmaosis infection because they suffered from repeated abortions and giving birth to deformed children). The blood sampled were put in plain test tubes (without anticoagulant) and left in the water bath for 15-30 minutes to obtain serum, then latex agglutination test was performed by using a suspension of formal in fixed latex particles coated with toxoplasma antigen to detect toxoplasma antibodies in the sera of patients. The kit used is called (Toxoplasmosis kit) from the Spanish company (Biokit) which contained the following:

A. Toxoplasma latex: Suspension of latex particles coated with *T.gondii* antigen and 0.1% Sodium azide as a preservative.

B. Positive control: Human serum and 0.1% Sodium azide

C. Negative control: Non-reactive human serum and 0.1% Sodium azide.

3. **Detection of blood group:** Bood group are detected (Maton et al .1997) was represented by the use of special solution

1. Anti-A detection of blood A.
2. Anti-B detection of blood B.
3. Anti-D detection of reiss Rh.

The work method was summarized by adding three drops of for sampleon the slide and then adding adrop of Anti-A solution to the first drope, adrop of Anti-B solution to the second drope and adrope of Anti-D to the

three drope then mixed by sticks to know the following:

1. In the case of coagulation of the first drope and non clotting the second,the blood type A.
2. In the case of non coagulation of the first drope and clotting the second,the blood type B.
3. In the case of coagulation first and second drope,the blood type AB.
4. In the case of non coagulation first and second drope,the blood type O.

As for Rh the occurrence coagulationin the third drope containing

An Anti-D solution indicates appositive test and the opposite is true.

Results and Discussion

The current study showed the importance of studying toxoplasmosis incidence in Baghdad city. Results in table (1) showed that the prevalence rate of toxoplasmosis was (61%) in pregnant women and (64%) in non-pregnant women. In comparing these results with the findings of other studies, it was found that ¹³ reported (12%) infection rate out of 100 pregnant women, while the study by ¹⁴ on 127 women who were suffering from repeated abortions reported (33.07%) infection rate by using the indirect hemagglutinin test and (40.15%) infection rate by using the complement fixation test.

Table (1): Infection rate with Toxoplasma gondii in Baghdad city

Women	Total Number	Positive (+ve)	%
Pregnant women	100	61	61
Non-pregnant women	50	32	64
Total	150	93	125

Table (2) shows the relationship between age and infection with toxoplasmosis. The highest infection number and rate 23 (77.66%) was found among pregnant women within the age group (26-30) years, while the lowest infection rate (25%) appeared among the two age range groups (15-20) years and (> 41) years. When comparing these results with those of non-pregnant women, it was found that the highest positive infection rate (77.8%) was found among non-pregnant women within the age group (36-40) years.

Table (2): Distribution of toxoplasmosis according to different age in the two groups of women

Age Group (Years)	Pregnant Women			Non-pregnant Women		
	Total Number	+ve	%	Total Number	+ve	%
15-20	4	1	25	5	3	60
21-25	19	10	52.63	10	6	60
26-30	30	23	76.66	5	3	60
31-35	31	21	67.74	8	4	50
36-40	12	5	41.66	18	14	77.8
> 40	4	1	25	4	2	50
Total	100	61	61	50	32	

Abortion period, times and types during infection with toxoplasma among both pregnant and non-pregnant women are shown in table (3). It is shown that the highest abortion rate (63.18%) occurred during the first trimester of pregnancy among pregnant women, while the highest abortion rate (63.37%) occurred during the first trimester of pregnancy among non-pregnant women, and these results agreed with²³ who recorded the highest incidence rate of toxoplasmosis during the first

trimester of pregnancy in comparison with the second and third trimesters which is attributed to the period and time of infection. Moreover, our results agreed with the results of²⁴ who reported that the transmission rate of toxoplasmosis from the mother to her fetus during the first trimester of pregnancy was 70% and during the second trimester was 25%, therefore, abortion rate will be higher in the first trimester than the second trimester of pregnancy which depends upon the infection severity.

Table (3): Period and type of abortion during infection with Toxoplasma gondii among pregnant and non-pregnant women

Type of Abortion	Pregnant Women		Non-pregnant Women	
	Number	%	Number	%
Stillbirth	13	5.90	8	6.23
First trimester of pregnancy	139	63.18	17	63.37
Second trimester of pregnancy	53	24.04	12	25.78
Third trimester of pregnancy	15	6.81	6	5.12
Total	220	100	43	100
Total number of pregnancies	449	-----	72	-----
Total number of child loss	229	48.99	35	70

*The data is recorded by the questionnaire sheet.

Table (4) shows the effect of toxoplasmosis on abortion frequency in pregnant and non-pregnant women. It is observed that abortion for two times recorded the highest percentage of abortion among pregnant women (42.37%), while abortion for three times recorded the highest percentage of abortion among

non-pregnant women (29.16%). However, these results were on the contrary of the findings of²⁶ who stated that seropositivity was the highest among women who had one abortion when compared with women with multiple abortions.

Table (4): Effect of toxoplasmosis and its relationship with abortion frequency among pregnant and non-pregnant women

Frequency of Abortion	Pregnant Women		Non-pregnant Women	
	Number	%	Number	%
One time abortion	10	16.94	8	11.11
Two time abortion	25	42.37	19	26.38
Three time abortion	9	15.25	21	29.16
Four time abortion	7	11.86	11	15.27
Five time abortion	4	6.77	7	9.72
Six time abortion	1	1.69	3	4.16
Seven time abortion	3	5.08	2	2.77
Eight time abortion	/	/	1	1.38
Total	59	100	72	100

*The data is recorded by the questionnaire sheet.

Relationship between toxoplasmosis and blood groups: Distribution of toxoplasmosis among pregnant and non-pregnant women with different blood groups showed that the highest infection rate was in the pregnant women with blood group A+ (98.3%) followed by the blood group O+ (27.8%)., the highest infection rate in the women with blood group A+ can be explained by the presence of A subgroups, which may help the parasite to be adapted with such groups, while for blood group O+,

it is attributed to the presence of a negative allele similar to that found in the *plasmodium vivax* parasite, which was reported by ^(27,28), and this can be explained by the presence of glycoproteins in the form of glycoporphines in this blood group, which can be used as nutrient for the parasite^(29,30) Regarding the infection rate among non-pregnant women, our study found that the highest infection rate was in the blood group O+ (31.25%) as seen in table (5).

Table (5): Distribution of toxoplasmosis according to the blood groups

Blood Group	Number	Positive	%	Number	Positive	%
B+	30	21	34.4	12	7	21.8
A-	/	/	/	2	1	3.125
A+	25	15	98.3	8	8	25
B-	/	/	/	2	1	3.125
AB+	15	8	13.11	8	4	12.5
AB-	/	/	/	/	/	/
O+	27	17	27.8	16	10	31.25
O-	3	/	/	2	1	3.125
Total	100	61	/	50	32	/

Conclusion

The results of laboratory diagnosis were showed that the infection rate with *toxoplasma gondii* was higher in non-pregnant women group Higher than the pregnant women group, Study of prevalence of toxoplasmosis

among women's' age groups revealed that the highest infection rate was in the age group (26-30) years, while the lowest infection rate was in the age groups (15-20) and (>41) years of the pregnant women, The results of the current study also revealed a high number of abortions in both pregnant and non-pregnant women

groups during the first trimester of pregnancy (139 in the pregnant and 17 abortions in the non-pregnant women). The results of abortion frequency demonstrated that two times abortion was most frequent among pregnant women, and three times abortions was most frequent among non-pregnant women. Finally, our results found that the highest infection rate (98.3%) was among the pregnant women with A+ blood group, and (31.25%) among non-pregnant women with O+ blood group.

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Middle Technical university, Institute of Medical Technology/Baghdad/Nursing Department, Iraq and all experiments were carried out in accordance with approved guidelines.

References

- Al-Kaysi AMJ. Toxoplasmosis among random sample of Iraqi women and premature infants with certain immunological aspect. M.Sc. thesis university of Al-mustansiryah.2001.
- Shani WS. Humeral and cellular immune response in women afflicted with Toxoplasmosis . Ph.D. Thesis. University of Basrah. 2004.
- Rashno MM, Fallahi S, Bahrami P. Alzheimer's disease and Toxoplasma gondii infection; seromolecular assess the possible link among patients. *Int J Geriatric Psychiatry*. 2017;32:232-4.
- Sharbatkhori M, Moghaddam YD, Pagheh AS, Mohammadi R, Mofidi HH, Shojaee S. Seroprevalence of Toxoplasma gondii infections in pregnant women in Gorgan city, Golestan province, Northern Iran-2012. *Iran J Parasitol*. 2014;9:181.
- ABHusain, Hadeel M Fiadh, Anaas A. Study the prevalence Toxoplasma gondii in aborted women by using agglutination and ELISA method. College of Veterinary Medicine, Anbar University2010.
- AL-Rubaia .Zahrira Abd AL-Hammza Abbas Comparative between enzyme linked immuno sorbent assay and enzyme linked fluorescent assay in diagnosis of Toxoplasma gondii in pregnant women and it's relationship with abortion cases and abnormalities in Diwaniya provinceB.S.C. Biology-2006 University of Al-Qadisiya-College of Science.
- Rashno MM, Fallahi S, Kheirandish F, Bagheri S, Kayedi MH, Birjandi M. Seroprevalence of Toxoplasma gondii infection in patients with Alzheimer's disease. *Arch Clin Infect Dis*. 2016;11(3).
- AL-Nasri ARGh, Daoud ISD.The changes in some biochemical tests among women infected with Toxoplasma gondii in salahaldin Provice college of Science, University of Tikrit, Tikrit, Iraq.2011.
- Yad MJY, Jomehzadeh N, Sameri MJ, Noorshahi N. Seroprevalence of anti-toxoplasma gondii antibodies among pregnant woman in South Khuzestan, Iran. *Jundishapur J Microbiol*. 2014;7(5).
- Parasites – Toxoplasmosis (Toxoplasma infection) Disease”. July 10, 2014. Archived from the original on 22 August 2015. Retrieved 22 August 2015
- HunterCA, SibleyLD. “Modulation of innate immunity by Toxoplasma gondii virulence effectors”. *Nature Reviews Microbiology*. November 2012;10 (11): 766–78. doi:10.1038/nrmicro2858. PMC 3689224. PMID 23070557.
- Cook TB, Brenner LA, Cloninger CR. Latent” infection with Toxoplasma gondii: association with trait aggression and impulsivity in healthy adults”. *Journal of Psychiatric Research*. 2015;60: 87–94.
- Fallahi S, Mazar ZA, Ghasemian M, Haghghi A. Challenging loop—mediated isothermal amplification (LAMP) technique for molecular detection of Toxoplasma gondii. *Asian Pacif J Trop Med*. 2015;8: 366-72.
- Fallahi S, Mazar ZA, Ghasemian M, Haghghi A. Challenging loop—mediated isothermal amplification (LAMP) technique for molecular detection of Toxoplasma gondii. *Asian Pacif J Trop Med*. 2015;8: 366-72.
- Ahmed A. Isolation and diagnosis of toxoplasma gondii parasite among aborted women in Tikrit Teaching Hospital. M.Sc thesis, College of education for girls. University of Tikrit. 2008
- Mohammad M. Seromolecular assess of Toxoplasma gondii infeaction in pregnant women and neonatal umbllical cord blood, Damghan Branch, Islamic Azad University, Damghan, Iran, 2019.
- Hussien JH, Mohammed A, Raghda HA.”Study the Effect of Acute Toxoplasmosis Infection on Some Hormones and the Phagocytic Activity

- of Neutrophils in Pregnant and Non-pregnant Women Before and After Treatment”. *Int. J. Curr. Microbiol. App. Sci.* 2015; 4(10): 459-465.
18. Salman YJ, Kalawish AM. “Relationship between *Toxoplasma gondii* and arthritis among patients in Kirkuk city”. *Int. Curr. Res. Aca. Rev.* 2015; 3(8):175-187.
 19. Ahmed HA, Shafik SM, Ali MEM, Elghamry ST, Ahmed AA. Molecular detection of *Toxoplasma gondii* DNA in milk and risk factors analysis of seroprevalence in pregnant women at Sharkia, Egypt. *Veterinary World*, 2014;7:594–600.
 20. Amdouni Y, Rjeibi MR, Rouatbi M, Amairia S, Awadi S, Gharbi M. Molecular detection of *Toxoplasma gondii* infection in slaughtered ruminants (sheep, goats and cattle) in Northwest Tunisia. *Meat Science*, 2017;133:180–184.
 21. -Boughattas S, Ayari K, Sa T, Aoun K, Bouratbine A. Survey of the parasite *Toxoplasma gondii* in human consumed ovine meat in Tunis City. *PLoS One*, 2014;9: e85044.
 22. Sadiqui S, Shah SRH, Almugadam BS, et al.: Dataset 1 in: Distribution of *Toxoplasma gondii* IgM and IgG antibody seropositivity among age groups and gestational periods in pregnant women. *F1000 Research*. 2018. <https://www.doi.org/10.5256/f1000research.15344.d224335>
 23. Ayi I, Kwofie KD, Blay EA, Osei JH, Frempong KK, Koku R, et al. Clonal types of *Toxoplasma gondii* among immune compromised and immune competent individuals in Accra, Ghana. *Parasitol Int.* 2016; 65(3):238-44. <https://doi.org/10.1016/j.parint.2016.01.004> PMID:26775819
 24. Mahmoudvand H, Saedi Dezaki E, Soleimani S, Baneshi MR, Kheirandish F, Ezatpour B, et al. Seroprevalence and risk factors of *Toxoplasma gondii* infection among healthy blood donors in south-east of Iran. *Parasite Immunol* 2015; 37: 362–67.
 25. Pappoe F, Cheng W, Wang L, Li Y, Obiri-Yeboah D, Nuvor SV, et al. Prevalence of *Toxoplasma gondii* infection in HIV-infected patients and food animals and direct genotyping of *T. gondii* isolates, Southern Ghana. *Parasitol Res.* 2017;116(6):1675-1685.
 26. Wallon M, François P. “Congenital Toxoplasmosis: A Plea for a Neglected Disease”. *Pathogens*. 2018; 7(1). pii: E25. DOI:10.3390/pathogens7010025
 27. Eman Z Younis1, Adela H, *Toxoplasma gondii* IgG, IgM, and IgA among Type-2 Diabetic Patients in Benghazi Libya: A Comparison Study, Faculty of Education-Ghemines, University of Benghazi, Benghazi, Libya, 2018.
 28. Ebrahimi M, Ahmadi A, Yaghfoori S, Rassouli M, Azizzadeh M. Evaluating the prior knowledge of toxoplasmosis among students of Ferdowsi university of Mashhad. *Med J Islam Repub Iran* 2015;29:163.
 29. Hadi H, Raad AK, Raheem TOAL.” seroepidemiological aspects for *toxoplasma gondii* infection in women of Qadisiyah province, Iraq”. *IJPRIF*. 2016;9(11):252-259.
 30. Nariman H, Rawaa A. Immunological and Molecular study of *toxoplasma gondii* from aborted women in Diyala, Iraq. 2018.

Assessment of Teachers' Knowledge about Child abuse at AL Nasiriya Primary Schools

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Abstract

Background: One of the most pressing issues concerning child health and well-being is child abuse; it remains to be particular and major risk to the emotional and social well-being of the children worldwide. As pupils spend long time in school, the teachers must be qualified to identify physical and behavioral fluctuations related to abuse to assuredly determine the reason and design interventions properly. The insufficient data and information result in a break in the vital duty of teachers in determination and initial assistance in case of child abuse.

Objectives: The aims of the study were to evaluate the information of the primary school teachers on identifying and reporting of child abuse and to identify any link between the teachers' knowledge with designated sociodemographic variables.

Methodology: A descriptive design was applied during the study, which include 100 primary school teachers from 6 selected schools in Al-Nasiriyah city. The tool used for data collection were a designed questionnaire on signs and symptoms of child abuse.

Results: Most of the school teachers (74%) had low knowledge on child abuse. Regarding association between knowledge and certain sociodemographic variables, no significant statistical association found except for Receive educational training courses in child abuse ($p < .05$).

Conclusion: Child abuse is an international concern, children experience abuse in several types, and additional awareness will assist in fighting this issues. Teachers' knowledge have to be improved by applying attentiveness programs on child abuse.

Keywords: *Assessment, knowledge, child abuse, primary school teachers.*

Introduction

Children all over the world must have the simple and basic human right to live safely, child abuse risk that right by engaging the child at danger of emotional and physical injuries and may be death. Child abuse and happen in all various groups all around the world despite ethnic, occupational, cultural, and socioeconomic differences⁽¹⁾.

Child maltreatment (child abuse) is generally defined by the World Health Organization (WHO) as "the abuse and neglect of people under 18 years of age. It includes all forms of physical and/or emotional ill-treatment, sexual abuse, neglect or negligent treatment or commercial or

other exploitation, resulting in actual or potential harm to the child's health, survival, development or dignity in the context of a relationship of responsibility, trust or power"⁽²⁾.

During 2016, around 4.1 million reports concerning 7.4 million child were reported to U.S. child protective service agencies⁽³⁾. Majority of these reports (65%) were by specialists who, while working, encountered the suspected child victim. With educational staffs, one of the major reporters of child abuse. In United States of America, educators introduce 16% of all reports⁽⁴⁾.

Teachers are in direct contact on day-to-day basis with a large number of children for a longtime as the

child devotes a lengthier period in school. Therefore, teachers can detect behavioral abnormalities in the child and consequently are in a good place to perceive and report child abuse, but are not prepared or are not sufficiently informed⁽⁵⁾. Teachers' attitudes can effect the awareness and perception of abuse and subsequently reporting cases⁽⁶⁾.

The teachers knowledge toward reporting of child abuse is a chief factor in dealing with the case. There are numerous components that may possibly be impacted by their attitude and recognition that may influence the quality of reporting and decision-creation of child abuse that teachers have to put in consideration⁽⁷⁾.

Some of the recognized impacts affecting active teacher reporting child abuse emerge from the attributes of the child's condition, for example, the recurrence and seriousness of the child's behaviour and injuries⁽⁸⁾. Others identify with institutional elements, for example, a steady workplace. Still, many determinants related to the teacher, such as the teacher's consciousness of the presence of a lawful obligation to report alleged child abuse, their insight of the content of that obligation⁽⁹⁾ and their disposition concerning the duty⁽¹⁰⁾.

It is vital for teachers to own positive mentalities concerning the reporting obligation, knowledge regarding communal and educational background of child abuse, and 'lawful literacy' about the lawful and policy-based commitments to report. This professional advancement of teachers should happen not just in in-service settings, but also in pre-service ones^(11, 12).

The deficiency of researches (especially in Iraq) in teachers' knowledge and training in the subject of child abuse is alarming. Therefore, this study aims to assess teachers' knowledge concerning child abuse and set basis for future studies and solutions to this problem in Iraq.

Material and Method

Study Design: Descriptive survey is conducted in the period from 19th of April 2019 to 1st of October 2019.

Setting of the Study: The study was applied at 10 primary schools in Al-Nasiriyah city, Thi-qar, Iraq.

Study Sample: A probability (random) sample of (100) teachers, who were working in 10 primary schools in Al-Nasiriyah city.

The Study Instrument: The authors constructed a questionnaire for the purpose of the study

Part 1: Demographic Data: Socio-demographic data sheet composed of six points that included (Marital status, gender, education, passing of educational training courses, income).

Part 2: Part II. Clinical information regarding blood transfusion and its reactions: The questionnaire is consisted of (12) items separated into three domains.

First Domain: (4) items connected to signs and symptoms of physical violence.

Second domain: (4) items related to signs and symptoms of emotional violence.

Third domain: (6) items linked to signs and symptoms of sexual violence.

These items were rated according to the following scale; ["know" is given (1); "Don't know" is given (2)]

Data Collection: Data were gathered by application of the constructed questionnaire after estimation of the reliability and validity through direct interview with the sample.

Pilot Study: In order to estimate the study instrument (questionnaire) reliability, A (10) teachers sample were designated; pilot study was applied in the period from 1st of April to 15th of April 2019. The pilot study sample was excepted from the total study sample.

Validity: Study instruments validity were determined by a group of (7) experts, that had more than five years of experience in the study field.

Reliability: Questionnaire reliability was estimated by the use of test re-test method on ten teachers. Outcomes displayed acceptable level of constancy and internal consistency of major items regarding responses' of the questionnaire, responses were calculated through applying the Alpha Cronbach parameter, which exhibit that the person correlation coefficient = (0.78).

Analysis of the Statistics: With the intention of analyze the study data, the statistical package of social sciences (SPSS) ver. (23) were used (Percentage, Frequency, Mean, Standard deviation, Mean of score, and Chi-square).

Results

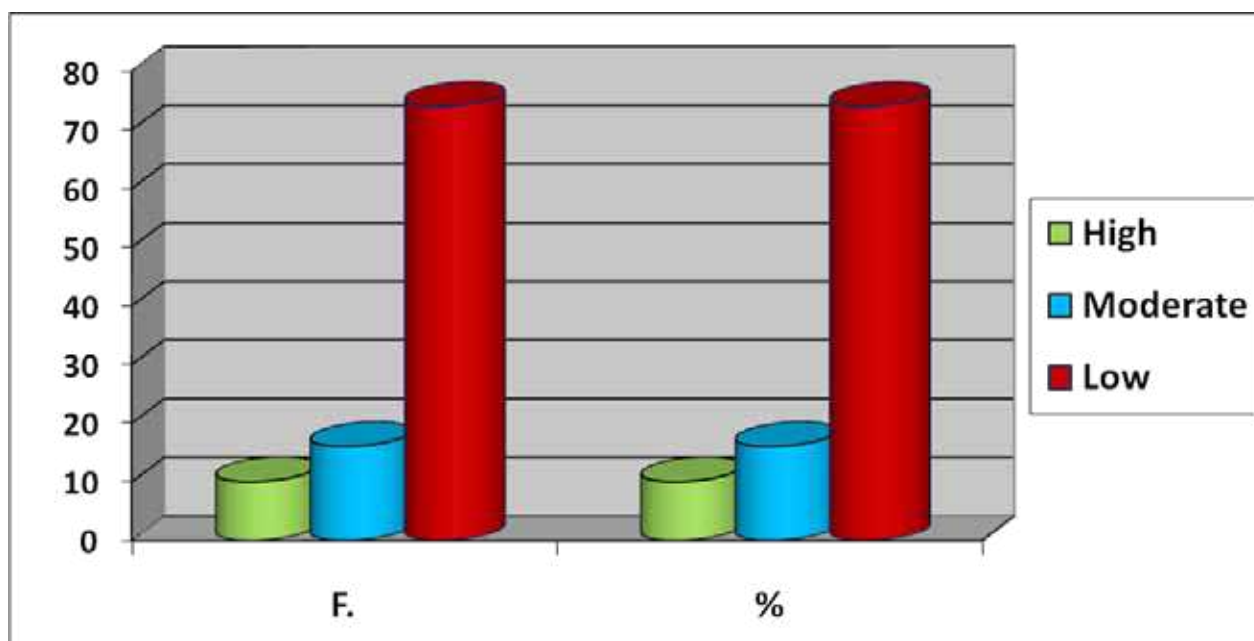
Table 1: Frequency of Sociodemographic characteristics of Teachers (N=100)

SDVs	Group	Frequency (F)	Percent (%)
Marital Status	Single	33	29
	Married	57	61
	Divorced	6	6
	Widowed	4	4
Gender	Male	39	39
	Female	61	61
Education	Diploma or Associated Degree	78	78
	Bachelor’s Degree or Higher	22	22
Receive educational training courses in child abuse	Yes	5	5
	No	95	95

SDVs = Sociodemographic variables, % = percentage, F = frequency, n = number of samples

Table (1) shows that the most of the study subjects were married (57%) Female (61%). The highest educational status of the participants was reported to

be (78%) of diploma or Associated Degree. Majority of the study subjects (95%). Have not Receive educational training courses in child abuse.



n = number of samples, F = frequency, % = percentage

Figure (1): Total teacher’s knowledge concerning child abuse

Figure (1) shows knowledge levels of teachers where most of them (74%) were have low level and (16%) were have moderate level, while only (10) were

have a high knowledge level regarding blood transfusion reactions.

Table (3): Relationship between SDVs and nurses knowledge regarding main domains

Main Domains \ SDVs	Marital status		Gender		Education		Receive educational training courses in child maltreatment	
	X ²	Sig.	X ²	Sig.	X ²	Sig.	X ²	Sig.
Signs and symptoms of physical violence	19.177	.574	3.278	.858	20.261	.122	26.359	.023
Signs and symptoms of emotional violence	27.747	.271	19.704	.012	23.658	.097	36.634	.002
Signs and symptoms of sexual violence	30.908	.275	14.074	.120	17.212	.509	34.428	.011
Total	64.694	.796	23.291	.561	60.847	.140	71.069	.027

SDVs: Sociodemographic variables, X²: Chi-square, Sig.: Significance.

Table (3) illustrates the relationship between SDVs and knowledge level concerning main domains and total level of knowledge.

Discussion

The issue of child abuse has substantial insinuations for pre-service teacher’s preparation and proficient development. They have an instructive role in interacting with suspected children, and a lawful and professional obligation to report alleged case. Teachers need provision and training to improve the particular knowledge and confidence wanted to interact with this multifaceted context.

The results of the current study presented that most of the sample were married (57%) Females (61%) and the highest educational status of the participants was reported to be (78%) of diploma or Associated Degree.

The most important finding concerning sociodemographic variables is that (95%) of the study sample have not receive educational training courses in child abuse (either pre- or in-service) and that is an extremely alarming result that indicate poor administrations performance in providing knowledge and training programs for teachers. Many studies find low or no content at all concerning child protection in teachers training programs during pre-service period^(12, 13). Also, some studies suggest that reporting of the teachers is affected by the level and context of teachers’ training programs in identifying abuse⁽¹⁴⁾.

Concerning total knowledge of the teachers regarding child abuse, the study exhibits that majority (74%) have low levels of knowledge. From the researchers’ viewpoint, that was expected because in Iraq (like in many of the developing countries) the

governmental administrations have a “bigger” problems to deal with until child abuse has become an unimportant issue compared to other problems!

The results also illustrated that there was statistically significant relationship ($p < .05$) related to knowledge score with sociodemographic data (Receiving educational training courses in child abuse in specific). The relationship between these two items is undeniable as many studies shows ^(7, 14).

Conclusion

Child abuse is an international concern that need urgent and effective interventions in order to manage appropriately. In developing countries including Iraq, this problem takes a less attention from the specialized administrations and organizations that subsequently result in unnoticed escalation that primarily affect the children.

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References

1. Garosi, B, Safizadeh, H, Dostmohamadi, L. The knowledge and attitudes of pediatric specialists and assistants on child abuse. Journal of Forensic Medicine. 2005;38:83-7.
2. Violence Info – Child maltreatment-WHO.

- Retrieved from <http://apps.who.int/violence-info/child-maltreatment/>. 2019; 16.
3. Child Maltreatment AD. Retrieved from <https://www.acf.hhs.gov/cb/research-data-technology/statistics-research/child-maltreatment>. 2019.
 4. Kenny MC. Teachers' attitudes toward and knowledge of child maltreatment. *Child Abuse & Neglect*. 2004; 28(12): 1311–1319.
 5. Goldman JG, Grimbeek P. Sources of knowledge of departmental policy on child sexual abuse and mandatory reporting identified by primary school student teachers. *Educational Review*. 2011;63(1): 1-18.
 6. Feng JY, Huang TY, Wang CJ. Kindergarten teachers' experience with reporting child abuse in Taiwan. *Child Abuse & Neglect*. 2010; 34(2): 124–128.
 7. Hynniewta B, Jose T, Anjali KG. Knowledge and attitude on child abuse among school teachers in selected urban English medium schools of Udipi District. *Manipal Journal of Nursing and Health Sciences*. 2017; 3(1): 32-36.
 8. Walsh K, Bridgstock R, Farrell A, Rassafiani M, Schweitzer R. Case, teacher and school characteristics influencing teachers' detection and reporting of child physical abuse and neglect: Results from an Australian survey. *Child Abuse & Neglect*. 2008; 32(10): 983-993.
 9. Ben Mathews (2011). Teacher Education to Meet the Challenges Posed by Child Sexual Abuse. *Australian Journal of Teacher Education*, 36(11), 13-32.
 10. Goebbels A, Nicholson J, Walsh K, De Vries H. Teachers' reporting of suspected child abuse and neglect: behaviour and determinants. *Health Education. Research*, 2008; 23(6):941-951.
 11. Mathews B, Walsh K, Rassafiani M, Butler D, Farrell A. Teachers reporting suspected child sexual abuse: results of a three-State study. *University of New SouthWales Law Journal*. 2009; 32(3): 772-813.
 12. Arnold L, Maio-Taddeo C. Professionals Protecting Children: Child Protection and Teacher Education in Australia. Australian Centre for Child Protection: Adelaide. 2007.
 13. Watts V, Laskey L. Where have all the flowers gone? Child protection education for teachers in Australian universities. *South Pacific Journal for Teacher Education*, 1997; 25(2): 171-176.
 14. Hawkins R, McCallum C. Mandatory notification training for suspected child abuse and neglect in South Australian schools. *Child Abuse & Neglect*. 2001; 25: 1603-1625.

Pharmacological Activities and Chemical Constituents and of Bryonia Dioica L.: A Review

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Abstract

Bryonia is one of the genera belong the Cucurbitaceae family (gourd family). *Bryonia dioica* distribute in Western Europe, this plant flowering in May as small, greenish and three or four flowers together in small cluster the stamens and pistils are found separated therefore consider a dioecious plant—growth as separate plant into (male and female). The phytochemical constituents of Leaves are Luteolin, flavonoids (kaempferol), alkaloids, Glycosides, phenol steroids, Carbohydrates, anthraquinone and terpenoids, while the part used of this plant (Roots) are Kempferol 3, 7-di-O-rhamnoside, polyphenols, sterols, triterpenes, alkaloids, heterosides-c, carbohydrates, saponins, terpenoids, flavonoids, tannins, alkaloids, quinones, reducing sugar and coumarin. The fruits containing triterpene, glucosides, calcium oxalate crystals and the flowers are Phenolic acid and flavonoids. The biological activity and pharmacological uses of all plant parts of *B. dioica* are antinociceptive effects, antimicrobial activities, antioxidant activity, hepatoprotective activity, Anticancer activity, hypercholesterolemia, diabetes and fertility disorders.

Keywords: *Bryonia dioica*, phytochemical constituents, biological activity and pharmacological uses

Introduction

Bryonia is one of the genera belong the Cucurbitaceae family (gourd family) which is flowering plant^(1,2). The genus name Bryonia, came from the bryo word (Greek bryo), which means shoot, or appears of sprout according to the active growth of the plant stems⁽³⁾. The best-known common name is Bryony^(4,5). *B. dioica* distributed in Western Europe⁽⁶⁻⁸⁾. it has five-pointed leaves with different flowers like blue or white⁽⁹⁾. This plant flowering in May as small, greenish and three or four flowers together in small cluster the stamens and pistils are found separated therefore *B. dioica* consider a dioecious plant – growth as separate plant into (male and

female) flowers with many petals (five greenish-white petals)⁽¹⁰⁾. Male flowers about 12 to 18 mm and having stalked bunches and loose. The stamens consist of one-celled and the anthers are yellow, while the female flowers about 10 to 12mm^(11,12). The fertile flowers, distinguish easily by the presence of an ovary beneath the calyx, in general without stalk (sessile) about two to five fertile flowers together when the stem and leaves are withered, The berries, hang about the bushes, about peas size when ripe, take pale scarlet color containing six seeds in large size and filly juice⁽¹³⁾. The stems of *B. dioica* plant containing a long tendrils, which use for climb and its springing from the stalks of leaves and the tendrils between the shrubs and trees extend for many yards during the summer season, and when the fruit is ripening the tendrils drying as vine shaped very rough with leaves and form like prick-hairs and its consider as general character for this plant⁽¹⁴⁻¹⁶⁾. The leaf blade is lobed, which is divided into five lobes and the middle one is longer than others, in general the leaves consider as curved stalked shape⁽¹⁷⁾. The part used of this plant is the root which collected in the autumn and used as fresh and dry state⁽¹⁸⁾. the fresh root take a dirty yellow

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or yellowish-white, when cutting the root obtain milky juice as a bitter, and acrid taste. . The root is simple, like a carrot and some time forked into two parts⁽¹⁹⁻²⁰⁾. The medicinal uses of *B. dioica* plant for Irritative, hydragogue and cathartic. But now don't recommended used as a purgative because its cause discomfort able and irritation⁽²¹⁻²³⁾. It is useful in different diseases but in small doses used in cough, influenza, bronchitis, pneumonia, pleurisy and whooping-cough . Also used for cardiac disorders caused by rheumatism and gout, also in malarial and zymotic diseases⁽²⁴⁾.

Vernacular Names: There are many common names for *B. dioica* plant like white bryony,mandrake, ladies' seal, Tetterbury, red bryony, Wild Vine, Wild Hops, Wild Nep. Tamus and in French Navet du diable⁽²⁵⁻²⁸⁾.

Scientific Classification	
Kingdom	Plantae
Clade:	Angiosperms
Order:	Cucurbitales
Family:	Cucurbitaceae
Subfamily:	Cucurbitoideae
Genus:	Bryonia
Species	Bryonia dioica L.



Figure (1): Leaves and fruits of *Bryonia dioica* L. plant

Table (1): Phytochemistry Review

Plant Part	Constituent Reported
Leaves	Luteolin, flavonoids(kaempferol)(29-31). alkaloids, Glycosides, phenol steroids, Carbohydrates and, anthraquinone and terpenoids(32-35).
Flowers	Phenolic acid, flavonoids(36).
Fruit	triterpene glucosides and calcium oxalate crystals(37).
Root	Kempferol3, 7-di-O-rhamnoside(38), polyphenols, sterols, triterpenes, alkaloids(39), heterosides-c, carbohydrates, saponins, terpenoids, flavonoids, tannins, alkaloids,quinones, reducing sugar, coumarin (40-43).

Pharmacological and Biological Activities:

1. Antinociceptive Effects: The antinociceptive activity of the leaves extract of *Bryonia dioica* plant confirm by hydroalcoholic extract of leaves by used standard test of tail flick and formalin which is one of the most common test used for measured the antinociceptive activity with acetic acid used as chemical stimulation the results were observed that dose of 300 mg/kg with $P < 0.01$ ⁽⁴⁴⁾. and the compared between the leaves extract and indomethacin shown that no significant difference between them at dose of 300 mg/kg of leaves extract

and the results determined the LD50 of the plant extract was 4200 mg/kg⁽⁴⁵⁾.

2. Antimicrobial Activities: The leaves extract of *Bryonia dioica* plant has a referred to antibacterial activity against many of pathogenic bacteria such as *E.coli*, *K. pneumoniae*, and *P. vulgaris*. the results significant that activity against gram negative bacteria. The maximum inhibition zone (MIC)was 227.3mg ml⁻¹ against *P. vulgaris* while 186 mg ml⁻¹ against *K.pneumoniae* and then against *E.coli* was 143.9 mg ml⁻¹^(46,47).

3. **Antioxidant Activity:** The phenols and flavonoids in the *B. dioica* plant act as antioxidant activities those active compounds found in different parts of this plant (leaves, stem and flower) and those active compounds act as radical scavenging capacity, the flowers of *B. dioica* consider an important part used rich in phytochemical compounds and act as antioxidant this study done by measured the scavenging activity by colorimetric assay DPPH and presented by IC₅₀ value, the polar stem extract concentration at 28.75 µg/ml shown highest radical scavenging activity and in non polar extract at 31.27 µg/ml, while in leaves extract were 76.08 µg/ml in polar and 83.62 µg/ml in non polar and finally in flower extract were 98.35 µg/ml in polar and 91.54 µg/ml in non polar^(48,49).
4. **Hepatoprotective Activity:** The hepatoprotective action of leaves extract of *B. dioica* plant was investigated by used oral dose about 250mg/kg plant leaves extract for week this study was used Rats model by histopathological effect in Rats liver which induce hepatotoxicity by used CCl₄ and investigated the hepatoprotective activity of this extract in serum tested as the biochemical marker for hepatotoxicity AST and ALT . The leaves extract shown decrease the enzymes level by decrease the CCl₄ cause the plant extract have very important constituents like flavonoids, alkaloids, terpenoids, sterols⁽⁵⁰⁾.
5. **Anticancer Activity:** In Algerian study which proved the local population used the extract of *B. dioica* roots for treatment of breast cancer used this root extract only or by mixed this extract with honey and this study reported treat cancer 26% this study attributed to presence the major active compound: Kempferol 3, 7-di-O-rhamnoside which induced cell death in cancer cell line and also the same study reported the root extract treat hypercholesterolemia (22%), diabetes (18%), fertility disorders (14%)⁽⁵¹⁾.

Conclusion

B. dioica one of the medicinal plant which widely used in traditional medicine and distribution in different countries specially in Western Europe and containing many active ingredients in all types of plant specially in root which consider as part used in this plant such as Kempferol 3, 7-di-O-rhamnoside and polyphenols which responsible for many biological activity and pharmacological uses such as antinociceptive effects, antioxidant activity, hepatoprotective activity,

Anticancer activity, hypercholesterolemia, diabetes and fertility disorders .

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Department of Pharmacognosy and Medicinal Plant, College Of Pharmacy, Mustansiriyah University, Iraq and all experiments were carried out in accordance with approved guidelines.

References

1. Volz S.M. Evolution of Dioecy in the Cucurbitaceae Genus Bryonia: A Phylogenetic, Phylogeographic, and SCAR-marker Approach. Dissertation, Ludwig Maximilian University of Munich 2008.
2. Gallego, E.C., Gallego, A.C. 2008. Usos, tradiciones y conocimientos de las plantas por las gentes de Sayago. ADERISA, Zamora, Spain.
3. Sallam, A.A., Hitotsuyanagi, Y., Mansour, E.S.S., Ahmed, A.F., Gedara, S., Fukaya, H. and Takeya, K., Cucurbitacins from *Bryonia cretica*. *Phytochemistry Letters*, 2010,3(3), pp.117- 121.
4. Volz SM, Renner SS . Hybridization, polyploidy, and switches between monoecy and dioecy in *Bryonia* (Cucurbitaceae), a clade with XY sex determination. (Submitted).
5. Wellmann M, ed (1906-1914, reprinted 1958) *Pedanii Dioscuridis Anazarbei De material medica libri quinque*. 3 vols. Reprinted Weidmann, Berlin (DE) (*Bryonia*, 2008, vol. 2, pp. 331-332
6. Scarborough J . *Sextius Niger*. In *Encyclopedia of Ancient Natural Scientists* (Keyser PT, Irby-Massie G, eds). Routledge. London and New York. 2008
7. Schröder S., Lunau K. Die oligolektische Sandbiene *Andrena florea* und die Rote Zaunrübe *Bryonia dioica* – Schnittstelle zweier spezialisierter Fortpflanzungssysteme. *Mitteilungen der Deutschen Gesellschaft für Allgemeine und Angewandte Entomologie*, 2001: 13: 529–533.
8. Assefa, B., Glatzel, G. and Buchmann, C., Ethnomedicinal uses of *Hagenia abyssinica* (Bruce) JF Gmel. among rural communities of Ethiopia. *Journal of ethnobiology and ethnomedicine*, 2010, 6(1). p.20.
9. Karageuzyan KG, Vartanyan GS, Agadjonov MI,

- Panossian AG, Hoult JR. 1998. Restoration of the disordered glucose-fatty acid cycle in alloxan-diabetic rats by trihydroxyoctadecadienoic acids from *Bryonia alba*, a native Armenian medicinal plant. *Plant Med* 1999;64:417-22.
10. Anderson RT. *Traditional Europe: Study in Anthropology and History*. Belmont: Wadsworth Publishing; 1971.
 11. Monika Kujawska and Ingvar Svanberg : From medicinal plant to noxious weed: *Bryonia alba* L. (Cucurbitaceae) in northern and eastern Europe. 2019. 15:22: 3-12.
 12. Traveset A., Richardson D.M.. Biological Invasions As Disruptors Of Plant Reproductive Mutualisms. *Trends Ecology & Evolution*, 2006, 21 (4): 208–216.
 13. Medeiros MFT. Historical ethnobiology. In: Albuquerque UP, Romeu R, Alves N, editors. *Introduction to ethnobiology*. New York: Springer International Publishing; 2016. p. 19–24.
 14. Voltz SM, Renner SS. Phylogeography of the ancient Eurasian medicinal plant genus *Bryonia* (Cucurbitaceae) inferred from nuclear and chloroplast sequences. *Taxon*. 2009;58(2):550–60.
 15. Allen DE, Hatfield G. *Medicinal Plants in Folk Tradition: An Ethnobotany of Britain and Ireland*. Portland: Timber Press; 2004.
 16. Kadhim EJ. Phytochemical investigation and hepato-protective studies of Iraqi *Bryonia dioica* (Family Cucurbitaceae). *Int J Pharm Pharm Sci* 2014; 6(4): 187-90.
 17. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of their detoxification capacity and protective effects (part 1). *Asian Journal of Pharmaceutical Science & Technology* 2015; 5(4): 257-70.
 18. Jeffrey C . A review of the genus *Bryonia* L. (Cucurbitaceae). *Kew Bulletin* . 1969, 23: 441-461
 19. Pieroni A. Medicinal plants and food medicines in the folk traditions of the upper Lucca Province, Italy *Journal of Ethnopharmacology* .2000,70;235–273
 20. Krauze BM, Cisowski C () Flavone C-glycosides from *Bryonia alba* and *B. dioica*. *Phytochemistry*.1995; 39: 727-729.
 21. Mankowsky A . Ueber *Bryonia alba*. In *Historische Studien aus dem Pharmakologischen Institut der Kaiserlichen Universität Dorpat* (Kobert R, ed). 1890; pp. 143-180
 22. Benarba, B., Meddah, B. and Aoues, A. *Bryonia dioica* aqueous extract induces apoptosis through mitochondrial intrinsic pathway in BL41 Burkitt's lymphoma cells. *Journal of ethno pharmacology*, 2012;141(1), pp.510-516.
 23. Gholivand, M.B. and Piryaei, M., The antioxidant activity, total phenolics and total flavonoids content of *Bryonia dioica* Jacq. *Biologija*, 58(3), 2012.
 24. Dhouioui, M., Boulila, A., Jemli, M., Schiets, F., Casabianca, H. and Zina, M.S., Fatty Acids Composition and Antibacterial Activity of *Aristolochia longa* L. and *Bryonia dioica* Jacq. Growing Wild in Tunisia. *Journal of Oleo Science*, 2016; 65(8), pp.655-661.
 25. Barreira JCM, Pereira E, Dueñas M, Carvalho AM, Santos-Buelga C, Ferreira ICFR. *Bryonia dioica*, *Tamus communis* and *Lonicera periclymenum* fruits: characterization in phenolic compounds and incorporation of their extracts in hydrogel formulations for topical application. *Ind Crops Prod* 2013; 49: 169-76.
 26. Rafael M, Barros L, Carvalho AM, Ferreira ICFR. Topical anti-inflammatory plant species: bioactivity of *Bryonia dioica*, *Tamus communis* and *Lonicera periclymenum* fruits. *Ind Crops Prod* 2011; 34: 1447-54.
 27. García-Herrera P, Sánchez-Mata MC, Cámara M, Tardío J, Olmedilla-Alonso B. Carotenoid content of wild edible young shoots traditionally consumed in Spain (*Asparagus acutifolius* L, *Humulus lupulus* L, *Bryonia dioica* Jacq. and *Tamus communis* L). *J Sci Food Agric* 2013; 93: 1692-8.
 28. Ukiya M, Akihisa T, Yasukawa K, Toduda H, Toriumi M, Koike K, et al. Anti-inflammatory and antitumor-promoting effects of cucurbitane glycosides from the roots of *Bryonia dioica*. *J Nat Prod* 2002; 65: 179- 83.
 29. Kokate C. K., Gokhale S. B., Purohit A. P. *A Textbook of Pharmacognosy*. 29th ed., Nirali Prakashan, 2009, 635p.
 30. Józef Banaszak, Lucyna Twerd, Halina Ratyńska, Weronika Banaszak-Cibicka, Teresa Zyś, *Andrena florea* Fabricius, 1793 (Hymenoptera, Apoidea, Apiformes): a rare bee species in Poland, related to the expansion of the alien plant *Bryonia dioica* JACQ. (Cucurbitaceae) *Polish Journal of*

- Entomology. 2018; 87 (3): 199–215.
31. Mohammad Bagher Gholivand, Marzieh Piryaee, The antioxidant activity, total phenolics and total flavonoids content of *Bryonia dioica* Jacq. *Biologija*. 2012. Vol. 58. No. 3. P. 99–105
 32. Echaimaa Chekroun, Nabila Benariba, Houria Adida, Asma Bechiri, Rachid Azzi, Rabeh Djaziri Antioxidant activity and phytochemical screening of two Cucurbitaceae: *Citrullus colocynthis* fruits and *Bryonia dioica* roots, *Asian Pac J Trop Dis* 2015; 5(8): 632-637
 33. Krishnaiah D, Sarbatly R, Nithyanandam R. A review of the antioxidant potential of medicinal plant species. *Food Bioprod Process* 2011; 89: 217-33.
 34. Marco Rafael, Lillian Barros, Ana Maria Carvalho, Isabel C.F.R. Ferreira, Topical anti-inflammatory plant species: Bioactivity of *Bryonia dioica*, *Tamus communis* and *Lonicera peryclimenum* fruits.
 35. Bachir Benarba, Boumedienne Meddah, Abdelkader Aoues *Bryonia dioica* aqueous extract induces apoptosis through mitochondrial intrinsic pathway in BL41 Burkitt's lymphoma cells *Journal of Ethnopharmacology*. 2012; 141; P.510– 516
 36. Stefanie M. Volz & Susanne S. Renner Phylogeography of the ancient Eurasian medicinal plant genus *Bryonia* (Cucurbitaceae) inferred from nuclear and chloroplast sequences *Taxon*. 2009, 58 (2): 550–560
 37. Oobayashi K, Yoshikawa K, Arihara S () Structural revision of bryonoside and structure elucidation of minor saponins from *Bryonia dioica*. *Phytochemistry*. 1992; 31: 943-946.
 38. Pohlmann J. Cucurbitacine in *Bryonia alba* and *B. dioica*. *Phytochemistry*. 1975; 14: 1587–9.
 39. Narendra, K., Swathi, J., Sowjanya, K.M., Reddi, K.R., Varaprasad, M.M., Padmavathi, C., Rao, G.V. and Satya, A.K., Studies on Chemical and Biological properties of *Bryonia epigaea* (Rottler). *Journal of Medicinal Plants Research*, 2015; 9(22), pp.664-673.
 40. De Pascual Teresa, J.; Urones, J. G.; Fernandez, A.; Vaquero Alvarez, M. D. Lipid components of *Aristolochia longa*. *Phytochemistry* . 1984; 23, 461-462
 41. Ali E Al-Snafi, and Mahdi M Thuwaini, Arabian Medicinal Plants With Hepatoprotective Activity *Research Journal of Pharmaceutical, Biological and Chemical Sciences* • 2018 9(5) P. 1469 .
 42. Krauze-Baranowska M, Cisowski W. Flavone C-Glycosides from *Bryonia alba* and *B. dioica*. *Phytochemistry*. 1994; 39(3): 727–9.
 43. Matsuda, H., Nakashima, S., Abdel-Halim, O.B., Morikawa, T. and Yoshikawa, M., Cucurbitane-type triterpenes with anti-proliferative effects on U937 cells from an Egyptian natural medicine, *Bryonia cretica*: structures of new triterpene glycosides, bryoniaosides A and B. *Chemical and Pharmaceutical Bulletin*, 2010; 58(5), pp.747-751.
 44. Mohammad Zarei; Saeed Mohammadi, Nasreen Abolhassani; Mahtab Asgari Nematian . The Antinociceptive Effects of Hydroalcoholic Extract of *Bryonia dioica* in Male Rats, *Avicenna J Neuro Psych Physio*. 2015; 2(1): e25761.
 45. Gholivand MB, Piryaee M. The antioxidant activity, total phenolics and total flavonoids content of *Bryonia dioica* Jacq. *Biologija* 2012; 58(3): 99-105.
 46. Mouna Dhouioui, Abdennacer Boulila, Maroua Jemli, Frederic Schiets, Herve Casabianca and Mongia Said Zina, Fatty acid composition and antibacterial activity of *Aristolochia longa* L. and *Bryonia dioica* Jacq growing wild in Tunisia : *Journal of Oleo Science* . 2016. 65(8): 655-661.
 47. Hinneburg, I., Dorman, H.D. and Hiltunen, R., Antioxidant activities of extracts from selected culinary herbs and spices. *Food Chemistry*, 2006; 97(1), pp.122-129.
 48. Amjed Haseeb Khamees, Enas Jawad Kadhim, Hayder Bahaa Sahib, Shihab Hattab Mutlag I In vitro Analysis of Antioxidant and Antimicrobial Activity of Iraqi *Bryonia dioica* *Int. J. Pharm. Sci. Rev. Res.*, 2017; 43(1), P. 248-252
 49. Enas Jawad Kadhim Phytochemicals Investigation And Hepato-Protective Studies Of Iraqi *Bryonia dioica* (Family Cucurbitaceae) *Int J Pharm Pharm Sci*, 2014; Vol 6, (4), 187-190
 50. Kadhim, E.J., Phytochemical investigation and hepatoprotective studies of Iraqi *Bryonia dioica* (Family Cucurbitaceae). *Int J Pharm Pharm Sci*, 2014; 6(4).
 51. Bachir Benarba; Ethnomedicinal study of *Bryonia dioica*, a plant used as anti-breast cancer herbal therapy in North West Algeria. *Journal of Medicinal Herbs and Ethnomedicine* 2015, 1: 113-115.

Risk of Cesarean Delivery and Low Bishop Score after Induction of Labor in Nulliparous Women in Tikrit City

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Abstract

This prospective study was carried out in Tikrit city in the period of 1st February to 1st of July 2019 on pregnant women admitted to the labor ward of Salahaddin general hospital to assess the risk factors of cesarean delivery associated with induction of labor in nulliparous women in relation to bishop score in unfavorable cervix. The study included 100 nulliparous pregnant women with singleton fetus in cephalic presentation who admitted for induction of labor for different indications. A total number of 100 pregnant women in whom spontaneous onset of labor was diagnosed at admission were assigned to the spontaneous onset group, which served as the control group. The cesarean delivery rate for women who were induced with an unfavorable cervix (Bishop score ≤ 4) was 27.14%; the rate for women who were induced with a favorable cervix was 10% (Figure 2). The induction of labor for women with an unfavorable cervix was associated with a significantly increased risk of cesarean delivery ($P < 0.002$). The study showed that Bishop score ≤ 4 was significant risk factor for C/S in addition to maternal age, gestational age and birth weight

Keyword: Bishop Score, Induction of Labor; Cesarean Rate; Nulliparous Women.

Introduction

Induction of labor is a common procedure in modern obstetrics. It is a relatively common procedure in modern obstetric practice; some of the obstetricians consider it to be quite simple, efficient, safe and psychologically well tolerated procedure and far superior to secondary interventions such as vacuum delivery or forceps delivery¹. However, cesarean section (CS) rates vary worldwide, ranging from approximately 10% in Sweden to about 80% in private-sector hospitals in Brazil². High rates are reported from regional, tertiary public and private hospitals. These high rates are probably due to large proportions of highrisk patients attending tertiary and regional². Regarding our country, almost 26% of Iraqi women giving birth at public hospitals do so via CS according to the 2010 health report for the Iraqi Health Ministry³; and in 2016, the rate was further increased to 29.25%¹. When a woman and her care provider decide that labor induction is desired, they must next choose a method of induction. In general, induction of labor is indicated when the risks of continuing the pregnancy outweigh the risks associated with delivery for the

mother and the baby⁵. In 1955, Bishop devised a cervical scoring system for multigravida patients in which 0–3 points are given for each of five factors⁶. Bishop score is a pre-labor scoring system assisting in predicting whether induction of labor will be required^(7,8). It has also been used to assess the likelihood of spontaneous preterm delivery¹. The Bishop scoring assign points for cervical effacement, dilatation, consistency, and position and for the depth of the fetal presenting part in the maternal pelvis⁵. He determined that the total score of at least 9 predicts the likelihood of vaginal delivery following labor induction and was similarly observed in patients with spontaneous onset of labor⁸. Thus Bishop's Score (BS) or the modified version is used universally to assess the favourability of the cervix with its characteristics of effacement and dilatation and the station of the presenting part and also used to predict the method and success of a medically indicated induction^(9,10). The aim of the study was to assess the risk factors of cesarean delivery associated with induction of labor in nulliparous women in relation to bishop score in unfavorable cervix.

Material and Method

This prospective study was carried out in Tikrit city in the period of 1st February 2019 to 1st of July 2019 on pregnant women admitted to the labor ward of Salahaddin general hospital. The study included 100 nulliparous pregnant women with singleton fetus in cephalic presentation who admitted for induction of labor for different indications. Exclusion criteria include: Multiparous women., Multiple gestations, Fetal anomalies, Preterm deliveries (>37 weeks), Elective cesarean deliveries for medical or obstetric reasons and Patients with Failed inductions. A total number of 100 pregnant women in whom spontaneous onset of labor was diagnosed at admission were assigned to the spontaneous onset group, which served as the control group.

Method

At admission to the labour ward, specific data including maternal age, history of previous abortion, and the indication for induction was recorded. Depending on bishop score at admission we decided which method of induction should be used. The modified bishop score was calculated (cervical dilatation 0 - 3 point, effacement 0 - 3 point and fetal station 0 - 3 point). From the first vaginal exam before labour induction or any method of cervical ripping used. Induction was performed using either

prostaglandin E2 vaginal gel alone, amniotomy alone, oxytocin in combination with or without amniotomy, or prostaglandin E2 vaginal gel followed by oxytocin, or amniotomy, or a combination of both. Based on the Bishop score at admission, the attending obstetrician decided which method of induction should be performed. In case of an unfavorable cervix, induction was usually started with prostaglandin E2 vaginal gel for ripening.

Statistical Analysis: Statistical analysis was performed using SPSS. Univariate analyses included the X² test followed by Scheffe' test for differences between groups. Known prognostic variables were included in a multivariable logistic regression analysis. A final model of risk factors for cesarean delivery was created using the maximum likelihood estimation (P >0.5).

Findings: The mean maternal age of induced pregnant women was 25.82+4.11 years with range 37-40 years. The mean gestational age of induced women was 39.5+1.87 week. The mean Bishop score of these pregnant women was as 3.2+0.23. However, body mass index (BMI) was significantly higher in both induction groups than in the spontaneous onset group. The gestational age in the spontaneous onset group was significantly lower than in the induced groups. Further differences between induced and spontaneous onset pregnant women were shown in Table 1.

Table 1: Characteristics of the studied women in the study

Parameters	Pregnant women of the study				P. value
	Induced		Spontaneous Onset (Control)		
	No.	%	No.	%	
Age (Years)					
Mean±SD.	25.5+ 4.11		27.7+ 5.6		0.59
BMI (Mean±SD.)	31.6+ 5.3		29.5+ 4.9		0.005 (HS)
Gestational age (weeks)					
37-37 ⁺⁶	9	9	10	10	0.82
38-38 ⁺⁶	17	17	18	18	
39-39 ⁺⁶	15	15	19	19	
40-40 ⁺⁶	38	38	33	33	
41-41 ⁺⁶	15	15	11	11	
≥42	6	6	9	9	
Mean±SD.	39.5+1.87		38.3+1.4		0.007

Parameters	Pregnant women of the study				P. value
	Induced		Spontaneous Onset (Control)		
	No.	%	No.	%	
Bishop score					
≤4	70	60	20	20	0.0001
5-8	30	40	40	40	
≥9	0	0	40	40	
Mean±SD.	3.2+0.23		7.7+0.23		0.0001
Range	0-8		0-12		
Dilatation (CM)					
0	40		2		0.001
1-2	55		28		
3-4	4		37		
≥5	1		33		

The study demonstrated that the cesarean delivery rate for women in spontaneous labor was 10%; women who were admitted for induction of labor were found to have a cesarean delivery rate of 22% with a significant difference between the 2 groups (P: 0.033) (Figure 1). The cesarean delivery rate for women who were induced

with an unfavorable cervix (Bishop score ≤ 4) was 27.14%; the rate for women who were induced with a favorable cervix was 10% (Figure 2). The induction of labor for women with an unfavorable cervix was associated with a significantly increased risk of cesarean delivery (P < 0.002).

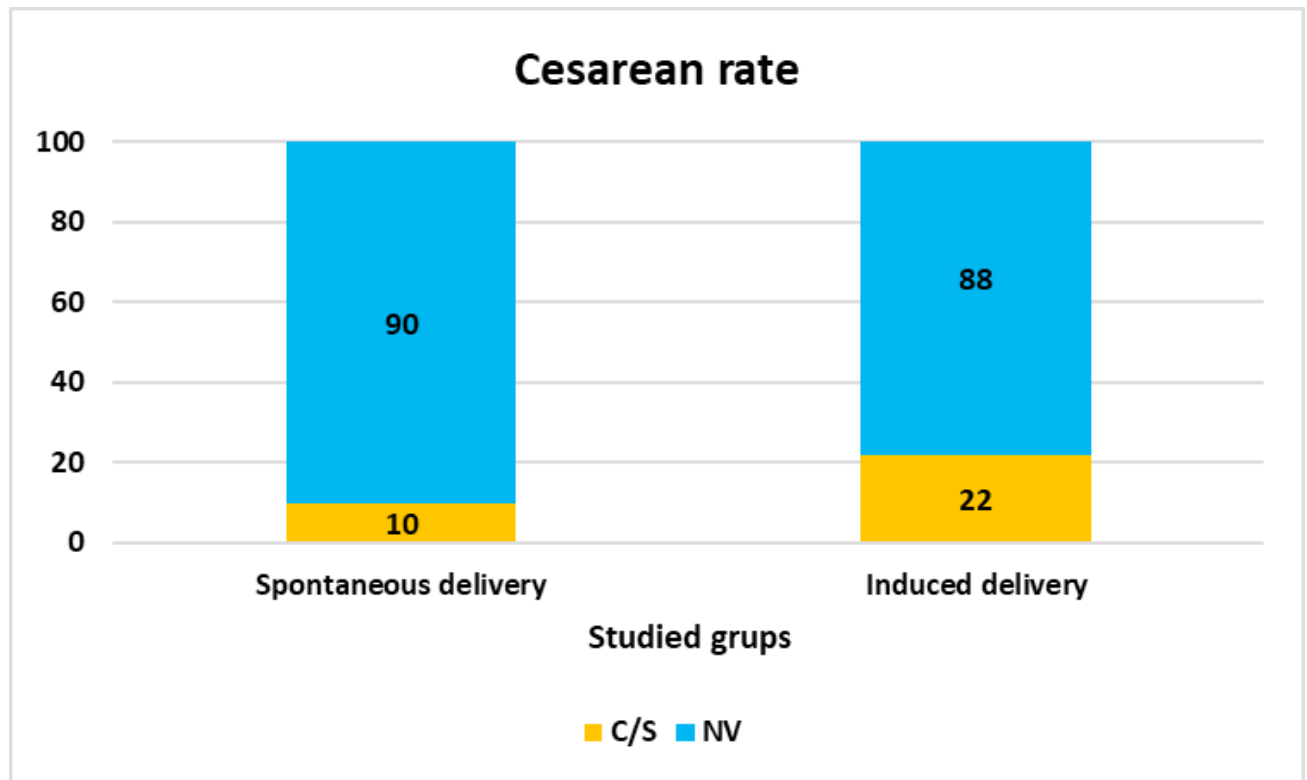


Figure 1: Cesarean delivery rate in induced and spontaneous delivery women

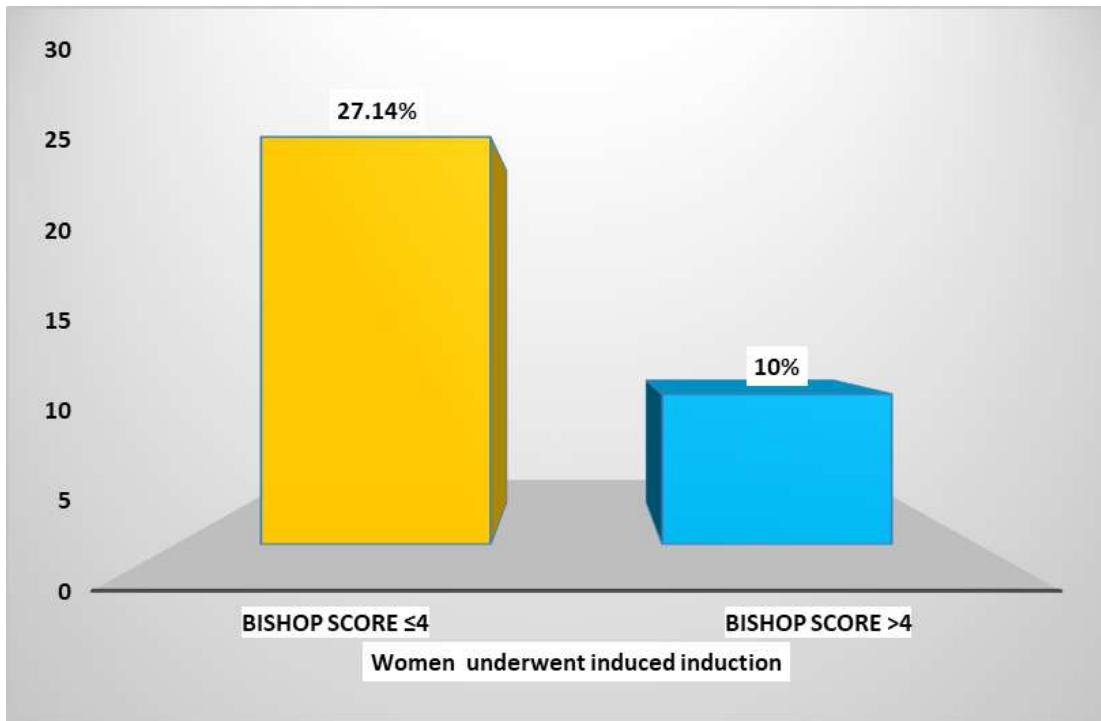


Figure 2: Cesarean delivery rate in women with favorable and unfavorable cervix

The four confounders in the logistic regression model were (1) maternal age of, (2) Bishop score, (3) birth weight and (4) baby’s gestational age in weeks. We also examined possible interactions between the exposure variables and the confounders. The study showed that Bishop score ≤ 4 was significant risk factor for C/S in addition to maternal age, gestational age and birth weight (Table 2).

Table 2: Adjusted odds ratio for a Cesarean Delivery with multiple logistic regression model

Risk Factor	Adjusted OR (95% CI)
Maternal Age	
≤ 19	1.32 (1.22-1.04)
20-24	0.94 (0.66-1.34)
25-29	0.94 (0.51-1.73)
30-34	1.54 (1.41-1.68)
≥ 35	1.66 (0.67-2.22)
Bishop Score	
≤ 4	2.04 (1.48-2.82)
>4	1.0
Birth Weight	
2.5-3	1.23 (1.01-1.73)
3-3.5	1.56 (1.0-1.78)

Risk Factor	Adjusted OR (95% CI)
3.5-4	1.0
4-4.5	1.55 (1.33-2.31)
4-4.5	1.99 (1.01-2.76)
Gestational Age	
37-37+6	0.46 (0.15-0.68)
38-38+6	0.66 (0.42-0.87)
39-39+6	0.56 (0.35-0.89)
40-40+6	0.85 (0.46-1.22)
41-42	1.1

Discussion

In this study, when Bishop score included as an extra covariable in the multivariable regression model with gestational age, maternal age and birth weight, there was significant increase in cesarean delivery rate predominantly related to unfavorable bishop score at admission^(11,12). The degree of cervical dilatation and station of the presenting part, rather than cervical length can be a considered as a predictors for risk of cesarean delivery there for a bishop score at admission of 4 or lower and not the induction per se is associated with a more than double risk in cesarean delivery rate regardless of the causes of induction. In the 2 groups, the cesarean delivery rate was significantly related to the Bishop

score at admission; dilatation was the most important item, and failure to progress during the first stage was the most common indication for cesarean delivery. After including the Bishop score as an extra covariable in the multivariable logistic regression model, no significant differences in cesarean delivery rate between the 2 groups could be demonstrated. Therefore, a Bishop score at admission of 5 or lower, and not the induction per se, is associated with a more than double risk in cesarean delivery rate, regardless of whether the labor is induced for a medical or an elective reason. This is in agreement with other studies that reported both labor induction and cervical ripeness as being of significance⁽²⁻⁴⁾. A possible limitation of this study was the absence of a prospectively determined method of induction in case of a certain Bishop score. Compared with the spontaneous onset group, women in both induction groups had a higher BMI. Body mass index was also an independent risk factor for cesarean delivery. Increased BMI was associated with an increase in the cesarean delivery rate, as demonstrated by others^(5,6). Because impending postterm pregnancy with its accompanying psychosocial problems was an indication for elective induction, and because postterm pregnancy was an indication for medical induction, it could have been expected that the lowest gestational age was found in the spontaneous onset group and the highest gestational age in the medical induction group^(7,8). Oxytocin stimulation during the first and second stages, and duration of the second stage were similar in the 3 groups. None of these factors had an independent relation to the cesarean delivery rate. As could be expected, more children with a birth weight below 2,500 g or 4,000 g or higher were born in the induction groups than in the spontaneous onset group. Birth weight was also an independent risk factor for cesarean delivery. Birth weight of 3,500 g or higher was associated with an increased cesarean delivery rate, again as mentioned by others⁽¹⁰⁻¹²⁾. The association between induction and increased risk for cesarean delivery has been documented in many studies especially when the focusing is placed specifically on nulliparous patients⁽¹³⁻¹⁵⁾. Studies that evaluated the induction of nulliparous patients consistently have shown an increased risk for cesarean delivery, although not always statistical significance has not always been reached. Seyb *et al*¹¹ prospectively studied 1561 nulliparous women at term in either spontaneous labor or awaiting induction. This included 437 women who labor was being induced both electively and for medical indications. The increased risk for cesarean delivery that

was attributed to induction was found to be significant. They included the results of the initial cervical examination by dilation and separately for effacement, but not together, to determine cervical favorability. They did note that the spontaneous labor group generally had more advanced dilation and effacement. They also did not determine the cesarean rates on the basis of the initial cervical assessment. This is in contrast to studies done earlier showed that that induction of labour in 67 nulliparous women from a total of 210 when medically or obstetrically indicated is not associated with an increased risk of cesarean delivery, instrumental delivery and favorable outcome for induction of labour both in low and high risk pregnancies^(16,17). This discrepancy may be explained by other method used for cervical ripening such as labour initiation by prostaglandins, improved fetal surveillance, and liberal use of analgesia along with more active approach to treatment of labour disorders which have been increasingly used during the last two decades. In the present study cesarean delivery rate was significantly related to maternal age, the higher the maternal age the higher the risk of cesarean delivery. In line with our observation several authors Maslow AS *et al*, Johnson DP *et al*, Heffner LJ *et al*, and Ecker JL *et al*. found that cesarean delivery risk increased with older maternal age and higher birth weight, induction without stated risk factors may not carry an increased risk of cesarean delivery⁽¹⁸⁻²⁰⁾.

Conclusions

The induction of labor for women with an unfavorable bishop score was associated with a significantly increased risk of cesarean delivery.

Conflict of Interest: Non

Source of findings: Self findings.

Ethical Clearance: This research was carried out with the patient's verbal and analytical approval before the sample was taken.

References

1. Yeast JD, Jones A, Poskin M. Induction of labor and the relationship to cesarean delivery: a review of 7001 consecutive inductions. *Am J Obstet Gynecol* 1999;180:628–33.
2. Smith LP, Nagourney BA, McLean FH, Usher RH. Hazards and benefits of elective induction of labor. *Am J Obstet Gynecol* 1984;148:579–85.

3. Osmundson S, Ou-Yang RJ, Grobman WA. Elective induction compared with expectant management in nulliparous women with an unfavorable cervix. *Obstetrics & Gynecology*. 2011 Mar 1;117(3):583-7.
4. Heffner LJ, Elkin E, Fretts RC. Impact of labor induction, gestational age, and maternal age on cesarean delivery rates. *Obstet Gynecol* 2003;102:287-93.
5. Ecker JL, Chen KT, Cohen AP, Riley LE, Lieberman ES. Increased risk of cesarean delivery with advancing maternal age: indications and associated factors in nulliparous women. *Am J Obstet Gynecol* 2001;185:883-7.
6. Crane SS, Wojtowycz MA, Dye TD, Aubry RH, Artal R. Association between prepregnancy obesity and the risk of cesarean delivery. *Obstet Gynecol* 1997;89:213-6.
7. Nuthalapaty FS, Rouse DJ, Owen J. The association of maternal weight with cesarean risk, labor duration, and cervical dilation rate during labor induction. *Obstet Gynecol* 2004;103:452-6.
8. Burke N, Burke G, Breathnach F, McAuliffe F, Morrison JJ, Turner M, Dornan S, Higgins JR, Cotter A, Geary M, McParland P. Prediction of cesarean delivery in the term nulliparous woman: results from the prospective, multicenter Genesis study. *American journal of obstetrics and gynecology*. 2017 Jun 1;216(6):598-e1.
9. Hants Y, Kabiri D, Elchalal U, Arbel-Alon S, Drukker L, Ezra Y. Induction of labor at term following external cephalic version in nulliparous women is associated with an increased risk of cesarean delivery. *Archives of gynecology and obstetrics*. 2015 Aug 1;292(2):313-9.
10. Burke N, Burke G, Breathnach F, McAuliffe F, Morrison JJ, Turner M, Dornan S, Higgins JR, Cotter A, Geary M, McParland P. Prediction of cesarean delivery in the term nulliparous woman: results from the prospective, multicenter Genesis study. *American journal of obstetrics and gynecology*. 2017 Jun 1;216(6):598-e1.
11. Seyb ST, Berka RJ, Socol ML, Dooley SL. Risk of cesarean delivery with elective induction of labor at term in nulliparous women. *Obstet Gynecol* 1999;94:600-7.
12. Dodd JM, Crowther CA, Grivell RM, Deussen AR. Elective repeat caesarean section versus induction of labour for women with a previous caesarean birth. *Cochrane Database of Systematic Reviews*. 2017;(7).
13. Alexander JM, McIntire DD, Leveno KJ. Forty weeks and beyond: Pregnancy outcomes by week of gestation. *Obstet Gynecol* 2000a;96:291.
14. Hoffman MK, Sciscione AC. Elective induction with cervical ripening increases the risk of cesarean delivery in Multiparous women. *Obstet Gynecol* 2003; 101:7S.
15. Maslow AS, Sweeny AL. Elective induction of labor as a risk factor for cesarean delivery among low-risk women at term. *Obstet Gynecol* 2000; 95:917,.
16. Nathan RO, Benjamin RE, Vasilios TA. High risk pregnancy outcome following induction of labour. *European Journal of Obstetrics & Gynecology And Reproductive Biology* 1997;72:153-158.
17. Macer JA, Macer CL, Chan LS. Elective induction versus spontaneous labour: A retrospective study of complication and outcome. *AM J Obstet Gynecol* 1992; 166:1690-1697.
18. Strobel E, Sladkevicius P, Rovas L, De Smet F, Karlsson ED, Valentin L. Bishop score and ultrasound assessment of the cervix for prediction of time to onset of labor and time to delivery in prolonged pregnancy. *Ultrasound Obstet Gynecol* 2006;28:298-30.
19. Vahratian A, Zhang J, Troendle JF, et al. Labor progression and risk of cesarean delivery in electively induced nulliparas. *Obstet Gynecol* 2005;105:698-704.
20. Melamed N, Yogev Y, Hadar E, et al. Preinduction cervical ripening with prostaglandin E2 at preterm. *Acta Obstet Gynecol Scand* 2008;87:63-7.

Histological Changes for *Stachybotryschartarum* Fungus in the Lungs and Nose for Infant White Mice

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Abstract

Stachybotryschartarum in one of fungi that cause respiratory system infection to human and animals therefore this study it done to evaluation histological changes in some respiratory organs such as nose and lung induced by this fungus suspension . Detection of *Stachybotryschartarum* fungus confirmed by cultured samples which collected from baths floor on potato dextrose agar in room temperature for seven days. Then the suspension of positive samples of this fungus diluted by phosphate buffer saline and counted the spores by using hemocytometer before used experimentally in lab animals (Balb/C mice) to study histological changes in respiratory system . Twelve mice used in this study divided into two groups. first group consist of six mice induced with 0.5 ml from one positive sample of fungus suspension contain 2×10^4 spore/mm³ (for month : one dose daily) according to count of hemocytometer to evaluate some histopathological changes in nose and lung .Second group induced with 0.5 ml from phosphate buffer saline only. The results revealed that the nose of mice injected with 0.5 ml contain 2×10^4 spore/mm³ from *Stachybotryschartarum* fungus suspension causefocal superficial necrosis of the respiratory epithelial cells with acute inflammatory cells and infiltration of the mucosa while the lung of group mice treated with same concentration of fungus has interstitial pneumonia with thickening of inter alveolar space due to infiltration and chronic inflammatory cells especially mononuclear cell.

Keywords: ??.

Introduction

Stachybotryschartarum is a fungus that has become notorious as a mycotoxin producer that can cause animal and human mycotoxicosis¹

Schartarum called a black mold that produces its conidia in slime heads found in soil and grain, but the mold is most often detected in cellulose-rich building materials from damp or water-damaged buildings² It requires high moisture content in order to grow and is associated with wet gypsum material excessive humidity, water leaks, water infiltration, or flooding as in bathrooms³.

(4,5)Fungal division from Deuteromycota and its single class Deuteromycetes and is a member of the order Moniliales and the family Dematiaceae⁶. *S. chartarum* capable of producing mycotoxins

that include both macrocyclic tricothecenes and nonmacrocyclictricothecenes. There are very few reports that toxigenic molds found inside homes can cause health conditions such as pulmonary hemorrhage or memory loss. The (Institute of Medicine⁷ found there was sufficient evidence to link indoor exposure to mold with upper respiratory tract symptoms, cough, and wheeze in otherwise healthy people, with asthma symptoms in people with asthma, and with hypersensitivity pneumonitis in individuals susceptible to that immune-mediated condition. Other recent studies⁸ have suggested a potential link of early mold exposure to development of asthma in some children, particularly among children who may be genetically susceptible to asthma development, and that selected interventions that improve housing conditions can reduce morbidity from asthma and respiratory allergies. Previous experiments used exposures of rats and mice to *S. chartarum*

spores intranasally and intratracheally; lung tissue was examined for histological changes and bronchoalveolar lavage for evidence of injury and inflammation^(9,10,11,12). *Schartarum* has been consistently reported to cause pulmonary hemorrhage, extensive inflammation and chemokine levels in response to intratracheally instilled spores of *S. chartarum* as well as apoptosis, cytokine release, DNA damage, and changes in gene expression^(13,14,15,16)

Schartarum is the only fungus that we know of to which BALB/c mice are more sensitive.¹⁷ We have previously shown that BALB/c mice respond more to pulmonary exposure to *S. chartarum* spores than do other strain mice¹².

Health problems related to this mold have been documented in humans and animals since the 1930s. More recently, *S. chartarum* has been linked with so-called sick building syndrome^(18,19). Blood tests confirmed the presence of a toxin produced by *S. chartarum*, and severe mold contamination was found in the home.²⁰

The aim of the current study: Evaluation the histological changes induced by *Stachybotryschartarum* fungus suspension intranasally in mice (Balb/c).

Material and Method

1. Samples collection and Lab tests:

Stachybotryschartarum fungus samples were collected from the bath ground and testing microbiological Laboratory that done by cultured on potato dextrose media and incubated at room temperature for 3-7 days in order to obtaining on *Schartarum* fungus. Dilution done by two –fold serial diluents in 8 tubes and harvesting of this fungus with normal saline.

One positive samples of this fungus was further used for the experimental study on laboratory animals (mice) after infected with 0.5 ml from fungus suspension contain 6×10^4 spore/mm³ counted by using hemocytometer chamber (white blood cells count chamber) for evaluation the effects of *Stachybotryschartarum* on respiratory tissues sections taken from these mice.

2. Experimental Study: A total of 12 males mice species Balb/c have aged one month and weight 25-30 g divided into two groups, the first group

consist of six mice infected intranasal with 0.5 ml from *Stachybotryschartarum* fungus suspension for one positive sample contain 6×10^4 spore/mm³ (for month as one time daily). The other as control group was received 0.5 ml of sterile phosphate buffer saline (PBS) according to method of²¹. After 7-14 days clinical signs were recorded in infected animals. Then the Experimental mice were sacrificed after anesthetization by chloroform and open abdomen cavity by medical scissors. Nose and lung tissue sections were collected for the experimentally infected mice and placed in formalin 10% for histological changes examination in later. Histological sections and staining were prepared according to method described by²⁷.

The histological changes were read by Dr. Nemah . H. AL-jabori/college of medicine/university of Babylon under the magnification power 10X and 40 X of light microscope.

3. Statistical Analyses: Using statistical package for social science (SPSS) version 13.0, two-way analysis of variance was conducted to test the significance of effects of groups and periods post injection on the examined traits. The statistical differences among means of the different treatments were tested By Duncan's multiple range test.

Results

1. Lab. Study Results: Culture microbiological testing in laboratory observed *Stachybotryschartarum* fungus on potato dextrose agar. 0.5 ml contain 6×10^4 spore/mm³ from this fungus suspension used with histological study in vivo (inside mice) to evaluation the histological changes in some organs of respiratory system (nose and lung) figure 1 and 2 shows these results the culture.



Figure (1): A culture of *S. chartarum* on PDA from top side



Figure (2): A culture of *S. chartarum* PDA from bottom side (see the roots).

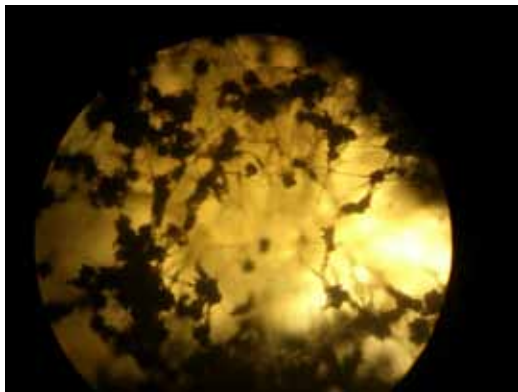


Figure (3): The mass of conidia of *S. chartarum* at the tip of the conidiophore networks. Under light microscopic magnification 4x.

2. Histological changes: Results of the current study revealed histological changes in nose and lung of mice infected with 0.5 ml contain 6×10^4 spore/mm³ from *Schartarum* fungus suspension, these changes shown in figure 4,6 while figures 5,7 represented control group of mice infected with 0.5ml phosphate buffer saline .

In this results figure (4) the nose of mice infected with 0.5 ml contain 6×10^4 spore/mm³ from *Schartarum* fungus suspension showsfocal superficial necrosis of the respiratory epithelial cells with acute inflammatory cells and infiltration of the mucosa.

The results in figure (6) lungs of mice infected with 0.5 ml 6×10^4 spore/mm³ from *Schartarum* fungus suspension indicated tointerstitial pneumonia with thickening of inter alveolar space due to infiltration and chronic inflammatory cells especially mononuclear cell.

While the figure (5,7) revealed to the nose and lungs of control mice infected with 0.5ml phosphate buffer saline. No histological changes observed in nose and lung control mice group.

The graph (8) shows the histological resulting column for compersation between injection and control groups after one month ago (one dose/ dailyfrom *Schartarum* fungus suspension).

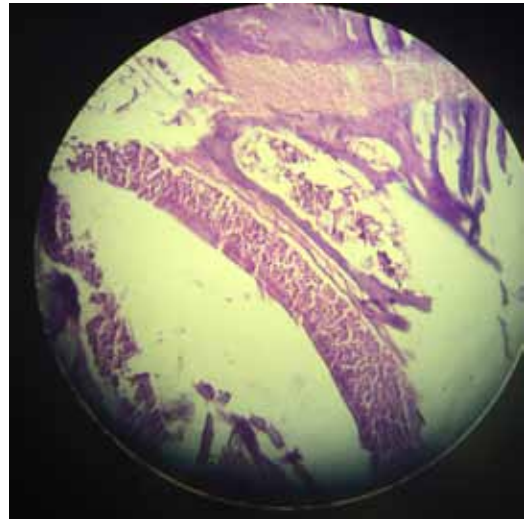


Figure (4): Nose of mice infected with0.5 ml contain 6×10^4 spore/mm³ from *Stachybotryschartarum* fungussuspension . This slide shows focal superficial necrosis of the respiratory epithelial cells with acute inflammatory cells and infiltration of the mucosa .E & H stain. Magnifications 20X.

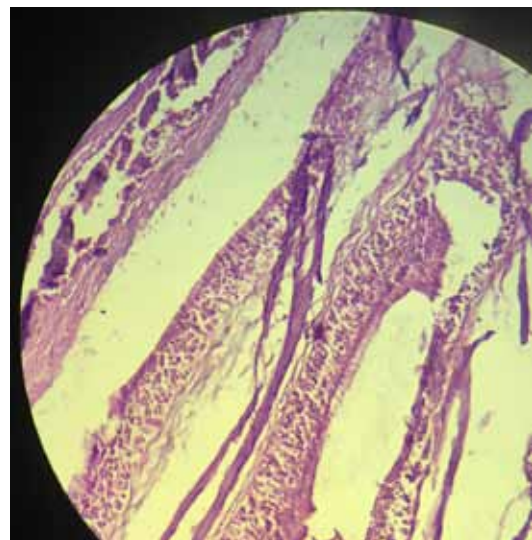


Figure (5): Control of Nose of mice infected with 0.5 ml phosphate buffer saline . There is normal appearance in respiratory epithelial cells of nose without any damage or destruction of epithelium cells. E & H stain. Magnification 20x.

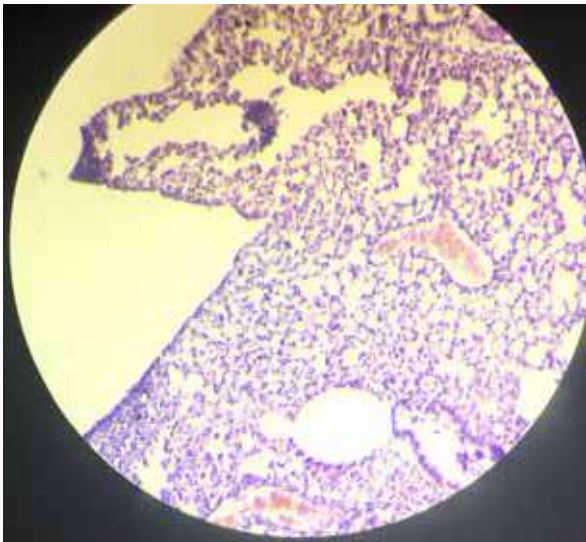


Figure (6): Lung of mice infected with 0.5 ml contain 6×10^4 spore/mm³ from *Stachybotrys chartarum* fungus. this slide shows interstitial pneumonia with thickening of inter alveolar space due to infiltration and chronic inflammatory cells especially mononuclear cells. E & H stain. Magnification 20x

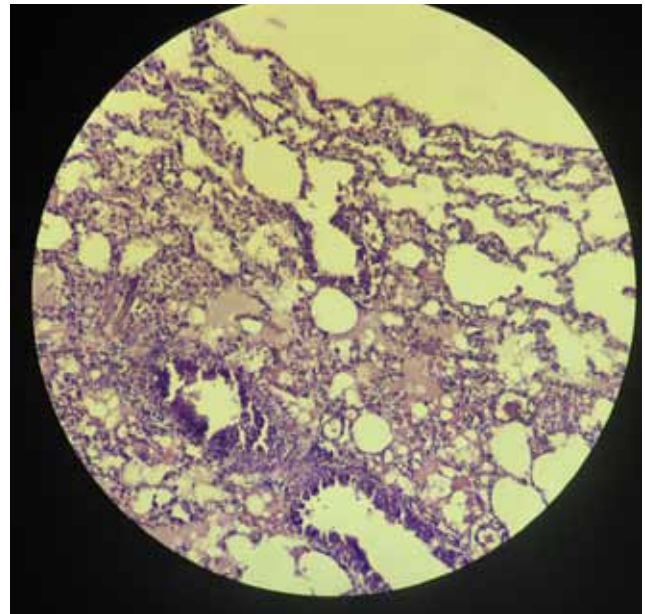
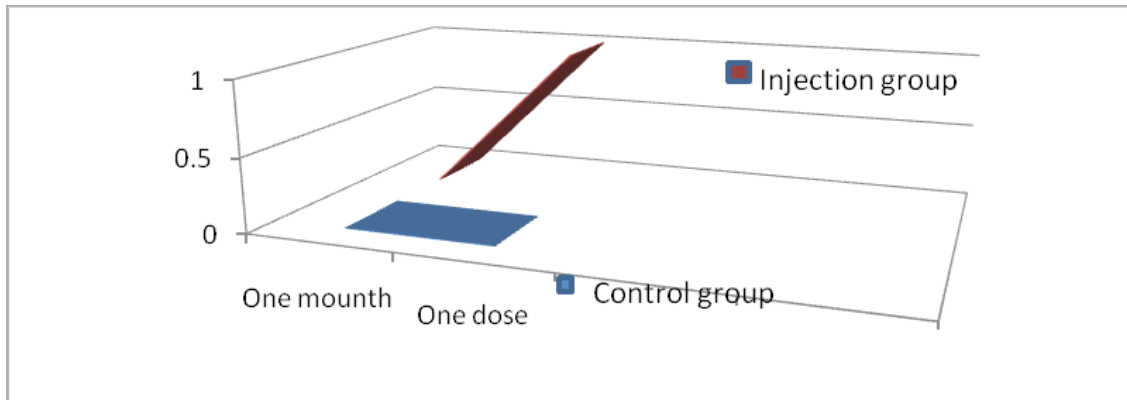


Figure (7): Control of lung of mice infected with 0.5 ml phosphate buffer saline. this slide shows normal inter alveolar space and normal cells of lung. (E & H 20X).



The graph (8) shows the histological results column for compared between injection and control groups.

Discussion

Stachybotrys chartarum was reported to induce sensory irritation, inflammatory, and/or pulmonary responses in mice and rats exposed via intranasal instillation, intratracheal instillation and inhalation²¹.

The results of present study about effects of *S. chartarum* suspension on nose and lung of mice which experimentally infected revealed to histological changes within nose and lung mice infected with 6×10^4 spore/mm³ from this fungus suspension. These histological

changes were observed in figure 3,5 figure (3) showed histological changes in nose represented in focal superficial necrosis of the respiratory epithelial cells with acute inflammatory cells and infiltration of the mucosa. Spores or spore components in the lungs of BALB/c mice persisted longer and thus may have elicited a greater response. This persistence might also explain how an extract of *S. chartarum* can also induce allergic asthma in BALB/c mice after repeated pulmonary exposures²². The first evidence that differences in spore clearance and macrophage susceptibility to spore-induced death may

contribute to strain differences in susceptibility to *S. chartarum* seen in vivo. (23,24)

This results similar to other studies mentioned that no inflammation or tissue damage was seen in the nasal cavity. ²⁵in spite of the interstitial inflammation with luminal hemorrhagic exudates were observed in nose of animals infected with this dose from fungus, as well as toxicity or mortality was seen⁹.

The results of lung mice infected with same concentration of this fungus shows in figure (5) lungs of mice infected with 6×10^4 spore/mm³ from *Schartarum* fungus suspension indicated to interstitial pneumonia with thickening of inter alveolar space due to infiltration and chronic inflammatory cells especially mononuclear cell.

This results similar to other studies mentioned that *Schartarum* cause severe alveolar, bronchiola and the higher concentration caused a significant

increase in monocytes, neutrophils, and lymphocytes in the lung (26,10). Genetic variability in human populations may account for some of the wide variation among individuals responding to mold exposure in contaminated occupational and domestic settings. In addition, other concomitant conditions, such as cigarette smoke exposure or bacterial infection, might further exacerbate poor spore clearance in susceptible populations. A Centers for Disease Control (CDC) report concluded that *S. chartarum* was responsible for acute idiopathic pulmonary hemorrhage in a cluster of infants^(27,28,29).

Causes of histopathological changes in nose and lung of infected mice perhaps due to the toxin that produce by *Schartarum* effect on some organs of respiratory system including the nose and lung^(30,31).

Conclusion: the *Stachybotrys chartarum* fungus suspension caused clear histological changes in nose and lung of mice (Balb/c) infected with 6×10^4 spore/mm³ from fungus suspension.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Faculty of bio-technologies, AL. Qasim Green University, Iraq and all experiments were carried out in accordance with approved guidelines.

References

1. Nelson D. "Stachybotrys chartarum. the toxic indoor mold". *APSnet*. American Phytological Society. National Center for Environmental Health. 2005.
2. Samson RA, Houbraken J, Thrane U, Frisvad JC, Andersen B. Food and Indoor Fungi. CBS-KNAW-Fungal Biodiversity Centre, Utrecht, the Netherlands. 2010;1-398.
3. Andersen B, Frisvad JC, Søndergaard I, Rasmussen IS, Larsen LS. Associations between fungal species and water damaged building materials. *Applied and Environmental Microbiology*. 2011.
4. Bae HK, Shinozuka J, Islam Z, Pestka JJ. Satratoxin G interaction with 40S and 60S ribosomal subunits precedes apoptosis in the macrophage. *Toxicol. Appl. Pharmacol*. 2009;237:137–145.
5. Hastings C, Rand T, Bergen HT, Thliveris JA, Shaw AR. Stachybotrys chartarum alters surfactant-related phospholipid synthesis and CTP: cholinephosphate cytidyltransferase activity in isolated fetal rat type II cells. *Toxicol. Sci*. 2005;84: 186–194.
6. Nelson BD. Stachybotrys chartarum: The Toxic Indoor Mold. *APSnet Features*. Online. doi: 10.1094/APSnetFeature-2001-1101. 2001.
7. Centers for disease control and prevention CDC . Questions and Answers on Stachybotrys chartarum and other molds. Internet address: <http://www.cdc.gov/nceh/airpollution/mold/stachy.htm>. Last updated on November 30, 2002. Last accessed on March 10, 2004.
8. World Health Organization, linking indoor mold exposure and respiratory illness in otherwise healthy children. In 2009, the World Health Organization issued additional guidance, the WHO Guidelines for Indoor Air Quality: Dampness and Mould, 978 92 4 159860 6. 2009.
9. Nikulin M, Reijula K, Jarvis B B, Veijalainen P, Hintikka EL. Effects of intranasal exposure to spores of Stachybotrys atra in mice. *Fundam. Appl. Toxicol*. 1997;35:182–188.
10. Nikulin M, Reijula K, Jarvis BB, Veijalainen P, Hintikka E-L. Effects of intranasal exposure to spores of Stachybotrys atra in mice. *Fundam Appl Toxicol*, 1997;35:182-188.
11. Rao CY, Burge HA, Brain JD. The time course of responses to intratracheally instilled toxic Stachybotrys chartarum spores in rats.

- Mycopathologia 2000;149: 27–34.
12. Rosenblum Lichtenstein JH, Molina RM, Donaghey TC, Brain JD. Strain differences influence murine pulmonary responses to *Stachybotryschartarum*. *Am. J. Respir. Cell Mol. Biol.* 2006;35: 415–423.
 13. Andersen B, Nielsen KF, Thrane U, Szaro T, Taylor JW, Jarvis BB. Molecular and phenotypic descriptions of *Stachybotryschlorohalonata* sp. nov. And two chemotypes of *stachybotryschartarum* found in water-damaged buildings. *Mycologia* 2003;95: 1227-1
 14. Chung YJ, Yang GH, Islam Z, Pestka J. Up-regulation of macrophage inflammatory protein-2 and complement 3A receptor by the trichothecenes deoxynivalenol and satratoxin G. *Toxicology* 2003b;186: 51–65.
 15. Dearborn DG, Yike I, Sorenson WG, Miller MJ, Etzel RA. Overview of investigations into pulmonary hemorrhage among infants in Cleveland, Ohio. *Environ. Health Perspect.* 1999;107 (Suppl. 3): 495–499.
 16. Islam Z, Hegg CC, Bae H K, Pestka JJ. Satratoxin G-induced apoptosis in PC- neuronal cells is mediated by PKR and caspase independent. *Toxicol. Sci.* 2008;105: 142–152.
 17. Jamie H Rosenblum Lichtenstein,^{*,1} Ramon M Molina,^{*} Thomas C Donaghey,^{*} Chidozie J Amuzie,[†] James J Pestka,[†] Brent A Coull,[‡] Joseph D Brain. Published online 2010 Apr 12. Pulmonary Responses to *Stachybotryschartarum* and Its Toxins: Mouse Strain Affects Clearance and Macrophage Cytotoxicity. (2010) Jul; 116(1):113–121.
 18. Heller RM, Heller TW, Sasson JM. "Mold: history of a confusion". *Perspect. Biol. Med.* 2003;46 (4): 588–91
 19. Page EH, Trout D B. "The Role of *Stachybotrys* Mycotoxins in Building-Related Illness". *AIHAJ - American Industrial Hygiene Association*. 2001;62 (5): 644.
 20. Gao P, Martin J. "Volatile metabolites produced by three strains of *Stachybotryschartarum* cultivated on rice and gypsum board". *Appl. Occup. Environ Hyg.* 2002;17 (6): 430–6.
 21. Scott A Masten. *Stachybotryschartarum*. National Toxicology Program (NTP). National Institute of Environmental Health Sciences (NIEHS). 2004.
 22. Viana ME, Coates NH, Gavett SH, Selgrade MK, Vesper SJ, Ward MD. An extract of *Stachybotryschartarum* causes allergic asthma-like responses in a BALB/c .2002; 77:213-218 Nikulin M, Reijula K, Jarvis BB, Hintikka E-L. Experimental lung mycotoxicosis in mice induced by *Stachybotrys* sp. *Int. J. Exp. Pathol., mouse model. Toxicol. Sci.* 1996;70, 98–109.
 23. Flemming J, Hudson B, Rand TG. Comparison of inflammatory and cytotoxic lung responses in mice after intratracheal exposure to spores of two different *Stachybotryschartarum* strains. *Toxicol Sci*, 2004;78:267-275.
 24. Dearborn DG, Smith PG, Dahms BB, Allan TM, Sorenson WG, Montana E, Etzel RA. Clinical profile of 30 infants with acute pulmonary hemorrhage in Cleveland. *Pediatrics* 2002;110:627–637.
 25. Korpi A, Kasanen JP, Raunio P, Kosma VM, Virtanen T, Pasanen AL. Effects of aerosols from nontoxic *Stachybotryschartarum* on murine airways. *Inhal. Toxicol*, 2002;14:521-540.
 26. Leino M, Makela M, Reijula K, Haahtela T, Mussalo-Rauhamaa H, Tuomi T, Hintikka E-L, Alenius H. Intranasal exposure to a damp building mould, *Stachybotryschartarum*, induces lung inflammation in mice by satratoxin-independent mechanisms. *Clin Exp. Allergy*, 2003;33:1603-1610.
 27. Luna LG. *Manual of histological staining method of the Armed Forces Institute of Pathology*, 3rd Ed. McGraw Hill. New York. 1968;195 - 196.
 28. Lynn Nielsen-Bohlman, Allison M Panzer, David A. Kindig, Editors; Committee on Health Literacy; Institute of Medicine IOM, *Stachybotryschartarum, Trichothecene Mycotoxins, and Damp Building-Related Illness: New Insights into a Public Health Enigma* 2004;104-4-26.
 29. Ahmed OH, Zahraa MA, Khansa H. Adequacy of Magnetic Resonance Image versus Electromyography in Patients with Back Pain. *J. Global Pharma Tech.* 2018;10(03): 225-228
 30. Ahmed OH. Histological Effect of Androgenic Anabolic Steroid Dianabol in Heart and Some Blood Parameters of Male Albino Rats. *J. Global Pharma Tech.* 2018;10(03): 215-219
 31. Ahmed OH. EFFECT OF FUMONISIN B1 ON HISTOLOGY OF SPLEEN OF BROILER CHICKEN GALLUS GALLUS. *Biochem. Cell. Arch.* 2018;18(2): 1755-1761,

Study the Activity of Lactate Dehydrogenase (LDH) and Some Biochemical Parameters in Atherosclerosis Patients

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Abstract

Atherosclerosis causes significant biochemical changes, serum biochemistry was studied to investigate the correlation of these factors to Atherosclerosis. Total of 100 subjects was studied, 40 healthy individuals and 60 Atherosclerosis patients. Blood samples were collected in gel tubes from Kirkuk, General Hospital. In this study, the high level of Lactate Dehydrogenase (LDH) activity ($P \leq 0.01$) were observed in Atherosclerosis patients. And a number of biochemical parameters were measured, a Significantly decreased at a level of probability ($p \leq 0.01$) in Antioxidant Superoxide Dismutase (SOD) Catalase (CAT) and increased at a level of probability ($p \leq 0.01$) in Antioxidant, Glutathione (GSH) and increased at level of probability ($p \leq 0.01$) in Lipids blood serum (TC) Total Cholesterol, (TG) Triglycerid for patients with Atherosclerosis as compared with the control group.

Keywords: Atherosclerosis, Lactate Dehydrogenase activity, SOD, GSH, CAT, TC, TG, HDL, K.

Introduction

Atherosclerosis is a pathogenic process that clinically affects all blood vessels, most notably cerebral, coronary and peripheral blood vessels¹. Atherosclerosis is a complex process involving the deposition of plasma lipoproteins and the proliferation of cellular elements in the artery wall. This condition is accelerated especially under conditions that help plaque rupture and platelet formation².

Fat is deposited on the inner walls of blood vessels so that they can grow to obstruct blood flow in any part of the body's arteries, causing stroke, an aneurysm in the abdomen, and heart attacks³.

The German histologist Felix Jacob Marchand first introduced the descriptive term "atherosclerosis" in 1904 to describe "porridge" as the accumulation of fatty substance within the hardened artery and suggested that atherosclerosis is responsible for blockage of the arteries⁴.

The enzyme (LDH EC 1.1.1.27) is an enzyme with a widespread in the tissues of the body where it stimulates the transformation of lactate to pyruvate as in the equation below, as the enzyme has five isomers,

which is a homogeneous or heterogeneous quadromes, which consists of sub-proteins H, M They encode LDHB and LDHA genes and these isomers differ in chemical composition, properties and tissue distribution⁵ The LDH enzyme is a multi-part enzyme Oligomeric and each of the sub-units of the enzyme LDH enzyme has the same function, the LDH enzyme four subunits Tetramers and has a molecular weight of about 140,000 Dalton, which means that the molecular weight of each of the subunits is about 35,000 Dalton. Subunits differ from each other in the composition of amino acids and are called the first type M-Form where there is a lot in the muscles that are linked to the skeleton and anaerobic tissues, where there is a lot in the heart muscles⁶ H-Form The other type is

The LDH enzyme is a specialized enzyme whose concentration in the tissues of the organism is very high compared with its concentration in plasma⁷ found in almost all cells and tissues of the body, especially in the heart, bones, smooth muscles and blood cells⁸.

Materials and Method

Selection of Patients: This study was conducted in the Department of Biochemistry lab in Kirkuk University, Iraq. It included 60 patients diagnosed with

Atherosclerosis and 40 controls were also involved in the study.

Serological Technique: All were informed regarding the study and written consent was obtained. General information such as name, age, gender, acute illness, height, weight, and drugs usage etc was recorded in case of history performa. Blood samples were collected in a gel tubes from normal and Atherosclerosis infected patients. The biochemical test included each of LDH activity was measured using the standard kits from Biolabo While (SOD,GSH, and CAT) manually measured While Cholesterol, Triglycerides, and HDL was measured using the standard kits from Biolabo and K was performed by commercially available kit (Rocha).

Table (1): Method used to estimate the biochemical parameters.

Biochemical Parameters	The Method
LDH	BioLabo ready measurement kit9
SOD	Diagnostic Tool Kit supplied by Elabscience 10
GSH	Using the modified method (Sedlak and Lindsay) 11
CAT	The concentration or effectiveness of this enzyme depends on the consumption of hydrogen peroxide 12.
TC	Richmond13
T.G	Use of Biolabo Diagnostic Kit14
HDL	Richmond13
K	BioLabo15

Statistical Analysis: In this study, the results include mean±S.D and significant differences (P.Value) between groups that examined an available statical SPSS 17.0 significant differences were estimated as the p. value equal or less than 0.01

Results and Discussion

Lactate Dehydrogenase (LDH): Results are shown in Table (2) showed that the effectiveness of the enzyme lactate dehydrogenase increased significantly at the level of probability ($p \leq 0.001$) for all age groups in serum in people with atherosclerosis and for both sexes compared with the healthy group and the highest rate of increase was recorded in the age group (70-61). The enzyme may be caused by tissue injury and hypertension, which in turn causes hypoxia¹⁶. The enzyme is caused by kidney dysfunction, leading to damage to blood vessels. And lack of oxygen in humans¹⁷ As a result of lack of oxygen will activate anaerobic decomposition which

is a predominant feature of blood vessels LDH due to high blood pressure, which leads to increased activity of the enzyme and lactate production. Serum enzyme concentration.¹⁸

Table (2): Mean±S.D of LDH activity for patients Atherosclerosis and control group

Age	The activity of LDH (IU/L) (Mean±S.D)	
40-50	Control	(221.0±43.17)
	Patients	(**689.3±44.76)
51-60	Control	(222.8±69.5)
	Patients	(**716.1±40.72)
61-70	Control	(13.6±70.7)
	Patients	(**732.3±46.4)

Antioxidant levels in the blood serum of males with atherosclerosis and compared with females:

The results shown in Table 3 showed a significant decrease at the probability level ($P \leq 0.001$) in the levels and effectiveness of antioxidants (CAT,SOD) in male patients with atherosclerosis and the results (0.0074 KU/L,0.8352 U/ml) respectively compared with the healthy group and the results(0.0190 KU/L,5.9316 U/ml) respectively. Significant decrease in female patients with atherosclerosis and the results were(0.0085 KU/L, 0.6788 U/ml) respectively compared to females for the control group, which reached (0.022 KU/L,4.9890 U/ml) respectively. to the oxidation component of the arteries. According to a study by colleagues and colleagues, increasing the levels of cholesterol in the arteries leads to an increase in the level of free radicals and weaken the role of antioxidants and low levels, causing endothelial damage to the arteries, leading to the development of atherosclerosis.¹⁹

The results of Sözmen, Bülent and his colleagues²⁰ showed a decrease in the activity of enzymatic antioxidant due to increased platelets of which leads to a decrease in the activity. This decrease can be explained by the effect of the increase of free radicals derived because the lower the activity concentration increases, CAT increases when peroxide concentrations are high. It also corresponded with studies Rande and colleagues²¹ and McMurray colleagues.²²

The serum level at the probability level ($P \leq 0.05$) of GSH male patients with atherosclerosis (12.552 $\mu\text{mol/L}$) compared to the control group (9.144 $\mu\text{mol/L}$), while the level increased at the same time.

Table 3: Shows the levels and effectiveness of antioxidants (SOD, CAT, GSH by age groups)

Age		SOD(U/ml)	CAT (KU/L)	GSH (µmol/L)
		(Mean±S.D)		
(40-50)	Control	(5.356±0.573)	(0.0183±0.0055)	8.945±0.678))
	Patients	(**0.807±0.099)	(**0.0084±0.0009)	(**12.870±0.546)
(51-60)	Control	(5.116±0.844)	(0.0246±0.0051)	(9.365±0.714)
	Patients	(**0.729±0.083)	(**0.0077±0.0009)	(**12.412±0.852)
(61-70)	Control	(6.150±0.363)	(0.0194±0.0085)	(9.220±0.425)
	Patients	(**0.689±0.076)	(**0.0080±0.0011)	(**12.795±0.985)

Lipid levels in serum males with atherosclerosis and compared with females–cholesterol, triglycerides, and high-density lipoproteins.) were measured in serum of females and males with atherosclerosis and compared with the control group.

The results shown in Table (4) show that the level of cholesterol increased significantly at the level of probability ($P \leq 0.05$) for all age groups in serum of people with atherosclerosis and for both sexes compared with the healthy group and that these results are consistent with the results of previous research that indicated a high level. This increase in cholesterol level is due to the decrease in the level of high-density lipoproteins in

the blood serum of patients as it helps to extract excess cholesterol deposited in the walls of blood vessels and provide it back to the liver for disposal. Gastrointestinal tract and helps to keep blood vessels dilated and thus enhance the blood flow better and it carries cholesterol (old), which was rejected by the cells and return it to the liver for recycling or excretion²³

High triglycerides and low high-density lipoproteins are characteristic of abdominal obesity, diabetes and insulin resistance²⁴. High-density lipoproteins are inversely related and cholesterol is transported from high-density lipoproteins to triglycerides rich in very-low-density lipoproteins²⁵

Table 4: Shows the lipid levels in serum males with atherosclerosis and compared with females

Age		TC (mg/dl)	T.G(mg/dl)	HDL(mg/dl)
		(Mean±S.D)		
(40-50)	Control	(95.44±6.37)	(94.16±8.02)	(40.65±3.93)
	Patients	(**229.6±27.91)	(**211.8±16.04)	(**21.69±3.21)
(51-60)	Control	(98.80±5.56)	(97.15±10.90)	(38.63±1.54)
	Patients	(**224.9±15.49)	(**199.3±13.91)	(**25.06±4.80)
(61-70)	Control	(79.46±4.91)	(99.56±15.77)	(3.56±40.95)
	Patients	(**228.2±21.81)	(**224.8±11.42)	(**21.88±4.34)

Potassium level in serum of males with atherosclerosis and compared with females. The results indicated in table (5) showed that the level of potassium decreased significantly at the level of probability ($P \leq 0.001$) for all age groups in serum in people with atherosclerosis compared with the healthy group and that the reason for the low level of potassium in patients may be due to high blood pressure due to imbalance

Potassium is transported through the smooth and vascular muscle cell membrane, which in turn regulates blood pressure²⁶. It may also be caused by a decrease in nitric oxide release by endothelial cells, which leads to narrowing of blood vessels and increased platelet aggregation, which increases blood pressure. Control of blood pressure regulation which in turn leads to low serum potassium level.²⁷

Table 5: Shows the Potassium level in serum

Age	K(U/L) (Mean±S.D)	
40-50	Control	(4.273±0.352)
	Patients	(**2.576±0.335)
51-60	Control	(4.083±0.277)
	Patients	(**2.676±0.310)
61-70	Control	(4.585±0.444)
	Patients	(**2.674±0.252)

Conclusion

An investigated of Atherosclerosis case was successfully performed, studying its effect on the Lactate Dehydrogenase activity. The main concluded points from this research were summarized as follow: the increase of Lactate Dehydrogenaseenzyme activity level; increasing the level of TC, TG, GSH, and decreasing the level of SOD,CAT,HDL, K.

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Department of Chemistry/ College of Science/Kirkuk University/Kirkuk, Iraq and all experiments were carried out in accordance with approved guidelines.

References

1. Clemmons DR. Atherosclerosis: Risks, Mechanisms, and Therapies. 2015.
2. Tribble D L, Nutrition Committee. Antioxidant Consumption and Risk of Coronary Heart Disease: Emphasis on Vitamin C, Vitamin E, and β-Carotene A Statement for Healthcare Professionals From the American Heart Association. *Circulation*, 1999;99(4):591-595.
3. JevonP. Angina and Heart Attack. Oxford University Press. 2012.
4. Konstantinov IE, Mejevoi N, Anichkov NM. Nikolai N. Anichkov and his theory of atherosclerosis. *Texas Heart Institute Journal*, 2006;33(4): 417.
5. Muzaffar, Sami Abdul Mahdi, *Biochemistry, Part II* 1981; 610.
6. Grimes AS. Human red cell metabolism Blackwell scientific, publication, Oxford. London. 1980; 165-233.

7. Kaplan LA. “ Clinical Chemistry: Theory, analysis, and correlation “ The C.V. Mosby Co., 2nd. edition., 1989;777:784-793.
8. FischbachF “ A Manual of laboratory and diagnostic tests”. Lippincott Williams and Wilkins. 6th edition., 2000;448.
9. Klin Z, Klin U. The enzymatic reaction for determination of lacticdehydrogenase. *Biochemistry J.*, 1972;10:182-187
10. Brown M, Faust J, Goldstein L. “Role of the low-density lipoprotein receptor in regulating the content of free and esterified cholesterol in human fibroblasts”. *J. Clin. Invest.* 1975;55:783-793
11. Aziz BN, Al-Kataan MA, Ali WK. Lipid Peroxidation and Antioxidant Status in Î²-Thalassemic Patients: Effect of Iron Overload. *Iraqi Journal of Pharmaceutical Sciences (P-ISSN: 1683-3597, E-ISSN: 2521-3512)*. 2017 Mar 30; 18(2):8-14.
12. Hofstad T, Kristoffersen T. Chemical characteristics of endotoxin from *Bacteroides fragilis* NCTC 9343. *Microbiology*. 1970;61(1):15-9.
13. Bunitis CA, Ashwood ER, Bruns DE. *Tietz Textbook of Clinical Chemistry and Molecular Diagnostics*. by Saunders, an imprint of ElsevierInc. USA. 2015;356:368
14. DLabbé al, *Ann. Biol. Clin.* 1996; 54: 285 – 289
15. HenryRF, et. al., *Clinical Chemistry Principles and Techniques*, 2nd ED., Harper and Row, Hagerstown, M.D., 1974.
16. Vinitha Padmini Mary, MChellatamizh, S Padmanaban. Role of serum LDH in preeclampsia as a prognostic factor – a cross-sectional case-control study in tertiary care hospital. *Int J Reprod Contracept Obstet Gynecol* 2017 Feb; 6(2): 595-598 .
17. DrMadole MB, Dr Bhave DP, DrMamatha MT, Dr Dharmesh Gamit,” Evaluation of serum uric acid and serum lactate dehydrogenase in hypertension. *Indian Journal of Basic and Applied Medical Research*; September 2016: Issue -4; 706-712.
18. Liggy Andrews, Nikunj Patel. Correlation of serum lactate dehydrogenase and pregnancy-induced hypertension with its adverse ones. *International Journal of Research in Medical Sciences* Andrews L et al. *Int J Res Med Sci.* 2016 Mary; 4(5): 1347-1350

19. GriendlingKK, FitzGeraldGA. Oxidative stress and cardiovascular injury part II: animal and human studies. *Circulation*, 2003;108(17):2034-2040
20. SözmenB, KazazC, TASKIRAND, AslanL, Akyol A, Sözmen EY. . Plasma antioxidant status and nitrate levels in patients with hypertension and coronary heart disease. *Turkish Journal of Medical Sciences*, 1998;28(5):525-532.
21. Dubois-RandeJL, ArtigouJY, Darmon JY, HabbalR, ManuelC, Tayarani I, Grosogeat Y. Oxidative stress in patients with unstable angina. *European heart journal*, 1994;15(2):179-183.
22. McMurrayJ, ChopraM, AbdullahI, SmithWE, DargieHJ. Evidence of oxidative stress in chronic heart failure in humans. *European heart journal*, 1993;14(11):1493-1498.
23. RizviNB, NagraSA. Minerals and Lipids Profiles in Cardiovascular Disorders in South Asia: Cu, Mg, Se, Zn and Lipid Serum Profiles for the Example of Patients in Pakistan. Springer Science & Business Media. 2013.
24. HaaseC L, Tybjærg-HansenA GrandeP, Frikke-SchmidtR. Genetically elevated apolipoprotein AI, high-density lipoprotein cholesterol levels, and risk of ischemic heart disease. *The Journal of Clinical Endocrinology & Metabolism*, 2010; 95(12): E500-E510.
25. TowfighiA, ZhengL, OvbiageleB. Sex-specific trends in midlife coronary heart disease risk and prevalence. *Archives of Internal Medicine*, 2009;169(19):1762-1766.
26. PikilidouMI, LasaridisAN, SarafidisA, TziolasIM, ZebekakisPE, DombrosNV, GiannoulisE. Blood pressure and serum potassium levels in hypertensive patients receiving or not receiving antihypertensive treatment. *Clinical and Experimental Hypertension*, 2007;29:563-573
27. PlantoneD, RennaR, KoudriavtsevT. Neurological diseases associated with autoantibodies targeting the voltage-gated channel complex: immunobiology and clinical characteristics, 2016;3:69.

Electrocardiographic Changes and Cardiac Arrhythmias in Hemodialysis Patients with End-Stage Renal Disease, at AL-Hussein Teaching Hospital

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Abstract

Background: Cardiovascular disease is the leading cause of mortality among patients on dialysis. When considering all causes of death, about 30% are classified as cardiac arrest, death of unknown cause or cardiac arrhythmia. The increasing time of ventricular depolarization and repolarization, measured non-invasively by measuring the QT interval on the electrocardiogram at rest, has emerged as a predictor of complex ventricular arrhythmias, a major cause of sudden cardiac death.

Objective: To evaluate electrocardiographic abnormalities in patients with Chronic kidney disease on Maintenance Hemodialysis.

Method: This cross sectional observational study design was carried out through the present investigation from Jun 2nd January/2019 to 2/July/2019 in order to achieve the objectives of the present study. A non-probability (purposive) sample of 120 patient which including (86) males and (34) females. Who were attending Hemodialysis Unit in AL- Hussein Teaching Hospital. The results according to the special criteria.

Results: Total number of patients included in the study was 124 Mean age of all patients was 49.9 ± 13.8 years, 106 (84.8%) had hypertension, 84 (70%) had diabetes mellitus, and 35 (29.9%) had known cardiovascular disease. Mean serum creatinine was $7. \pm 3.4$ mg/dl, mean eGFR was 10.6 ± 9.2 ml/min/1.73m². Overall 78.4% of all CKD patients have one or more ECG abnormality. Left ventricular hypertrophy (40%), Q waves (27.2%), ST segment elevation or depression (23.4%), prolonged QRS duration (19.2%), tachycardia (17.6%) and left and right atrial enlargement (17.6%) were the most common abnormalities.

Conclusion: ECG abnormalities are common in hospitalized CKD patients in local population. All hospitalized CKD patients should undergo ECG to screen for cardiovascular disease.

Keywords: *Chronic Kidney Disease; ECG abnormalities; Cardiac Arrhythmias.*

Introduction:

Cardiovascular disease is a major cause of mortality and morbidity among subjects on hemodialysis. It is responsible for up to 50% of deaths among subjects on dialysis¹ Cardiac arrhythmias are frequent among the hemodialysis population, particularly during and immediately after a dialysis session.² These arrhythmias may be caused by the rapid changes in intracellular and extracellular electrolytes during the dialysis session.³ Despite development of modern technologies electrocardiogram (ECG) remains an essential tool for

evaluation of cardiovascular disease. ECG is important in detection of cardiac rhythm abnormalities, cardiac conduction defects and detection of myocardial ischemia.⁴ Resting ECG abnormalities are common in patients with CKD and they independently predict future cardiovascular events.^{5,6} However, there is wide variation in reported prevalence of various ECG abnormalities in different studies.^{8–15} Left ventricular hypertrophy (LVH) has been found in 27.6–83% percent of CKD population.^{10–14} Similarly prolonged corrected QT interval (QTc) was found in 16.9–66%.^{8,9} right bundle branch block (RBBB) in 2.2–12.8%, left bundle

branch block (LBBB) in 6.0–9.6%,^{8,12} and left atrial enlargement in 21.6–30% of CKD patients in different studies^{7,8}.

Material and Method

This cross sectional observational study design was carried out through the present investigation from Jun 2nd January/2019 to 2/July/2019 in order to achieve the objectives of the present study. A non-probability (purposive) sample of 120 patient which including (88) males and (32) females. Who were attending Hemodialysis Unit in AL- Hussein Teaching Hospital. The results according to the following criteria.

Inclusion Criteria: Those patients who are on hemodialysis for > 6 months. Adult patients. Both sexes. Patients who were in stable condition. No other chronic disease except hypertension and diabetes mellitus. Persons who are free from psychiatric illness with the drugs. Patients who agreed to conduct the questionnaire.

Exclusion criteria: Those patients of < 6 months duration of dialysis. Patients known to have H/o CAD or intervention to cardiac problem 12 LEAD ECG was taken in all patients. Patients were excluded if they had an implantable pacemaker in place or if they have severe hyperkalemia (serum potassium >6.0 meq/L), severe hypokalemia (serum potassium <3.0 meq/L) and hypocalcaemia (correct serum calcium <8.0 mg/dl).

The questionnaire consisted of two parts which:

Part I: Demographic and Clinical information: Patient's history, medical records and laboratory information were reviewed to obtain data on patient's age, sex, history of diabetes mellitus, hypertension, duration of hypertension and diabetes mellitus cardiovascular disease, heart rate, blood pressure, serum creatinine, eGFR and urine protein to creatinine ratio.

Part II: All patients underwent 12 lead electrocardiograms (ECG) at the time of admission. Subsequent ECGs if done were not analyzed for study purpose. ECG was interpreted by a qualified physician trained in interpretation of ECG abnormalities. ECG abnormalities were defined based on accepted standard criteria^{9,10}. PR interval was considered to be prolonged if it was above 200 msec. Thresh hold criteria for prolonged QRS duration was above 100 msec Corrected QT interval (QTc) was calculated by using following formula: $QTc = QT \text{ interval} / \sqrt{RR}$

interval (in seconds). QTc was considered prolonged if it was above 446 msec in females and 444 msec in males. Tachycardia was defined as heart rate above 100 beats/min and bradycardia was defined as heart rate less than 60 beats/min respectively. Right axis was defined as presence of negative QRS deflection in lead I and positive QRS deflection in lead aVF. Left axis was defined as presence of positive deflection of QRS complex in lead I and negative deflection in lead II. ST segment depression was considered to be present if there was down word or horizontal sloping of ST segment greater than 0.05 mV below baseline measured at 0.08 second after J point in two contiguous leads. ST segment elevation was considered to be present if ST segment elevation was present by equal or greater than 0.1 mV and by equal or greater than 0.2 mV in leads V2 and V3, measured at the J point. Q wave was considered to be present if there was any Q-wave in leads V2–V3 equal or more than 0.02 s or Q-wave equal or more than 0.03 s in other leads. Skolow-Lyon indices were used to establish left ventricular hypertrophy.¹⁸ Right ventricular hypertrophy (RVH), left and right atrial enlargement, left and right bundle branch blocks and fascicular blocks were identified using accepted standard criteria.¹¹.

Results

Total 120 patients were included in this study. Mean age of the study group was 44.7±12.3years . Men were 86 and women were 34 in number . Mean duration of dialysis is 2.5±6 months. At least one ECG abnormality was observed in 89(74.9%) patients. Mean duration of dialysis is 27.4±25.9 months. At least one ECG abnormality was observed in 87(72.5%) patients. hypertension, 84 (70%) had diabetes mellitus, 32 and 35 (29.9%) had known cardiovascular disease. (26.7%) were smokers, 22 (18.3%) had dyslipidemia Mean serum creatinine was 7.2±3.4 mg/dl, mean eGFR was 10.6±9.2 ml/min/1.73m² and mean urine protein to creatinine ratio was 3.8±3.9. Of all patients 85.7% had stage V CKD, 7.6% had stage IV CKD and 5.9% had stage III CKD. Majority of the patients (101) had permanent vascular access (84.1%) and only 11 patients had Jugular catheter (9.1%). Rhythm abnormalities were seen in 32 patients (26.6%) and the remaining 88 patients (73.4%) .

Only one patient had sinus arrhythmia and 25 patients had sinus tachycardia. Six patients had ventricular ectopic beats. Mean heart rate in the study group was 90.7±15 seconds. Mean PR interval was 149.75±31.8millisec and mean QRS duration was 95.43±19.20 millisec,

Mean QTc interval was 431.9±27.3 milliseconds. Prolonged PR interval was observed in 12 patients and a prolonged QTc was noted in 16 patients (table 1). Factors influencing prolonged QTc and prolonged PR interval could not be studied.

Table 1: Average heart rate, PR, QRS and corrected QT interval in patients with CKD

Mean heart rate (beats/min)	91.8±18.3
Mean PR interval (ms)	137.9±22.3
Mean QRS duration (ms)	93.4±22.2
Mean corrected QT interval (ms)	400.1±57.9

Table 2: CKD patients with abnormal heart rate or intervals

Abnormal Rate or Intervals	Percentage	Frequency
Sinus tachycardia	25	20.8%
VPCs	6	5%
Prolonged PR interval	12	10%
Prolonged QRS duration	12	10%
Prolonged QTc interval	16	12.8%

On resting ECG, most common abnormality found was left ventricular hypertrophy (50%) and T wave changes (34%). Left atrial enlargement was observed in 22.5% and ST segment changes were seen in 23%. LBBB was least common, noted in only 2.5% of study population (table 2).

Table 3: Average heart rate, PR, QRS and corrected QT interval in patients with CKD

Abnormal Findings on ECG	Percentage	Frequency
Left ventricular Hypertrophy	53	45.2%
Left atrial enlargement	24	18.9%
RBBB	14	10.3%
LBBB	5	4.9%
ST segment changes	29	23.4%
T wave changes	41	34.16%
Abnormal Q waves	8	7.4%
Bifascicular block	1	0.8%
Premature atrial beats	6	4.8%
Premature ventricular beats	18	14.4%
Right axis deviation	14	10.4%
Left axis deviation	18	14.4%
Rhythms other than sinus	1	0.8%

Discussion

Our study showed that ECG abnormalities are

common in local CKD population with LVH being the most common ECG abnormality. At least one ECG abnormality was noticed in 78.4% of all CKD patients. In other studies, abnormal ECG findings were noticed in 50–86% of all patients.^{12,13} LVH was found in 41.6% of our patient population. Our study results are consistent with Bignotto et al¹³ and Stewart et al¹⁴. However, in a study by Chijiokie et al. LVH was found in 27.6% of all patients.⁸ Other studies have shown a much higher prevalence of LVH (66–83%) in CKD patients.¹⁵ However, the later study showing significantly higher prevalence of LVH was done in hemodialysis patients. Our study population entirely comprised of pre-dialysis CKD patients. Finding of LVH on ECG is significant as it is independently associated with adverse cardiovascular outcomes.²² Left atrial enlargement was found in 22.5% of our patients compared to other studies which have reported a frequency of 21.6–30%.⁷

In our study, frequency of RBBB and LBBB was found to be 12.8% and 2.5% respectively. Our results are consistent with Nwanko et al which showed a frequency of 15.1% and 10.1% respectively.¹⁶ Kestenbaum B et al. found a lower frequency of RBBB as 2.2% and LBBB as 6.0%.⁸

Presence of Q waves and ST segment deviation were found in 5% and 27.2% in our study similar to frequency of myocardial ischemia/infarction as 28% in another study.⁷

Widening of QRS complex was found in 10% of our patients. Prolonged QTc was found in only 12.8% of our patients. Other studies have reported a significantly higher frequency of prolonged QTc ranging from 16.9% to roughly 2/3rd of CKD patients.^{16,17}

Reason for lower frequency of prolonged QTc in our patient population is not clear but it may be due to difference in patient population, relatively younger age, exclusion of patients with electrolyte abnormalities and infrequent use of medications associated with prolonged QT interval in our patient population.

ECG abnormalities in CKD patients have been found to independently predict cardiovascular event and mortality.^{7,8} CKD patients with ECG abnormalities may benefit from close follow up and consultation with cardiologist to help reduce cardiovascular event or mortality. Our study has several limitations including relative small sample size, single center and cross-sectional study design. In addition, our study was

conducted in hospital setting with large proportion of patients with advanced CKD. This may have resulted in over-estimation of frequency of ECG abnormalities

in CKD patients. However, our study population's characteristics are reflective of patient's profiles in tertiary care facilities in Iraq.

Table 5: Comparison of ECG findings in the studies available.

Variables	Shafi et al	Manjusha and Kumaraswamy	Present
Total no of patients	120	124	120
Mean Age	44.7±12.3	49.9±13.8	44.7±12.3
ECG abnormalities	72.5%	78.4%	74.9%
LVH	41.6%	40.8%	45.2%
LAE	22.5%	17.6%	18.9%
RBBB	5.8%	12.8%	10.3%
LBBB	2.5%	9.6%	4.9%
ST segment changes	23.3%	23.4%	23.4%
Q waves	5%	27.2%	7.4%
Prolonged QT interval	13.3%	49.1%	12.8%

Conclusion

In summary, our study shows that resting ECG abnormalities are common in CKD patients who were hospitalized. LVH is the most common electrocardiographic abnormality. All hospitalized CKD patients should undergo ECG to detect any abnormal findings. Further studies are needed to see whether abnormal ECG findings predict cardiovascular events or mortality in our patient population.

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the College of Nursing and all experiments were carried out in accordance with approved guidelines.

References

- De Lima J, Sesso R, Abensur H et al. Predictors of mortality in long-term hemodialysis patients with a low prevalence of co morbid conditions. *Nephrol. Dial. Transplant* 1995; 10 (9): 1708-1713.
- Familoni O, Alebiosu C, Ayodele O et al, Effects and outcome of hemodialysis on QT intervals and QT dispersion in patients with chronic kidney disease. *Cardiovascular J S Afr* 2006 Jan-Feb; 17(1):19-23.
- Krachler M, Scharfetter H, and Wirnsberger G. Exchange of alkali trace elements in hemodialysis Patients: a comparison with Na (+) and K(+). *Nephron* 1999; 83(3):226-36.
- Prutkin JM. ECG tutorial: Basic principles of ECG analysis [Internet]. [cited 2016 Mar 21]. Available from: <http://www.uptodate.com/contents/ecg-tutorial-basicprinciples-of-ecg-analysis>.
- Deo R, Shou H, Soliman EZ, Yang W, Arkin JM, Zhang X, et al. Electrocardiographic Measures and Prediction of Cardiovascular and Non-Cardiovascular Death in CKD. *JAm Soc Nephrol* 2016;27(2):559–69.
- Kestenbaum B, Rudser KD, Shlipak MG, Fried LF, Newman AB, Katz R, et al. Kidney function, electrocardiographic findings, and cardiovascular events among older adults. *Clin J Am Soc Nephrol* 2007;2(3):501–8.
- Dutta P, Das S. Value of electrocardiogram in predialytic chronic kidney disease patient without known coronary artery disease. *Int J Med Res Health Sci* 2014;3(4):967–74.
- Chijioke A, Makusidi AM, Kolo PM. Electrocardiographic abnormalities among dialysis naïve chronic kidney disease patients in Ilorin

- Nigeria. *Ann Afr Med* 2012;11(1):21–6.
9. Hancock EW, Deal BJ, Mirvis DM, Okin P, Kligfield P, Gettes LS, et al. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part V: electrocardiogram changes associated with cardiac chamber hypertrophy: a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society: endorsed by the International Society for Computerized Electrocardiology. *J Am Coll Cardiol* 2009;53(11):992–1002.
 10. Surawicz B, Childers R, Deal BJ, Gettes LS, Bailey JJ, Gorgels A, et al. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part III: intraventricular conduction disturbances: a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society. Endorsed by the International Society for Computerized Electrocardiology. *J Am Coll Cardiol* 2009;53(11):976–81.
 11. Rautaharju PM, Surawicz B, Gettes LS, Bailey JJ, Childers R, Deal BJ, et al. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part IV: the ST segment, T and U waves, and the QT interval: a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society: endorsed by the International Society for Computerized Electrocardiology. *J Am Coll Cardiol* 2009;53(11):976–81.
 12. Chijioke A, Makusidi AM, Kolo PM. Electrocardiographic abnormalities among dialysis naïve chronic kidney disease patients in Ilorin Nigeria. *Ann Afr Med* 2012;11(1):21–6.
 13. Bignotto LH, Kallás ME, Djouki RJ, Sasaki MM, Voss GO, Soto CL, et al. Electrocardiographic findings in chronic hemodialysis patients. *J Bras Nefrol* 2012;34(3):235–42.
 14. Stewart GA, Gansevoort RT, Mark PB, Rooney E, McDonagh TA, Dargie HJ, et al. Electrocardiographic abnormalities and uremic cardiomyopathy. *Kidney Int* 2005;67(1):217–26.
 15. Nwankwo EA, Ummate I, Wudiri W. Prevalence of electrocardiographic left ventricular hypertrophy among incident dialysis patients in Maiduguri Nigeria. *Res J Med Med Sci* 2007;2:1–4.
 16. Kestenbaum B, Rudser KD, Shlipak MG, Fried LF, Newman AB, Katz R, et al. Kidney function, electrocardiographic findings, and cardiovascular events among.
 17. Sherif KA, Abo-Salem E, Panikkath R, Nusrat M, Tuncel M. Cardiac repolarization abnormalities among patients with various stages of chronic kidney disease. *Clin Cardiol* 2014;37(7):417–21.
 18. Manjusha Y and Kumaraswamy P. Resting ECG Abnormalities in Patients on Maintenance Hemodialysis – A Clinical Study Volume 16, Issue 8 Ver. VII (Aug. 2017), PP 62-64.

Screening of Bio-active Chemical Composition of *Vespa Orientali* and Investigation of its Anti-Fungal Activity

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Abstract

Screening of Bioactive Chemical Composition of *Vespa orientali* was assayed for *in vitro* anti-fungal activity against *Asp. flavus*, *Asp. Terreus.*, *Penicillium expansum*, *Asp. fumigatus*, *T. horzianum*, *S. cerevisiae.*, *Candida albicans*, *T. viride*. GC-MS analysis of *Vespa orientali* revealed the existence of the, Thi-eno- furan-3, 2-amino-4, 6-dihydro, Z-8--Methyl-9-tetra-decenoic acid, I-Propyl-9-tetra-decenoate, Octa-decatrienoic, 2-[(tri-methylsilyl)oxy]-1-[(tri-methyl, 17-Octa-decynoic acid, Oxime-, methoxy-phenyl-, Edulanll, p-Menth-1-en-3-one, semi-carbazone, 5,7-dodeca diyn-1,12-diol, Methyl 2-O-benzyl -d- arabinofuranoside, Ery-thritol, d- D-Glucose, 6-O- α -D-galactopyranosyl-, Gala-ido- octonic, Desulphosingrin, 2(3H)-Furanone, 3-butyl dihydro-, 24,25- triol, (3 β ,5Z,7E)-, N-(4, 6-dinyl)- 4-(4-nitro benzylidene amino) benzel, 2,7-Di-phenyl-1,6-dioxopyri-dazino [4,5:2',3'] pyrrolo[4',5'-d]pyridazin, 2-Methyl-9- β -d-ribofuranosylhypoxanthine, Ergosta-5,22-dien-3-ol, acetate, (3 β ,22E)-, 10-Hepta-decen-8-tri-methoxy-2,3-dimethyl-, 1-Methyl-8-propyl-3, 6-diazahomoadamantan-5-dimethyl-aminomethyl-1H-[1,2,3] triazole, and 6-Octa-decenoic acid. The results of its activity showed that all compounds were highly effective to suppress the growth of *Asp. terreus*.

Keywords: *Vespa orientali*, GCMS, Bioactive chemical compounds, Anti-fungal, peptides.

Introduction

The Oriental hornet, *V. orientalis*, is an insect of the family Vespidae. *V. orientalis* can be found in Asia, Northeast Africa, and parts of Southern Europe¹. Peptides have a range of anti-bacterial and anti-fungal activities. They have a promising capacity in the therapeutic and prophylactic. They have a good capacity in the healthing and precaution. Insect are found throughout the world, with the possible exception of the arctic and Antarctic areas, the ocean depths, and the tops of high mountain peaks. Some are so small, a microscope is needed to see them, others are several inches long. They are so widespread that they can be studied practically everywhere in cities and in farms in the backyard or garden in the home or in the park. However, some insects are harmful. They can truly be regarded as people major competitors for food on this earth. They destroy crops by eating the roots, seeds, stems, leaves or of fruit of plants. They attack livestock, weakening or sometime killing it. They even get into processed food, forcing you to discard it. These peptides display an anti-microbial outcome by

destroy the microbic membrane and do not simply allow microbes to initiate pharmaceutical resistance. Currently, membrane mechanisms underlying the anti-microbial effects of peptides are proposed by different modes: the toroidal-pore, barrel-stave mode, and disorganized toroidal-pore are the typical modes.

Materials and Method

Vespa orientalis specimens were collected from rural areas - the center of Iraq. The whole body were crushed in a clean mortar using pestle. Methanol was used as solvent control.

Antimicrobial Assay: The microorganisms used in the antifungal screening assays were:

The studied yeast and fungi, *Asp. flavus*, *Asp. terreus*, *Penicillium expansum*, *Asp. fumigatus*, *T. horzianum*, *Saccharomyces cerevisiae*, *C. albicans*, *T. viride*. were maintained in potato dextrose agar. In triplicate the tests were carried out.

Gas-chromatography – mass spectrum analysis:

The GCMS analysis of the insect powder was made in a (Agilent 789 A) instrument. About 1microletters of the methanol extract was injected into the GCMS apply a micro syringe and the examine was done for 45 minutes. Results of the study were based on examination of variance (ANOVA).

Results and Discussion

Identification of Biochemical Compounds: Insect vary in their growth patterns. All begin as eggs and end up as adults. But between the egg and the adult stage there is an intermediate growth from called the immature stage. It’s during this stage which differs in different groups of insect that growth takes place. Insect growth is accompanied by series of periodic shedding of the exoskeleton.

V. orientalis displayed a good effect against different types of fungi. *Asp.terreus* was the most sensitive. Chromatogram GCMS examination of the methanol extract of *Vespa orientali* showed 39 major peaks. *Asp. flavus* 3.96±0.18 mm, *Aspergillusterreus* 4.01±0.20, *Penicilliumexpansum* 1.59±0.09, *Aspergillusfumigatus* 3.91±0.19, *Trichodermahorzianum* 1.89±0.09, *Saccharomyces cerevisiae* 2.04±0.10, *Candida albicans* 4.00±0.20, *Trichodermaviride* 2.63±0.08. *V.orientali* produce important metabolites with medicinal activities. Greatest zone initiate against *Asp.terreus* (4.01±0.21mm) mm, Table 1. These peptides display an anti-microbial outcome by destroy the microbic membrane and do not simply allow microbes to initiate pharmaceutical resistance.

Table 1. Anti-fungal activity of Vespa orientali metabolites.

Fungi	Anti-biotics/Metabolite produce Vespa orientali			
	Metabolite produce of Vespa orientali	Amphotericin B	Fluconazol	Miconazole nitrate
Asp.flavus	3.96±0.18	1.03±0.08	1.80±0.20	1.04±0.04
Asp.terreus	4.01±0.20	2.07±0.09	0.89±0.07	1.95±0.08
P.expansum	1.59±0.09	1.99±0.07	3.80±0.28	0.86±0.03
Asp.fumigatus	3.91±0.19	0.89±0.05	2.09±0.25	1.11±0.06
T.horzianum	1.89±0.09	1.09±0.03	2.05±0.20	1.08±0.04
S.cerevisia	2.04±0.10	1.36±0.07	1.91±0.21	2.09±0.15
C.albicans.	4.00±0.20	0.97±0.09	0.81.±0.04	1.87±0.11
T.viride.	2.63±0.08	1.98±0.06	1.40±0.11	1.39±0.09

Conclusion

39 active constituents had been fixed from *Vespa orientali* by GCMS technique. *In vitro* anti-fungal estimate of metabolite of *Vespa orientali* forms a platform for development of new anti-fungal compounds.

Ethical Clearance: Experimental protocols were confirmed under Dep. of Biology and all tests were carried out with advisable guidelines.

References

1. Cezard C, Pires V, C. Mullie, Sonnet P. Antimicrobial peptides: A review. Science against microbial pathogens: communicating current research and technological advances. Eds, Mendez-Vilas, A.: FORMATEX. 2011; 926-937.
2. Joerger RD. Alternatives to antibiotics: Bacteriocins, antimicrobial peptides and bacteriophage. Poultry Science. 2003; 82: 640-647.
3. Chiou SY, S Kotanen, A Cerstiaens, Daloze D. Purification of toxic compounds from larvae of the gray fleshfly: The identification of paralytins. Biochemical & Biophysical Research Communications. 1998; 246: 457.
4. Meylears K, ACerstiaens, E. Vierstraete, G. Baggerman, C.W. Michiels, Loof A, Schoofs L. Antimicrobial compounds of low molecular mass are constitutively present in insects: Characterisation of β-alanyl-tyrosine. Current Pharmaceutical Design. 2002; 8: 99-110.

5. Bulet P, M Charlet, Hetru C. In *Innate Immunity*, Eds., Ezekowitz RA, Hoffman JA: Humana Press, Totowa, N.J, 2003; pp: 89-107.
6. Cirioni O, R Ghiseli, C Silvestri, W Kamsay, F Orlando, F Mocchegiani, FD Matteo, Riva A. Efficacy of tachyplesin III, colistin, and imienem against a multiresistant *Pseudomonas aeruginosa* strain. *Antimicrobial Agents Chemotherapy*. 2007; 51: 2005- 2010.
7. Jakopic J, R Veberic, Stampar F. Extraction of phenolic compounds from green walnut fruits in different solvents. *Acta Agriculturae Slovenica*. 2009; 93: 11-15.
8. Gordon YJ, Romanowski EG, McDermott AM. A review of antimicrobial peptides and their therapeutic potential as anti-infective drugs. *Curr Eye Res*. 2005;30(7):505–515.
9. Wright GD. The antibiotic resistome: the nexus of chemical and genetic diversity. *Nat Rev Microbiol*. 2007;5:175–186.
10. Fleet GH. In: *Yeast Technology*. Spencer JFT, Spencer DM, editor. Berlin: Springer; 1990. Food spoilage yeasts.
11. Kumarasamy KK, Toleman MA, Walsh TR, Bagaria J. Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study. *Lancet Infect Dis*. 2010;10(9):597–602.
12. Anderson ET, Young LS, Hewitt WL. Antimicrobial synergism in the therapy of gram-negative rod bacteremia. *Chemotherapy*. 1978;24(1):45–54.
13. Kreger BE, Craven DE, McCabe WR. Gram-negative bacteremia. IV. Re-evaluation of clinical features and treatment in 612 patients. *Am J Med*. 1980;68(3):344–355.
14. Guardabassi L, Kruse H. Overlooked aspects concerning development and spread of antimicrobial resistance. Central European symposium on antimicrobial resistance, Brijuni, Croatia, 4–7 July, 2003. *Expert Rev Anti Infect Ther*. 2003;1(3):359–362.
15. Hancock RE, Diamond G. The role of cationic antimicrobial peptides in innate host defences. *Trends Microbiol*. 2000;8(9):402–410.
16. Hujer AM, Bethel CR, Hujer KM, Bonomo RA. Antibiotic resistance in the institutionalized elderly. *Clin Lab Med*. 2004;24(2):343–361.
17. Adams ME, Herold EE, Venema VJ. Two classes of channel-specific toxin from funnel web spider venom. *J Comp Physiol A*. 1989;164(3):333–342.
18. Chan TK, Geren CR, Howell DE, Odell GV. Adenosine triphosphate in tarantula spider venoms and its synergistic effect with the venom toxin. *Toxicon*. 1975;13(1):61–66.
19. Wullschleger B, Nentwig W, Kuhn-Nentwig L. Spider venom: enhancement of venom efficacy mediated by different synergistic strategies in *Cupiennius salei*. *J Exp Biol*. 2005;208(Pt 11):2115–2121.
20. Harvey AL, Robertson B. Dendrotoxins: structure-activity relationships and effects on potassium ion channels. *Curr Med Chem*. 2004;11(23):3065–3072.
21. Koh DC, Armugam A, Jeyaseelan K. Snake venom components and their applications in biomedicine. *Cell Mol Life Sci*. 2006;63(24):3030–3041.
22. Dani MP, Richards EH, Isaac RE, Edwards JP. Antibacterial and proteolytic activity in venom from the endoparasitic wasp *Pimpla hypochondriaca* (Hymenoptera: Ichneumonidae) *J Insect Physiol*. 2003;49(10):945–954.
23. Perumal SR, Gopalakrishnakone P, Thwin MM, Chow TK, Bow H, Yap EH, Thong TW. Antibacterial activity of snake, scorpion and bee venoms: a comparison with purified venom phospholipase A2 enzymes. *J Appl Microbiol*. 2007;102(3):650–659.
24. Fennell JF, Shipman WH, Cole LJ. Antibacterial action of a bee venom fraction (melittin) against a penicillin-resistant *Staphylococcus* and other microorganisms. USNRDL-TR-67-101. *Res Dev Tech Rep*. 1967;5:1–13.
25. Benli M, Yigit N. Antibacterial activity of venom from funnel web spider *Agelenalabyrinthica* (Araneae: Agelenidae) *J Venom Anim Toxins incl Trop Dis*. 2008;17(4):641–650.
26. Budnik BA, Olsen JV, Egorov TA, Anisimova VE, Galkina TG, Musolyamov AK, Grishin EV, Zubarev RA. De novo sequencing of antimicrobial peptides isolated from the venom glands of the wolf spider *Lycosagingoriensis*. *J Mass Spectrom*. 2004;39(2):193–201.
27. Stiles BG, Sexton FW, Weinstein SA. Antibacterial effects of different snake venoms: purification and characterization of antibacterial proteins from

- Pseudechisaustralis (Australian king brown or mulga snake) venom. *Toxicon*. 1991;29(9):1129–1141.
28. Torres-Larios A, Gurrola GB, Zamudio FZ, Possani LD. Hadrurin, a new antimicrobial peptide from the venom of the scorpion *Hadrurusaztecus*. *Eur J Biochem*. 2002;267(16):5023–5031.
 29. Wikler MA, Cockerill FR, Craig WA, Dudley MN. Method for dilution antimicrobial susceptibility tests for bacteria that grow aerobically, approved standard, Volume 26. 7. Wayne (PA): Clinical and Laboratory Standards Institute; 2006.
 30. Zasloff M. Antimicrobial peptides of multicellular organisms. *Nature*. 2002;415(6870):389–395.
 31. Xu C, Ma D, Yu H, Li Z, Liang J, Lin G, Zhang Y, Lai R. A bactericidal homodimeric phospholipases A2 from *Bungarusfasciatus* venom. *Peptides*. 2007;28(5):969–973.
 32. Gao B, Xu J, Rodriguez Mdel C, Lanz-Mendoza H, Hernández-Rivas R, Du W, Zhu S. Characterization of two linear cationic antimalarial peptides in the scorpion *Mesobuthuseupeus*. *Biochimie*. 2010;92(4):350–359.
 33. Yan L, Adams ME. Lycotoxins, antimicrobial peptides from venom of the wolf spider *Lycosacarinensis*. *JBiolChem*. 1998;273(4):2059–2066. doi: 10.1074/jbc.273.4.2059.
 34. Biggs JS, Rosenfeld Y, Shai Y, Olivera BM. Conolysin-Mt: a conus peptide that disrupts cellular membranes. *Biochemistry*. 2007;46(44):12586–12593. doi: 10.1021/bi700775p.
 35. Shukla R, Siravatava B, Kumar R, Dubey NK. Potential of some powders in reducing infection of chickpea by *Callosobruchusmaculatus* (Coleoptera: Brauchidae). *J. Agricultur. Technol*. 2007; 3(1): 11-19.
 36. Hamza LF, Kamal SA, Hameed IH. Determination of metabolites products by *Penicillium expansum* and evaluating antimicrobial activity. *Journal of Pharmacognosy and Phytotherapy*. 2015; 7(9): 194-220.
 37. Shareef HK, Muhammed HJ, Hussein HM, Hameed IH. Antibacterial effect of ginger (*Zingiberofficinale*) roscoe and bioactive chemical analysis using gas chromatography mass spectrum. *Oriental Journal of Chemistry*. 2016; 32(2): 20-40.
 38. Gundappa, S, Jayappa J, Chandrashekara K. Bioprospecting for antimicrobial peptides from insects: In vitro antimicrobial activity of acidified methanol extract of dung beetles. *Journal of Entomology Research*. 2012; 36: 41- 44.

Interleukin-4 Genetic Polymorphism -590 C/T in Type- 2 Diabetes Patients from Al-Diwaniyah Hospital of Iraq

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Abstract

This study aims to found the relationship of interleukin-4(IL-4) genetic polymorphism -590 C/Tin association of type-2 diabetes (T2D)development. (50) blood samples were collection from the patients with T2D and (30) samples from healthy group individual from Al-Diwaniyah Hospital. PCR-RFLP was carried out for detection IL-4 genetic polymorphism (-590 C/T) of T2D patients and healthy blood samples .The IL-4 gene polymorphism genotype frequencies were studied in the patients and healthy group, for the CC, CT and TT genotypes, the result revealed significant ($p<0.05$) presence of these genotypes in the patients group compared with healthy group. Also found the TT genotype increased the risk more than 20% in T2D compared with healthy group 3.33%,and CT genotype increased the risk more than 57% in T2D compared with healthy group 30%,while CC was decreased the risk 26% in the T2D compared with healthy group 66.66% . Frequency of allele T increased to 46% in the T2D compared with healthy group 20%. While frequency of allele C was not show any signification. The allele C and T carriage rates were examined, and there was no significant changes in carriage rate for C alleles. However, a significant changes was noticed in carriage rate of T allele(78.7%) in the patients population compared to healthy population. Also the results revealed there were a significant ($p<0.05$), effect of the sex and family history parameter on the IL-4 genetic polymorphism, the females and positive family history of disease 58% and 72% respectively were revealed more occurrence of this genotype in their samples with percentage. Our study was concluded that genotype C/T may be is risk factor in the T2D.

Keywords: *Interleukin-4; Genetic Polymorphism -590 C/T; Type- 2 Diabetes; Iraq.*

Introduction

T2D is thought to be a multicauses disease that effected by environmental and genetic factors. Persons that share genetic factors and have family history of the disease are at a more risk of developing T2D the in addition to probably similar environment^[1]. Recent studies have shown that numerous environmental and genetic factors are associated with T2D ^[2].

T2D is a disease dependent on immunity that have changes in the cytokine expression pattern ^[3]. Many studies focused on cytokines and its receptors for their essential role in T2D (2). Increased inflammatory cytokines level in serum including interleukin, interferon- γ , and TNF- α , are documented in T2D^[4,5]. IL-4 is the most important cytokines gene, it was originally discovered as a polypeptide consist from 129 amino acids derived from T cell, which is encoded on chromosome 5q23.31. Also it is produced by natural killer (NK), helper T cells and by innate immune system cells, including basophils, eosinophil's and mast cells,^[6]. IL-4 play important role in regulates gene expression,cells proliferation and apoptosis, also differentiation in several hematopoietic cells, like, it leads convert the Ig class to the IgE and IgG1^[7]. The relation of IL-4 in immunological disturbance such

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as diabetes mellitus is well established^[8,9]. Many of studies showed that polymorphisms in -590 region can be affected on IL-4 production^[10]. Studies showed that T2D is associated with a systemic inflammations due to increased blood level markers and mediators of immune-response. This due to association of increase levels of plasma interleukin with patient have T2D, also with increased insulin resistance, which suggesting its latent role in the T2D development^[11].

Therefore, This study aims to found the relationship of IL-4 genetic polymorphism -590 C/T in association of T2D.

Method

Collections of blood Samples: (50) blood samples were collection from the patients with T2D and (30) samples from healthy group, individual from Al-Diwaniyah Hospital, then the samples storage in freezer until use.

DNA Extraction: DNA were extracted from blood samples by using genomic DNA Mini Kit, (Geneaid. USA). This was done by using Proteinase K for frozen Blood extraction. Then, the extracted genomic DNA purity and concentration were checked by Nanodrop spectrophotometer, after that stored in freezer at -20°C.

PCR RFLP: PCR RFLP used for detection IL-4 gene polymorphism (-590 C/T) of T2D patients and healthy blood samples. The technique was done according to^[12]. The forward primers (5'-TAAACTTGGGAGAACATGGT-3) and reverse primers (5'-TGGGGAAAG ATAGAGTAATA-3). (Bioneer company. Korea). After that used AccuPower[®] PCR PreMix kit. (Bioneer. Korea) to prepare PCR master mix. PCR premix tube contains dried- freeze pellet of (dNTPs 250µM, Taq DNA polymerase, Tris - HCl (pH 9.0) 10mM, MgCl₂ 1.5mM, stabilizer, KCl 30mM, and tracking dye) then the PCR master mix consist from 5µl of pure gDNA and 3µl of 10pmole of forward and reverse primers, then the volume complete into 20 µl by add deionizer water and mixed by vortex centrifuge. The reactions were done in a thermocycler T100 Thermal

cycler (Biorad.USA) as the following thermocycler conditions, initial denaturation 95°C for 5 minutes, then 35 cycle at denaturation 95° C for 30 second, annealing 53° C for 30 second, and extension 72° C for 1 minute and finally extension at 72° C for 5 minutes. The electrophoresis used to examine 195bp PCR products in a 2% agarose gel, and visualized under UV illumination. RFLP step done by using (AvaII, Biolabs, UK) restriction enzyme. products of PCR RFLP were using for detection IL-4 gene polymorphism include CC wild type homozygote, the product undigested by restriction enzyme 195bp band. The C/T heterozygote, the product digested by restriction enzyme into 195bp, 175bp and 20bp band. The RFLP PCR fragments were separated by 3% agarose gel electrophoresis and visualized under UV Transilluminator.

Statistical Analysis: Genotype and allele frequencies were calculated in patients and healthy groups by direct genes counting. Used SPSS software (version 25). For detected odds ratio to compare the importance of various risk factors. P value <0.05 was considered significant.

Results

The present study investigated the effect of sex and family history of disease on the IL-4 genotypes in the T2D patients group compared to the control group. The result revealed that there was a significant effect (p<0.05) of the sex parameter on the IL-4 genetic polymorphism. Family history parameter effect on the IL-4 genetic polymorphism was also investigated, the results in table (1) revealed a significant increased (p<0.05) of the IL-4 genetic polymorphism within the positive family history of disease in the patients group. The IL-4 genotype frequencies were studied in the patient and healthy group, for the CC, CT and TT genotypes (figure. 1), the results showed a significant (p<0.05) presence of these genotypes in the patients group. In addition, this study investigated the allele C and allele T frequencies in the patients group as well as in the healthy group, and the results revealed a significant shifting of two alleles in the patient group (table 3).

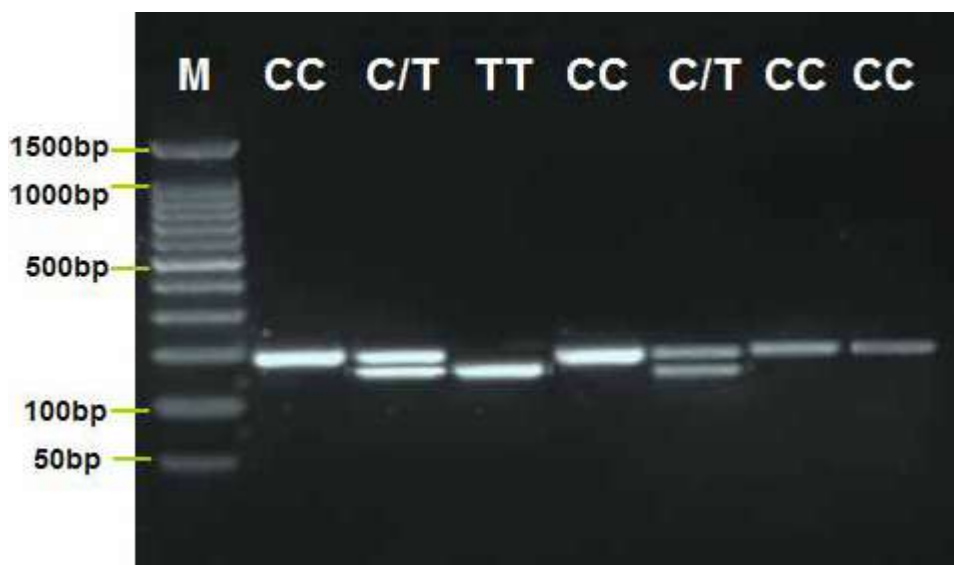


Figure 1: Image show RFLP-PCR product analysis for IL-4 gene polymorphism (-590 C/T) of T2D patients and healthy blood samples by use Agarose gel electrophoresis. This done by using *avaII* restriction enzyme in 3% agarose. Where M: marker (1500-100bp), (CC) wild type homozygote lanes, the product undigested by restriction enzyme and still as 195bp band. The (C/T) heterozygote lanes, the restriction enzyme digested product into 195bp, 175bp and invisible 20bp band. Whease the (TT) mutant type homozygote lanes, the restriction enzyme digested product into 175bp and invisible 20bp band.

The carriage rate for allele C and T were studied in the patients population compared to the healthy population, and no significant changes was noticed

in carriage rates for C allele. However, a significant changes was noticed in carriage rate of T allele in the patients group (Table 4,5).

Table (1): Clinical data of patients and healthy groups

Clinical Data		Healthy Group (30 Cases)	Patients Group (50 Cases)	P value
Sex	Male	13 (43.33%)	21 (42%)	0.07
	Female	17 (56.67%)	29 (58%)	
Family History of Disease	+	11 (36.66%)	36 (72%)	0.07
	-	19 (63.33%)	14 (28%)	

Signification at level 0.05

Table (2): IL-4 Genotype frequencies

Genotype	Healthy Group (30 Cases) N and (%)	Patients Group (50 Cases) N and (%)
CC	20 (66.66)	13 (26)
CT	9 (30)	27 (54)
TT	1 (3.33)	10 (20)
P value	0.04	

Table (3): IL-4 Allele Frequencies

Type	Healthy Group (30 Cases) N and (%)	Patient Group (50 Cases) N and (%)
C	48 (80)	54 (54)
T	12 (20)	46 (46)
Odds ratio (95% CI)	0.668	
P value	0.008	

Table (4): Allele C Carriage Rate

Type	Healthy Group (30 Cases) N and (%)	Patient Group (50 Cases) N and (%)
C(+)	24 (80)	57(89.06)
C(-)	6 (20)	7(10.93)
Odds ratio(95% CI)	4.623	.638

Table (5): Allele T Carriage Rate

Type	Healthy Group (30 Cases) N and (%)	Patient Group (50 Cases) N and (%)
T(+)	10 (21.3)	37 (78.7)
T(-)	20 (62.5)	12 (37.5)
Odds ratio(95% CI)	.340	2.099

Discussion

Complications of T2D become a main causes of death worldwide. The immunity play important roles in the T2D development, cytokines are a important part of the immunity that involve in development T2D complications^[13]. Researchers in immunology said the T2D is associated with cytokines disturbance and altered immunity response pattern ^[14]. Our study used molecular method (PCR method) to detect association between IL-4 genetic polymorphism (-590 C/T) and T2D patients that agreed with some researchers that used same the technique ^[15,16]. The current study found that IL-4 gene -590 C/T Polymorphism showed significant correlation with T2D, this study also suggested that SNP -590 which is located in the IL-4 gene promoter region may be a risk factor to develop of T2D. Mediators of inflammation such as family of cytokines and certain chemokine’s have proposed to be involved in the events result in diabetes mellitus^[17,18,19]. This might give a suggestion that there are a strong link between T2D and IL-4 genetic polymorphisms which might considered as prognostic biomarker for development of T2D. Our study agreed with Bid and colleagues that were reported a significant association between T2D and IL-4 polymorphism in the population of north Indian^[20]. Another research found the IL-4-590 C/T heterozygous

genotypes might be as risk factor, while the -590 C/C homozygous wild types might be considered protective to T2D^[15].

Another study showed there was no signification between IL-4 genotypes in patients and control groups (9). Also^[21] Didn’t show any significant differences in the IL-4 genetic polymorphism between T1D patients and control groups. The difference between our previous results and those may be that population are different in genetics and race from our studied population.

The IL-4 polymorphisms were more pronounced in the T2D patients, particularly the CC, CT and TT and it revealed a significant relation with family history of disease and sex parameters. This genotypes of the IL-4 gene showed more occurrence in the females with 58%. So, IL-4 polymorphisms revealed that the frequency C/T alleles were a significant increased in T2D patients group. This lead to suggest that SNP has a important role in susceptibility to T2D development.

Also, our study found that the allele C carriage rate (.638) was lower than that in allele T carriage rate (2.099) in T2D group, which is confirmed the previous results. Also our study found that TT genotype increases the risk up to 20% in patients compared to control group 3.33%, and CT genotype increases the risk up to 57%

in T2D compared to control group 30%. While, CC was decreases the risk 26% in the patients compared to control group 66.66%. Frequency of Allele T increased to 46% in the patients compared to control group 20%. While, frequency of allele C not show any significant result. This results suggested that genotypes and alleles are correlated with development of T2D. The current data provided a sight on the cytokine gene heterogeneity role in development of T2D. Additionally, the cytokine genes variants may be a probable indicator for disease susceptibility in Iraq population.

Conclusion

Our study was concluded that genotype C/T may be is risk factor in the T2D.

Conflict of Interest: : The author has no disclosures to report.

Source of Funding: Self.

Ethical Clearance: Not required.

References

1. Doria A, Patti M.-E. and Kahn, C. R. The emerging genetic architecture of type 2 diabetes. *Cell Metabolism*.2008; 8: 3 pp:186–200.
2. Nathanson D, Nystrom T. Hypoglycemic pharmacological treatment of type 2 diabetes: Targeting the endothelium. *Mol Cell Endocrinol*. 2009;297 pp:112-26.
3. Cruz M, Maldonado-Bernal C, et al .Glycine treatment decreases proinflammatory cytokines and increases interferon-gamma in patients with type 2 diabetes. *J Endocrinol Invest*. 2008;31 pp:694-9.
4. Skopinski P, Rogala E, Duda-Krol B, et al. Increased interleukin-18 content and angiogenic activity of sera from diabetic (Type 2) patients with background retinopathy. *J Diabetes Complications*. 2005;19:6 pp:335-8.
5. Pickup JC, Chusney GD, Thomas SM, Burt D. Plasma interleukin-6, tumour necrosis factor alpha and blood cytokine production in type 2 diabetes. *Life Sci*. 2000;67:291-300.
6. Voehringer D, Reese T A, Huang X, Shinkai K and Locksley RM . Type 2 immunity is controlled by IL-4/IL-13 expression in hematopoietic non-eosinophil cells of the innate immune system. *Journal of Experimental Medicine*, 2006; 203. 6, pp” 1435–1446.
7. Ueta M, Sotozono C, Inatomi T, Kojima K, Hamuro J and Kinoshita S. Association of combined IL-13/IL-4R signaling pathway gene polymorphism with Stevens-Johnson syndrome accompanied by ocular surface complications. *Investigative Ophthalmology and Visual Science*.2008; 49:5 pp: 1809–1813.
8. Bugawan TL, Mirel DB, Valdes AM, Panelo A, Pozzilli P, Erlich HA. Association and interaction of the IL4R, IL4, and IL13 loci with type 1 diabetes among Filipinos. *Am J Hum Genet*. 2003;72 pp:1505-14.
9. Arababadi MK, Pourfathollah AA, Daneshmandi S, et al. Evaluation of relation between IL-4 and IFN- γ polymorphisms and type 2 diabetes. *Iran J Basic Med Sci*. 2009;12 pp:100-4.
10. Arababadi MK, Pourfathollah AA, Jafarzadeh A, et al. Evaluation of Relation between Polymorphisms in -590 Region of IL-4 and Occult HBV Infection. *J Guil Univ Med Sci*. 2009;18 pp:1-8. Persian.
11. Pradhan, A. D., Manson, J. E., Rifai, N., Buring, J. E. & Ridker, P. M. C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. *Jama*.2001; 286pp: 327-334.
12. Arababadi MK. Interleukin-4 Gene Polymorphisms in Type 2 Diabetic Patients With Nephropathy. *Iranian Journal of Kidney Diseases*.2010; 4, 4 pp302-306.
13. Alhazmi AS, Hussein YM, Al Omari A, El Askary A and Damiati L. Interleukin-4 (IL-4), Tumor Necrosis Factor- α (TNF- α), and its receptors Gene Polymorphism in Type 2 Diabetes Mellitus. *Clinical Journal of Diabetes Care and Control*.2019;2.1pp:1-9.
14. Nosratabadi R, Arababadi MK, Hassanshahi G et al. Evaluation of IFN- γ serum level in nephropathic type 2 diabetic patients. *Pakistan Journal of Biological Sciences*.2009; 12, 9 pp. 746–749.
15. Alsaid A, El-Missiry M, El-Sayed H, Tarabay M and Settin A. Association of IL-4-590 C>T and IL-13-1112 C>T Gene Polymorphisms with the Susceptibility to Type 2 Diabetes Mellitus.2013.35,4pp:243-247.
16. Hassan I B, Nazzal M F, Qadir H T and Hammadi I A T. A Genetic Polymorphism of Interleukin-4 Gene at Position 590 in Type-1 Diabetes of Iraqi Patients.2017;10,9 pp:641-645.

17. Cilenšek I, Hercegovac A, Starčević JN, Vukojević K, Babić M S and Živin A M. Polymorphisms of interleukin-4, -10 and 12B genes and diabetic retinopathy. *Cent. Eur. J. Biol.*2011; 6(4)pp: 558-564.
18. Tripathi A K, Shukla, S, Tripathi J K, Saket R D, kol S, Mishra P, Chauhan U K and Indurkar M. Association of Genetic Polymorphism of Inflammatory Genes (IL-1 β and IL-4) with Diabetes Type 2. *J. Genet. Mol. Cell Biol.*2015; 1,1pp:1-9.
19. Alsaid A, El-Missiry M, Hatata S, Tarabay M and Settin F. Association of IL-4-590 C>T and IL-13-1112 C>T Gene Polymorphisms with the Susceptibility to Type 2 Diabetes Mellitus Disease. *Markers.* 2013; 35, 4pp: 243–247.
20. Bid HK, Konwar R, Agrawal CG, Banerjee M. Association of IL-4 and IL-1RN (receptor antagonist) gene variants and the risk of type 2 diabetes mellitus: a study in the north Indian population. *Indian J Med Sci.* 2008;62pp: 259-66.
21. Jahromi M, Millward A, Demaine A. A CA repeat polymorphism of the IFN-gamma gene is associated with susceptibility to type 1 diabetes. *J Interferon Cytokine Res.* 2000;20pp:187-90.

Challenges of Continuous Nursing Education in Health Agencies

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Abstract

Background: Many factors effects on continuous nursing education, like environment of the study or teaching method, stimulation of employees to participate in the courses and participant's satisfaction or outcome, so evaluating such unit is so vital and can strengthen weak points and this leads to better patient outcome and high rates of nurses job satisfaction.

Aims: This study aims to evaluate continuous nursing education in three parts structure, process and outcome, and knowing factors affecting it.

Methodology: Descriptive study design, data collected from three educational hospitals and eight primary health care centers, the approval to conduct the study was obtained from Training and Development Centre in Babylon Health institution, Ethical committee in the nursing college of Babylon and official permissions from Al-Hilla Teaching Hospital, Babylon Maternity and Children Teaching Hospital, Murjan Medical City and Al-Hilla health sectors 1 & 2.

Structure and process data gathered by researcher from continuous nursing education unit manager by answering questionnaire which reviewed by (20) nursing experts, the outcome assessed by nurses who participated in continuous nursing education courses by answering the questionnaire by (250) nurse, convenient sampling.

Results: The finding refers to several infrastructure weak points, low funds leads to decreased learning preparations like smart screens or advanced laboratories and medical equipment for training. The courses scheduling which set by health ministry are less than applied actually, and low focusing about nursing competencies in these courses, there wasn't any coordination between health institutions and higher education to fill knowledge gaps or decrease subjects repetition for nurses, and few nurses takes courses out of their hospitals (abroad).

High rates of participant nurses didn't get money reward and most of them used participation certificate for promotion purposes, though, high rates of nurse's satisfaction about continuous nursing education role, timing commitment, gaining knowledge and scientific materials provided.

Conclusion: The purpose of this article was to describe our evaluation process. Continuous nursing education evaluation is central to the mission and integrity of nursing programs in preparing successful nurses, advanced practice nurses, leaders, and scholars. At a more immediate level, continuous nursing education evaluation is an integral component of continuous quality improvement and of significant benefit in planning and implementing intentional, data-driven, program changes.

Putting continuous nursing education units in high priority in hospitals policies or primary health care centers in financial support will improve its performance and provide an appropriate environment, tools, hiring highly educated lecturers or participating in abroad of their governances or even country, for studying and learning new skills.

Coordination with educational institutions will provide variety in teaching method and filling gaps in the learner knowledge chain, further studies in this field is required that focuses in Health ministry curriculum, separation of hospitals and primary health care centers, and about nurses that didn't engaged in continuous nursing education courses.

Keywords: CNE, continuous nursing education.

Introduction

At all times, human beings have created their lives and started in the world through work. In recent decades work has undergone big transformations, administrative perspective in organizations in general have diminished due to the influence of knowledge of technology, theories, economics business, and technical, social, political, and cultural changes of community. Health care organizations was part of this process.¹

The originator and founder of modern nursing Florence Nightingale. Her notes, "Notes on Nursing," she mentioned the nurses should always learn, by seeking new knowledge and new evidences not only through experience and observation. Florence identified that caring "the same technique we usually perform it" didn't certainly recover clients' health or maintain the best likely setting to support healing and rescue.⁵

The significance of transporting skills and knowledge from theories to clinical practice is vital in establishing credibility in clinical. Achieving it must integrate simulation, practice and theory. The Simulation considered as method to develop deeper education and a dynamic curricular improvement. Mixing of nursing knowledge and skills is improved by simulation use, which result in theoretical conceptions that readily applied more to the patients and their disorders suffering²

According to the World Health Organization (WHO), the global standards for nursing education include activities such as:

1. Establishing a global approach to the provision of evidence-based educational programs
2. Applying established competencies to provide a guide for curriculum development
3. Stimulating the creation of nursing (or midwifery) schools and programs to meet national, regional and societal needs and expectations
4. Establishing benchmarks for continuous quality

improvement and the progression of education in nursing and midwifery⁹.

Nurses Learning: Active learning increases learners' retention of information, improves performance on course assessments, and increases standardized test scores. Results from this study support the concept that when learner nurses are connected with course content, learning outcomes improve over-all. Active learning also improves nurses' perceptions of inclusiveness in the classroom and their self-efficacy. A meta-analysis of science, technology, engineering, and mathematics courses demonstrated that learners in lecture courses were 1.5 times more likely to fail when compared with those in active learning courses. In addition, average examination scores of the active learning course participants were 6% higher than lecture course participants³.

Within nursing, there is a paradigm shift away from a passive to a more active learner approach. Team based learning uses concept analysis, critical thinking, and problem solving to actively engage the learner, which is especially important in ethics education. In addition, the use of teams may translate well into the use of team based learning for inter-professional ethics education.

The application of learning concepts built into team based learning method reinforces the three components of moral competence-moral perception, moral judgment, and moral behavior. Ultimately, this approach helps to prepare new nurses who are able to embody everyday ethical comportment⁶

⁴demonstrates that without explicit guidance from regulatory nursing colleges, self-care competencies that are important to nursing practice and job sustainability (i.e., relationship, emotional, and spiritual self-care) are not necessarily taught in nursing education programs. The relative lack of attention to self-care competencies in nursing professional practice standards and entry-to-practice competency guidelines may indeed be reflected in a gap between the perceived importance and teaching

of self-care competencies within current nursing education programs.

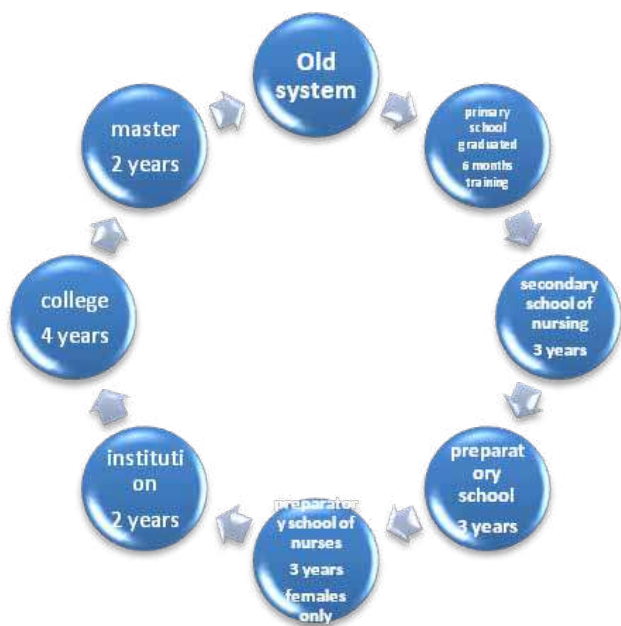


Figure 2.1 Nursing education in past few decades

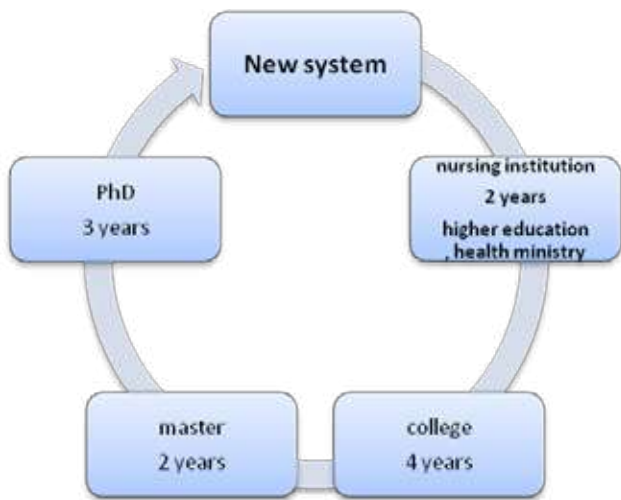


Figure 2.2 nursing education nowadays

Methodology

Study Design: Quantitative research, descriptive study design was used to evaluate continuous nursing education by dividing it into three parts (structure, process, and outcome)

Administrative Arrangements: To conduct this study, approved formal administrative permissions has been gathered before data collection as shown in appendix (B) as follow:

1. Ethical committee in the nursing college of Babylon accepted the instrument to use in the study.

2. Training and Development Centre in Babylon Health institution approved hospitals access consent form

3. An official permissions were received from Al-Hilla Teaching Hospital, Babylon Maternity and Children Teaching Hospital, Murjan Medical City and Al-Hilla health sectors 1 & 2.

Setting of the Study: The study has been conducted at the continuous nursing education unit of Babylon Maternity and Children Teaching Hospital, Al-Hilla Teaching Hospital, Murjan Medical City and Al-Hilla health sector 1 & 2.

Population and Sampling Plan: The target population (250) nurse which was included in this study, who works in the main teaching hospitals and primary health care centers in Al-Hilla city.

Any nurse who met the research criteria was included in this study regardless of their gender, specialties, or unit. This strategy was used to reflect the general characteristics of continuous nursing education, reduce sampling error, and enhance the representation of the study sample.

Ethical Considerations: Nurses were asked for voluntary participation. Research aims and benefits were explained to participants to help them determine whether to take part or not. Later on they agreed to be a component of the survey, participants were paid an anonymous questionnaire to maintain participants' confidentiality.

Survey Instrument: A great body of relevant literature was extensively reviewed to ascertain the appropriate tool for the recent field. A three part questionnaire was used to evaluate structure, process and outcomes of the continuous nursing education unit, the questionnaire reviewed by (20) expert in nursing profession for validation.

Instrument Description: This scale is an instrument composed of three parts (structure 8 items, process 13 items and outcome 14 items)

Part one (structure) include infrastructure and the media of the CNE units, its items filled by researcher by asking the CNE unit manager.

Part two (process) includes mechanisms, rules, subjects types and resources and competencies, filled by researcher by asking the CNE unit manager.

Part three (outcome) estimates the satisfaction of nurses about CNE, filled by nurses.

Validity of the Questionnaire: The questionnaire was translated (forward and back) by two independent bilingual content expert. The Arabic version that is closest to the original one after it was translated back to English was used in this study. The instrument was presented to (20) panel of content experts.

Reliability of the Questionnaire: Reliability is an instrument ability to measure the attributes of internal consistency of the questionnaire (Wood and Haber, 2014). Data were gathered out of (30) nurse, (10) from Marjan Medical City, (10) from Al-Hilla Teaching Hospital, (10) from Babylon maternity and children teaching hospital. Reliability-testing was used as a statistical analysis method to measure the internal consistency and find out the concordance among the items of the outcomes of CNE unit, which it is the third part in the questionnaire, the satisfaction of the nurses in CNE unit, using the reliability coefficient. The scale had an acceptable level of internal consistency, as determined by a Cronbach’s alpha of 0.76.

Data Collection: After the researcher obtained all the required approvals, the process of data collection began in 31th March 2019 to 29th of April 2019..

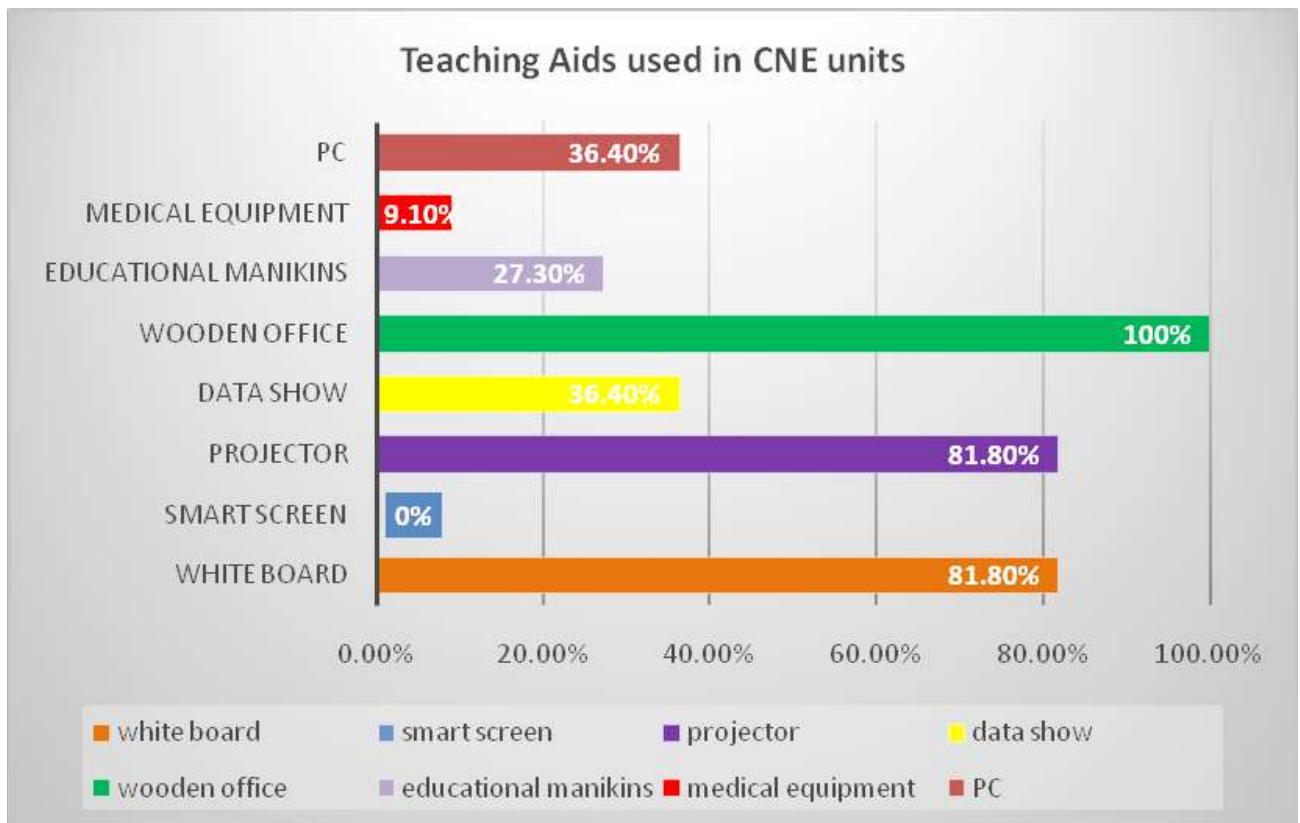
Statistical Data Analysis: Several statistical measures were used by using Statistical Package of Social Sciences (SPSS) version 24, and Microsoft excel (2016).

Results of the Study

Structure:

Lecturers’ Certificate	Freq.	Perc.
Diploma degree	9	81.8
Bachelor degree	2	18.2
Number of halls dedicated to formal nursing education	Freq.	Perc.
No Hall	2	18.2
One Hall	8	72.7
Two Halls	1	9.1
Total	11	100.0

The lecturers graduation certificate who controls the CNE unit have diploma (81.8%) which was the dominate Percentage, and the highest Percentage of formal hall is one dedicated to CNE is (72.7%).



(9.1%) of CNE units who own medical equipment like stethoscope, sphygmomanometer and measurement tapes etc. While only (36.4%) of CNE units having (PC) personal computer. All of the studied CNE units don't have smart screen.

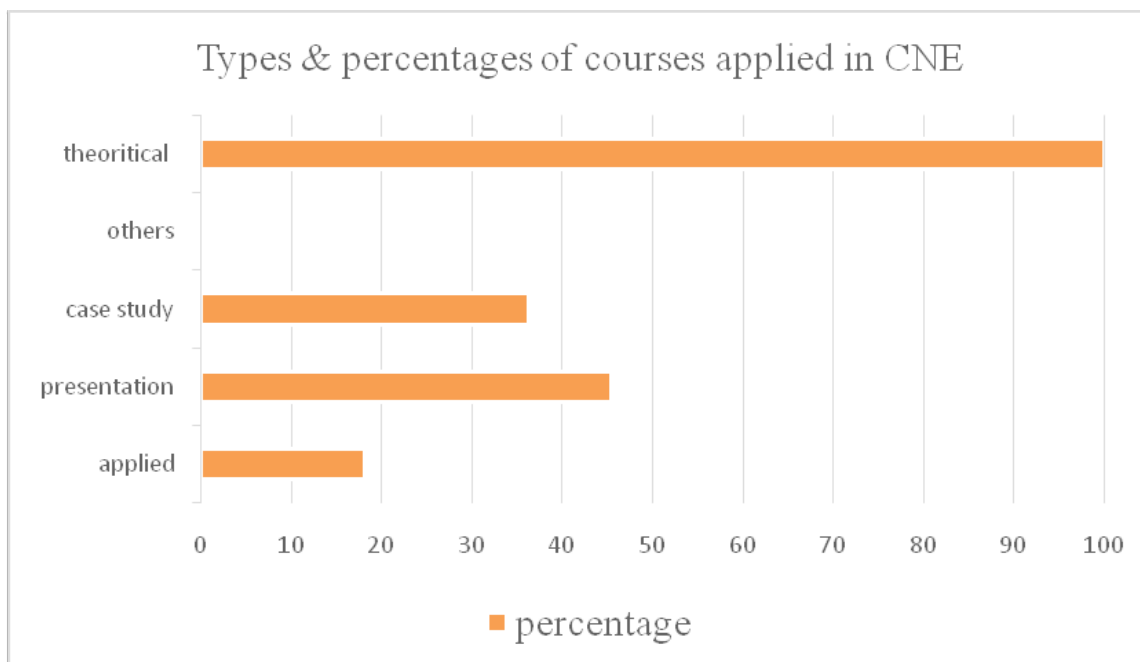
The highest percentage (81.8%) having at least one whiteboard as a teaching aids, (81.8%) have one projector at least used to CNE units. (36.4%) of CNE units own Data show. All of the studied CNE units have a wooden office.

Process:

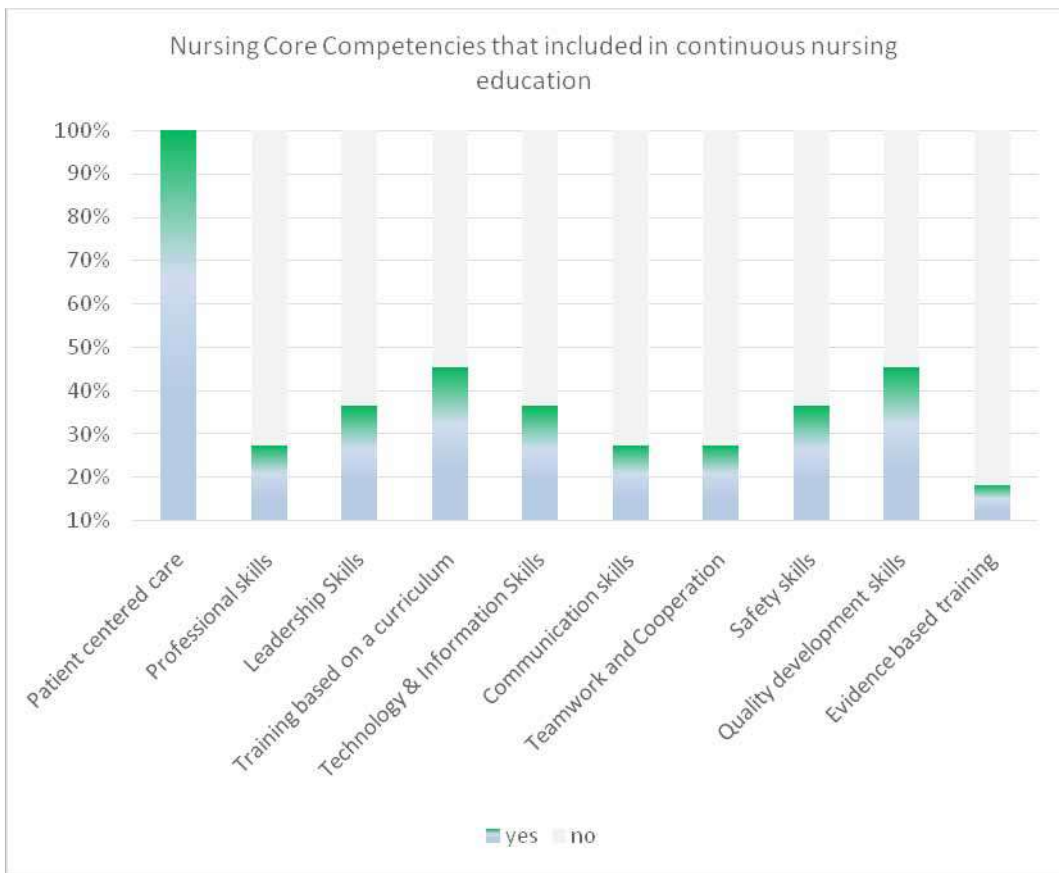
Number of courses scheduled within a month			
		Freq.	Perc.
Valid	1-3 Courses	2	18.2
	4-6 Courses	1	9.1
	More than 7 Courses	8	72.7
	Total	11	100.0
Number of courses completed within one month			
		Freq.	Perc.
Valid	1-3 courses	3	27.3
	4-6 courses	3	27.3
	More than 7 courses	5	45.5
	Total	11	100.0

Number of courses delivered outside the governorate/ outside the country/year			
		Freq.	Perc.
Valid	None	8	72.7
	Twice	3	27.3
	Total	11	100.0
Is there any instructions that coordinate courses with educational institutions to fill knowledge gaps or non-repetitions in scientific topics?			
		Freq.	Perc.
Valid	No	11	100.0

Number of courses scheduled in the curriculum within a month was (7) courses and more, with percentage (72.7%) while the actual applied courses was 5 courses per month with (45.5%), The number of courses delivered outside the governorate/outside the country was (2) in year with percentage (27.3%) while (72.7%) didn't receive any abroad courses. There wasn't any instructions that coordinate curriculum with educational institutions to fill knowledge gaps or non-repetitions in scientific topics.



This chart (4.4) shows percentages of courses types that applied in CNE, (100%) uses theoretical technique while case study technique (36.4), while (45.5%) using seminar presentation technique, the applied (clinical dependent) technique was (18.2%) and no any other type more than that.



This chart (4.6) shows percentages of Nurses core competencies that included in continuing nursing education, (100%) CNE units included patient centered care in their courses, (27.3%)Professional skills, (36.4%)Leadership Skills, (45.5%)Training based on a curriculum, (36.4%) Technology and Information Skills, (27.3%) Communication skills, (27.3%) Teamwork and Cooperation, (36.4%) Safety skills, (45.5%) Quality development skills and (18.2%) Evidence based training.

Third part/outcome:

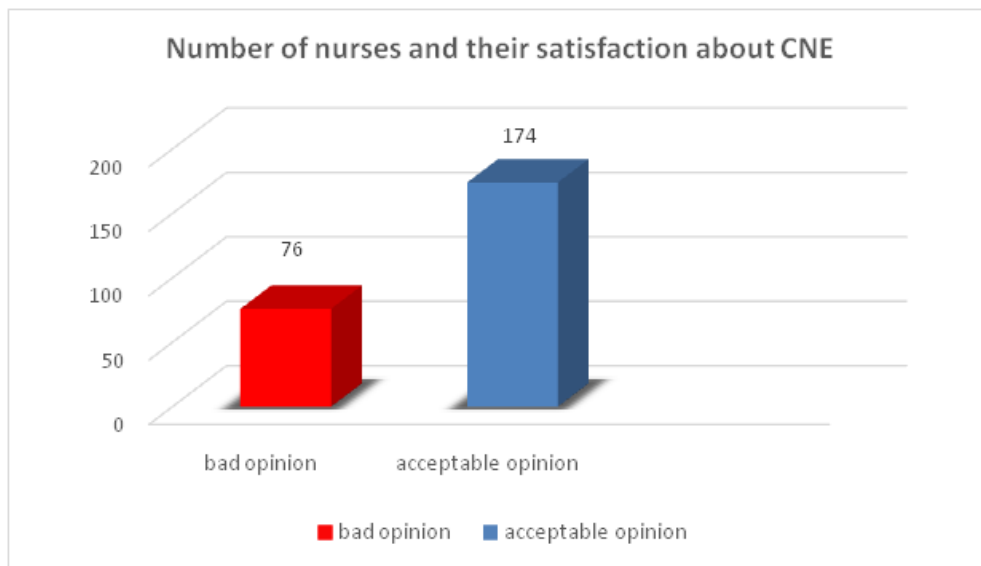


Chart (4.8) shows the total scores of nurse’s satisfaction toward CNE activities (76) Nurse expressed their bad opinions or dissatisfied of their CNE units, (174) nurse showed acceptable opinions of CNE units.

Discussion of the Study Results

Part One/Structure: The most remarkable result to emerge from the data is that most of CNE units are managed by one person who controls courses scheduling, teaching, assessing and evaluating weak points in the institution and this is manifested by nurse's shortage in health institutions.

Most of CNE unit managers have diploma certificate and teach higher than his academic level which is related to the health ministry policies which prevents nurses with bachelor degree to work in PHC centers. Some of the halls which dedicated to CNE have less chairs than participants and more than half of them do not have supporting halls which is due to weak infrastructure of these institutions, lack or decreased financial support leads to few of these halls have computer, medical equipment, data show and smart screen, so variation in teaching method or simulation labs is not available.

Part two/process: The most surprising aspect of the data in this part is the lack of commitment of the CNE manager to the curriculum timing because the course scheduling didn't met with actual application and this due to nurse's shortage and/or absence of CNE evaluation. More than two thirds of nurses didn't get any abroad course or at least out of their governance, so getting big image of community problems, taking preventive measures and varying in teachers or method of teaching is difficult to afford.

The finding shows complete absence of coordination between educational and health institutions, filling knowledge gaps to nurses, the reasons for this result are not yet entirely understood which will leads to decreased patients care quality⁸ reached that CNE decreases reality shock and fills theory-practice gap.

Part Three: (76) Nurse expressed their bad opinions or dissatisfied of their CNE units, (174) nurse showed acceptable opinions of CNE units.

The majority of nurses recognized that CE activities were effective in improving their knowledge, clinical practice, quality of patient care and motivation for learning.

This result supported by ⁷ Education and the acquisition of knowledge are likely to have an impact on nurses' job satisfaction and self-concept

Conclusion

This study showed that the present approach of nurses' continuing education needs modification so as to meet nurses' needs and leads to better patient outcome.

Although high percentage of nurse's acceptancy and satisfaction about CNE unit but still the other parts of this study shows weakness of infrastructure and in the mechanism of choosing and applying the curriculum specially in competencies application

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the College of Nursing and all experiments were carried out in accordance with approved guidelines.

References

1. BackesV, PradoM, Erdmann A, FerrazF. Continued nursing education in university hospitals in southern Brazil. *Journal of Continuing Education in Nursing*, 2008;39(8): 368–374.
2. Bevan Ann L, Joy Rosalyn, Keeley Sarah BP. *Learning to Nurse : Developing knowledge and skills for practice* Authors, 2015;(0).
3. Bristol T, HaglerD, Mcmillian-bohler J, Wermers R, Hatch D, Oermann MH. Nurse educators ' use of lecture and active learning. *Teaching and Learning in Nursing*, 2019;14(2):94–96.
4. Docherty-skippen SM, HansenA, Engel J. Nurse Education in Practice Teaching and assessment strategies for nursing self-care competencies in Ontario ' s nursing education programs. *Nurse Education in Practice*, 2019;36:108–113.
5. Gonda S. *Continuing Nursing Education Listings*. *New Mexico Nurse*, (October), 2017;10. <https://doi.org/10.1177/0898010108328313>
6. HickmanSE, Wocial LD. Team-Based Learning and Ethics Education in Nursing. *Journal of Nursing Education*, 2014;52(12):696–700. <https://doi.org/10.3928/01484834-20131121-01>
7. HoeveY, JansenG, RoodbolP. The nursing profession : public image, self-concept and professional identity . A discussion paper, (April), 2013;295–309. <https://doi.org/10.1111/jan.12177>

8. HuybrechtS, Loeckx W, Quaeyhaegens Y, Tobel DDe, Mistiaen W. Nurse Education Today Mentoring in nursing education : Perceived characteristics of mentors and the consequences of mentorship. YNEDT, 2011;31(3):274–278.
9. World Health Organization. Global standards for the initial education of professional nurses and midwives. Nursing & Midwifery Human Resources for Health. World Health Organization, Nursing & Midwifery Human Resources for Health Global. 2009.

Role of 14-3-3 η (Eta) Protein as Immunological Marker for Disease Activity in Patients with Rheumatoid Arthritis

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Abstract

Background: There are few studies had addressed the effect of 14-3-3 η (Eta) protein in the activity of rheumatoid arthritis. Therefore, this study mainly aims to evaluate whether 14-3-3 η (Eta) protein is related to disease activity in a sample of Iraqi patients with rheumatoid arthritis.

Method: The case- control study included 50 patients with the rheumatoid arthritis, 3 males and 47 females as group I, 34 non rheumatoid arthritis (apparently healthy) control as group II. Serum levels of 14-3-3 η (Eta) protein was measured by sandwich ELISA using ELISA minikits (MyBioSource-USA).

Results: Rheumatoid arthritis found high in individuals of age group (45-54). There is a significant ($P=0.02$) association between this age of patients and the susceptibility to rheumatoid arthritis. There was a high significant ($P=0.0001$) difference between males and females among patients with rheumatoid arthritis, the association was non-significant ($P=0.27$) between family history and rheumatoid arthritis patients. According to patient's history of smoking, there was a high significant ($P=0.002$) relationship between rheumatoid arthritis patients and smoking history compared with control. The serum level of 14-3-3 eta protein have a significant ($p=0.025$) association with susceptibility to rheumatoid arthritis while Anti CCP showing a high significant $P<0.001$ association with the disease. Also there was a non- significant association between Anti CCP, 14-3-3 eta protein with disease activity score-28. Regarding disease duration, 14-3-3 eta protein showing a significant ($P=0.01$) association with early rheumatoid arthritis.

Conclusion: There was a significant association between the 14-3-3 eta protein serum level and susceptibility to rheumatoid arthritis. Also, this study was reported a non-significant association between 14-3-3 eta protein and disease activity score -28.

Keywords: Rheumatoid arthritis, Disease activity score-28, 14-3-3 η (Eta) protein.

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease resulting from both genetic and ecological factors. It has been hypothesized that genetic predilection, in combination with environmental factors, leads to a cascade of events causing synovitis and eventually destructive arthritis¹, affecting nearly 1% of the world population². The clinical manifestation of symmetrical joint involvement include arthralgia, swelling, redness and limiting the range of motion³.

Chronic inflammation of the synovium in RA is the cause of the clinical manifestations of joint involvement characterized by interactions of resident cells such as fibroblast-like synoviocytes (FLS) with cells of the adaptive (T, B lymphocytes) and innate (macrophages, dendritic cells, mast cells, NK cells and neutrophils) immune system¹. Several research on probable risk factors has focused on triggers setting off disease, such as microbial/viral agents, cigarette smoking and environmental pollution⁵.

Patients with RA live three to 12 years less than the healthy individuals, particularly due to cardiovascular disease, especially in those with high disease activity. The biologic therapies may extend life in those with RA by reversing progression of atherosclerosis⁶. The 14-3-3 preserved regulatory proteins family includes seven isoforms: α/β , γ , δ/ζ , ϵ , η , θ/τ and σ . These proteins normally exist as ubiquitous intracellular chaperones that interact with over 200 intracellular proteins and contribute to the modulation of their activities. 14-3-3 eta protein was detectable at significantly higher levels in the synovial fluid and/or serum from patients with RA when compared with healthy or subjects with other autoimmune condition and bacterial/viral infections. Extracellular 14-3-3 eta protein at detectable concentrations in RA patient serum acts as a signal of cell damage that effectively induces bone-degrading enzymes and pro-inflammatory cytokines⁷.

Materials and Method

Fifty RA patients were clinically-diagnosed, 3 males and 47 females, at age ranged between (25- 64) years old, attending to the Rheumatology clinic in AL-Sader Medical City in Najaf Province during the period from October 2018 to February 2019 were included as the test group. In addition, 34 non-RA (apparently healthy) age matched patients attending the outpatient clinic were recruited as control subjects. All participants underwent a complete screening panel, including medical history, clinical examination, and assessment of BMI. Five ml of venous blood were collected from each patients and control groups, collected in gel tubes, slow withdrawal of the blood sample via the needle of syringe to prevent hemolysis. The sample dropped into clean disposable gel tube, serum was separated after 20 minutes at room temperature. The samples were then centrifuged at 3500 rpm for 5 minute and then stored at freeze condition(-20C) until analyzed.

Human 14 -3- 3 (eta) protein ELISA test: Serum levels of 14-3-3 η protein were determined by classic sandwich-ELISA using ELISA minikits (MyBioSource-USA).

Statistical Analysis: All statistical analyses were performed by using Statistical Package of Social Science software (SPSS) computer program (Version 22, SPSS Inc., Chicago, IL, USA).

Result

There is a significant association between the age of patients (45-54) and the susceptibility to rheumatoid arthritis ($P= 0.02$), as shown in table-1. The patients comprised 46 (92%) about females and 4(8%) about males while in control 16 (47%) as female and 18 (53%) as male. There was a high significant ($P= 0.0001$) difference between females and males among patients with RA and compared with control. However, the association was non-significant ($P=0.27$) between family history and RA patients. There was a high significant association ($P=0.002$) between RA patients and smoking history compared with control, as shown in table-2.

Mean BMI among patients was (19.30) compared to (24.47) for control, there is a highly significant difference in the distribution of patients and control subjects ($P< 0.001$), 48 patients (96%) were rheumatoid factor positive, whereas 2(4%) patients were RF negative, giving a mean of 1.04 ± 0.03 , Erythrocyte sedimentation rate (ESR) ranged between (20.0-110.0) among patient group, giving a mean of 50.98 ± 2.69 , The mean of Anti CCP antibodies in RA patients was significantly higher ($P<0.001$) than in controls, (3.56 ± 0.24) and (1.52 ± 0.07), respectively. 14-3-3 eta protein showing a significant ($P =0.025$) association with patients group, giving a mean of 5.13 ± 0.25 and a mean of 4.38 ± 0.17 among control group, as in table-3.

The mean of Anti CCP antibodies level in RA patients was (3.82 ± 0.30) in high grade of disease activity score-28 (DAS28) and (2.82 ± 0.31) in moderate grade. There was a non-significant association ($P=0.07$) between Anti CCP antibodies and DAS-28. Also, 14-3-3 eta protein giving a mean of (5.21 ± 0.28) and (4.90 ± 0.55) among high and moderate grade of DAS-28 respectively. There is a non-significant association ($P=0.58$) with DAS-28 of RA patients, as in table-4. Regarding disease duration, early rheumatoid arthritis (less than one year) and established (more than 3 years), rheumatoid factor and 14-3-3 eta protein showing a significant association with early RA, giving a mean of 1.14 ± 0.10 and 6.11 ± 0.62 respectively in early RA and a mean of 1.00 ± 0.00 and 4.75 ± 0.22 respectively in established RA, whereas Anti-CCP showing a non- significant association giving a mean of 3.91 ± 0.55 in early RA and a mean of 3.43 ± 0.27 in established RA, as in table -5.

Table 1: Age distribution among rheumatoid arthritis patients

Age/Years	R.A Patients No. (%)
25-34	5(10%)
35-44	10(20%)
45-54	21(42%)
55-64	14(28%)
Total	50(100%)

Table 2: Distribution of the studied groups according to gender, family history, and smoking habit.

Variable	Cases N(%)	Controls N(%)	P	OR	95% C.I.
Gender					
Female	46(92%)	16(47%)	0.000**	12.9	3.8-44
Male	4(8%)	18(53%)			
Family History					
Positive	3(6%)	0(0%)	0.27	1.7	1.4-2.1
Negative	47(94%)	34(100%)			
Smoking					
Yes	11(22%)	0(0%)	0.002**	1.9	1.5-2.3
No	39(78%)	34(100%)			
Total	50(100%)	34(100%)			

**Highly significant p value, RA = rheumatoid arthritis, OR = odds ratio, C.I. = confidence intervals

Table 3: Serum level of rheumatoid arthritis patients and controls

Parameters	RA Patients N=50 Mean±SE (Range)	Controls N=34 Mean±SE (Range)	P
Body mass index	19.30±0.21(17.51-23.46)	24.47±0.33(20.76-29.48)	P<0.001**
RF (IU/ml)	1.04±0.03(1.00-2.00)	-----	-
ESR (mm/hour)	50.98±2.69(20.0-110.0)	-----	-
Anti-CCP (IU/ml)	3.56±0.24(8.07-1.87)	1.52±0.07(0.75-2.40)	P<0.001**
14-3-3 eta protein (ng/ml)	5.13±0.25(2.38-10.84)	4.38±0.17(1.71-6.59)	0.025*

*significant p value **highly significant p value, RA = rheumatoid arthritis, SE = standard error of mean, RF = rheumatoid factor, ACCP = Anti-cyclic citrullinated peptide, ESR = erythrocyte sedimentation rate

Table 4: Comparison between the 14-3-3 eta protein and Anti-CCP in rheumatoid arthritis patients according to grade of disease activity score 28.

Parameters	High Grade N=37 Mean±SE	Moderate Grade N=13 Mean±SE	P-value
Anti-CCP (IU/ml)	3.82±0.30	2.82±0.31	0.07
14-3-3 eta protein (ng/ml)	5.21±0.28	4.90±0.55	0.58

ACCP = Anti-cyclic citrullinated peptide

Table 5: Comparison between early and established rheumatoid arthritis cases according to different Parameters

Parameters	Early RA N=14 Mean±SE	Established RA N=36 Mean±SE	P value
RF(IU/ml)	1.14±0.10	1.00±0.00	0.02*
Anti-CCP(IU/ml)	3.91±0.55	3.43±0.27	0.38
14-3-3 eta protein(ng/ml)	6.11±0.62	4.75±0.22	0.01*

*significant p value, RA = rheumatoid arthritis, RF = rheumatoid factor, ACCP = Anti-cyclic citrullinated peptide

Discussion

Rheumatoid arthritis was found high in individuals of age group (45-54) years old, at a percentage (42%). There is a significant association ($P= 0.02$) between the age group (45-54) of patients and the susceptibility to rheumatoid arthritis. This result was associated with a study conducted by⁸ who revealed that the majority of RA patients are (40-50) years old. Another study by⁹ showed that a peak age of onset is Forties. In the current study, there was a highly significant ($P=0.000$) difference between study groups in the gender. The scattering of RA is higher among females than males. This finding similar to the study by¹⁰ who revealed the sex ratio is typically around 3:1 about females compared with males.

Also, The association was non-significant ($P=0.27$) between family history and RA. A study conducted by¹¹, exhibited that RA family history do not related with RA and this result was in the same line with the present study. in contrary,¹² demonstrate that family history is still a significant risk factor for RA.

In addition, there was statistically significant association ($P=0.002$) between smoking and RA in present study and this result was in the same line with a study conducted by¹³ and¹⁴, whose found a significant relationships between cigarette smoking and development of rheumatoid arthritis. In contrary with¹⁵ who revealed that smoking is independent risk factor for progression in RA . In the current study there was a significant ($p= 0.025$) association between the level of 14-3-3 eta protein and rheumatoid arthritis. The present study in the same line with a study conducted by¹⁶ who showed that measurement of 14-3-3 η complements RF and anti-CCP antibody tests in RA and may improve diagnostic sensitivity. In contrary¹⁷ who demonstrated that measurement of 14-3-3 η ETA offered limited additional diagnostic value when compared to RF and ACPA. Furthermore, This study was reported a non-significant ($p= 0.58$) association between 14-3-3 eta protein and disease activity score -28 in contrary with¹⁸ whose reported that 14-3-3 η positive RA patients have higher disease activity score. Otherwise, The current study also revealed a non- significant ($P=0.07$) association between Anti CCP antibodies and DAS-28. This result was in contrast¹⁹ whose demonstrate that ACCP positive patients exhibited more active disease, expressed by higher disease activity scores -28 ($p<0.001$).

Moreover, in the current study there was a significant ($p =0.02$) association between rheumatoid factor and early RA and this result was associated with²⁰ who revealed that RF seropositivity was found to be more common in much early RA patients while present study reported a non-significant ($p =0.38$) association of ACCP with the early and established RA. In contrast²¹ revealed that ACCP in early RA diagnosis is more than 80%. This study also showed that 14-3-3 eta protein was significantly ($p= 0.01$) high in patients with early RA and this result agreed with²² who reported that 14-3-3 η protein were detectable at significantly higher levels in patients with early RA than in healthy subjects and patients with various autoimmune disorders and other arthritides. The differences of these results may be due to the ethnicity in different populations and may be due to the small volume of samples in this study.

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the University of Karbala and all experiments were carried out in accordance with approved guidelines.

References

1. Angelotti F, Parma A, Cafaro G, Capecci R, Alunno A, Puxeddu I. pathogenesis of rheumatoid arthritis. Clin Exp Rheumatol. 2017;35(3):368-378.
2. Gibofsky A. Overview of epidemiology, pathophysiology, and diagnosis of rheumatoid arthritis. 2012;S295-302.
3. Qiang Guo, Yuxiang Wang, Dan Xu, Johannes Nossent, Nathan J, et al., pathological mechanisms and modern pharmacologic therapies 2018. doi: [10.1038/s41413-018-0016-9].
4. Carbone F, Bonaventura A, Liberale L, Paolino S, Torre F, Dallegri F, et al., Atherosclerosis in Rheumatoid Arthritis: Promoters and Opponents. Clin Rev Allergy Immunol. [PubMed] 2018.
5. Cutolo M, Nikiphorou E, Don't neglect nutrition in rheumatoid arthritis! 2018.. doi:10.1136/rmdopen-2017-000591.
6. Friedewald VE, Ganz P, Kremer JM, Mease Pj, O'Dell JR, Pearson TA, et al. rheumatoid arthritis and atherosclerotic cardiovascular disease. Am

- J Cardiol 2010. DOI: <https://doi.org/10.1016/j.amjcard.2010.04.005>.
7. Carrier N, Marotta A, de Brum-Fernandes AJ, Liang P, Masetto A, Ménard HA, Maksymowych WP, et al. Serum levels of 14-3-3 η protein supplement C-reactive protein and rheumatoid arthritis-associated antibodies to predict clinical and radiographic outcomes in a prospective cohort of patients with recent-onset inflammatory polyarthritis. 2016. doi: 10.1186/s13075-016-0935-z.
 8. Bryl E, Witkowski JM. Autoimmunity and autoimmune diseases in the elderly. 2009.
 9. Oliver JE, Silman AJ. Why are women predisposed to autoimmune rheumatic diseases? 2009, doi: 10.1186/ar2825.
 10. Miriovsky BJ, Michaud K, Thiele GM, O'Dell JR, Cannon GW, Kerr G, Richards JS, Johnson D, Caplan L, Reimold A, Hooker R, Mikuls TR. Anti-CCP antibody and rheumatoid factor concentrations predict greater disease activity in men with rheumatoid arthritis. 2010. doi: 10.1136/ard.2009.122739.
 11. Frisell T, Saevarsdottir S, Askling J. Does a family history of RA influence the clinical presentation and treatment response in RA? 2016. doi: 10.1136/annrheumdis-2015-207670.
 12. Jiang X, Frisell T, Askling J, Karlson EW, Klareskog L, Alfredsson L, Källberg H. To what extent is the familial risk of rheumatoid arthritis explained by established rheumatoid arthritis risk factors? 2015. doi: 10.1002/art.38927.
 13. Sugiyama D, Nishimura K, Tamaki K, Tsuji G, Nakazawa T, and Morinobu A, et al. Impact of smoking as a risk factor for developing rheumatoid arthritis: A meta-analysis of observational studies. 2010. doi: 10.1136/ard.2008.096487.
 14. Di Giuseppe D, Discacciati A, Orsini N, Wolk A. Cigarette smoking and risk of rheumatoid arthritis: A dose-response meta-analysis. 2014. doi: 10.1186/ar4498.
 15. de Rooy DP, van Nies JA, Kapetanovic MC, Kristjansdottir H, Andersson ML, Forslind K, van der Heijde DM, Gregersen PK, Lindqvist E, Huizinga TW, Gröndal G, Svensson B, van der Helm-van Mil AH. Smoking as a risk factor for the radiological severity of rheumatoid arthritis: a study on six cohorts. 2014. doi: 10.1136/annrheumdis-2013-203940.
 16. Kadavath S, Chittalae S, Nidal Shuaib O, Soon Goh K, Tosic M, Giles J, et al. SAT0211 14-3-3 ETA Protein: A Novel Biomarker for the Diagnosis of Rheumatoid Arthritis. 2014.
 17. Vasconcellos A, Chittalae s, Efthimiou p. Does 14-3-3 ETA Protein Offer Any Additional Diagnostic Value in Rheumatoid Arthritis? 2015.
 18. Chao R, Das M, Purat N, Efthimiou P . AB0296 14-3-3eta positivity is associated with higher rheumatoid arthritis disease activity measured by multi-biomarker disease activity assay. 2018.
 19. Papadopoulos NG, Tsiaousis GZ, Pavlitou-Tsiontsi A, Giannakou A, Galanopoulou VK .Does the presence of anti-CCP autoantibodies and their serum levels influence the severity and activity in rheumatoid arthritis patients? 2008.
 20. Othman MA, Ghazali WS, Yahya NK, Wong KK. Correlation of Demographic and Clinical Characteristics with Rheumatoid Factor Seropositivity in Rheumatoid Arthritis Patients. 2016. doi: 10.21315/mjms2016.23.6.6.
 21. Shilkina NP, Luzinova MS, Vinogradov AA., [Anticitrullin antibodies--modern markers of rheumatoid arthritis] 2011. PMID: 21446207
 22. Maksymowych WP, Naides SJ, Bykerk V, Siminovitch KA, van Schaardenburg D, Boers M, et al. Serum 14-3-3 η is a novel marker that complements current serological measurements to enhance detection of patients with rheumatoid arthritis. *J Rheumatol*. 2014. doi: 10.3899/jrheum.131446. [PubMed].

An Epidemiological Study of Scabies by Age Groups, Regions and Gender in Diwaniya Governorate

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Abstract

This study included the investigation of scabies parasites, which is one of the external parasitic. It is becoming more polluted and less clean. The diagnosis from the cases reviewed to the dermatologist at Diwaniyah Teaching Hospital showed that there were many cases of skin infections with fungi and bacteria. However, the study was about scabies. The number of cases during 90 days was 120 cases after examination and diagnosis. The study showed the increase in pollution of the city center as well as the lack of ventilation, and the number of injury 29 and by 24 percent, while the lowest number was in two areas are AL- Shafaia and AL-Sudair 13 and the proportion of 10.8 percent. The number of males was 75 and 62.5%, while females were 45 and 37.5% .As for the age groups, the highest number was 41 cases in the ages of 10 years and less than 20 years and by 34% and in the age of less than 10 years were 28 and 23%. The lowest number of cases in 120 cases were 8 cases in children under 30 and over 20 years, and 6.6% .

Keywords: *Epidemiological, scabies, Diwaniya Governorate.*

Introduction

Scabies, also known as the seven-year itch, is a contagious skin infestation by the mite *Sarcoptes scabiei*.^[1] The most common symptoms are severe itchiness and a pimple-like rash.^[2] Occasionally, tiny burrows may be seen in the skin.^[2] In a first ever infection a person will usually develop symptoms in between two and six weeks.^[2] During (a second infection symptoms) may begin in as little as 24 hours.^[2] These symptoms can be present, across most of the body or just certain areas such as the wrists, between fingers, or along the waistline.^[2] The head may be affected, but this is typically only in young children.^[2] The itch is often worse at night.^[2] Scratching may cause skin breakdown and an additional bacterial infection of the skin.^[2] Scabies is caused by infection with the female mite *Sarcoptes scabiei* var. *hominis*.^[3] The mites burrow into the skin to live and deposit eggs.^[3] The symptoms of scabies are due to an allergic reaction to the mites.^[2] Often, only between 10 and 15 mites are involved in an infection.^[2] Scabies is most often spread during a relatively long period of

direct skin contact with an infected person (at least 10 minutes) such as that which may occur during sex or living together.^[3] Spread of disease may occur even if the person has not developed symptoms yet. Crowded living conditions, such as those found in child-care facilities, group homes, and prisons, increase the risk of spread.^[3] Areas with a lack of access to water also have higher rates of disease.^[4] Crusted scabies is a more severe form of the disease.^[3] It typically only occurs in those with a poor immune system and people may have millions of mites, making them much more contagious.^[3] In these cases, spread of infection may occur during brief contact or by contaminated objects.^[3] The mite is very small and usually not directly visible.^[5] Diagnosis is based on the signs and symptoms.^[6]

A number of medications are available to treat those infected, including permethrin, crotamiton, and lindane creams and ivermectin pills.^[7] Sexual contacts within the last month and people who live in the same house should also be treated at the same time.^[8] Bedding and clothing used in the last three days should be washed in

hot water, and dried in a hot dryer.^[9] As the mite does not live for more than three days away from human skin, more washing is not needed.^[10] Symptoms may continue for two to four weeks following treatment.^[1] If after this time symptoms continue, retreatment may be needed.^[10]

Scabies is one of the three most common skin disorders in children, along with ringworm and bacterial skin infections.^[11] As of 2015, it affects about 204 million people (2.8% of the world population).^[8] It is equally common in both sexes.^[12] The young, and the old are more commonly affected.^[1] It also occurs more commonly in the developing world and tropical climates.^[12] The word scabies is from Latin: scabere, “to scratch”.^[13] Other animals do not spread human scabies.^[3] Infection in other animals is typically caused by slightly different but related mites and is known as sarcoptic mange.

Scabies has been observed in humans since ancient times. Archeological evidence from Egypt and the Middle East suggests scabies was present as early as 494 BC.^[14] The first recorded reference to scabies is believed to be from the Bible – it may be a type of (leprosy) mentioned in Leviticus c. 1200 BC^[15] or be mentioned among the curses of Deuteronomy 28.^[16] In the fourth century BC, Aristotle reported on (lice) that “escape from little pimples if they are pricked) a description consistent with scabies.^[17]

The Roman encyclopedist and medical writer Aulus Cornelius Celsus (c. 25 BC – 50 AD) is credited with naming the disease (scabies) and describing its characteristic features.^[18] The parasitic etiology of scabies was documented by the Italian physician Giovanni Cosimo Bonomo (1663–1696) in his 1687 letter, (Observations concerning the fleshworms of the human body).^[50] Bonomo’s description established scabies as one of the first human diseases with a well-understood cause.^[19]

Pathophysiology: The symptoms are caused by, an allergic reaction of the “host’s body” to mite proteins, though exactly which proteins remains a topic of study. The mite proteins are also present, from the gut, in mite feces, which are deposited under the skin. The allergic reaction is both of; the delayed “cell-mediated” and immediate ((antibody-mediated)) type, and involves IgE antibodies, it is presumed, mediate the very rapid, symptoms on reinfection.^[30] The allergy-type symptoms (itching) continue for some days, and even several

weeks, after all mites are killed. New lesions may appear for a few days after mites are eradicated. Nodular lesions from scabies may continue to be symptomatic for weeks after the mites have been killed.^[31]

Rates of scabies were negatively related to temperature, and positively related to humidity.^[32]

Diagnosis: Scabies may be diagnosed clinically in geographical areas where it is common when diffuse itching presents along with either lesions in two typical spots or itchiness is present in, another household member.^[33] The classical sign of scabies is the burrow made by a mite within the skin.^[34] To detect the burrow, the suspected area is rubbed with ink from, a fountain pen or a topical tetracycline solution, which glows under a special light. The skin is then wiped, with an alcohol pad. If the person is infected with scabies, the characteristic, zigzag, or S pattern of the burrow will appear across the skin; however, interpreting this test may be difficult, as the burrows are scarce and may be obscured by scratch marks.^[11] A definitive diagnosis is made by finding either the scabies mites or their eggs and fecal pellets.^[35] Searches for these signs involve either scraping a suspected area, mounting the sample in potassium hydroxide and examining it under a microscope, or using dermoscopy to examine the skin directly.^[36]



Figure (3): Photomicrograph of an itch mite (S. scabies)

Differential Diagnosis: Symptoms of early scabies infestation mirror other skin diseases, including dermatitis, syphilis, erythematic multi form, various urticaria-related syndromes, allergic reactions, ringworm-related diseases, and other ectoparasites such as lice and fleas.^[30]

Prevention: Mass-treatment programs that use topical permethrin or oral ivermectin have been effective in reducing the prevalence of scabies in a number of populations.^[37] No vaccine is available for scabies. The simultaneous treatment, of all close contacts is recommended, even if they show no symptoms of infection “asymptomatic”, to reduce rates of recurrence.^[38] Since mites can survive for only two to three days without a host, other objects in the environment; pose little risk of transmission except in the case of crusted scabies, thus cleaning is of little importance.^[39] Rooms used by those with crusted scabies require thorough cleaning^[40].

Materials and Method

A. Material

1. Microscope .
2. Collect 120 samples .
3. Glass slides for dignosis .
4. Potassium hydroxide.

B. Method: The classic mark of scabies are burrows that are shaped by mites inside the skin. To detect burrows, ^[41] rub the ink-contaminated areas of an ink pen or topical tetracycline solution, which shines under a special light. The skin is then wiped with a cloth containing alcohol. If the person is infected with scabies, the S pattern or the scaly will appear across the skin from the hole area; However, the interpretation of this test may be difficult because burrows are rare and can mask scratch marks. Accurate diagnosis is performed by finding either moths, eggs, and fecal pellets. The search for these markers involves either scavenging the suspected area and collecting the sample in potassium hydroxide and examining it under a microscope, or using a microscope to examine the skin directly. ^[42]

Results and Discussion

The results shown in Table (1) indicate the percentage of people with scabies in Diwaniyah city center and its districts and areas with the highest incidence of scabies

in the city center, where the percentage of infection was 24.16%, while the lowest rate of infection in the district of Sudair and Shafei area 10.8%, while the percentage of infection in the rest of the districts and districts was different. The percentage of infection in the Sunni areas was 16.6%, Al-Daghara 12.5%, Afak and Al-Hamzah Al-Sharqi each 12.5%.

Table (1): Shows the comparison of numbers and percentage of scabies between thy city center and the district

Regions	Number of Infections	Percentage
1. City center	29	24.16%
2. The dagara	15	12.5%
3. Al-sudair	13	10.8%
4. The Sunni	20	16.6%
5. Afak	13	10.8%
6. The shafaia	15	12.5%
7. Eastern Hamza	15	12.5%

Table 2 shows the percentage of infection by sex. The results indicate that males have the highest incidence of infection, with a percentage of 62.5%. The percentage of infection among females is 37.5%. In the present study male patients represent (62.5%) compared with (37.5%) females which come on concordance with that reported by Mustafa et al (1997) reported that on turkey scabietic males represent (52.38%) compared with (47.62%) females. This may be attributed to the similarity on socioeconomic and demographical conditions between Iraq and turkey. This result disagree with that recorded by Lassa et al (2011)^[46], they recorded that there was a significantly greater infestation rate between females relative to males in UK which might be attributed to study design and the possibility of exposure to infestation as are results of the type of works that achieving by females beside hygiene measures .Walton et al (2004) ^[47], discordance with this study the reported that the prevalence of scabies isn't affected by sex.

Table (2): Shows the numbers of infections and percentage of scabies between the male and female.

Sex	Numbers of Infections	Percentage
Male	75	62.5%
Female	45	37.5%

Table (3) shows the percentage of cases of scabies by age group. The highest age group (10-20 years) was the most infected. The percentage of infection was 34.16%, while the age group (20 years) (30%) was the

lowest in the age group, with a percentage of 6.6%, while the percentage of the infection was different among the other age groups. The percentage of infection among the age group (10 years) was 23.3% Where the percentage of infection of the age group less than (10) years, 23.3%, while The percentage of infection among the age group (30-40) years was 11.6%. The percentage of infection among the age group (40-50) years was 7.5%. The percentage of infection among the age group (50-60) (10.8%), where the percentage of infection in the age group and those aged over(60) years 5.8%.

Scabies is most popular in children and young adults, but may happen at any age. These are possible related to customs, family size, and social agents rather than inherent susceptibility. Overcrowding, which is the popular in the underdeveloped countries and is linked with poorness and poor hygiene, help the spread of scabies, among between children and young adults. In such as disease whose transmission requires close personal contact, cultural agents are very important. Therefore transmission especially occurs within families, when one member (fathers and mothers in our study) of a family demand scabies entire family sometimes becomes infested as well as. In a study to identify the source of infestation prison, and military personal were the important agents in the spread of infestation. This may due to overcrowding, population movement. To an extent the wars are a composite of factors. It is probably that war may be translate minor increasing on the incidence of scabies, into a more substantial epidemical. Allergic sensitivity to the mite or it is products appears to play important role on determining the development of lesions other than burrows, and in producing itching . yet, the sequence of immunological events is not clear and demands in addition to elucidation. [45]

Table (3): Shows the numbers and percentages of infection by age groups.

Age Groups	Numbers of Infection	Percentages
Less than 10 years	28	23.3%
10-20	41	34.16%
20-30	8	6.6%
30-40	14	11.6%
40-50	9	7.5%
50-60	13	10.8%
Over 60 years	7	5.8%



Figure (1): Show child infected by scabies

Conclusions

The study showed that the highest infection of scabies was in the center of the city due to population congestion and low ventilation of houses for small area .The study showed clear and high rates of infection in rural areas and villages .Male infection rates were higher than that of females .Through the examination and distribution of infection by age groups, the study showed that the highest percentage of infection was in the young ages of males and females .There were a number of obvious injuries in large ages

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Al-Qadisiyah University, Iraq and all experiments were carried out in accordance with approved guidelines.

References

1. Gates H. Infectious disease secrets (2. ed.). Philadelphia: Elsevier, Hanley Belfus. 2003; 355.
2. “Parasites – Scabies Disease”. Center for Disease Control and Prevention. 2010.

3. "Epidemiology & Risk Factors". Centers for Disease Control and Prevention. 2015; 2.
4. "WHO -Water-related Disease". World Health Organization. Archived from the original on 2010: 10-22..
5. "Scabies". World Health Organization. 2015.
6. Ferri, Fred F. Chapter S". Ferri's differential diagnosis : a practical guide to the differential diagnosis of symptoms, signs, and clinical disorders (2nd ed.). Philadelphia, PA: Elsevier/Mosby.2010.
7. "Parasites – Scabies Medications". Center for Disease Control and Prevention, 2010.
8. GBD 2015 Disease and Injury Incidence and Prevalence, Collaborators. "Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study ". *Lancet*. 2015; 388 (10053): 1545–1602.
9. Dressler C, Rosumeck S, Sunderkötter C, Werner RN, Nast A. "The Treatment of Scabies". *DeutschesArzteblatt international*. 2016; 113 (45): 757–62.
10. "Parasites - Scabies Treatment". Center for Disease Control and Prevention. 2010.
11. Andrews RM, McCarthy J, Carapetis JR, Currie BJ. Skin disorders, including pyoderma, scabies, and tinea infections". *Pediatr. Clin. North Am*. 2009; 56 (6): 1421–40.
12. Vos T. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010". *Lancet*. 2012; 380 (9859): 2163–96
13. Mosby's Medical, Nursing & Allied Health Dictionary (4 ed.). Mosby-Year Book Inc. 1994; 1395.
14. Georgis' Parasitology for Veterinarians (10 ed.). Elsevier Health Sciences. 2014. p. 68.
15. CDC web site >DPDx – Laboratory Identification of Parasites of Public Health Concern > Scabies "Archived copy". 2009.
16. Hay RJ. "Scabies and pyodermas—diagnosis and treatment". *Dermatol Ther*. 2009; 22 (6): 466–74.
17. Markell E, David C, Petri W. Markell and Voge's medical parasitology (9th ed.). St. Louis, Mo: Elsevier Saunders. 2006.
18. "Scabies" (PDF). *Derm Net NZ*. New Zealand Dermatological Society Incorporated. Archived (PDF) from the original on 2009.
19. Bouvresse S, Chosidow O. Scabies in healthcare settings". *Curr Opin Infect Dis*.2010; 23 (2): 111–18.
20. Hicks MI, Elston DM. "Scabies". *Dermatol Ther*. 2009; 22 (4): 279–92.
21. "DPDx – Scabies". Laboratory Identification of Parasites of Public Health Concern. CDC. 2009.
22. Walton SF, Currie BJ. "Problems in Diagnosing Scabies, a Global Disease in Human and Animal Populations". *Clinical Microbiology Reviews*. 2007; 20 (2): 268–79
23. Walton SF, Currie BJ. "Problems in Diagnosing Scabies, a Global Disease in Human and Animal Populations". *Clinical Microbiology Reviews*. 2007; 20 (2): 268–79.
24. Carol T, Jeffrey S. *The Encyclopedia of Skin and Skin Disorders*. New York: Facts on File inc.2006.
25. Chosidow O. Clinical practices. Scabies". *N. Engl. J. Med*. 354 (16): 1718–27.
26. "Scabies – Fast Facts". American Social Health Association. 2006.
27. FitzGerald D, Grainger J, Reid A. Interventions for preventing the spread of infestation in close contacts of people with scabies". *The Cochrane Database of Systematic Reviews*. 2: CD009943.

Investigation of Escherichia Coli Fim H Gene Occurrence Isolated from Clinical and Environmental Samples

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Abstract

Background: *Escherichia coli* consider as commensal bacterium that can be inhabitant in the small intestinal micro-biota of warm-blooded animals, Urinary tract infections cause by Uropathogenic *Escherichia coli* (UPEC) Are among the most branded infectious diseases in humans. Due to their recurrently incidence in the community and nosocomial infection and evolution of resistance to ordinarily recommended antimicrobial agents.

Objective: The aim of current study was Investigation of *FimH* gene occurrence a virulence factor in *Escherichia coli*.

Materials and Method: Sixty urine samples of women with urinary tract infection symptoms. In addition, samples from different environmental places involving poultry, knacker shops, drainage water, fresh water and sewage water were collected during 22^{ed} November 2017 to 28^{ed} February 2018. Twenty one clinical and twenty three environmental isolates of *Escherichia coli*. The data were analyzed by using the statistical package social system (SPSS).

Results: The biofilm formation were 14(66.6%) strong, 7(33.30%) moderate and weak biofilm producers not exit in clinical isolates, while 13(41%) strong, 8(34.70%) moderate and 2(8.60%) for weak biofilm formation in environmental isolates. Moreover, PCR assay of *FimH* was applied. So, 20 isolates (95.23%) were positive results for clinical isolates and 17 isolates (73.9%) positive results for environmental

Conclusion: Uropathogenic *E. coli* had the higher occurrence rate for fimbriae gene (*Fim H*) compared with environmental isolates, Stronger biofilm formation by clinical *E. coli* isolates than by environmental isolates. There is a significant correlation between biofilm formation and probability of *Fim H* occurrence in both clinical and environmental isolates.

Keywords: *Escherichia coli*, *FimH* gene, Biofilm formation.

Introduction

E. coli consider as commensal bacterium that can be inhabitant in the small intestinal micro-biota

of warm-blooded animals, it's a member of the fecal coliform group adumbrated as "indicator organism" that occurrence in environment point to fecal contamination, accordingly, utmost strains are harmless but specific can be pathogenic thus represent important issues to human health¹.

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Biofilm defined as; a community of microorganisms encased within a secreted matrix of exo-polysaccharide or EPS, that attached to a surface this term modeled by Dr. Bill Costerton in 1974. Biofilm formation is

considered to be substitute idea to cells grow and lived only in planktonic or single cell state². Urinary tract infections cause by Uropathogenic *Escherichia coli* (UPEC) Are among the most branded infectious diseases in humans. Due to their recurrently incidence in the community and nosocomial infection and evolution of resistance to ordinarily recommended antimicrobial agents³. The critical stage in the infection procedure is the establishment to the urinary tract. Ordinarily, without join to epithelia cells bacteria can be wash away by urination route. Uropathogenic *Escherichia coli* or UPEC have many diverse tools for adherence to the uroepithelium, including : fimbriae, which defined as appendages with rod-like shape ascends from the surface of bacterial cell crowning in a top adhesion; fimbrillae, flexible, prolonged conformations with adhesions present throughout the structure for example not only at the top; and afimbrial adhesions such as autotransporters. Moreover, Extensive regulatory systems coordinate expression of these different adhesions⁴. Type 1 fimbriae coded by the genome of *E. coli* about 99% of their strains, Type 1 fimbriae compromise from FimA,

the main structural subunit, several minor subunits, and FimH, the adhesion which is found at the top of fimbriae⁵.

Subjects and Method:

Ethically, data collection and the design of the study groups were accomplished after the approval on the research proposal was done by Research Ethics Committee of Kerbala Health Directorate to work in its hospitals.

Sixty morning midstream urine were collected from women with urinary tract infection aged from 18 to 60 years. In addition, Samples were taken from different environmental places involving poultry, knacker shops, drainage water, fresh water, and sewage water. Biofilm formation assay and quantification was performed using method followed by⁶ with some modifications. Colony PCR method followed by⁷ was used for extraction of genomic DNA of *E. coli* isolates and appropriate statistical and descriptive analysis were performed using IBM SPSS V21.

Results

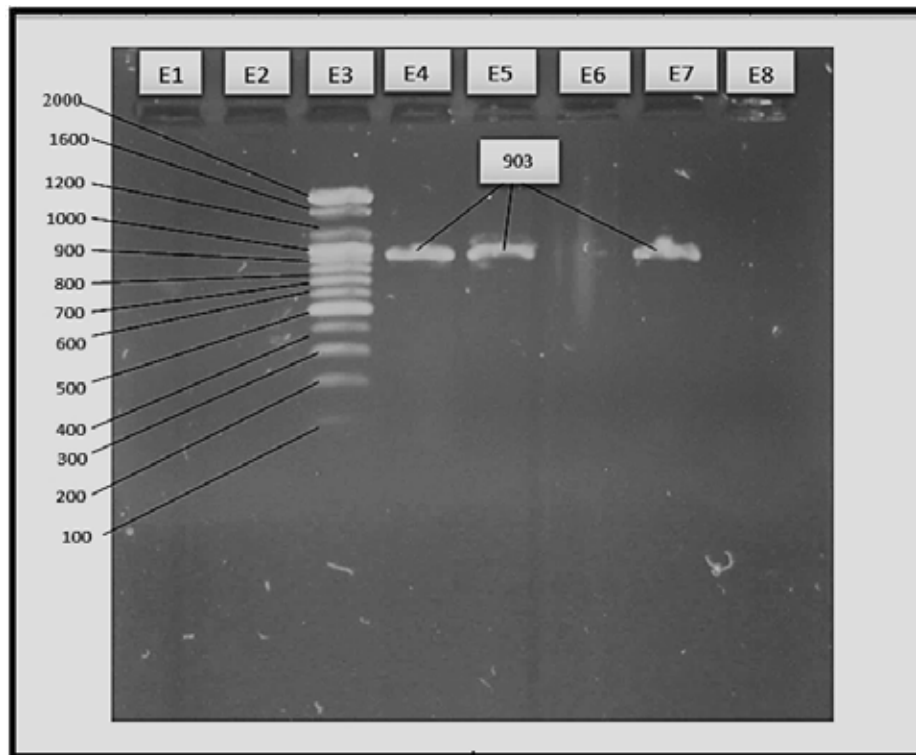


Figure (1): Agarose gel electrophoresis for PCR product of FimH gene, 1.5% agarose, visualized under UV after staining with ethidium bromide at 4volt/cm for 1 hours. laneE1 and E2 negative controls for FimH gene. Lane E3 is size marker (bp). Lane E4 and E5 and E7 is FimHPCR product (903 pb). Lane E6 and E8 is negative results of FimH PCR, All numbers in figure are in base pair.

Biofilm was performed on 21 clinical of *E. coli* isolates comparing with control which contented media only. *E. coli* isolates formed strong and moderate biofilm as the following: 14(66.6%) strong, 7(33.30%) moderate, while weak biofilm producers not exit in clinical isolates, *E. coli* isolates formed strong, moderate and weak biofilm as the following: 13(41%) strong, 8(34.70%) moderate and 2(8.60%) for weak or non-biofilm formation in environmental isolates. In current study PCR was applied on 21 clinical and 23 environmental isolates for *FimH* gene as showed in figure (1). Results showed that *FimH* gene had the higher occurrence represent 95.2% in clinical isolates. While *FimH* gene had lower occurrence represent 17(73.9%) in environmental isolates.

Discussion

Besides all human infectious diseases, urinary tract infections had a high prevalence and in the majority of cases *Escherichia coli* is a dominance bacterium which can cause pyelonephritis and cystitis⁸. Additionally, virulence genes as well as patients-related factors are equally responsible for the development of infections and also that virulence genes may help such isolates to persist even with appropriate chemotherapy and be responsible for recurrent infections⁹. Consequently, the aim of the present study was determination occurrence of the *FimH* gene that associated with adherence to host surface leading to UTI initiation. Moreover, study by Bronzato *et al.*, 2017¹⁰ emphasized that high frequency of *FimH* gene, the adhesion-encoding gene is associated with epithelial cell invasion in uropathogenic *E. coli*.

In current study; the results were obtained for the biofilm formation in clinical isolates, which seem to be similar to study emphasized by Neupane *et al.*, 2016¹¹ which found higher occurrence of strong and moderate biofilm other than weak biofilm in uropathogenic strains of *E. coli*.

Moreover, biofilm formation in environmental isolates, results approximate similar to study ascertain by Wang *et al.*, 2016¹² this study emphasized the ability of *E. coli* to biofilm forming from poultry and found sizable rate of weak biofilm formation among them.

Also, Correlation coefficient statistically measured between biofilm formation and probability of *FimH* occurrence (r) = 0.5542 for 21 clinical isolates while (r) = 0.34 for 23 environmental isolates.

Conclusion

Uropathogenic *E. coli* had the higher occurrence rate for fimbriae gene (*FimH*) compared with environmental isolates. Stronger biofilm formation by clinical *E. coli* isolates than by environmental isolates. There is a significant correlation between biofilm formation and probability of *FimH* occurrence in both clinical and environmental isolates.

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Department of Microbiology, Iraq and all experiments were carried out in accordance with approved guidelines.

References

1. Cedillo Martin, C . Isolation and Characterisation of Shiga Toxin-Producing Escherichia Coli from Norwegian Bivalves (Master's thesis, The University of Bergen) 2017.
2. COSTERTON, J William, STEWART, Philip S, GREENBERGE, Peter. Bacterial biofilms: a common cause of persistent infections. *science*, 1999;284(5418): 1318-1322.
3. FOXMAN Betsy. Urinary tract infection syndromes: occurrence, recurrence, bacteriology, risk factors, and disease burden. *Infectious disease clinics of North America*, 2014;28(1): 1-13.
4. SNYDER Jennifer A, et al. Coordinate expression of fimbriae in uropathogenic Escherichia coli. *Infection and immunity*, 2005;73(11): 7588-7596.
5. KLEMM P, et al. The major subunit of Escherichia coli type 1 fimbriae is not required for D-mannose-specific adhesion. *Molecular microbiology*, 1990; 4(4): 553-559.
6. WOJNICZ Dorota, et al. Medicinal plants extracts affect virulence factors expression and biofilm formation by the uropathogenic Escherichia coli. *Urological Research*, 2012; 40(6): 683-697.
7. WALKER Kaiti. Identification of Bacterial Species Using Colony PCR. 2015.
8. KARIMIAN Aazam, MOMTAZ Hassan, MADANI Mahbobeh. Detection of uropathogenic Escherichia coli virulence factors in patients with urinary tract infections in Iran. *African Journal of Microbiology*

Research, 2012; 6(39): 6811-6816.

9. CHAKRABORTY Arindam, et al. Molecular characterisation of uropathogenic *Escherichia coli* isolates at a tertiary care hospital in South India. *Indian journal of medical microbiology*, 2017; 35(2): 305.
10. BRONZATO Greiciane França, et al. Genotypic characterization of *Escherichia coli* strains isolated from dairy cattle environment. 2017.
11. NEUPANE Sanjeev, et al. Correlation between biofilm formation and resistance toward different commonly used antibiotics along with extended spectrum beta lactamase production in uropathogenic *Escherichia coli* isolated from the patients suspected of urinary tract infections visiting Shree Birendra Hospital, Chhauni, Kathmandu, Nepal. *Antimicrobial resistance and infection control*, 2016; 5(1): 5.
12. WANG Yang, et al. Isolation, phylogenetic group, drug resistance, biofilm formation, and adherence genes of *Escherichia coli* from poultry in central China. *Poultry science*, 2016;95(12): 2895-2901.

Dental Health Status among Adult Population in Karbala City

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Abstract

This study done to evaluate the oral health status (dental caries, periodontal disease and treatment needs) in Karbala city the adult individuals sample include 250 individuals age ranging between 20-40 years of both sexes using sharp dental caries explorers with W.H.O periodontal probs to detect periodontal health by use of DMFT index of W.H.O (1997) and CPITN by W.H.O (1987).

The mean DMFT for the total sample was (3.98 + 0.15) which was increased with increasing age for different age groups with significant difference in the mean DMFT for total boys and girls has been found. The results also showed that the total number of health 468 with a mean of 1.12 tooth/person in need of treatment is the most prevalent needed one surface filling And 308 teeth with a mean 1.01 tooth/person needed two or more surface filling.

According to highest CPITN there was significant difference between boys and girls in calculus at $P \leq 0.05$ and shallow pockets at $P \leq 0.01$. The results also revealed that the mean number of healthy sextants for the total sample was 4.13 while for bleeding and calculus were 0.82 and 0.31 respectively. It means that the treatment need for periodontal disease is more toward oral hygiene procedure and prophylaxis as general. The dental health education program is an essential activity for promoting optimal oral health and preventing oral disease.

Keywords: *Dental Health Status, DMFT of Adult, CPITN OF Adult.*

Introduction

The periodontal disease is one of the most wide spread disease all over the world and more prevalent among population of the developing countries. Periodontitis is a bacterial infecting of all parts of the periodontium including gingiva, periodontal ligament, bone and cementum, which results in irreversible destruction to the tissue of periodontium⁽¹⁻³⁾

Usually periodontal disease begins at childhood as gingivitis which increases in severity in the early “ ten “ years and it may lead to the development of periodontitis which is associated with pocket formation.⁽³⁻⁵⁾

While there are many factors that affect prevalence and severity of dental caries and periodontal disease, the most important factors are age, sex level place of residence, parental influences education level and socioeconomic status⁽⁶⁻⁸⁾

The purpose of this study were to estimate the prevalence and severity of dental caries and periodontal disease in adult population in karbala city can help in planning preventive dental health program

Material and Method

The survey was conducted during the period between October 2017 to April 2018 on 250 randomly selected in karbala city of adult people seeking for dental treatment in different departments of dental college (in karbala city), age ranging between 20 - 40 years old, divided in to 2 age groups of 10 years intervals 20 - 30 and 30 - 40 years respectively.

The clinical examination was carried out by one examiner at the dental college using plane mouth mirrors, sharp dental caries explorer and W . H . O periodontal probes to detect periodontal health

The indices used for assessment of dental condition were as follows

1. DMFT by W . H . 0 methodology for caries status and treatment need (1997)⁽⁷⁾ to obtain and calculate decayed (D) missing (M) and filled (F) for each tooth
2. Community periodontal index of treatment needs (CPITN) by WHO (1987)⁽⁹⁾ for assessment of gingival and periodontal health status and their treatment needs Each sextant was assigned a code number which recorded the condition of the Worst affected site in the sextant the subject were classified in to treatment need

Categories according to the highest code number assigned to any of the sextants in particular individual

The statistical analysis of the data included the means, standard deviation and standard error by using duncan’s multiple range test, analysis of variance (ANOVA), F test and KruskalWallis test

Results

The age and gender distribution of 250 subjects comprising 132 males and 118females was divided into 2 age groups with an interval of 10 years for age group (table 1) .

Table (2) showed there was no significant difference in the mean DMFT for total males (3.90) and total females (3 . 60), but there was significant difference in the mean DMFT and its components between different age groups and the caries prevalence was increased with age of both sexes,

Table (3) illustrated the number of teeth in the total sample that required treatment, it showed that the

treatment need for person for the total sample was in need of one surface filling, followed by two or more surface filling.

Table (4) Showed that the total sample distributed according to the highest CPITN code by age and sex it has been found that only (88) person are healthy in all age groups and the highest value was in the age group (30-40) years the most frequently periodontal condition was calculus it has been found the significant difference between males and females for calculus of $p \leq 0, 05$, and deep pocket at $p \leq 0.01$.

Table (5) showed the mean number of sextants by person the mean number of healthy sextants for the total sample was (9.79) while for bleeding (5, 06) an for calculus was (1,11).

The mean number of healthy Sextant for all age groups were nearly the same, while bleeding code was decreased with increasing age the mean number for calculus and pocket sextants was increased with age but not for all age groups.

Females tended to have health and had less bleeding and calculus Sextants compared to males .

Table (6) demonstrated the distribution of sample in need to oral hygiene education Scaling and those with no need for treatment more than half of the sample showed no need to any type of periodontal treatment (score 0) and less than half of sample need oral hygiene instruction.

Table (1): Distribution of the sample by age and sex

Age (Year)	Male No	Female No	Total No
20-30	68	64	132
30-40	64	54	118

Table (2): The mean DMFT and its components

Age	Sex	No.	DMFT		DT		MT		FT	
			Mean±SD	SE	Mean±SD	SE	Mean±SD	SE	Mean±SD	SE
20-30	Male	68	1.69±1.92	0.12	1.21±1.42	0.11	0.13±0.20	0.02	0.12±1.02	0.02
	Female	64	1.49±1.92	0.22	1.20±1.63	0.41	0.21±0.41	0.11	0.35±1.12	0.23
	Total	132	3.16±3.48	0.34	2.41±3.05	0.52	0.34±0.61	0.5	0.56±2.14	0.25
30-40	Male	64	2.21±1.21	0.11	3.21±2.81	0.41	0.40±1.23	0.21	0.60±1.69	0.35
	Female	54	2.13±1.20	0.21	4.32±3.61	0.72	0.81±1.21	0.21	0.37±0.52	0.08
	Total	118	4.34±2.41	0.32	7.53±6.42	1.13	1.21±2.54	0.42	0.97±2.21	0.43
	Total Males	132	3.90±4.33	0.32	7.53±6.42	1.13	1.21±2.54	0.41	0.97±2.21	0.30
	Total Females	118	3.60±3.12	0.43	5.52±4.24	1.10	0.42±1.62	0.32	0.72±1.63	0.31

SD: Standard Deviations SE: Standard Error

Table (3): Dental Treatment Need.

Types of Dental Treatment	No. of Teeth	Treatment Need
One surface of filling	467	1.22
Two or more surface filling	379	0.91
Extraction	18	0.07
Pulp care	12	0.01
Crown or removal replacement	232	0.43

Table (4): Number and percentage of sample distributed According to highest CPTIN code by age and sex.

Age	Sex	No.	No.	%	1No.	%	2No.	%	3No.	%	4No.	%
20-30	Male	49	21	11.9	13	7.7	13	7.5	3	1.1	0	0.0
	Female	13	7	14.2	4	1.1	2	3.0	1	0.62	1	1.2
	Total	62	28	12.4	17	8.0	15	6.6	4	1.0	1	0.2
30-40	Male	14	9	18.3	3	2.0	3	4.7	2	1.7	1	1.1
	Female	10	7	19.7	1	1.3	2	5.5	1	1.5	0	0.0
	Total	24	16M< 0.001	18.9> 0.05	4M< 0.001	1.4F< 0.01	5M< 0.05	5.0F> 0.05	3M< 0.05	1.7F> 0.05	1M< 0.05	0.6F> 0.05

Scores: 0:healthy, 1:Bleeding, 2:aculus, 3:Shallow pockets, 4:Deep pocket, Ns: Not significant

Table (5): Mean number of sextants affects person for each stage of disease by age and sex.

Age	Sex	No.	0 Mean±SD	1 Mean±SD	2 Mean±SD	3 Mean±SD	4 Mean±SD
20-30	Male	49	1.78	0.93 0.92	0.21 1.12	0.08 0.14	0.00 0.00
	Female	13	1.62	0.82 0.87	0.11 0.72	0.12 0.31	0.20 0.22
	Total	62	1.42	0.54 0.93	0.42 2.31	0.09 0.25	0.03 0.13
30-40	Male	14	1.82	0.91 0.98	0.12 0.8	0.19 1.21	0.02 0.12
	Female	10	1.63	0.22 0.99	0.23 1.31	0.14 1.04	0.00 0.00
	Total	24	1.52	0.94 0.89	0.12 1.21	0.23 0.91	0.03 0.16

Scores: 0: healthy 1: bleeding 2: calculus 3: shallow 4: deep pocket, M: male F: female T: total, SD: Standard Deviation

Table (6): Periodontal treatment need expressed as percentage of sample distributed according to type of treatment required by age and sex

Age	Sex	No.	0 Mean±SD	1 Mean±SD	2 Mean±SD	3 Mean±SD
20-30	Male	49	21 17.3	40 23.2	23 16.3	0 0.0
	Female	13	9 20.2	14 29.3	5 12.2	1 2.3
	Total	62	30 62.3	54 23.2	28 14.1	2 0.8
30-40	Male	14	8 22.3	12 25.4	9 23.2	1 3.2
	Female	10	7 11.3	9 18.4	4 22.4	0 0.0
	Total	24	15 18.4	21 22.6	13 23.0	2 2.1

Treatment Need: 0: no need 1: oral hygiene instruction 2: scaling 3: oral hygiene instruction, Scaling: M: male F: female T: total SD: standard Deviation

Discussion

Caries experience was measured by the DMFT index while is valid, simple and reproducible index for assessment of dental caries this method ensures that the data collected in a wide range of environment is comparable it is also provides a standard measurement of oral disease and condition as base for planning and evaluating oral health.

The results of this study have shown that there was increase in caries prevalence with increasing age for both sexes, this increase in caries experience with age may be attributed to differences in dietary habits,

The results of this study have also shown that there was no significant difference in the mean DMFT values for total males and total

Females this was in accordance with studies conducted in developed and developing countries ^(10,11)

Concerning treatment needs, it has been shown the majority of the sample required one surface filling followed by 2 or more surface filling.

This was in contrast with study conducted on adult population on in Spain^(11,12)

The world wide acceptance of the CPITN which has proved to be simple and effective method for measuring

and minority the prevalence and severity of periodontal disease at the community level^(14,15)

The CPITN has been increasingly adopted in dental health services and has proven to be a useful tool for planning and monitoring periodontal treatment and establishing population periodontal health goals^(14,15)

Results also revealed that there was a significant difference between males and females in ‘calculus at $p \leq 0.05$ and pocket more than 5mm depth at $p \leq 0.01$ level females tended to have higher percentage of healthy gingiva .this may be due to the fact that there were differences in practice of oral hygiene between sexes, girls tend to practice better oral hygiene .this results was in agreement with other study⁽¹⁵⁾

The results showed that calculus was the most frequently observed periodontal condition in the total population while in the age group 30-40 years the periodontal condition most frequently observed was shallow pocket. The findings of this study suggested that periodontal disease prevalence range from low to moderate, when compared with other studies

The prevalence of gingival bleeding was lower in the first age group and higher in the second age groups the mean number of health sextants for two age groups are nearly the same as the bleeding which will decrease with increasing age .it was in agreement with other studies^(16,17)

The results indicated that treatment need for periodontal disease is more toward oral hygiene procedure followed by scaling.

Conclusion

Dental caries and periodontal disease are very important public health problems in the most of developing countries therefore, an efficient dental health care instruction program showed be constructed to achieve an acceptable standard of oral hygiene, so dental health education program for those people is an essential activity for promoting establishing and maintaining optimal oral health and preventing oral diseases.

While the need for treatment was concentrated on instruction in oral hygiene and prophylaxes which can be developed by dental hygiene staff.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq.

Conflict of Interest: The authors declare that they have no conflict of interest.

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References

- Jenkins WMM, Popanou PN . Epide miology of periodontal diseases in children and adolescents. *Periodontal* 2008; 34 :40-44
- Din: EI. Periodontal conditions and treatment ‘needs (CPITN) in a worker population in Araraquara SP. Brazil. In *Dent J*.2014,24: 211-232
- Oliver RC, Brown LJ, LÖEH. Periodontal disease in the United states population. *J Periodontal* .1998; 69(2):269-278.
- Waker A, Grogory J, Brandnock G, Nunn J, White D. National diet and nutrition Survey : young people aged 4 to 8 years Report of the Oral Health Survey. Vol. 2. London HMSO.2009; P: 28- 30.
- Boross E, Molnar L Caries intensity and oral hygiene in adult patient in Budapest. *J Fogory SZ*.2008; 101(9): 110-1 18
- Pilot T, Barmas DE, leclereq MH, Mccombe BJ,Sardo infirrij. Periodontal conditions in adults 35-44 years of age, an over view of CPITN data in the WHO global oral data bank,Community Dent oral Epidemiol. 1996, 24: 410-416.
- World Health organization .Oral Health Survey: Basic Method. 4thed WHO. Geneva, Switzerland.1997
- Makan: LA.oral hygiene and gingival health among adolescents and adult population (15-44) years in sharkhan village, Ninevah.Iraq.AL-rafidian Dent. J.2011.1 (1): 1-7.
- World Health Organization Oral Health survey: Basic Method.3rd WHO. Geneva Switzerland.1987
- Hayes C. the effect of non cariogenic sweeteners of the prevention of dental caries :A review the evidence.*J Dent Educ*. 2009 73(17) 102-110.
- AL-Vara ZAA, AL-Varaz RJA,Den JM, Fernandez VJ,Villa VM.DMFT and treatment needs in adult population of Oviedo, Spain. *Community Dental oral Epidemiol*, 1996; 24(1): 17-20.
- Harris NO, christen AG. Primary preventive dentistry .4thed Stamford Connecticut 1998;P:126-B2.
- Peterson PE, Razanamihaja N.oral health status in children and adult in Madagascar. *Int dent J*.2017:54:62-77.
- Hussein SA,Doumit M,Doughan BN,El-nadeef M oral health in Lebanon of pilot pathfinder Survey. *East mediterr health J*.2008; 14:301-330
- Watson MR.Horowitz AM, caries I,Conto MT. caries condition among 2-5 years old immigrant Latino children related to parent’s oral health knowledge, opinions and practices. *communit dent oral Epidemiol* .2009:37:12-23
- Havt RJ. Behavioral and sociode mographic risk factors for caries In:Bader JD(ed). *risk Assess. It in Dentistry*. Chapel. Hill university of north Carolina dental Ecology.1990;P:50-59.
- Murray JJ.Nunn JH, steele JG. The preventive of oral disease 4thed Oxford. New York. 2010; P42-52.

The Diagnosis of Metastatic Malignancy in Ascites and Pleural Effusion by Fluid Tumor Marker in Comparison to Cytology

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Abstract

Study objective is measurement the sensitivity of CA125,CA15-3, CA19-9, CEA, NSE, and α -FP in the both pleural effusion and ascites and diagnosis their etiology in comparison with cytology.

Method: This study is prospective study, 98 patients who admitted to Al-Hilla Surgical Teaching Hospital, 42 patients with pleural effusion and 56 patients with ascites. The investigations were done and include sugar and protein analysis, direct smears, tumor markers tests (CA125,CA15-3, CA19-9, CEA, NSE, and α -FP), and cytology are done for diagnosis of metastatic cancer in both effusions, or by histopathology if negative cytology are result.

Results: Pleural effusion (42 patients) are divided into 16 (38.1%) and 26 (61.9%) for benign and malignant effusion respectively, ascites (56 patients) are 33(58.9) and 23(41.1%) for benign and malignant ascites. The age group 71-80 and male gender group is the higher percentage in both effusions. Sensitivity and accuracy in pleural fluid CEA (30.8% and 57.1%), CA15-3 (26.9%,54.8%) respectively, and in ascitic fluid CA125 and CA19-9 (26.1%, 69.6%). Tumor markers have significant association in pleural effusion (CEA and CA15-3) and ascitic fluid (CEA, CA125, and CA19-9). Sensitivity and specificity of cytology in ascitic fluid (65.2%, 96.9%) and in pleural effusion (57.7%,93.8%) respectively with significant association in both effusion . In pleural effusions, CEA+ cytology result 44.2%, 64.3%, and In ascitic effusion, CA125 + cytology show 45.7%+77.7%, for sensitivity and accuracy respectively.

Conclusion: Tumor marker of both effusions have low sensitivity and high specificity. The combination tumor markers with each other and with cytology resulting in considerable increase in their diagnostic efficacy and they can use as director for invasive procedure cytology remain the highest sensitivity (in compare to tumor markers) and would be one before other invasive tools.

Keywords: Pleural effusion, Ascites, Cytology, Fluid tumor makers.

Introduction

According to data 2015 of World Health Organization, there are about 10 million of new cancer disease per year and about 6 million cancer patients are die from that disease⁽¹⁾.

The pleural effusion is collections of fluid in the pleural cavity and 90% of its etiology are related to congestive heart failure, cancer, and pneumonia⁽²⁾.

Ascites is pathological collection of liquid in

peritoneal cavity⁽³⁾ and it caused by enterocoelia and peritoneum malignancies, tuberculosis, kidney disease, heart insufficiency, and others⁽⁴⁾.

Cytological procedure may not give final diagnosis up to 40% from all cases and so, there is additional diagnostic techniques such as fluid-soluble tumor marker are added⁽⁵⁾.

The CA125, CEA, and NSE are applied for initial detection of lung cancer⁽⁶⁾ and CA19-9 with CEA for pancreatic malignancy⁽⁷⁾. Also, there are widespread

tumor markers that are applied for clinical used and they include α -fetoprotein (α -FP), CA125, and CEA⁽⁸⁾.

The aim of this research is to study the sensitivity of CA125, CA15-3, CA19-9, CEA, NSE, and α -FP in the both pleural effusion and as cites and to diagnose their metastatic cancer in comparison with cytology .

Method

This research is prospective study, and it included entire 98 patients who admitted to Al-Hilla Surgical Teaching Hospital, 42 patients with pleural effusion and 56 patients with as cites. The study is done in period between January/2016 to September/2018.

The biochemical (sugar and protein analysis), direct smears, tumor markers tests (CA125, CA15-3, CA19-9, CEA, NSE, and α -FP), and cytology are done for diagnosis of metastatic cancer causing both effusions, and approved by clinical findings.

Benign ascitic and pleural fluid patients shows inflammatory or tuberculosis cytology. Malignant ascitic and pleural fluid is approved by positive cytology or previous diagnosis by histopathology.

Cut off value of tumor markers according to the company kits are CEA: <2.5ng/ml, CA125: <35U/ml, CA19-9: < 30U/ml, CA15-3: < 30U/ml, α -FP: < 10U/ml, NSE : < 12.5 ng/ml. This cut value are represent the upper normal limit healthy individuals .

The 98 patients are divided into 70 male and 28 female with age group that ranging between 40-80 years old.

The pleural and peritoneal fluid samples are divided into two specimens, one fluid specimen for cytology and other samples for measurement of fluid tumor markers level.

The statistical evaluation of present research was using SPSS software (version 22) . Continuous data are calculated as median, mean \pm SD, and range. Pearson's chi square (X²) and Fisher's Exact Test are valued to demonstrate the association between categorical data. P value \leq 0.05 is regarded as significant.

Results

The among 98 patients, 42 patients with pleural effusion are divided into 16 (38.1%) and 26 (61.9%) for benign and malignant effusion respectively, and 56 patients with as cites are 33(58.9) and 23(41.1%) for also benign and malignant as cites.

The age group 71-80 is the higher percentage that demonstrate 50% and 53.8% in benign and malignant pleural effusion respectively, at the same time, the male is more percentage than female. While, patients with as cites, there are the similar findings regarding age group 71-80 and gender male (Table 1).

Table 1: Association of age and gender with benign and malignant effusion in both pleural and ascitic sites .

Parameters		Benign Pleural Effusion N(%)	Malignant Pleural Effusion N(%)	P Value
Age (Binned group) (years old)	40-50	2(12.5%)	2(7.7%)	*0.545
	51-60	4(25%)	3(11.5%)	
	61-70	2(12.5%)	7(26.9%)	
	71-80	8(50%)	14(53.8%)	
Gender	Male	10(62.5%)	21(80.8%)	*0.281
	Female	6(37.5%)	5(19.2%)	
		Benign ascitic fluid N(%)	Malignant ascitic fluid N(%)	P Value
Age (Binned group) (years old)	40-50	6(18.2%)	4(17.4%)	^0.849
	51-60	7(21.2%)	5(21.7%)	
	61-70	7(21.2%)	6(26.1%)	
	71-80	13(39.4%)	8(34.8%)	
Gender	Male	24(72.7%)	15(65.2%)	^0.548
	Female	9(27.3%)	8(34.8%)	

*Fisher's Exact Test, ^Pearson chi-Square

Most tumor markers (in comparison benign and malignant cases) of ascitic fluid (CEA, CA125, CA19-9, and CA15-3) show more significant difference (P value =0.009, 0.003, 0.003, and 0.064 respectively), in contrast to pleural effusion are also had association but less significant P value (CEA= 0.016, and CA15-3=0.033).

In other side, cytology reveals highly significant association in both pleural and ascitic fluid (P =0.001 and 0.000 respectively) and with its value has higher level in positive malignant of both fluid (Table 2).

Table 2: Comparison of tumor markers and cytology between pleural and ascitic fluid regarding their etiological bases (benign and malignant).

Tumor markers	Benign pleural effusion N(%)		Malignant pleural effusion N(%)		P Value
	Positive	Negative	Positive	Negative	
CEA(ng/ml)	0(0%)	16(100%)	8(30.8%)	18(69.2%)	*0.016
CA125(U/ml)	0(0%)	16(100%)	6(23.1%)	20(76.9%)	*0.067
CA19-9(U/ml)	0(0%)	16(100%)	4(15.4%)	22(84.6%)	*0.28
CA15-3(U/ml)	0(0%)	16(100%)	7(26.9%)	19(73.1%)	*0.033
α-FP(U/ml)	0(0%)	16(100%)	1(3.8%)	25(96.2%)	*1.00
NSE(ng/ml)	0(0%)	16(100%)	1(3.8%)	25(96.2%)	*1.00
Cytology	1(6.2%)	15(93.8%)	15(57.7%)	11(42.3%)	^0.001
	Benign ascitic fluid N(%)		Malignant ascitic fluid N(%)		P Value
	Positive	Negative	Positive	Negative	
CEA(ng/ml)	0(0%)	33(100%)	5(21.7%)	18(78.3%)	*0.009
CA125(U/ml)	0(0%)	33(100%)	6(26.1%)	17(73.9%)	*0.003
CA19-9(U/ml)	0(0%)	33(100%)	6(26.1%)	17(73.9%)	*0.003
CA15-3(U/ml)	0(0%)	33(100%)	3(13%)	20(87%)	*0.064
α-FP(U/ml)	0(0%)	33(100%)	2(8.7%)	21(91.3%)	*0.164
Cytology	1(3.1%)	32(96.9%)	15(65.2%)	8(34.8%)	^0.000

*Fisher’s Exact Test, ^Pearson chi-Square

Tumor markers are generally low level of sensitivity and high specificity (100%). Sensitivity and accuracy are more in pleural fluid CEA (30.8% and 57.1%), CA15-3 (26.9%,54.8%), and CA125 (23.1%,52.4%) respectively. However, both ascitic fluid CA125 and CA19-9 have upper value in sensitivity and accuracy

(26.1%, 69.6%). Cytology is important parameter in differentiate between malignant and benign pleural and ascitic fluid. Sensitivity and specificity of cytology in ascitic fluid (65.2%, 96.9%) are more than pleural effusion (57.7%,93.8%)respectively (Table 3).

Table 3: Tumor markers and cytology are measured by sensitivity, specificity, positive predictive, negative predictive, and accuracy in both pleural effusion and ascitic fluid.

Markers	Sensitivity %	Specificity %	Positive predictive value %	Negative predictive value %	Accuracy %
Pleural Effusion					
CEA (ng/ml)	30.8%	100%	100%	47.1%	57.1%
CA125 (U/ml)	23.1%	100%	100%	44.4%	52.4%
CA19-9 (U/ml)	15.4%	100%	100%	42.1%	47.6%
CA15-3 (U/ml)	26.9%	100%	100%	45.7%	54.8%
α-FP (U/ml)	3.8%	100%	100%	39.0%	40.5%

Markers	Sensitivity %	Specificity %	Positive predictive value %	Negative predictive value %	Accuracy %
NSE (ng/ml)	3.8%	100%	100%	39.0%	40.5%
Cytology	57.7%	93.8%	93.8%	57.7%	71.4%
Ascitic Fluid					
CEA (ng/ml)	21.7%	100%	100%	64.7%	67.9%
CA125 (U/ml)	26.1%	100%	100%	66.0%	69.6%
CA19-9 (U/ml)	26.1%	100%	100%	66.0%	69.6%
CA15-3 (U/ml)	13.0%	100%	100%	62.3%	64.3%
α -FP (U/ml)	8.7%	100%	100%	61.1%	62.5%
NSE (ng/ml)	0%	100%	0%	58.9%	58.9%
Cytology	65.2%	96.9%	100%	78.0%	83.9%

Table 4 shows that combination of tumor markers alone without cytology yield no change or may be lower value of sensitivity specificity, positive predictive, negative predictive, and accuracy but the *p* value is

highly significant more than the *p* value in Table 2 when the tumor markers and cytology are alone without combinations.

Table 4: The combination tumor markers and cytology are analyzed by statistical parameters level (sensitivity, specificity positive predictive, negative predictive, accuracy, and p value) in both pleural effusion and ascitic fluid.

Tumor Markers	Sensitivity %	Specificity %	Positive predictive value %	Negative predictive value %	Accuracy %	P value
Pleural effusion						
CEA(ng/ml)+CA125(U/ml)	26.9%	100%	100%	45.7%	54.8%	^0.001
CEA(ng/ml)+CA125(U/ml)+CA19-9(U/ml)+CA15-3(U/ml)	24.0%	100%	100%	44.8%	53.0%	^0.00
CEA(ng/ml)+CA15-3(U/ml)	28.8%	100%	100%	46.4%	56.0%	^0.001
CA15-3(U/ml)+Cytology	42.3%	96.9%	95.7%	50.8%	63.1%	^0.00
CEA(ng/ml)+Cytology	44.2%	96.9%	95.8%	51.7%	64.3%	^0.00
CA125(U/ml)+Cytology	40.4%	96.9%	95.5%	50.0%	61.90%	^0.00
Ascitic fluid						
CEA(ng/ml)+CA125(U/ml)	23.9%	100%	100%	65.3%	68.8%	*0.00
CEA(ng/ml)+Cytology	43.5%	100%	100%	71.7%	76.8%	^0.00
CA19-9(U/ml)+Cytology	45.7%	100%	100%	72.5%	77.7%	^0.00
CA125(U/ml)+Cytology	45.7%	100%	100%	72.5%	77.7%	^0.00

*Fisher's Exact Test, ^Pearson chi-Square

Discussion

The ascitic effusion has etiological risk of malignancy, the cytology is main non-invasive procedure for diagnosis such disease, but this procedure is resulting 30%-50% negative test in malignant as cites, and this negative result in cytology is overcome or decrease by using laparoscopy⁽⁹⁾.

It recommended that combined ascitic CEA with cytology may helpful in distinction between benign and malignant as cites and this must be done with each doubtful malignant patient when cytology is negative⁽¹⁰⁾. In present study, that combination of many tumor markers with cytology leads to increase sensitivity of these markers. So combination of CEA and CA19-9 with cytology in as cites lead to change sensitivity from 21.7%

and 26.1% to 43.5% and 45.7% respectively. *P* value is also changed from 0.016 and 0.28 to 0.00 and 0.00 for CEA and CA19-9 respectively and it is become highly significant.

In compared to other studies with as cites, Sari et al⁽¹¹⁾ found sensitivity and specificity in as cites for CA19-9 are 19% and 94.5% respectively. Kaleta et al⁽¹²⁾ got sensitivity and specificity for CEA are 31% and 95%; for CA19-9 are 30% and 95%; and for α -FP are 17% and 95% respectively. Jume et al⁽¹³⁾ has results that sensitivity and specificity in as cites for CA125 are 39.7% and 98.8% respectively. Fang et al⁽⁴⁾ found sensitivity and specificity for CA15-3 are 23.4% and 98.56% respectively. Fang et al⁽⁴⁾ and Jume et al⁽¹³⁾ found that sensitivity of cytology in as cites are 56.81% and 65.5% respectively. So the reflection idea from our (in table 3 and table 4) and these above data in as cites, the sensitivity of these tumor markers is low to be diagnostic for malignant as cites, but their specificity are high enough to exclude malignant as cites. In our study, The higher accuracy is for cytology (83.9%) to differentiate between benign and malignant ascitic fluid.

Also, we compared to other studies with pleural effusions, Q-L Laing et al⁽¹⁴⁾ shows that sensitivity ranges of CA125, CA15-3, and CA19-9 are 17%-100%, 30%-80%, and 13%-89% respectively, and their specificity are 50%100%, 75%-100%, and 73%-100% respectively, and this is approximately similar to our result (table 3). Gulden et al⁽¹⁵⁾ use cut off value of kit company (similar to our study) to yield diagnostic role of CEA, CA15-3, CA19-9, and CA125 in pleural effusions because most of studies (above researches) is depend on using receiver operator characteristic analysis to give the highest sensitivity and specificity in association with specific tumor marker concentration.

Gulden et al⁽¹⁵⁾ demonstrate that sensitivity of CEA, CA15-3, CA19-9, and CA125 are 41.66%, 38.8%, 25.7%, and 85.7% respectively. Their specificity are 100%, 100%, 92.4%, and 41.2% respectively, this is slightly difference from our result except for CA125 that show highly difference in sensitivity and specificity (table 3). Also, Gulden et al⁽¹⁵⁾ combined many tumor markers to show if there changing in sensitivity and result that sensitivity of CEA+CA15-3 and CEA+CA125 are 28.6% and 31.4% respectively, this outcome value of this combination is proximate to our result that yield sensitivity 28.8% and 26.9% for CEA+CA15-3 and CEA+CA125 respectively.

A combined unsuitable tumor markers may lead loss their efficacy for diagnosis and particularly when primary tumor was undiagnosed⁽⁵⁾.

The sensitivity of pleural cytology examination in our study is 57.7%. many studies give similar result, Kjeldsberg et al⁽¹⁶⁾ and Light et al⁽¹⁷⁾ show that result of pleural cytology are 50%-60% and 70% respectively. This difference because the sensitivity level of cytology is correlated on the amount of good morphological cancer cells and cytopathologist skills and that is specifically for pleural effusion because problem in differentiation between normal (or reactive) mesothelial cells from malignant mesothelioma cells⁽¹⁸⁾.

Several studies provide that relationship between tumor markers in benign and malignant effusions (as cites and pleural fluid) are significant (comparable to our study) and those are Gulden et al⁽¹⁵⁾ and Antonangela et al⁽⁵⁾.

The conclusion of this study, tumor marker of both as cites and pleural effusion have low sensitivity and high specificity, and we cannot confirm malignant diagnosis with first result (low sensitivity) but we can exclude it (high specificity). Also, the combination tumor markers with each other and with cytology lead considerable increase in diagnostic efficacy of tumor markers but to be dependable level for malignant diagnosis and they can use as guide for invasive procedure to be highly diagnostic. The *P* value show association of tumor marker and cytology with both malignant effusions and this value is highly significant when there combination of tumor markers together and with cytology.

Finally, cytology remain the highest sensitivity (in compare to tumor markers) and it can be used as first line for investigation before invasive histopathological examination.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: The authors declare that they have no conflict of interest.

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References

1. Travis WD, Brambilla E, Burke AP, Marx A,

- Nicholson AG. WHO Classification of Tumours of the Lung, Pleura, Thymus and Heart. 4th ed. Series: who Classification of Tumours (vol. 7). Geneva, Switzerland: World Health Organization; 2015.
2. Trapé J, Sant F, Franquesa J, Montesinos J, Arnau A, Sala M, et al. Evaluation of two strategies for the interpretation of tumour markers in pleural effusions. *Respir Res* 2017;18:103. <https://doi.org/10.1186/s12931-017-0582-1>.
 3. Turnage RH, Li DLB, McDonald JC. Abdominal wall umbilicus, peritoneum, mesenteries, omentum. In: Sabiston Textbook of Surgery – The biological basis of modern surgical practice. 17th edn. Philadelphia.
 4. Liu F, Kong X, Dou Q, Ye J, Xu D, Shang H, Xu K, Song Y. Evaluation of tumor markers for the differential diagnosis of benign and malignant ascites. *Ann Hepatol*.2014;13(3):357-63.
 5. Antonangelo L., R. K. Sales, A. P. Corá, M. M. P. Acencio, L. R. Teixeira, and F. S. Vargas. Pleural fluid tumour markers in malignant pleural effusion with inconclusive cytologic results. *Curr. Oncol*. 2015;22 (5):336–341.
 6. Ahn JM, Cho JY . Current Serum Lung Cancer Biomarkers. *J Mol Biomark Diagn S4:001*. 2013. doi:10.4172/2155-9929.S4-001
 7. Swords D. S., Firpo M. A., Scaife C. L., & Mulvihill S. J. . Biomarkers in pancreatic adenocarcinoma: current perspectives. *Oncotargets and therapy*.2016; 9: 7459.
 8. Nolen B. The expansion and advancement of cancer biomarkers. *Cancer Biomarkers: Section A of Disease Markers*. 2011;10:61–2.
 9. Bedioui H, Ksantini R, Nouria K, Mekni A, Daghfous A, Chebbi F, et al. Role of laparoscopic surgery in the etiologic diagnosis of exudative ascites: a prospective study of 90 cases. *Gastroenterol Clin Biol*. 2007;31: 1146-1149.
 10. Torresini RJ, Prolla JC, Diehl AR, Morais EK, Jobim LF. Combined carcinoembryonic antigen and cytopathologic examination in ascites. *Acta cytol*. 2000;44:778-82.
 11. Sari R, Yidirim B, Sevinc A, Bahceci F, Hilmioğlu F. The importance of serum and as cites fluid alpha-fetoprotein, carcinoembryonic antigen, CA 19-9, and CA 15-3 levels in differential diagnosis of as cites etiology. *Hepatogastroenterology*. 2001;48:1661-21.
 12. Kaleta EJ, Tolan NV, Ness KA, O’Kane D, Algeciras-Schimmich A. CEA, AFP and CA 19-9 analysis in peritoneal fluid to differentiate causes of as cites formation. *Clin Biochem*. 2013;46 (9): 814-8.
 13. JAUME TRAPÉ, GABRIEL GURT, JOSEFINA FRANQUESA, JESÚS MONTESINOS, ANNA ARNAU, MARIA SALA, et al. Diagnostic Accuracy of Tumor Markers CYFRA21-1 and CA125 in the Differential Diagnosis of Ascites. *ANTICANCER RESEARCH*. 2015; 35: 5655-5660 .
 14. Q-L Liang, H-Z Shi, X-J Qin, X-D Liang, J Jiang, H-B Yang. Diagnostic accuracy of tumor markers for malignant pleural effusion: a meta-analysis. 2008 BMJ Publishing Group and British Thoracic Society. *Thorax Online First*, published on June 15, 2007 as <http://dx.doi.org/10.1136/thx.2007.077958>.
 15. Gülden Paşaoğlu, Adil Zamani, Gülsüm Can, Oktay İmecik. DIAGNOSTIC VALUE OF CEA, CA-19-9, CA 125 AND CA 15-3 LEVELS IN MALIGNANT PLEURAL FLUIDS. *Eur J Gen Med*. 2007;4(4):165-171.
 16. Kjeldsberg CR, Knight JA. Pleural and pericardial fluids. In: Kjeldsberg CR, Knight JA. *Body Fluids: Laboratory Examination of Amniotic, Cerebrospinal, Seminal, Serous and Synovial Fluids*. 3rd ed. Chicago, IL: ascp Press. 1993; 159–222.
 17. Light RW. Clinical practice. Pleural effusion. *N Engl J Med*. 2002;346:1971-1977.
 18. Hewitt SM. Design, construction, and use of tissue microarrays. *Method Mol Biol*. 2004;264:61–72.

Clinicopathological Evaluation of Odontogenic Tumors in Iraq (A Fifteen Years Retrospective Study)

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Abstract

Background: The purpose of this study was to determine the occurrence of clinically and histopathological diagnosed odontogenic tumors during the period of 15 years in Iraqi population.

Materials and Method: A total of 3652 biopsy specimens from the histopathological report's archive of oral pathology laboratory in Oral Diagnosis Department/College of Dentistry/Baghdad University were assessed histologic finding of odontogenic tumors for 15-year (1999-2015). Clinical data regarding age, gender, and site of lesions were collected from biopsy reports and patient's files.

Results: A total of 145 (3.97%) odontogenic tumors were reported. Ameloblastoma was very mutual odontogenic tumor 49(33.8%), then keratocystic odontogenic tumors 29 (20%), peripheral odontogenic fibroma 18 (12.4%), odontogenic myxoma 13(9%), and odontoma 11(7.6%), only 5 cases (2.8%) had malignant change, (97.2%) of cases were benign. Odontogenic tumors occurred more in males with most cases appearing in the second and third decades of life. Conclusion: odontogenic tumors shown a low incidence among oromaxillofacial lesions and low rate of malignancy changing.

Keywords: *Odontogenic Tumors; Clinicopathological Evaluation.*

Introduction

Odontogenic tumors (OTs) are uncommon objects that set up a varied group of illnesses with different clinical and histopathological structures^(1,2). In 2005 histological typing of this lesion and some pathological changes were update and renewing by WHO⁽³⁾. The Para keratinized variant of odontogenic keratocyst is considered one of common changing and update and now viewed as keratocystic odontogenic tumor (KCOT)^(4,5). Many articles and studies collected related to frequency and incidence of OT from different parts of world⁽⁶⁻¹¹⁾, but no one of these studies had data on prevalence of OT in Iraq. So the aim of this study was to define the frequency and prevalence of OTs as WHO classification from the histopathological report's archive of oral pathology laboratory in Oral Diagnosis Department/College of Dentistry/Baghdad University were assessed histologic finding of odontogenic tumors

for 15-year (1999-2015) and to match these data with studies from further geographical areas of the world.

Method

The histopathological report's archive of oral pathology laboratory in Oral Diagnosis Department/College of Dentistry/Baghdad University, were reviewed retrospectively for OTs from (1999-2015). Odontogenic tumors were categorized into 2 chief groups: benign plus malignant and 3 subdivisions based on the types of odontogenic tissues involved: epithelial odontogenic tumors (odontogenic epithelium with mature fibrous stroma, without odontogenic ectomesenchyme) (EOTs), mixed odontogenic tumors (odontogenic epithelium with odontogenic ectomesenchyme, with/without tissue formation) (MixOTs), and mesenchymal odontogenic tumors (mesenchyme and/or ectomesenchyme, with or without odontogenic epithelium) (MOTs). Demographic

variables: age, gender, type of histopathological changes and place were data collected. 2 anatomic areas, maxilla and mandible were allocated: anterior (begin from the midline and end to the distal surface of the 2nd premolar teeth), posterior (begin from the mesial surface of the 1st molar and end more distally). Our data was analysis by using SPSS 22, were P-value less than 0.05 considered significant.

Results:

Frequency:145 persons from 3652 patients were identified such as odontogenic tumors, frequency of OTs was 3.97% from total biopsied specimens, 140 patients (97.2%) were benign, while only 5 patients 5(2.8%) were malignant. So according WHO classification 95 patients (65.5%) identified as epithelial odontogenic tumors 19(13.1%) cases were mixedodontogenic tumors,and 31(21.4%) cases were mesenchymal odontogenic

tumors. Ameloblastoma (AME) was the more common tumor 49 patients (33.8%) which involving of entirely histological kinds, followed by keratocystic odontogenic tumors (KCOT) 29 (20%), odontogenic fibroma (OF)18 (12.4%), odontogenic myxoma (OMYX) 13(9%), and odontoma (OD)11(7.6%).The rest were other tumors 25 (17.2%). (Figure 1,2,3).

Age and sex: Of the 145 odontogenic tumors patients, 79 (54.48%)were males and 66(45.52%) were females. According to the age of patients it is differ from 2 years old to 80 years old, mean 32.19 years. The most incidence rate of occurrence in 3rd decades of life then by 2nd decade, and most common OT occur in 2nd decade of life was KCOT, then AMEs. While most common OTs occur in 4th decade was AMEs. Regarding malignant OTs the five reported cases appeared to occur in later decades of life as show in tables (1,2).

Table (1): Occurrence frequency, gender, and gender ratio of OTs

Tumor type	Frequency		Male	Female	Male/Female ratio
	No.	%			
AME	49	33.8%	25	24	1.04:1
KCOT	29	20%	19	10	1.9:1
OF	18	12.4%	8	10	0.8:1
OMYX	13	9%	5	8	0.625:1
OD	11	7.6%	5	6	0.83:1
CEOT	9	6.2%	6	3	2:1
AMF	5	3.4%	5	-	-
AC	3	2%	2	1	2:1
AFOD	3	2.1%	2	1	2:1
AD OD TUM	2	1.4	-	2	-
MGCT	1	0.7%	1	-	-
Clear cell Od t.	1	0.7%	1	-	-
Sq Od t	1	0.7%	-	1	-
Total	145	100%	79	66	1.19:1

Table (2): Distribution of age according to OTs occurrence in decades of life.

Tumor	0-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	Total
AME	1	6	13	16	8	3	2	0	49
KCOT	2	3	15	4	1	1	2	1	29
OF	0	4	6	3	2	3	0	0	18
OMYX	0	2	8	1	2	0	0	0	13
OD	1	7	3	0	0	0	0	0	11
CEOT	1	3	3	0	1	0	0	1	9
AMF	3	0	2	0	0	0	0	0	5

Tumor	0-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	Total
AC	1	0	0	1	0	1	0	0	3
AFOD	0	2	1	0	0	0	0	0	3
ADOT	1	1	0	0	0	0	0	0	2
MGCT	0	0	0	0	1	0	0	0	1
CCOT	0	0	0	0	1	0	0	0	1
SqOT	0	0	1	0	0	0	0	0	1
Total	10	28	52	25	16	8	4	2	145

Location: the site distribution of OT revealed that the maxilla was exaggerated in 46(31.72%) cases while mandible in 93(64.13%) cases with five cases include both maxilla and mandible and the remaining two cases with no site mentioned in the available reports. The

posterior region of the mandible appeared to be involved more than anterior region while the anterior maxilla area was further main site than the posterior as show in table (3).

Table (3): Site distribution of OTs.

Tumor type	Maxilla	Mandible	Maxilla and Mandible	Unknown site	Total
AME	5	43	-	1	49
KCOT	9	18	1	1	29
OF	11	7	-	-	18
OMYX	4	9	-	-	13
OD	10	1	-	-	11
CEOT	2	2	4	1	9
AMF	1	4	-	-	5
AC	1	2	-	-	3
AFOD	1	2	-	-	3
AD OD TUM	1	1	-	-	2
MGCT	-	1	-	-	1
C.C.Od.T,	-	1	-	-	1
Sq Od t	1	-	-	-	1
Total	46	91	5	3	145

Discussion

OTs are originated from epithelial, mesenchymal and or ectomesenchymal basics of the tooth-forming system. These varied tumorseven though uncommon but carriage an important therapeutic as well asdiagnostic trial, so awareness offrequency and plain clinical structures have good use in diagnosis and management⁽¹⁰⁾. So many studies done in different countries shown significant geographic difference in the frequency of OTs ^(10,11,12,17,18). In this study the frequency rate was (3.97%) of total oral lesions documented from January

1999 to December 2015, this results similar to study done in Asia (3.9%)⁽⁷⁾, more than middle east (1.9%)⁽⁶⁾, south America was (1.82%)^(10,15), but in north America was (1.55%) and in Iran was (1.9%)⁽¹¹⁾. but in south Africa was lower than this study (9.6%)⁽¹⁹⁾, in India was (5.7%)⁽⁹⁾, while in turkey was 7.38%⁽²³⁾. In current study show that benign tumors are most common OTs, agreement with prior studies done in many countries wild word, while just five cases were malignant^(6,7,8,9,10,11). Epithelial OTs were the most frequent subdivision of OTs followed by the mesenchymal ones .This finding come in agreement with previous reports from China, Egypt, Brazil, and

Libya, but in contrast to series from other countries like: USA, Mexico, Turkey^(16,20,21-7,8,10,13) world^(10,13,15,16,20).

In the present study, Ameloblastoma was the most frequent OT, followed by keratocystic odontogenic tumors, odontogenic fibroma, and odontogenic myxoma.

AME also considered the most common OTs this show in many studies done in many countries in middle east Asia and Africa in there population^(6,8,9,13,14,17-19). While another studies reported that KCOT was most common OTs^(7,15,16,20).

According to the gender, male is more to have tumors than female except in OF, OD and OMYX. This results is against the results appear in studies done in Iran, turkey, Brazil and Mexico this studies show that females most have tumor than males except in AMEs and OFs^(6,10,15,16). While other studies done in India and China and Egypt show that malignant tumors were more significant and usual in males patients and agreed with this fact^(7,9,17).

According to the age of patients it is differ from 2 years old to 80 years old, mean 32.19 years, the most incidence rate of occurrence in 3rd decades of life then by 2nd decade, this results agreed and similar to previous studied done in Iran⁽⁶⁾.

and most common OT occur in 2nd decade of life was KCOT, then AMEs, disagree with other studies done in turkey show that OD was more common OTs occur in 2nd as well as 3rd decade followed by KCOT⁽²³⁾.

In current study AMEs was most common tumors occur in 4th decade of life this is agree with previous study from turkey displayed that usual and common OT in 5th as well as 6th decades were AMEs plus KCOTs, this highly incidence of tumor in elderly age group may due to multicystic epithelial features of EOTs^(23,12,21).

Regarding malignant OTs the five reported cases appeared to occur in later decades of life. In patient with OD, occur more in age group less than 30 years old, study done in turkey agreed with this results⁽²³⁾, but not agree with other studies done in many countries in world^(6-8,10,11,14,15,18,20,22) the site distribution of OT revealed that the maxilla was exaggerated in 46 (31.72%) cases while mandible in 93 (64.13%) cases, this is more occur in mandibular lesions, with exception for complex odontomas, the maxilla to mandible proportion (3:6.5) this is similar to studies done in many sites in

Data obtainable in the patients with tumor placed posteriorly or anteriorly was very limited, so AMEs showed highly significant of occurrence in posterior part of mandible, while OD occurred more in anterior part of the maxilla, this results agreed and similar to study done in other countries^(7, 8, 13, 15, 16, 20, 23).

Conclusion

The present study provides epidemiological information about relative frequency of OTs, which in relation to other geographical areas revealed great variation that may be attributed to socioeconomic and genetic factors.

Retrospective studies of the frequency of OTs and tumors in many region in world will help the examiner (pathologist, maxillofacial surgeon) to understanding this lesions and managing it.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

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References

1. Kramer I, Pindborg J, Shear M. Histological typing of odontogenic tumors, WHO. 2nd. ed. Berlin: Springer-Verlag; 1992.
2. Barnes L, Eveson JW, Reichart P, Sidransky D. Pathology and genetics of head and neck tumors. Lyon: IARC Press; 2005.
3. Philipsen HP, Reichart PA. Classification of odontogenic tumors. A historical review. J Oral Pathol Med. 2006; 35: 525–529.
4. Dandena, V. et al. A comparative study of odontogenic keratocyst and orthokeratinized odontogenic cyst using Ki67 and α smooth muscle actin. Journal of Oral and Maxillofacial Pathology 21, 458–459 (2017).
5. Rangiani, A. & Motahhary, P. Evaluation of bax and bcl-2 expression in odontogenic keratocysts and orthokeratinized odontogenic cysts: A comparison of two cysts. Oral Oncology 45, (2009).

6. Saghravani N, Jafarzadeh H, Bashardoost, Pahlavan N, Shirinbak I. Odontogenic tumors in an Iranian population: a 30-year evaluation. *J Oral Sci* 2010; 52: 391–396.
7. Luo HY, Li TJ. Odontogenic tumors: A study of 1309 cases in a Chinese population. *Oral Oncology* 2009; 45: 706–711.
8. Tawfik MA, Zyada MM. Odontogenic tumors in Dakahia, Egypt: analysis of 82 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2010; 109: e67–e73.
9. Bhawna G, Ponniah I. The pattern of odontogenic tumors in a government teaching hospital in the southern Indian state of Tamil Nadu. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2010; 110: e32–e39.
10. Taylor MA, Montes CL, Sandova SC, Robertson JP, Rivera LMRG et al. Odontogenic tumors in Mexico. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1997; 84: 672–675.
11. Buchner A, Merrell PW, Carpenter WM. Relative frequency of central odontogenic tumors: A study of 1,088 cases from northern California and comparison to studies from other parts of the world. *J Oral Maxillofac Surg* 2006; 64: 1343–1352.
12. Günhan O, Erseven G, Ruacan S, Celasun B, Aydintug Y, Ergun E. Odontogenic tumors: a series of 409 cases. *Aust Dent J* 1990; 35: 518–522.
13. Olgac V, Koseoglu BG, Aksakalli N. Odontogenic tumors in Istanbul: 527 cases. *Br J Oral Maxillofac Surg* 2006; 44: 386–388.
14. Jing W, Xuan M, Lin Y, Wu LL, Zheng X, Tang W et al. Odontogenic tumors: a retrospective study of 1642 cases in a Chinese population. *Int J Oral Maxillofac Surg*. 2007; 36: 20–25.
15. Osterne RL, Brito RG, Alves AP, Cavalcante RB, Sousa FB. Odontogenic Tumors: a 5-year retrospective study in a Brazilian population and analysis of 3406 cases reported in the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2011; 111: 474–481.
16. Avelar RL, Antunes AA, Santos TS, Andrade ESS, Dourado E. Odontogenic tumors: clinical and pathology study of 238 cases *Rev Bras Otorrinolaringol* 2008; 74: 668–73
17. Sriram G, Shetty RP. Odontogenic tumors: a study of 250 cases in an Indian teaching hospital. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2008; 105: e14–e21.
18. Lu Y, Xuan M, Takata T, Wang C, He Z, Zhou Z et al. Odontogenic tumors: A demographic study of 759 cases in a Chinese population *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1998; 86: 707–714.
19. Ladeinde AL, Ajayi OF, Ogunlewe MO, Adeyemo WL, Arotiba GT, Bamgbose BO et al. Odontogenic tumors: a review of 319 cases in a Nigerian teaching hospital. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2005; 99: 191–195.
20. Gehani R, Orafi M, Elarbi M, Subkashraj K. Benign tumors of orofacial region at Benghazi, Libya: A study of 405 cases. *J CranioMaxillofacSurg* 2009; 37: 370–375.
21. Tamme T, Soots M, Kulla A, Karu K, Hanstein SM, Sökk A et al. Odontogenic tumours, a collaborative retrospective study of 75 cases covering more than 25 years from Estonia *J CraniomaxillofacSurg* 2004; 32: 161–165.
22. Tekkesin MS, Pehlivan S, Olgac V, Aksakalli N, Alatlı C. Clinical and histopathological investigation of odontomas: review of the literature and presentation of 160 cases. *J Oral MaxillofacSurg* 2012; 70: 1358–1361.
23. Figen izmeci şenel1, ezherhamza dayisoylu1, şafak ersz2, nurayyilmaz altintaş1, emre tosun1, cem-ngr1, fatih taşkesen1 the relative frequency of odontogenic tumors in the black sea region of turkey: an analysis of 86 cases *turk j med sci* 2012; 42 (sup.2): 1463-1470

Prevalence of bla_{VIM} , bla_{IMP} and bla_{NDM} Genes in Carbapenem Resistant *Pseudomonas Aeruginosa* Isolated from Different Clinical Infections in Diyala, Iraq

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Abstract

The study aimed to determine the prevalence of *bla*-genes (bla_{IMP} , bla_{VIM} and bla_{NDM}) encoding MBLs among the isolates of *P. aeruginosa*, which were recovered from various clinical samples from hospitalized patients in Diyala hospitals. This study was carried out during the period from February 2018 to August 2018. Out of 326 specimens, 81 isolates of *P. aeruginosa* were recovered. All isolates were tested toward the different class of clinically important antipseudomonal agents(18) by using agar diffusion method. The results of resistance were as following: piperacillin 74.07%, ticarcillin 85.18%, Amoxicillin-Clavulanic acid 93.82%, Ticarcillin/clavulanic acid 71.60%, ceftriaxone 87.65%, cefotaxime 85.18% and ceftazidime 75.30%, cefepime 80.24%, streptomycin 90.12%, gentamicin 85.18%, tobramycin 65.43%, amikacin 56.79%, ciprofloxacin 67.90%, levofloxacin 72.83%, ofloxacin 69.13%, Aztreonam 50.61%, Imipenem 11.11% and Meropenem 23.45%. In this investigation, antibiotic susceptibility testing of the *P. aeruginosa* isolates showed that 20(24.69%), 25(30.8%), 27(33.33%), and 9(11.11%) of the isolates were MDS, MDR, XDR and PDR, respectively. Based on the results from susceptibility testing, 19 (23.45%) of *P. aeruginosa* isolates were found to be resistant to at least one of carbapenems. Out of 19 of carbapenem resistant *P. aeruginosa* isolates, 16 (84.21%) were found to produce MBL. Among 16 phenotypic Metallo β -lactamase isolates the results achieved by using PCR revealed that 9 (56.25%) isolates have bla_{VIM} genes, while 4 (25%) isolates carried bla_{NDM} genes. No bla_{IMP} was detected among carbapenem resistant strains in this study.

Keywords: *P. aeruginosa*, Antimicrobials, Carbapenems, MBL, bla_{VIM} , bla_{IMP} , bla_{NDM} .

Introduction

Pseudomonas aeruginosa strains, especially multidrug-resistant, have caused serious problems in many countries, including Iraq. The increasing prevalence of nosocomial infections produced by multidrug-resistant (MDR), extensively drug resistant (XDR) and pandrug-resistant (PDR) *Pseudomonas aeruginosa* strains poses a grim challenge for antimicrobial therapy^[1]. *P. aeruginosa* is an opportunistic pathogen involved in many infections worldwide, such as respiratory infections, urinary tract infections, hospital-acquired pneumonia, wound and soft tissue infections, and bacteremia in immunocompromised patients, including patients with thermal injuries^[2,3]. *Pseudomonas*

aeruginosa infections are problematic due to its intrinsic as well as acquired resistance to many effective groups of antibiotics^[4].

Carbapenem resistance among clinically isolated *Pseudomonas aeruginosa* is a great concern worldwide, as this class of antibiotics is among the last resorts to eradicate infections with Gram-negative species^[5]. The prevalence of multidrug-resistant *P. aeruginosa* (MDRP) non-susceptible to quinolones and aminoglycosides in addition to beta-lactams is reported worldwide^[6]. Carbapenems are β -lactam antibiotics. It binds to penicillin binding proteins (PBP) and hinders the production of cell wall of microorganism^[7]. *Pseudomonas aeruginosa* isolates acquire resistance to carbapenems via several

mechanisms including overexpression of efflux systems, change or lack of outer membrane proteins (such as OprD porin), chromosomal AmpC beta-lactamase, production of carbapenemases and production of metallo- β -lactamases (MBLs). The presence of these mechanisms can lead to treatment failure in Carbapenem therapy of *P. aeruginosa* infections overall named heteroresistance^[8]. The most important carbapenemases produced by *P. aeruginosa* are zinc-dependent metallo-beta-lactamases (MBLs) capable of hydrolyzing imipenem, meropenem, ertapenem, and cephalosporins, but not monobactams and aztreonam^[9]. There are various MBL genes among carbapenem-resistant *P. aeruginosa* including Verona integron-encoded MBL (VIM), imipenemase (IMP), Germany imipenemase (GIM), New Delhi MBL (NDM), Sao Paulo MBL (SPM), and Florence imipenemase (FIM)^[10].

Genes responsible for the MBL productions in *P. aeruginosa* are typically part of an integron structure and are carried on transferable plasmids or transposons, but also might be a part of chromosomes. Accordingly, due to its integron-associated genecassettes, *P. aeruginosa* isolates producing MBL are capable for resistant to the several antibiotics in addition to carbapenems, causing the advent of MDR *P. aeruginosa*. Moreover, these genetic determinants are transferable to other Gram-negative species, extending the antimicrobial resistance rate and complicating the treatment of infected patients^[11]. MBL-producing organisms infections is linked with greater rates of mortality, morbidity, and healthcare costs. The international epidemiology of MBL-producing *P. aeruginosa* is still unknown in most countries^[12], which at least due to partly lack of proper screening and recommendations. Therefore, it is necessary to understand the epidemiology, molecular characteristics, and resistance mechanism of Metallo- β -lactamase-producing *Pseudomonas aeruginosa* (MPPA) to control infection and prevent a possible global health crisis. However, little information is available on the distribution of MBL producing isolates and colonial infections with these isolates in Diyala, Iraq. The aim of this study was to determine the prevalence of *bla*-genes (*bla*_{IMP}, *bla*_{VIM} and *bla*_{NDM}) encoding MBLs among *P. aeruginosa* isolated from clinical specimens in some hospitals in Diyala.

Materials and Method

Isolation and Identification of Bacterial Isolates:

A total of (326) clinical specimen from both gender

with different age were collected from the beginning of February 2018 to the end of August 2018, from patients in different hospitals of Baquba city. The isolates were identified by their colony characteristic, gram-stain and confirmed by the pattern of biochemical profiles using Vitek 2-GN system.

Antibiotic Susceptibility Testing: To estimate potential resistance of *P. aeruginosa* isolates against 18 items of antibiotics from different classes, all isolates had been subjected to antibiogram test according to (CLSI-2017)^[13], for Piperacillin, Ticarcillin, Amoxicillin-Clavulanic acid, Ticarcillin/clavulanic acid, Cefotaxime, Ceftriaxone, Ceftazidime, Cefepime, Ciprofloxacin, Levofloxacin, Ofloxacin, Gentamicin, Amikacin, Tobramycin, Streptomycin, Aztreonam, Imipenem and Meropenem. Detection of *P. aeruginosa* phenotypes based on the drug resistance patterns. Multidrug-resistant (MDR) phenotype is defined as *P. aeruginosa*, which is resistant to more than one antimicrobial agent in three or more antimicrobial categories. Extensively drug-resistant (XDR) phenotype is defined as *P. aeruginosa*, which is resistant to more than one antimicrobial agent in all the antimicrobial categories, except in two or less. Pan drug-resistant (PDR) phenotype is defined as a bacterium which is resistant to all antimicrobial agents in all antimicrobial categories.

Phenotypic detection of MBL: Imipenem-EDTA combined disc test (CDST) was used for identification of MBL-producing isolates according to^[14].

DNA Extraction and polymerase chain reaction (PCR) amplification: Genomic DNA was extracted from isolates using extraction Kits of Genomic DNA, Purification depending on instruction of manufacturing company (Promga USA). All carbapenem-resistant isolates were screened by standard PCR conventional using specific primers for *bla*_{IMP}, *bla*_{VIM} and *bla*_{NDM} genes as shown in table (1). PCR reaction tubes were transferred into thermal cycler that was programmed as following: initial denaturation for 5 mins at 95°C, (the conditions for each cycle were: 30 sec. at 94 °C, 30 sec. at 54, 55, 60°C and 30 sec. at 72°C), and final extension at 72°C for 5 mins. Amplified PCR products were detected by agarose gel electrophoresis.

Table (1): The primers used for MBLs genes detection

Primer	Oligo sequence (5'-3')	Product size bp	Annealing temp°C	Reference
bla _{IMP}	F-5' CTACCGCAGCAGAGTCTTTG3' R-5' AACCCAGTTTTGCCTTACCAT3'	587	54	15
bla _{VIM}	F-5'-GTTTGGTCGCATATCGCAAC-3' R-5'-AATGCGCAGCACCAGGATAG-3'	384	55	16
bla _{NDM}	F5'-AATGGAATTGCCCAATATTATGC-3' R-5'-CGAAAGTCAGGCTGTGTTGC-3'	491	60	17

Statistical Analysis: Statistical analysis was performed with Graph Pad Prism version 6 software, percentages were used for the comparison between samples of the study. Data analysis was done using Chi-square for the comparison of categorical data.

Results and Discussion

A total of 81 clinical isolates of gram negative bacteria primary identified as *Pseudomonas aeruginosa* were collected from different clinical sources. The source of these isolates were as follows : 24(29.62%) isolates from Wounds, 21(25.92%) isolates from Burns, 17 (20.98%) isolates from urine, 13 (16.04%) isolates from ears and the last 6 (7.40%) isolates from sputum.

Antimicrobial Sensitivity Test: Eighty one *P. aeruginosa* isolates were screened for their resistance to 18 different types of antibacterial agents. Results in table (2) show that isolate varied in their resistance and sensitivity to the antibiotics. It was found high resistance to beta lactams, aminoglycosides and fluoroquinolones. Resistance to monobactam was moderate when 50.61% of isolates being resistant to aztreonam. While the lowest resistance was observed for carbapenems. Profile of antibiotic resistance to other antibiotics is shown in table (2). In this investigation, antibiotic susceptibility testing of the *P. aeruginosa* isolates showed that 20(24.69%), 25(30.8%), 27(33.33%), and 9(11.11%) of the isolates were MDS, MDR, XDR and PDR, respectively.

Table (2): Antibigram susceptibility of *Pseudomonas aeruginosa* isolates

Antibiotic	Resistant isolates No. & %	Sensitive isolates No. & %	p-value ^a
Pipracilin	60 (74.07%)	16 (19.75%)	0.008
Ticarcillin	69 (85.18%)	9 (11.11%)	0.005
Ticarcillin/clavulanic acid	58 (71.60%)	17 (20.98%)	0.009
Amoxicillin/Clavulanic acid	76 (93.82%)	4 (4.93%)	0.001
Cefotaxime	69 (85.18%)	8 (9.87%)	0.005
Ceftriaxone	71 (87.65%)	5 (6.17%)	0.004
Ceftazidime	61 (75.30%)	18 (22.22%)	0.008
Cefepime	65 (80.24%)	12 (14.81%)	0.017
Ciprofloxacin	55 (67.90%)	26 (32.09%)	0.073
Levofloxacin	59 (72.83%)	22 (27.16%)	0.056
Oflaxacin	56 (69.13%)	18 (22.22%)	0.042
Gentamicin	69 (85.18%)	10 (12.34%)	0.008
Amikacin	46 (56.79%)	27 (33.33%)	0.051
Tobramycin	53 (65.43%)	17 (20.98%)	0.038
Streptomycin	73 (90.12%)	6 (7.40%)	0.007
Aztreonam	41 (50.61%)	30 (37.03%)	0.064
Imipenem	9 (11.11%)	65 (80.24%)	0.023
Meropenem	19 (23.45%)	50 (61.72%)	0.038

a: P-value was calculated using the Chi-square test in terms of the R & S group.

Pseudomonas aeruginosa isolates across countries are increasingly resistant to a higher number of antimicrobial agents. Ali [18] described that among 60 isolates of *P. aeruginosa*, 30% resist to 14 different antibacterial agents. Study by Tawfeeq [19] in Iraq revealed that resistance percentage to Cefotaxim (60.34%) and Piperacillin (59.48%). Results conducted in current study agreement with Al-Wasity [20] who reported that *P. aeruginosa* isolates from Baghdad hospitals developed resistance to different antibiotic classes, including fluoroquinolones in high resistance rates were 64.5%, 74.2% of isolates resistant to ciprofloxacin and Levofloxacin, respectively.

Based on the results from susceptibility testing, 19 (23.45%) of *P. aeruginosa* isolates were found to be

resistant to at least one of carbapenems. Susceptibilities of the isolates to imipenem and meropenem are listed in table (2). Imipenem showed better activity (72.83%) than meropenem (61.72%) in study period. Resistance for carbapenems by disk diffusion was originating in 9 (11.11%) isolates for both meropenem and imipenem, and in 10 (12.34%) isolates for meropenem alone, respectively.

Metallo β -lactamase production in *P. aeruginosa*:

All *P. aeruginosa* isolates that were resistant to carbapenems (n=19) were further investigated for the presence M β Ls genes. Among 19 isolates of *P. aeruginosa* 16 (84.21%), of the isolates were MBL producers, the remaining *P. aeruginosa* isolates 3 (15.78%) were non-MBL producers (Fig. 1).

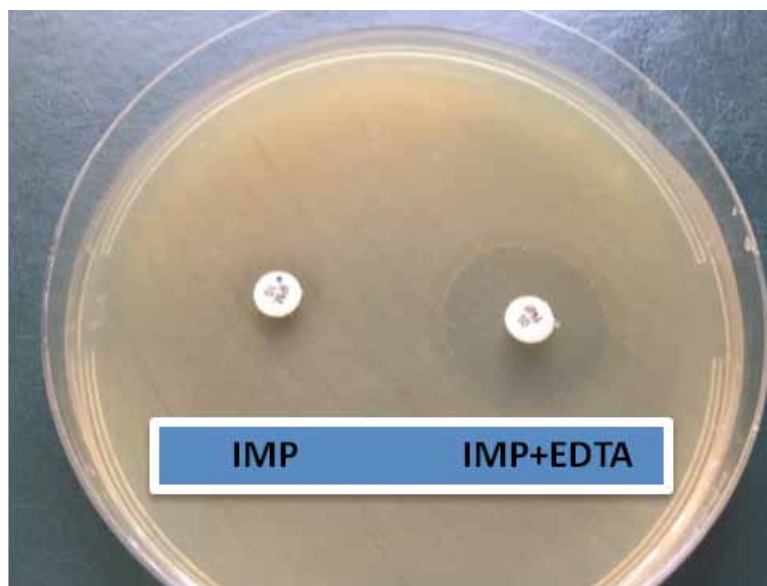


Figure (1): Combined disc diffusion test MBL positive

In the present study, 84.21% of carbapenem resistant *P. aeruginosa* isolates have Metallo β -lactamase, and this result agreed with Al-Shara [21] who found that 78% of carbapenem resistant *P. aeruginosa* isolates from patients have MBL enzyme, also agreed with Kazeminezhad [16], who demonstrate 73% of carbapenem resistant isolates in have MBL enzyme in Tehran/Iran. Early detection of these MBL producing isolate in a routine laboratory could help to avoid treatment failure, as often the isolates producing this enzyme show a susceptible phenotype in routine susceptibility testing.

Molecular detection of MBLs genes: Among 16 phenotypic Metallo β -lactamase isolates the results achieved by using PCR revealed that 9 (56.25%) isolates have *bla*_{VIM} genes (Fig. 2), while 4 (25%) isolates carried *bla*_{NDM} genes (Fig. 3). No *bla*_{IMP} was detected among Imipenem resistant strains in this study. The percentage of *bla*_{VIM} gene in the current study was higher than previous study in Saudi Arabia was noted *bla*_{VIM} appeared in 29.4% of isolates [22]. In another study in Some Hospitals in Bagdad (60%) of isolates carried *bla*_{VIM} genes, this result agreed with current study [23].

While studyin Wasit province by^[24]showed that 94.44% percentage of carbapenems resistant *P. aeruginosa* isolates have *bla_{VIM}* gene, this result disagreed with current study.

The percentage of *bla_{NDM}* genein the current study was lower than previous studyinIraq by^[25], showed that 50% percentage of carbapenems resistant *P. aeruginosa* isolates have *bla_{NDM}* gene. In Slovakia, study was reported *bla_{NDM}* gene in 6 isolates(20%).

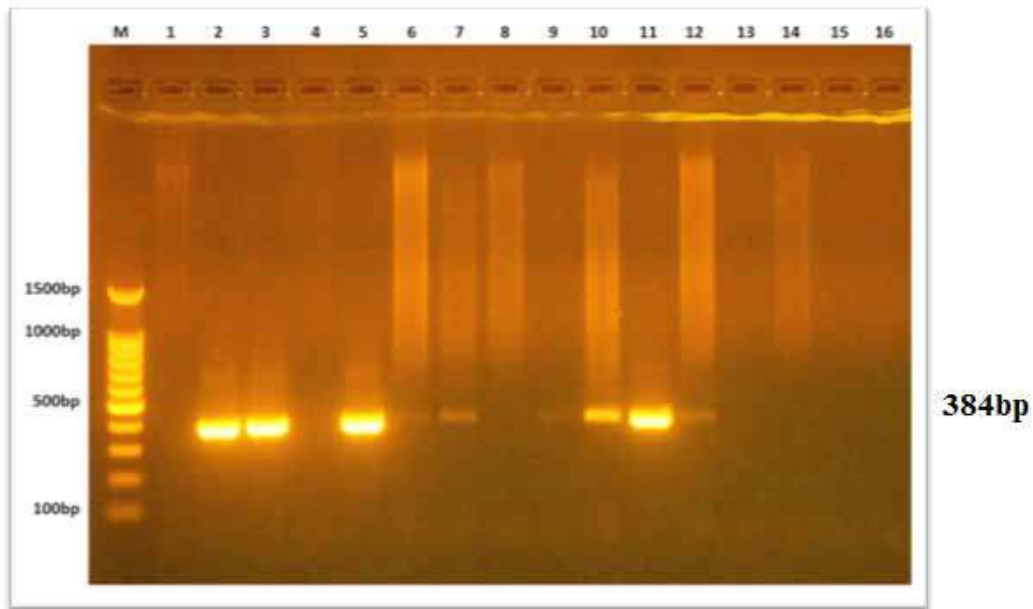


Fig. (2): Gel electrophoresis of amplified PCR product for the detection of MβL*bla_{VIM}* gene (384bp) run on 1% agarose (90 min at 70 volt), stained with ethidium bromide, lane 1-16 *P. aeruginosa* isolates; M:Marker DNA ladder (100bp); Lanes 2, 3, 5, 6, 7, 9, 10, 11, 12 positive for *bla_{VIM}*

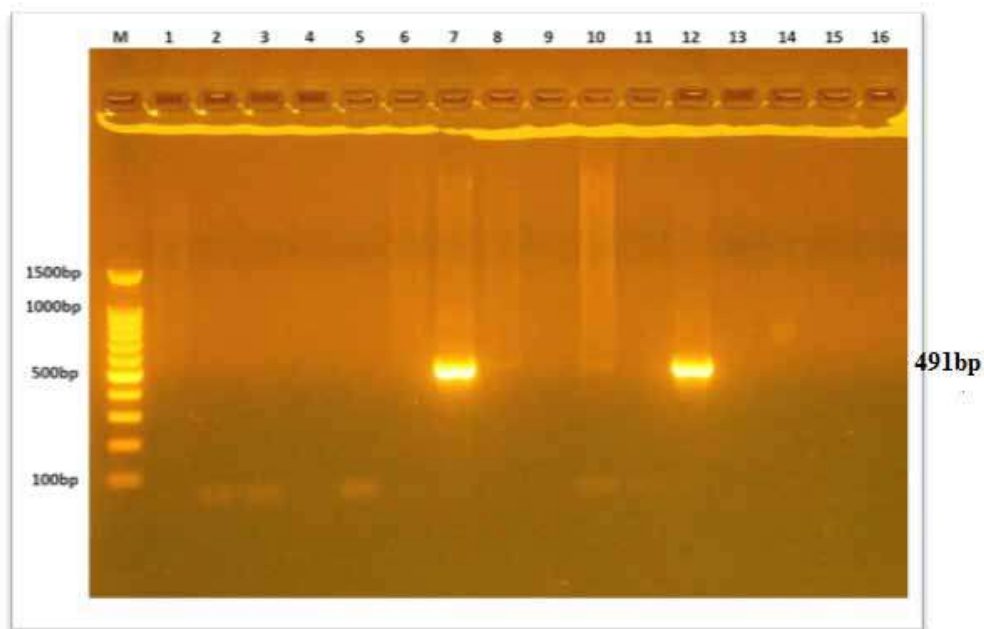


Fig. (3): Agarose Gel electrophoresis of amplified PCR product for the detection of MβLs *bla_{NDM}* gene (491bp) run on 1% agarose (90 min at 70 volt), stained with ethidium bromide, lane 1-16 *P. aeruginosa* isolates; M: Marker DNA ladder (100bp); Lanes 7, 8, 10, 12 positive for *bla_{NDM}*.

Conclusions

We can conclude Rate of occurrence of *bla*_{VIM} and *bla*_{NDM} producers was highest among carbapenem-resistant *Pseudomonas aeruginosa* isolated from clinical samples in Diyala hospitals. Therefore, the detection of *bla*_{VIM} and *bla*_{NDM} positive *P.aeruginosa* isolates in this study indicates importance of strengthening surveillance to prevent the nosocomial infection and dissemination of *blagenes* in Diyala.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: The authors declare that they have no conflict of interest.

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References

1. El Zowalaty ME, Al Thani AA, Webster TJ, El Zowalaty AE, Schweizer HP, Nasrallah GK, Marei HE, Ashour HM. *Pseudomonas aeruginosa*: arsenal of resistance mechanisms, decades of changing resistance profiles, and future antimicrobial therapies. *Future Microbiology*. 2015 Oct;10(10):1683-706.
2. Al-Azawy AN, Al-Taai HR, Al-Saadi LA. Effect of Inhibitors β -Lactamase on Recovery Effectiveness of Some β -Lactam Antibioticis Against *Pseudomonas aeruginosa*. *Diyala Journal of Medicine*. 2013;5(2):43-53.
3. Weiner LM, Webb AK, Limbago B, Dudeck MA, Patel J, Kallen AJ, Edwards JR, Sievert DM. Antimicrobial-resistant pathogens associated with healthcare-associated infections: summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2011–2014. *infection control & hospital epidemiology*. 2016 Nov;37(11):1288-301.
4. Mohamad SM, Rostami S, Zamanzad B, Gholipour A, Drees F. Detection of exotoxins and antimicrobial susceptibility pattern in clinical *Pseudomonas aeruginosa* isolates. *Avicenna Journal of Clinical Microbiology and Infection* 2017 4(4):1-6.
5. Davodian E, Sadeghifard N, Ghasemian A, Noorbakhsh S. Presence of *bla*_{PER-1} and *bla*_{VEB-1} beta-lactamase genes among isolates of *Pseudomonas aeruginosa* from South West of Iran. *Journal of epidemiology and global health*. 2016 Sep 1;6(3):211-3.
6. Sadari H, Owlia P. Detection of multidrug resistant (MDR) and extremely drug resistant (XDR) *P. aeruginosa* isolated from patients in Tehran, Iran. *Iranian journal of pathology*. 2015;10(4):265.
7. El-Gamal MI, Brahim I, Hisham N, Aladdin R, Mohammed H, Bahaaeldin A. Recent updates of carbapenem antibiotics. *European journal of medicinal chemistry*. 2017 May 5;131:185-95.
8. Bakhat S, Taj Y, Hanif F. Carbapenem Resistance Of *Pseudomonas Aeruginosa*: A Review 2019.
9. Cornaglia G, Giamarellou H, Rossolini GM. Metallo- β -lactamases: a last frontier for β -lactams?. *The Lancet infectious diseases*. 2011 May 1;11(5):381-93.
10. Labarca JA, Salles MJ, Seas C, Guzmán-Blanco M. Carbapenem resistance in *Pseudomonas aeruginosa* and *Acinetobacter baumannii* in the nosocomial setting in Latin America. *Critical reviews in microbiology*. 2016 Mar 3;42(2):276-92.
11. Hong DJ, Bae IK, Jang IH, Jeong SH, Kang HK, Lee K. Epidemiology and characteristics of metallo- β -lactamase-producing *Pseudomonas aeruginosa*. *Infection & chemotherapy*. 2015 Jun 1; 47(2):81-97.
12. Sunite A, Ganju R C, Guleria SB, Anil K K. Screening for metallo- β -lactamase producing *Pseudomonas aeruginosa* in clinical isolates in a tertiary care hospital in North India. *Medical Journal of Dr. D.Y. Patil University* 2016; 8(3): 334-336.
13. Patel JB, Weinstein M, Eliopoulos G, Jenkins S, Lewis J, Limbago B, Mathers AJ, Mazzulli T. M100 Performance standards for antimicrobial susceptibility testing. United State: Clinical and Laboratory Standards Institute (CLSI) 2017, p.240.
14. Bhalerao DS, Roushani S, Kinikar AG, Akhter I. Study of Metallo-beta lactamase producing *Pseudomonas aeruginosa* in Pravara Rural Hospital. *Pravara Medical Review*. 2010;5(3):16-9.
15. Doosti, M, Ramazani A. Garshabi M. Identification and characterization of metallo- β -lactamases producing *Pseudomonas aeruginosa* clinical isolates in University Hospital from Zanjan Province, Iran. *Iranian biomedical journal*, 2013 17(3), p.129.

16. Kazeminezhad B, Rad AB, Gharib A, Zahedifard S. bla_{VIM} and bla_{IMP} Genes Detection in Isolates of Carbapenem Resistant *P. aeruginosa* of Hospitalized Patients in Two Hospitals in Iran. *Iranian journal of pathology*. 2017;12(4):392.
17. Bubonja-Sonje M, Matovina M, Skrobonja I, Bedenic B, Abram M. Mechanisms of carbapenem resistance in multidrug-resistant clinical isolates of *Pseudomonas aeruginosa* from a Croatian hospital. *Microbial Drug Resistance*. 2015 Jun 1; 21(3):261-9.
18. Ali H S. Genetic and Phenotypic characterization of *Pseudomonas aeruginosa* Isolated from Inpatients in Baghdad hospitals. M.Sc. Thesis, College of Medicine, University of Al-Qadissiyah 2016.
19. Tawfeeq SM, Maaroo MN, Al-Ogaidi I. Synergistic effect of biosynthesized silver nanoparticles with antibiotics against multi-drug resistance bacteria isolated from children with diarrhoea under five years. *Iraqi Journal of Science*. 2017;58(1A):41-52.
20. Al-Wasity, M.A.I. Biosynthesis of ZnO Nanoparticles and Evaluate Its Effects on Biofilm Formation and psl^Á Gene Expression in *Pseudomonas aeruginosa* from Clinical Samples. Ph.D. Thesis in Microbiology Institute of Genetic Engineering and Biotechnology. University of Baghdad, Iraq 2018.
21. Al-Shara, J.M.R.. Phenotypic and molecular detecting of carbapenem resistant *Pseudomonas aeruginosa* in Najaf Hospitals. Ph.D. Thesis. Faculty of Science. University of Kufa. Iraq 2013.
22. Al-Agamy MH, Jeannot K, El-Mahdy TS, Samaha HA, Shibl AM, Plésiat P, Courvalin P. Diversity of molecular mechanisms conferring carbapenem resistance to *Pseudomonas aeruginosa* isolates from Saudi Arabia. *Canadian Journal of Infectious Diseases and Medical Microbiology*. 2016;2016.
23. AL-Thwani AN. Detection of β -lactam Genes in *Pseudomonas aeruginosa* Isolates in Some Hospitals in Bagdad Governorate by using Multiplex PCR. In *Jornal of Babylon Univ. Special Issue-Prociding of 5th International Conference of Environmental Scince University of Babylon/Environmental Research Center 2013 Dec (Vol. 3, p. 5)*.
24. Hussein ZK, Shamkhi IJ. Detection of bla_{-VIM} gene in carbapenem-resistant *pseudomonas aeruginosa* isolated from clinical samples in Wasit hospitals. *Basrah Journal of Veterinary Research* 2018, 17(3): 239-246.
25. Hussein ZK, Kadhim HS, Hassan JS. 3. Detection of New Delhi Metallo-Beta-Lactamase-1 (BLANDM-1) in Carbapenem-Resistant *Pseudomonas Aeruginosa* Isolated from Clinical Samples in Wasit Hospitals. *Iraqi Journal of Medical Sciences*. 2018;16(3):239-46.

Estimation of Caspase-8 in Patients with Systemic Lupus Erythematosus and its Relationship with Disease's Activity

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Introduction

Many research groups studied the relationship between SLE & apoptosis as some enzymes of apoptosis considered to be the cause of relapsing of disease, such as caspases 8 & 3. So the correlation between both is still a debate issue. This study aimed to: Assess level of caspase-8 among SLE patients. This done by:

1. Measurement of caspase 8 level by ELISA technique.
2. Clarify the relationship between caspase 8 levels and SLE activity by measuring ds-DNA and ANA levels.

Method: Subjects enrolled in this study were categorized into two groups: patients and control groups, The patients were of both sexes with ages ranging from (10-55 year), The study carried out during the period from December, 2017 through August, 2018. This study was conducted on patients attending Al-Sadder Medical City, AL Hakeem General Hospital in Al-Najaf, AL-Hussein Medical City in Karbala and Marjan Medical City in Babyl, All these provinces in Iraq. From the Rheumatology and Nephrology out clinics in those hospitals. Forty Five patients (5 males & 40 females), Collect appropriate amount of blood from each patient for: Assessment of ds- DNA and ANA. Assessment of apoptosis marker (caspase-8) using ELISA technique.

Results: The level of caspase 8 show significant correlation among patients with SLE than control (P. value = 0.023) . furthermore, ANA and ds-DNA were high significant in patients compare with control (P-value < 0.001 and P. = 0.001) respectively .

Keywords: Caspases-8; systemic lupus erythematosus; Apoptosis; ds-DNA; ANA.

Introduction

Systemic lupus erythematosus (SLE) is an auto-immune disease with a wide spectrum of clinical immunological abnormalities⁽¹⁾. A characteristic hallmark of SLE is the production of autoantibodies

against nuclear components⁽²⁾. To understand the pathogenesis of SLE it is important to know how self antigens become available and immunogenic to immune system, many researchers believed that apoptosis play a crucial role in autoimmunity, including SLE⁽³⁾. Disturbances in apoptosis and any defect in clearance of apoptotic cells, increases exposure of modified autoantigens to the immune system⁽⁴⁾. Apoptosis is a programmed cell death that follows characteristic biochemical and morphological features. Apoptosis can be induced by extrinsic (e.g., Fas ligand), or intrinsic factors (e.g., DNA damage)⁽³⁾. Accompanied with changes in chromatin structure and composition⁽⁵⁾. cells finally disintegrate into apoptotic blebs⁽⁶⁾. These stimuli

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lead to activation of caspases and changes in the plasma membrane⁽⁷⁾. SLE Disease Activity Index (SLEDAI), developed at the University of Toronto in 1992, is a global score reflecting all aspects of disease activity⁽⁸⁾. SLEDAI has certain limitations in that it does not score some life threatening manifestations such as pulmonary haemorrhage and haemolytic anaemia. It is heavily weighted for central nervous system and does not take into account the severity of manifestations. Gladman et al⁽⁹⁾. defined that an increase in SLEDAI score of more than three was a flare, SLEDAI score that was within three points of the previous score was persistent disease and a score of zero was remission. A change of SLEDAI score of more than 12 is a severe flare according to another study^(10,11). The mechanism between caspase-8 and SLE is complicated, The level of caspase-8 have an inverse relationship with the activity of the disease, So the current study aimed to: Assess level of caspase- 8 among SLE patients. This done by:

1. Measurement of caspase 8 level by ELISA technique.
2. Clarify the relationship between caspase 8 levels and SLE activity by measuring ds-DNA and ANA levels .

Subject and Method

Study Population: Patients group: This study was conducted on patients attending Al-Sadder Medical City, AL Hakeem General Hospital in Al-Najaf, AL-Hussein Medical City in Karbala and Merjan Medical City in Babyl these provinces in Iraq. From the Rheumatology and Nephrology out clinics in these hospitals. Forty Five patients (5 males & 40 females) with age range between 10-55 years, and duration of disease between 1 year -25 years included in this study who were clinically checked by Specialist and laboratory diagnosed as SLE.

Control group For the purpose of comparison, a group of 45 (5 males and 40 females) apparently healthy control persons were included (healthy, normal subjects with no family history of SLE, without any medical disease and chronic disease) with age range between 10-55 years. Their age ranges and gender is matched to that of patients. All groups (patients & control) have been informed about the study and its aims and their agreement were taken.

Specimen collection: Five ml of venous blood were drawn from each patients and control groups, collected in gel tubes, slow withdrawal of the blood sample via the needle of syringe to prevent hemolysis. The sample

dropped into clean disposable gel tube, serum was separated after 20 minutes at room temperature The samples were then centrifuged at 3500 rpm for 5 minute and then stored in to separated three eppendorf tubes at freeze condition (-20C) until analyzed. Assessment of ANA, dsDNA and Assessment of apoptosis marker (caspase-8).

Laboratory Assays:

Kits	Source
Human CASP3 (Caspase 3) ELISA Kit	Elabscience
Human CASP8 (Caspase 8) ELISA Kit	Elabscience
dsDNA-G Kit	CHORUS
ANA- screen Kit	CHORUS
(C4) Kit	Genrui
(C3) Kit	Genrui

Statistical Analysis: Data of both studied groups were entered and analyzed using the statistical package for social sciences (SPSS) version 25. Descriptive statistics presented as mean, standard deviation, standard error, range, frequencies and proportions. All continuous variables were tested for statistical normal distribution using histogram and normal distribution curve, statistical tests were applied according to the distribution and type of variables. Student's t test for two independent samples was used to compare two means of a continuous normally distributed variable, and Mann-Whitney U test for two independent samples was used to compare non-normally distributed continuous variables. Chi-square and Fisher's exact (when chi-square inapplicable) tests used alternatively to compare frequencies. Bivariate Pearson's and Spearman's correlation test, and regression curve estimation analysis were used to assess the correlations. Correlation coefficient (R) is an indicator of the strength and direction of correlations; its value ranged zero (complete no correlation) to one (perfect correlation) the higher R value close to one indicated stronger correlation, the positive (no sign) R value indicated a direct (positive) correlation and the negative signed R indicated an inverse correlation. Level of significance of ≤ 0.05 was considered as significant difference or correlation. Results and findings were presented in tables and figures with explanatory paragraphs using the Microsoft Office 2010 for windows.

Results

The mean caspase 8 of SLE patients was (27.73±1.16) which was significantly lower than that

of controls which was (30.51±1.21), (P. value = 0.023), (Table 6).

Table 6. Comparison of Caspase-8 levels of SLE patients and controls

Caspase 8	SLE Patients (n = 45)	Controls (n = 45)	P. value
Mean	27.73	30.51	0.026 Mann-Whitney U test
SE of Mean	1.16	1.21	
Minimum	3.56	19.01	
Maximum	32.92	32.92	

The comparisons of mean Antinuclear Antibodies (ANA) levels of SLE patients and controls revealed that SLE patients had significantly much higher mean ANA than controls, 6.41±0.69 and 0.92±0.41, respectively, (Table 2), (P<0.001).

Table 2. Comparison of ANA levels of SLE patients and controls

ANA	SLE Patients (n = 45)	Controls (n = 45)	P. value
Mean	6.41	0.92	< 0.001 Mann-Whitney U test
SE of Mean	0.69	0.41	
Minimum	0.40	0.22	
Maximum	12.00	2.30	

The mean Anti ds-DNA antibodies level in SLE patients was significantly higher than in controls, (74.59±11.02) and (11.37±4.69), respectively, (P.value = 0.001), (Table 3)

Table 3. Comparison of Anti ds-DNA levels of SLE patients and controls

Anti ds-DNA	SLE patients (n = 45)	Controls (n = 45)	P. value
Mean	74.59	11.37	0.001 Mann-Whitney U
SE of Mean	11.02	4.69	
Minimum	7.00	7.00	
Maximum	180.0	35.5	

Discussion

Based on recent findings as described above, our work focused on the association the caspase 8 and immunological marker of SLE.

Apoptosis is a highly controlled process (12), and plays an important role in pathogenesis of SLE. In current study, we examined the level of Caspase-8 in seria patients and control using and protein levels using

ELISA technique and aclarify the relationship between caspase 8 levels and SLE activity by measuring ds-DNA and ANA levels.

The current study, found that the main first result is comparisons of mean Antinuclear Antibodies (ANA) levels of SLE patients and controls revealed that SLE patients had significantly much higher mean ANA than controls.

The main second result is the mean Anti ds-DNA antibodies level in SLE patients was significantly higher than in controls.

The main third result is the mean caspase 8 of SLE patients was significantly lower than that of controls which was, (P. value = 0.023), (Table 6) which was consistent with our results⁽¹³⁾showed that the expression level of FasL, caspase 8 was decreased in SLE patients and in female, which was in agreement with the results of some previous studies.

Another study corresponds with our study, Mass et al (2002) assessed the expression level of a number of genes involved in apoptosis in SLE patients, and observed the reduced level of caspase 8 in these patients⁽¹⁴⁾.

Comparing the results of male and female SLE patients in present study we showed that apoptosis rate was decreased, and expression of caspase 8 in gene level was lower in female than male. The reason for this difference between male and female patients is not clear, but differences in sex hormones may be involved⁽¹⁵⁾. And others indicated that the level of prolactin was increased in female and male SLE patients, and the level of DHEA and progesterone as hormones having immunosuppressive effects were decreased⁽¹⁶⁾.

Previous study that shown, Apoptotic rate is increased in patients with systemic lupus erythematosus, Interaction of death receptor (Fas) with its ligand (FasL) activates caspase-8 which is necessary for transduction of apoptosis signals in extrinsic Pathway In the intrinsic pathway, any decrease in antiapoptotic proteins such as Bcl-2 leads to the activation of caspase-9 and the transduction of apoptosis signals⁽¹⁵⁾.

The results in previous study⁽¹⁷⁾ showed that there was no significant difference in apoptosis rate in protein level neither among lupus patients and control groups nor between male and female patients with their appropriate controls, which was in accordance with results of some previous studies⁽⁴⁾.

In a number of previous studies, apoptosis rate has been reported to be increased in patients with SLE⁽³⁾, whereas in other studies no difference was observed between SLE patients and controls when Fas molecule was assessed instead of apoptosis⁽³⁾, which was not compatible with our results.

Caspase-8 deficiency has been recently associated with human diseases, Caspase-8 also carries important non-apoptotic functions⁽¹¹⁾.

Most SLE patients enrolled in the present study were in the early stages of SLE and either took no drugs or consumed corticosteroids. Wang et al reported increased apoptosis rate in SLE patients, while nothing was mentioned in their study about the medications used for patients⁽⁴⁾. and Caricchio et al⁽¹⁸⁾ studied 13 and 25 SLE patients with similar drug dose as our study, respectively, and reported that the percentage of apoptotic cells and the expression level of Fas molecule was the same in SLE patients and healthy controls, which was comparable to our results. Different study results seem to be to some extent influenced by differences in patients' medication regimens. The differences may also be partly affected by different methodologies used in several studies.

In the current study, the mean caspase 8 of SLE patients was (27.73±1.16) which was significantly lower than that of controls which was (30.51±1.21), (P. value = 0.023)

In Iraq in Tropical-Biological Researches Unit, College of Science, University of Baghdad⁽¹⁹⁾ confirmed that The sera of SLE patients were positive for ANA (100.0%) while none of the control⁽¹⁹⁾.

Another study in Iraq, where explained that ANA was Positive in 90% with SLE patients and with rare present in healthy control, Antibodies to dsDNA in patients serum are increased comparing with the control⁽²⁰⁾.

These results were confirmed in the present study, the level of caspase 8 is low with the increase activity of disease also caspase3 in (table 7) that mean the level of extrinsic pathway correlate with serology and clinical SLE activity in our patients, the anti-dsDNA antibodies is more specific than ANA in diagnostic SLE .

Many studies did not correspond to our current study, Previous study show the presence of anti-ANA

antibodies is not in itself diagnostic or even predictive of disease in some cases⁽²¹⁾.

Previous study, sustained anti-dsDNA antibody production may appear that may relate to SLE. In the other situation, a transient antibody profile may appear that may not relate at all to SLE⁽²²⁾.

Other study confirmed differences in levels anti-dsDNA, This study was specifically focused on those patients with changing anti-dsDNA levels, and it became clear that changes in anti-dsDNA content associated with the three different complement components (C1q, C4, and C3).

Some methodological limitations should be considered in the interpretation of our results: the small sample size of the groups studied, different genetic variation between countries, most of our patients they take medication, also to technical failure because ELISA may fail to detect caspases, in general because of the different techniques used in the measurement of caspases, ANA & ds-DNA.

Conclusion: there are important changes in the level of caspase-8 in SLE, The level of caspase-8 have an inverse relationship with the activity of the disease.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq.

Conflict of Interest: The authors declare that they have no conflict of interest.

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References

1. Wallace D, Hahn BH. Dubois' Lupus Erythematosus and Related Syndromes E-Book: Expert Consult-Online: Elsevier Health Sciences; 2012.
2. Muñoz LE, Lauber K, Schiller M, Manfredi AA, Herrmann M. The role of defective clearance of apoptotic cells in systemic autoimmunity. *Nature Reviews Rheumatology*. 2010;6(5):280.
3. Munoz LE, van Bavel C, Franz S, Berden J, Herrmann M, Van Der Vlag J. Apoptosis in the pathogenesis of systemic lupus erythematosus. *Lupus*. 2008;17(5):371-5.

4. Xue C, Lan-lan W, Bei C, Jie C, Wei-hua F. Abnormal Fas/FasL and caspase-3-mediated apoptotic signaling pathways of T lymphocyte subset in patients with systemic lupus erythematosus. *Cellular immunology*. 2006;239(2):121-8.
5. Cohen G, Sun X, Snowden R, Dinsdale D, Skilleter D. Key morphological features of apoptosis may occur in the absence of internucleosomal DNA fragmentation. *Biochemical Journal*. 1992;286(2):331-4.
6. Coleman ML, Sahai EA, Yeo M, Bosch M, Dewar A, Olson MF. Membrane blebbing during apoptosis results from caspase-mediated activation of ROCK I. *Nature cell biology*. 2001;3(4):339.
7. Heyder P, Gaip US, Beyer TD, Voll RE, Kern PM, Stach C, et al. Early detection of apoptosis by staining of acid-treated apoptotic cells with FITC-labeled lectin from *Narcissus pseudonarcissus*. *Cytometry Part A*. 2003;55(2):86-93.
8. Bombardier C, Gladman DD, Urowitz MB, Caron D, Chang CH, Austin A, et al. Derivation of the SLEDAI. A disease activity index for lupus patients. *Arthritis & Rheumatism: Official Journal of the American College of Rheumatology*. 1992;35(6):630-40.
9. Gladman D, Goldsmith C, Urowitz M, Bacon P, Bombardier C, Isenberg D, et al. Sensitivity to change of 3 systemic lupus erythematosus disease activity indices: International validation. *The Journal of rheumatology*. 1994;21(8):1468-71.
10. Petri M, Buyon J, Skovron M, Kim M. Reliability of SLENA SLEDAI and flare as clinical trial outcome measures. *Arthritis & Rheumatism*. 1998;41(9):S218.
11. Chun HJ, Zheng L, Ahmad M, Wang J, Speirs CK, Siegel RM, et al. Pleiotropic defects in lymphocyte activation caused by caspase-8 mutations lead to human immunodeficiency. *Nature*. 2002;419(6905):395.
12. Krueger A, Fas SC, Baumann S, Krammer PH. The role of CD95 in the regulation of peripheral T-cell apoptosis. *Immunological reviews*. 2003; 193(1):58-69.
13. McNally J, Yoo D-H, Drappa J, Chu J-L, Yagita H, Friedman SM, et al. Fas ligand expression and function in systemic lupus erythematosus. *The Journal of Immunology*. 1997;159(9):4628-36.
14. Maas K, Chan S, Parker J, Slater A, Moore J, Olsen N, et al. Cutting edge: molecular portrait of human autoimmune disease. *The Journal of Immunology*. 2002;169(1):5-9.
15. Rastin M, Hatef MR, Tabasi N, Mahmoudi M. The pathway of estradiol-induced apoptosis in patients with systemic lupus erythematosus. *Clinical rheumatology*. 2012;31(3):417-24.
16. Zandman-Goddard G, Peeva E, Shoenfeld Y. Gender and autoimmunity. *Autoimmunity reviews*. 2007;6(6):366-72.
17. Rastin M, Mahmoudi M, Hatef M, Sahebari M, Tabasi N, Haghmorad D, et al. T lymphocyte apoptosis in systemic lupus erythematosus patients. *Iranian journal of basic medical sciences*. 2013;16(8):936.
18. Caricchio R, Cohen PL. Spontaneous and induced apoptosis in systemic lupus erythematosus: multiple assays fail to reveal consistent abnormalities. *Cellular immunology*. 1999;198(1):54-60.
19. Abbas AH, Melconian AK, Ad'hiah AH. Detection of anti-cytomegalovirus antibodies in sera of Iraqi systemic lupus erythematosus women patients. *Iraqi Journal of Science*. 2016:317-20.
20. Deane KD, El-Gabalawy H. Pathogenesis and prevention of rheumatic disease: focus on preclinical RA and SLE. *Nature Reviews Rheumatology*. 2014;10(4):212.
21. Olsen NJ, Karp DR. Autoantibodies and SLE—the threshold for disease. *Nature Reviews Rheumatology*. 2014;10(3):181.
22. Rekvig O. Anti-dsDNA antibodies as a classification criterion and a diagnostic marker for systemic lupus erythematosus: critical remarks. *Clinical & Experimental Immunology*. 2015;179(1):5-10.

Gold Nanoparticles Targeting Human Cervical Cancer Cells

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Abstract

The most disturbing gynecologic malignancies is cervical cancer particularly in the developing world with the same high incidence in Iraqi women. Cervical carcinoma has a high rate of mortality. The high death rate is associated with presence of human papillomavirus (HPV) infection. Cervical carcinoma is hard to treat, and conventional therapies are very aggressive which lead for the need for new approaches of therapy. Nanoparticles is a promising treatment modality to produce non-toxic and efficient cancer therapy. Gold nanoparticles (AuNPs) accumulate in cancer cells selectively. The current work was aimed to study cytotoxicity and cell death induced by AuNPs on cervical carcinoma cells. Method: Cytotoxicity of AuNPs was assessed by MTT viability assay and analysed using multiple comparison ANOVA tests. Results: AuNPs nanoparticles from 12.5 up to 50 µg/mL for 72 hours showed concentration-dependent killing activity.

Keywords: Gold nanoparticles (AuNPs), cytotoxicity. Cell death.

Introduction

The most disturbing gynecologic malignancies is cervical cancer particularly in the developing world⁽¹⁾. The new cervical cancer cases are about 569,847 diagnosed annually worldwide (estimates for 2018)⁽²⁾. Human Papillomavirus (HPV) infection is associated with the cervical cancer⁽³⁾. In Iraq, cervical cancer ranked 9th most common cancer in Iraqi women aged 15 to 44 years⁽⁴⁾. The most frequent type of cervical cancers is squamous cell carcinoma (SCC) which is about 85%⁽⁵⁾. There are known risk factors associated with cervical cancer in addition to HPV infection, such as cigarette smoking and smoke carcinogen (benzo[a]pyrene, BaP)⁽⁶⁾. Human papilloma virus (HPV) subtypes that cause cancer is genotype 16 that cause SCC and genotype 18 that cause adenocarcinoma⁽⁷⁾. It is well reported the importance of HPV infection in different type of benign and malignant tumors. It is well established that there is association between HPVs with cervical cancer⁽⁸⁾. Moreover,

environmental pollutions associated with conflicts may be another source for increase cancer related cases⁽⁹⁾. There were numerous attempts to overcome resistance to conventional therapies to accomplish a considerable therapeutic effect in malignant tumors by using gold nanoparticles^(10, 11). The resistant of cancer while there is treatment for long time, will cause progressive type of malignant tumors, requires the development of novel therapeutic modalities to overcome chemo-resistance and enhance prolong surviving effect⁽¹²⁾. Nanoparticles is a promising treatment modality to produce non-toxic and efficient cancer therapy^(13, 14). Nanoparticles carry unique chemical and physical features⁽¹⁵⁾, these features utilized in biomedical applications⁽¹⁶⁾ such as cancer⁽¹⁷⁾. Nanoparticles were combined with other cancer targeting agents to enhance therapeutic effects⁽¹⁴⁾. The search for more effective therapy is needed, therefore we designed the current study to use Gold (AuNPs) nanoparticles as anti-cervical cancer therapy which hold promise for clinical application.

Materials and Method

Maintenance of Cell Cultures: The human cervical cancer cell line, Hela were cultured in basic MEM media (Usbiological, USA) supplemented by 10% fetal bovine serum (FBS), 100 units/mL penicillin and 100 µg/mL streptomycin (Capricorn- Scientific, Germany).

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The cell line is authenticated regularly. Hela cell line was subcultured using trypsin-EDTA when confluent monolayer was achieved and incubated at 37°C in 5% CO₂ humidified incubator^(18,19).

Gold Nanoparticles: The current work used highly stable gold nanoparticles (AuNPs) of 10nm size, they are designed for biomedical applications⁽¹¹⁾.

Cytotoxicity determination using MTT assay: The Hela cells were seeded at concentration of 10000 cells/well in 96 multi-well microplates. The cells were suspended in 10% FBS MEM medium and allowed to grow for 80% confluency. Gold NPs were added at several concentrations from 3.2 to 100µg in triplicate and incubated for 72 hrs. at the end point, the MTT stain was added at a concentration of 2µg/ml. After 3h incubation at 37°C, Dimethyl Sulfoxide (DMSO) was added to all wells. The measurement of absorbance was done at 580 nm using biochrom microplate reader. Results of the assay were shown as a percentage of proliferation relative to control cells^(20, 21).

Statistical Analysis: The collected data were statically analyzed using multiple comparison ANOVA tests using Graph Pad Prism 6.07; values were presented as the mean±S.D of the triplicates.

Results

Gold NPs suppress Hela cervical cancer cells: The killing effect of Gold nanoparticles on human cervical carcinoma cells Hela after 72h of exposure was shown in figure 1. The cytotoxicity of GNPs on Hela cervical carcinoma cells was significant in compare to control not treated cells. The GNP cytotoxicity was significantly elevated with the increase in concentration as shown in

table 1. the effective concentrations were 12.5, 25 and 50µg/ml. The results of the cytotoxicity experiment suggest that gold nanoparticles can be valuable anti-cervical cancer therapy. Hela cells treated with AuNPs exhibited detachment and pathological morphological changes. IC₅₀, which is the inhibitory concentration that kills 50% of the cells, was 8.713µg (Figure-2). The cytopathological changes revealed apoptotic induction in Hela cells when observed under phase contrast inverted microscope. The untreated cells displayed that the cells preserved their unique morphology; most of the untreated cells were attached to the tissue culture plate.

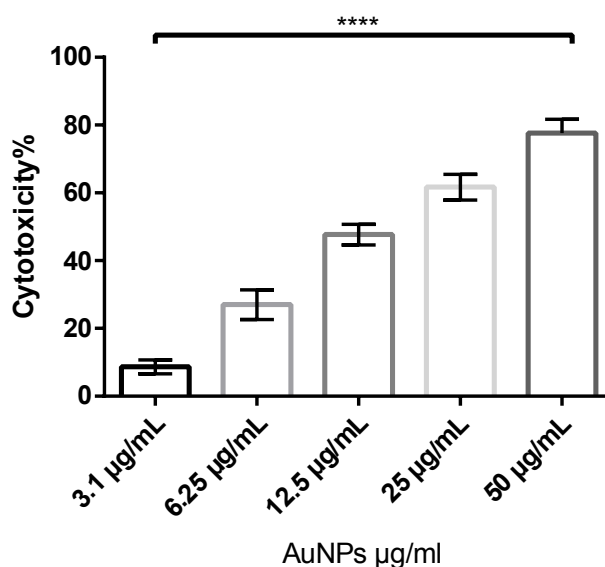


Figure 1: Killing effect of gold nanoparticles in cervical cancer Hela cells was measured via the MTT viability assay. The Hela cells were exposed to gold NPs for 72 h with different concentrations. The effective concentration of AuNPs nanoparticles were from 12.5 to 50 µg/ml.

Table 1, The cytotoxicity assay effect were analyzed using multiple comparison ANOVA tests

Tukey's multiple comparisons test	Mean Diff.	95% CI of diff.	Significant?	Summary
3.1 µg/mL vs. 6.25 µg/mL	-18.33	-27.90 to -8.770	Yes	***
3.1 µg/mL vs. 12.5 µg/mL	-39.00	-48.56 to -29.44	Yes	****
3.1 µg/mL vs. 25 µg/mL	-53.00	-62.56 to -43.44	Yes	****
3.1 µg/mL vs. 50 µg/mL	-69.00	-78.56 to -59.44	Yes	****
6.25 µg/mL vs. 12.5 µg/mL	-20.67	-30.23 to -11.10	Yes	***
6.25 µg/mL vs. 25 µg/mL	-34.67	-44.23 to -25.10	Yes	****
6.25 µg/mL vs. 50 µg/mL	-50.67	-60.23 to -41.10	Yes	****
12.5 µg/mL vs. 25 µg/mL	-14.00	-23.56 to -4.436	Yes	**
12.5 µg/mL vs. 50 µg/mL	-30.00	-39.56 to -20.44	Yes	****
25 µg/mL vs. 50 µg/mL	-16.00	-25.56 to -6.436	Yes	**

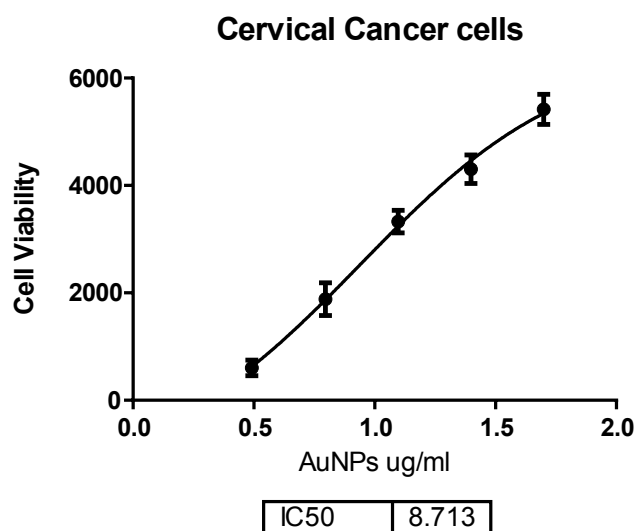


Figure 2: IC₅₀ value for Gold NPs in Hela cells was 8.7 μ g/ml, this dose reflects sensitivity of cervical cancer cells to nano gold.

Discussion

In the current experiment, the antiproliferative activity of AuNPs nanoparticles to human cervical cancer cells was investigated. Nanoparticles is considered an important drug delivery method for cervical Cancer treatment (22). Gold nanoparticles reported to have an anti-cervical cancer properties(23). The study results showed that AuNPs exposure to cancer cells cause significant cytotoxicity in most doses tested. Gold nanoparticles caused viability reduction in exposed cancer cells. It is reported that biosynthesized gold nanoparticles exposed to Hela cervical cancer cells cause DNA damage, G2/M arrest, and apoptotic cell death via caspase activation (23). Cell death cytological features of rounding and cell detachment as observed under the inverted microscope. Furthermore, generation of reactive oxygen species (ROS) is enhanced by gold nanoparticle treatment(10,24). Moreover, couple of studies (25,26) showed that 20nm gold nanoparticles decrease cancer cells growth mouse model. AuNPs may also use as delivery agents for phytochemicals such as Gallic acid or chemotherapeutic agents such as doxorubicin can be used as replacement for cervical cancer therapy to decrease radiotherapy and chemotherapy side effects (27, 28). Retinoic acid loaded on gold nanoparticle showed promising anti-cervical cancer effect (29). The IC₅₀ dose estimated was 8.713 μ g/ml in cervical carcinoma cells. Pharmacokinetic and bio-distribution investigation for AuNPs in tumor bearing animal model showed that gold nanoparticles have high stability when

conjugated with therapeutic agents and radiotherapeutic enhancement(30). Nanoparticles hold very promising activity against cervical cancer (31). Furthermore, cervical cancer and HPV need to find alternative treatments. Nanoparticles suggested promising in cervical cancer treatment by the capacity to target and internalize cancer cells(32). In conclusion, the present study proved that gold nanoparticles can be used for cervical cancer therapy.

Conclusion

Gold nanoparticles have anti-cervical carcinoma cells activity by cell death induction.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: The authors declare that they have no conflict of interest.

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References

1. Small Jr W, Bacon MA, Bajaj A, Chuang LT, Fisher BJ, Harkenrider MM, et al. Cervical cancer: a global health crisis. *Cancer*. 2017;123(13):2404-12.
2. Bruni L, Albero G, Serrano B, Mena M, Gómez D, Muñoz J, et al. ICO/IARC information centre on HPV and cancer (HPV information centre). Human papillomavirus and related diseases in the world Summary report. 2019.
3. Munoz N, Bosch FX, de Sanjose S, Herrero R, Castellsague X, Shah KV, et al. Epidemiologic classification of human papillomavirus types associated with cervical cancer. *N Engl J Med*. 2003;348(6):518-27.
4. Bruni L, Albero G, Serrano B, Mena M, Gómez D, Muñoz J, et al. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). Human Papillomavirus and Related Diseases in Iraq Summary Report. 2019.
5. Bourgioti C, Chatoupis K, Mouloupoulos LA. Current imaging strategies for the evaluation of uterine cervical cancer. *World journal of radiology*. 2016;8(4):342-54.
6. Alam S, Conway MJ, Chen H-S, Meyers C. The

- Cigarette Smoke Carcinogen Benzo[*a*]pyrene Enhances Human Papillomavirus Synthesis. *Journal of Virology*. 2008;82(2):1053-8.
7. Schiffman M, Clifford G, Buonaguro FM. Classification of weakly carcinogenic human papillomavirus types: addressing the limits of epidemiology at the borderline. *Infectious agents and cancer*. 2009;4(1):8.
 8. Tulay P, Serakinci N. The role of human papillomaviruses in cancer progression. *J Cancer Metastasis Treat*. 2016;2:201-13.
 9. Al-Shammari AM. Environmental pollutions associated to conflicts in Iraq and related health problems. *Reviews on Environmental Health* 2016. p. 245.
 10. Ali Z, Jabir M, Al-Shammari A. Gold Nanoparticles Inhibiting Proliferation of Human Breast Cancer Cell line. *Research journal of biotechnology*. 2019;14(S1):79- 82.
 11. Jabir MS, Taha AA, Sahib UI, Taqi ZJ, Al-Shammari AM, Salman AS. Novel of nano delivery system for Linalool loaded on gold nanoparticles conjugated with CALNN peptide for application in drug uptake and induction of cell death on breast cancer cell line. *Materials Science and Engineering: C*. 2019;94:949-64.
 12. Elshimali YI, Wu Y, Khaddour H, Wu Y, Gradinaru D, Sukhija H, et al. Optimization Of Cancer Treatment Through Overcoming Drug Resistance. *Journal of cancer research and oncobiology*. 2018;1(2):107.
 13. Sharma H, Kumar K, Choudhary C, Mishra PK, Vaidya B. Development and characterization of metal oxide nanoparticles for the delivery of anticancer drug. *Artificial Cells, Nanomedicine, and Biotechnology*. 2016;44(2):672-9.
 14. Al-Shammari AM, Zainal IG, Kachi W, editors. *Oncolytic Virotherapy and Cobalt Ferrite Nanoparticles as Breast Cancer Therapy*. MOLECULAR THERAPY; 2018: CELL PRESS 50 HAMPSHIRE ST, FLOOR 5, CAMBRIDGE, MA 02139 USA.
 15. Zainal IG, Al-Shammari AM, Kachi W. Characterization of the modified nickel-zinc ferrite nanoparticles coated with APTES by salinization reaction. *AIP Conference Proceedings*. 2018;1968(1):030008.
 16. Kachi W, Al-Shammari AM, Zainal IG, editors. Cobalt ferrite nanoparticles: Preparation, characterization and salinized with 3-aminopropyl triethoxysilane. *Energy Procedia*; 2019.
 17. Alsabari I, Thahab S, Al-Shammari A, Saadon B, Allebban Z. Nano-drug delivery system as a model for the treatment of breast cancer. *The Breast*. 2017;32:S28-S9.
 18. Al-Shammari AM, Alshami MA, Umran MA, Almukhtar AA, Yaseen NY, Raad K, et al. Establishment and characterization of a receptor-negative, hormone-nonresponsive breast cancer cell line from an Iraqi patient. *Breast Cancer : Targets and Therapy*. 2015;7:223-30.
 19. Al-Shammari AM, Al-Juboory A, Asmaa A, Ali AM, Al-Hili ZA, Yaseen NY, editors. Establishment and characterization of a chemoresistant glioblastoma cell line from an Iraqi patient. Abstract presented at the 105th Annual Meeting of the American Association for Cancer Research; 2014.
 20. Al-Hilli Z, Al-Shammari AM, Al-Jumaily EFA, Yaseen NY. The antiangiogenic effect of polyphenolic fraction of *Cyperus Rotundus L.* on human Glioblastoma cell line. First Scientific Conference on Nanotechnology, Advanced Material and Their applications, At: University of Technology; Baghdad, Iraq 2009. p. 168 - 80.
 21. Al-Shammari AM, Ismaeel FE, Salih SM, Yaseen NY. Live attenuated measles virus vaccine therapy for locally established malignant glioblastoma tumor cells. *Oncolytic Virother*. 2014;3:57-68.
 22. Ordikhani F, Erdem Arslan M, Marcelo R, Sahin I, Grigsby P, Schwarz JK, et al. Drug Delivery Approaches for the Treatment of Cervical Cancer. *Pharmaceutics*. 2016;8(3):23.
 23. Jeyaraj M, Arun R, Sathishkumar G, MubarakAli D, Rajesh M, Sivanandhan G, et al. An evidence on G2/M arrest, DNA damage and caspase mediated apoptotic effect of biosynthesized gold nanoparticles on human cervical carcinoma cells (HeLa). *Materials Research Bulletin*. 2014;52:15-24.
 24. Engelberth SA, Hempel N, Bergkvist M. Development of nanoscale approaches for ovarian cancer therapeutics and diagnostics. *Critical reviews in oncogenesis*. 2014;19(3-4):281-315.
 25. Arvizo RR, Miranda OR, Thompson MA, Pabelick CM, Bhattacharya R, Robertson JD, et al. Effect of nanoparticle surface charge at the plasma membrane

- and beyond. *Nano Lett.* 2010;10(7):2543-8.
26. Mukherjee P, Bhattacharya R, Wang P, Wang L, Basu S, Nagy JA, et al. Antiangiogenic properties of gold nanoparticles. *Clin Cancer Res.* 2005;11(9):3530-4.
 27. Tomoaia G, Horovitz O, Mocanu A, Nita A, Avram A, Racz CP, et al. Effects of doxorubicin mediated by gold nanoparticles and resveratrol in two human cervical tumor cell lines. *Colloids Surf B Biointerfaces.* 2015;135:726-34.
 28. Daduang J, Palasap A, Daduang S, Boonsiri P, Suwannalert P, Limpai boon T. Gallic acid enhancement of gold nanoparticle anticancer activity in cervical cancer cells. *Asian Pac J Cancer Prev.* 2015;16(1):169-74.
 29. Ye L, Song Q. Promising potency of retinoic acid-poly(ethylene glycol)-thiol gold nanoparticle conjugates for cervical cancer treatment. *International journal of clinical and experimental medicine.* 2015;8(7):10501-7.
 30. Geng F, Xing JZ, Chen J, Yang R, Hao Y, Song K, et al. Pegylated glucose gold nanoparticles for improved in-vivo bio-distribution and enhanced radiotherapy on cervical cancer. *Journal of biomedical nanotechnology.* 2014;10(7):1205-16.
 31. Zaman MS, Chauhan N, Yallapu MM, Gara RK, Maher DM, Kumari S, et al. Curcumin Nanoformulation for Cervical Cancer Treatment. *Scientific Reports.* 2016;6:20051.
 32. Medina-Alarcón KP, Voltan AR, Fonseca-Santos B, Moro IJ, de Oliveira Souza F, Chorilli M, et al. Highlights in nanocarriers for the treatment against cervical cancer. *Materials Science and Engineering: C.* 2017;80:748-59.

Bacteriological and Molecular Typing of Acne Vulgaris Etiology in the City of Baghdad

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Abstract

This study focuses and diagnosis bacteria involved in acne vulgaris . Method (culture, biochemical test, vitek 2 system, api 20 A, PCR) were used for isolation and identification. Results recorded that the most frequent etiological bacteria isolated anaerobically from acne patients was prevalence Propionibacterium acnes (40%), and the most common aerobic pathogen bacteria species were Staphylococcus epidermidis (27%), Staphylococcus aureus (24%) specific primer design for *recA* gene of *P. acne* confirmed and suggesting higher outbreak in the acne lesions with sever form, and the specific primers design for *mecA* gene of *S.epidermidis* were detected for methicillin resistant *Staphylococcus epidermidis* (MRSE) using target gene *mecA* confirmed and suggesting outbreak with mild form acne patients.

Keywords: *Acne vulgaris*, *P. acne*, *S. epidermidis*, *S.aureus*.

Introduction

Acne vulgaris is one of the most common dermatological disorders that afflict people in their adolescence. Many of the risk factors that may affect the occurrence of the disease, such as genetic factors, hormonal, stress, increased sebum secretion, abnormal pore different that cause local duct obstruction, bacterial biology of the local duct⁽¹⁾, anaerobic bacteria *Propionibacterium acnes* and *Staphylococcus epidermidis* plays an important role in causing acne^{(2),(3)}. Androgen secretion is the main cause of adolescent acne and other environmental factors. Conditions of stress and emotional disorders may aggravate acne⁽⁴⁾. There is significant evidence suggesting a possible pathogenesis acne vulgaris role for *Staphylococcus aureus* . This is in variance to some study which implicated both *S. epidermidis* and *P. acnes* as cause bacteria acne vulgaris⁽⁵⁾. The isolate microbial flora from patient of acne that appear possible to lead to pathogenesis acne includes: *P. acnes*, *S. epidermidis*, *S. aureus*^{(6),(7)}.

Materials and Method

One hundred discharging pus samples were taken from patients suffering from inflammatory acne skin condition with mild (29), moderate (50) and sever (21)

degree and include (48 males and 52 females) with ages (11-30) years by using a sterile cotton swab, during the first of February 2019 until the end of May 2019, from Al-Kindi Teaching Hospital/section of Dermatology,

Isolation and Identification of *P. acnes*: was done as described by ⁽⁸⁾, using blood (Oxoid, UK) and brucella agar media (Himedia, India), Gram stains, biochemical Tests and API 20A test (BioMerieux, France) ⁽⁹⁾ DNA was “extracted from broth samples by “employment of Genomic DNA” “Purification kit” (Promega, USA). Primers design for (*recA gene*) of *P. acne* were used” (forward, 5’-CTGTGCCTTTATTGACGCCG-) and” (reverse, 5’-CGCACCGGTCATCT-) (NCBI, Bioneer, Korea) expected products of amplification was (283bp), PCR “amplifications were carried” out in total reaction “volumes” of 20 ul containing Forward primer (1.5 ul) and Reverse primer (1.5 ul) D.W (12 ul) Template DNA (5ul). The “amplification” thermo “cycle parameters” condition were 5min at 95°C 30 cycles of 30 sec at 95°C, 30sec at 58°C, 30sec at 72°C 5min at 72°C .

Isolation and Identification of *S.epidermidis*: was done as described by ⁽¹⁰⁾, using blood (Oxoid, UK) agar media and. Culture Mannitol salt (Himedia, India), Gram stains, biochemical Tests: catalase, coagulase sensitive to the antibiotic novobiocin disk, Vitek 2

system(bioMérieux, France),DNA was “extracted from broth samples by “employment of Genomic DNA” “Purification kit” (Promega, USA).Primers design for(*mecA gene*)forisolateswere detected by Polymerase Chain Reaction (PCR) formethicillin resistant *Staphylococcus epidermidis*(MRSE) using target gene *mecAS. epidermidis*wereused”(forward,5' - A A A G G G C G T G G A A G T A A C G A -) and”(reverse,5'-TTT GAT GGC TTA TGCGCACG-) (NCBI,Bioneer,korea)expected products of amplification was216bp,PCR “amplifications were carried” out in total reaction “volumes” of 20 ulcontainingForward primer (1.5 ul) andReverse primer(1.5 ul)D.W(12 ul) Template DNA(5ul). The “amplification” thermo “cycle parameters” condition werewere5min at 95°C30cycles of 30 sec at 95°C,30sec at 60°C,30sec at 72°C5min at 72°C.

Isolation and Identification of *S.aureus*: was done as described by⁽¹¹⁾,using blood (Oxoid,UK) agar media andCulture Mannitol salt (Himedia, India),Gram stains,biochemical Tests:catalase, coagulase sensitive to the antibioticnovobiocin disk, Vitek 2 system (bioMérieux, France).

Results and Discussion

Results suggested the most frequent etiological agent isolated anaerobically bacteria from acne patients was *Propionibacterium acnes* (50%), and the most common aerobic pathogen bacteria species were *Staphylococcus epidermidis*(29%), *Staphylococcus aureus* (24%) as presumptive isolates.

Current data were in agreement with the study done in Iran by: ⁽¹²⁾showed a predominance of *P. acnes* (57%), followed by *S. epidermidis* (32%) and *S. aureus* (5%) and with the other study done in Cairo ⁽¹³⁾ showed *P.acne* (56%) cases and *S.epidermidis* (39%),*S. aureus* (14%),but with another results done in India ⁽⁶⁾ presented by cultured aerobic and anaerobic condition showed *P.acne* (66%), *S.aureus* (65%)and *S.epidermidis* (5%),

But another studies by ⁽¹⁴⁾ examined the species of bacteria aerobically and anaerobically isolated from 100 Korean acne patients. Among the bacteria isolated, *S. epidermidis* (36 patients) was the most common, followed by *P. acnes* (30 patients), dis agreement with a study from⁽¹⁵⁾inIndia found that the average of infection with *S. epidermidis* was (53%), *S. aureus*, and *P. acnes* were (41%), (33%) respectively,and in another results in Erbil city⁽¹⁷⁾ found *S.epidermidis* (27%), *P.acne* (13%), *S.aureus* (3.6%) and found 23 other types of bacteria .There is different results microbial profile in our study because the variations geographic location; diet, quality of the life, strains of bacteria, treatment used and others factor can be effect on the results ⁽¹⁶⁾.

*P.acne*colonies on BBA appeared as glistening, round and opaque with difference colors, included white, yellowish and gray. The colonies grew larger in size over time compare with young colonies (1-2) mm. Also, colonies with weak or no hemolysedwhen grow on BBA,Gram positive bacillus, pleomorphicand was appeared in different arranging. These results coincide as mentioned with pervious results in Iraq^{(18),(19)}.

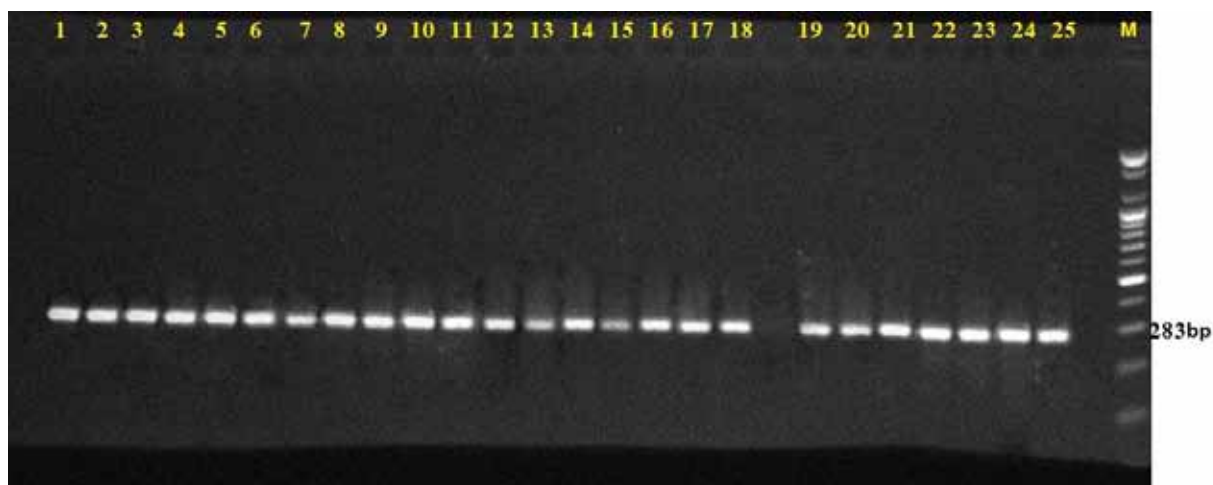


Figure (1): Agarose gel electrophoresis of PCR amplification produce for *Propionibacterium acnes*,expected products of amplification are 283bp (lanes 1-25: samples,lane M: marker 1000bp, 1% agrose gel and 70 Volt for 1 hr. in TBE buffers.

The presumptive *P. acnes* isolates showed positive results for indole, gelatin, catalase and negative results for esculin and urea. The results agreed with⁽²⁰⁾, 43% of *P. acnes* were confirmed according to API 20 A system carried out quickly and easily for the biochemical test identification of anaerobic bacteria. Our result as shown in figure (1) presents the PCR product electrophoresis on agarose gel (1%), PPA specific primer design for *recA* gene of *Propionibacterium acne* (283bp) (design by NCBI, Bioneer) were used to perform PCR. (40%) isolates were confirmed as *P. acnes*, suggesting higher outbreak in the acne lesions with severe form⁽²¹⁾. A study by⁽²²⁾, revealed that *p.acne* in samples was confirmed with aid of analysis of *recA* gene sequence. Genotype of *P. acnes* is *recA* (types I, II, and III) each of the *recA* genotypes has a characteristic phenotype and *recA* type I is dominant in isolates from acne vulgaris⁽²²⁾. Molecular method approach has been largely performed in several laboratories, due to its high sensitivity and specificity as well as rapid.

Colonies of *S. epidermidis* appeared white, opaque and smooth colony on blood agar media, by Gram stain showing Gram positive cocci, clusters, which often

in groups similar to grapes. Results agreed with⁽²³⁾. Positive results for catalase, coagulase negative, mannitol non fermenter and sensitive to the antibiotic novobiocin results agreed with⁽²⁴⁾.

The result of Vitek 2 system (bioMérieux) was used for confirmation of *S. epidermidis* isolates, the results showed that out of (29%) presumptive isolates (27%) of them were confirmed as *S. epidermidis* by Vitek-2 GP system and agreed with the study by⁽²⁵⁾. Our result as shown in figure (2) presents out of (29%) presumptive isolates, (27%) of them were positive for methicillin resistant *Staphylococcus epidermidis* MRSE target gene *mecA*, confirmed and suggesting outbreak with mild form acne patients⁽³⁾. The increasing antibiotic resistance confuses a great deal for the management of infections and shows that the isolation recurrence of methicillin resistant *S. epidermidis* (MRSE) can reach 80%⁽²⁶⁾ and the patterns of resistance of *S. epidermidis* to antimicrobial agents is essential for the diagnosis and directing infections^{(27),(28)}. Random overuse of antibiotics has led to the development of antibiotic-resistant strains which are occurring more frequently.

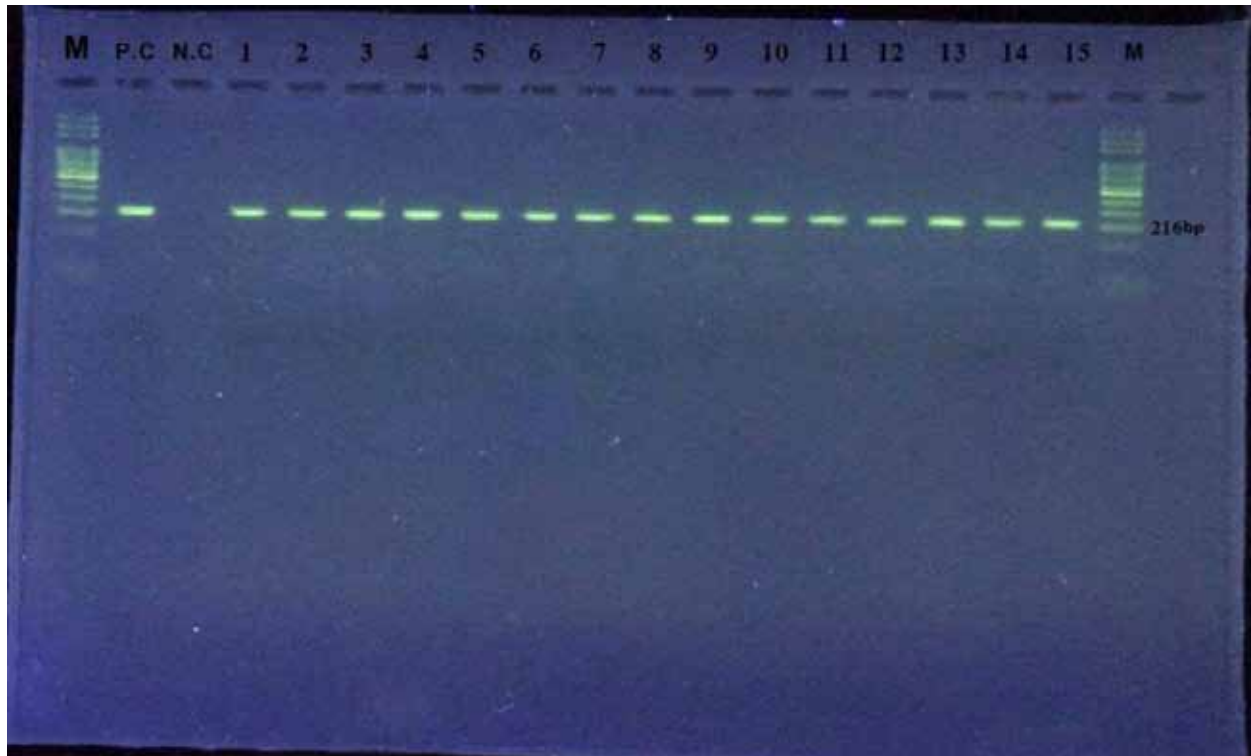


Figure (2): Agarose gel electrophoresis of PCR amplification products (*mecA*) *S. epidermidis*, expected amplification products are 216bp (lanes 1-15: samples, lane M: marker 1000bp, 1% agarose gel and 70 Volt for 1 hr. in TBE buffers).

Colonies *S.aureus* appeared smooth golden yellow, produce clearing zone surrounding their growth on blood agar media and by Gram stain showing Gram positive cocci under a microscope and forms grapes-like clusters, results was coincided as mentioned by⁽²⁹⁾. The results coagulase and catalase positive and mannitol salt agar fermenter yellow color and susceptible to novobiocin results was coincided with a study in⁽³⁰⁾ final identification was confirmed by vitek 2GP system (bioMérieux) with moderate acnes cases presented given highest *S.aureus* this result agree with the study⁽³¹⁾ was conducted to assess the new VITEK 2 system (bioMérieux) for identification and antibiotic susceptibility tests of gram-positive cocci. The GP card provide a speed and reliable identification of most species, whatever their origin

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

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References

1. Sitohang, I. B. S., Fathan, H., Effendi, E., & Wahid, M. The susceptibility of pathogens associated with acne vulgaris to antibiotics. *Medical Journal of Indonesia*, 2019;. 28(1), 21-7.
2. Dagnelie, M., Corvec, S., Mélanie, S., Valérie, B., Jean-Michel, N., Amir, K. and Brigitte D.. Decrease in Diversity of Propionibacterium acnes Phylotypes in Patients with Severe Acne on the Back. *Acta. Derm. Venereol.*, 2018; 98: 262–267.
3. Tabri, F., Massi, N., Sjahrir, R., Patellongi, I., Wahab, S., & Djawad, K.. Identification of Methicillin-Resistant Staphylococcus Epidermidis (MRSE) in Mild, Moderate and Severe Acne Patients. *American Journal of Clinical and Experimental Medicine*, 2017;. 5(1), 5-9.
4. Manarisip, C. K., Billy, J. K. and Sefty S. R. "HUBUNGAN STRES DENGAN KEJADIAN ACNE VULGARIS PADA MAHASISWA SEMESTER V (LIMA) PROGRAM STUDI ILMU KEPERAWATAN FAKULTAS KEDOKTERAN UNIVERSITAS SAM RATULANGI MANADO." *ejournal Keperawatan (e-Kep)*. 2015;. 3(1):1-6.
5. Khorvash F., Abdi F., Kashani H. H., Naeini F. F., and Narimani T. Staphylococcus aureus in Acne Pathogenesis: A Case-Control Study. *North American Journal of Medical Science*, 2012;. 4(11): 573–576.
6. Biswal, I., Gaiind, R., Kumar, N., Mohanty, S., Manchanda, V., Khunger N., Ramesh V., Manorama D. In vitro antimicrobial susceptibility patterns of Propionibacterium acnes isolated from patients with acne vulgaris. *J Infect Dev Ctries*; . 2016; 10(10):1140-1145.
7. Kumar, B., Pathak, R., Mary, P.B., Jha, D., Sardana, K., Gautam, H. K. New insights into acne pathogenesis: Exploring the role of acne-associated microbial populations. *Dermatologica sinica*, 2016;. 34(2), 67-73.
8. Patrick S. and McDowell A. The Actinobacteria, part B. Order XII Propionibacteriales ord. nov., p 1137–1155. In Goodfellow M, Kampf P, Busse H-J, Trujillo M, Suzuki K-I, Ludwig W, Whitman W (ed), *Bergey's manual of systematic bacteriology*, 2012;. 2nd ed, vol 5. Springer, New York, NY.
9. Versalovic, J.; Carroll, K.C.; Funke, G.; Jorgensen, J.H.; Landry, M.L. and Warnock D.W. *Manual of clinical Microbiology*. 10th Edition. American Society for Microbiology, Washington, D.C.; 2011.
10. Brooks, G. F., Butel, J. S. and Morse, S. A. *Medical Microbiology*. . 2007;. 24th ed. Mc Graw Hill company Inc.
11. Biswas, S., Karmakar, A., & Ghosh, C.. Multidrug resistant pathogenic Staphylococcus aureus in the pimples. *Medical Science*, 2015. 16(66), 41-50.
12. Zandi, S., Vares, B., Abdollahi, H. Determination of microbial agents of acne vulgaris and Propionibacterium acnes antibiotic resistance in patients referred to dermatology clinics in Kerman, Iran. *Jundishapur. J. Microbiol.*, 2011 . 4: 17-22.
13. El-Tonsy, T. M. K., Mohammed, M. A., Hamed, Y.A. & Tawfik, S. H. Bacteriological study of Acne Vulgaris in Cairo Egypt. *Egyptian Journal of Hospital Medicine*, 2018. 72(9):3-9.
14. Sang, H. M., Hyun S. R., Young H. K. Jeong E.K., Joo Y. K., Young S. R. Antibiotic resistance of microbial strains isolated from Korean acne patients. *The Journal of Dermatology*. 2012, 39(10); 833-837.
15. Hassanzadeh, P., Bahmani, M., Mehrabani, D. Bacterial resistance to antibiotics in acne vulgaris:

- an in vitro study. *Indian J Dermatol*;(2008), 53(3):122-4.
16. Yousif, N. I. M. and Dabbagh, R. A. Isolation and identification of microorganisms in acne patients. *Zanco J. Med. Sci.*,2016. 20 (2):1330-1336.
 17. Hassan, I. A., Hassan, M. A., Embarek, M. S., Attallah D. A., El Mokhtar, M. A., Alaa Eldin G. M. Antibiotic Susceptibility Patterns of *Propionibacterium Acnes* Isolated from Acne Vulgaris in Assiut University Hospitals, Egypt. *Egyptian Journal of Medical Microbiology*,2015. 24 (4); 67-72.
 18. Holland C.. Proteomic identification of secreted proteins of *Propionibacterium acnes*. *BMC Microbiology* 2010.10: 230.
 19. Patrick S. and McDowell A.. The Actinobacteria, part B. Order XII *Propionibacteriales* ord. nov., p 1137–1155. In Goodfellow M, Kampf P, Busse H-J, Trujillo M, Suzuki K-I, Ludwig W, Whitman W (ed), *Bergey's manual of systematic bacteriology*,2012, 2nd ed, vol 5. Springer, New York, NY.
 20. Naghdi, N. and Ghane, M.. Identification of the *Propionibacterium acnes* using Polymerase Chain Reaction (PCR) in the Acne vulgaris lesions. *Molecular and Biochemical Diagnosis (Journal)* 2014,1(3): 205-212.
 21. Rollason J., McDowell A., Albert H.B., Barnard E., Worthington T., Hilton A.C., Vernallis A., Patricks S., Elliott T., Lambert P. Genotyping and antimicrobial characterization of *Propionibacterium Acnes* isolates from surgically excised lumbar disc herniations. *BioMed Research International*. 2013,1-7.
 22. Bruggemann, H., Lomholt, H.B., Tettelin, H., Kilian, M.. CRISPR/cas loci. (of type II *Propionibacterium acnes* confer immunity against acquisition of mobile elements present in type I P. acnes. *PLoS One*. 2012;7(3):e34171.
 23. Flayyih, M. T. and Abd rabaa M. K. Isolation, identification and treatment of Vancomycin-Resistant *Staphylococcus epidermidis*. *Iraqi Journal of Science*, .2015, 56, (1C): 701-707.
 24. Nguyen, Thuan H., Matthew D. Park, and Michael Otto.. “Host Response to *Staphylococcus Epidermidis* Colonization and Infections.” *Frontiers in Cellular and Infection Microbiology*2017, (1-7).
 25. Bobenchik, A. M., Hindler, J. A., Giltner, C. L., Saeki, S., Humphries R. M. Performance of Vitek 2 for Antimicrobial Susceptibility Testing of *Staphylococcus* spp. and *Enterococcus* spp. *Journal of Clinical Microbiology*,2014,52(2); 392–397.
 26. Watanabe, K., Nakaminami, H., Azuma, C., Tanaka, I., Nakase, K., Matsunaga, N. .Methicillin-Resistant *Staphylococcus Epidermidis* Is Part Of The Skin Flora On The Hands Of Both Healthy Individuals And Hospital Workers. *Biol Pharm Bull.*;2016, 39: 1868-75.
 27. Iorio, N.L.P., Azevedo M.B., Frazão V.H., Barcellos A.G., Barros E.M. Pereira EM, . Methicillin-Resistant *Staphylococcus Epidermidis* Carrying Biofilm Formation Genes: Detection Of Clinical Isolates By Multiplex PCR. *Int Microbiol.*;2011, 14 13-7.
 28. Nakase, K., Nakaminami H, Takenaka Y, Hayashi N, Kawashima M, Noguchi N. Relationship Between The Severity Of Acne Vulgaris And Antimicrobial Resistance Of Bacteria Isolated From Acne Lesions In A Hospital In Japan. *Journal of Medical Microbiology*;. 2014, 63: 721-8.
 29. Delost, G.R., Delost, M.E., Armile, J. and Lloyd, J. *Staphylococcus aureus* carriage rates and antibiotic resistance patterns in patients with acne vulgaris. *J Am Acad Dermatol* .2016.;74(4):673-8.
 30. Adetutu, A. A., Oritsewehinmi B., Ikhiwili O. M., Moradeke A. O., Odochi A. S. and Adeola O. E. Studies on *Staphylococcus aureus* isolated from pimples. *Pak. J. Biol. Sci.*,2017. 20(7): 350-354.
 31. Delmas, J., Chacornac, J. P., Robin, F., Giammarinaro, P., Talon, R., & Bonnet, R. Evaluation of the Vitek 2 system with a variety of *Staphylococcus* species. *Journal of clinical microbiology*,. 2008, 46(1), 311-313.

Determination of the Best Level of Cognition for Category-10 Table-Tennis Athletes with Special Needs

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Abstract

The research addressed the importance of cognitive abilities in the field of physical education in general and table tennis in particular. The aim of the current research was to identify the best level of cognitive abilities for category-10 table-tennis athletes with special needs (C-10-TTASN), hence the importance of the research was to increase the knowledge and provide the sport science literature with valuable information about the C-10-TTASNs through research in the psychological areas of different levels in this class and the search for the role of the psychological aspect in this level. There are significant differences between the psychological profiles of the three categories (high, medium, and weak) which have effects on the classification of C-10-TTASNs. The research methodology and field procedures were also included. The descriptive methodology was used involving three players from the Iraqi national team. The results showed that there was a variation in the level of the profile between the three players according to the ten levels. The profile of the first player was better than that for the other players. The profile of the second player was better than that for the third player.

Keywords: Cognition, Reha Com.

Introduction

The game of ping-pong was originated in 1890 emanating from the game of tennis, which was then widespread in England and France, and was practiced at home using different types of rackets and balls made of cork and wood. It was also played on the dining tables and was called using the name (ping pong) because of the sound of the ball while hitting the surface of the table. Then, the game had spread in Europe gradually⁽¹⁻³⁾.

Table tennis is one of the most famous games among the players with special needs who can compete with the healthy ones. The game requires a high degree of vigilance and attention by the player's commitment and control to return the light ball to the opponent and requires a large degree of reactions by making quick decisions as required by the game⁽⁴⁻⁶⁾. The psychological factors associated with sport training and competitions clearly affect the individual's sport level and have not received adequate attention from scientists or trainers until very recently, and there are still many psychological problems associated with sport

activity that urgently needs to be addressed by research. It has been referred to the psychological profile as a set of tests representing psychological dimensions or knowledge and skills of that determines the strength and weakness of an individual and is in the form of graphic representation. The profile is an important model in the field of evaluation of psychological preparation for the competition and aims to help the player to identify the strength and weakness in a range of factors related to performance in the sport competition. The players with special needs are the group of athletes that were not adequately highlighted through research conducted despite the advanced results they have achieved in local and international competitions, which sometimes, outperforming the results of the healthy peers^(7,8).

The aim of the current research was to identify the best level of cognitive abilities for category-10 table-tennis athletes with special needs (C-10-TTASN) by identifying the differences between psychological profiles and their impact on the classification of players for three levels (high, medium, and weak). There are significant differences between the psychological

profiles of the three categories (high, medium, and weak) that have effects on the classification of category-10 table-tennis athletes with special needs (C-10-TTASN).

Materials and Method

Sample Players: The research sample was selected, which includes 10 players from category-10 table-tennis athletes with special needs (C-10-TTASN) of the Iraq national team, and three players were chosen in a deliberate manner representing the strong, medium, and weak levels according to their classification in the last tournament that took place.

Experimental Design: The researcher used the descriptive method of case study and comparisons to address the research problem.

Tests:

Vigilance Test: The technical aspects associated with the nature of this game requires a high degree of alertness and concentration of attention of the player, so the researchers conducted the vigilance test after a direct look at the RehaCom system, <https://www.rehacom.com/what-is-rehacom.html>. Through the use of the sources of the test and conducting personal interviews and direct inquiry, it was easy conducting and identifying accurately the accredited results of the test.

This test has an advantage over the paper and pen tests in obtaining objective results as it is characterized by high credibility as the system RehaCom is a global and codified system, as well as ensures us to save effort through computerized automated presentation.

Test form:

The reaction time in vigilance is checked under two circumstances: First: In order to measure the intrinsic alertness to maintain the response for as a long period of time as possible, a geometric shape appears at a fixed location that changes randomly within short intervals. The task of the subject is to react as quickly as possible to the shape that was changed by pressing the required keyboard button

Second: In order to measure the phasic alertness (short-term attention concentration), the figure appears on the screen at a fixed location that before changing at a random interval, a warning signal is heard.

Method of Application: The test begins with

a message on the screen in case the reaction is early, before the appearance of the shape and before changing it randomly, and the exercise phase does not end unless the reactions are correct in all attempts to exercise, and the performance of the test in two parts and called simple design ABBA as follows:

- Try without a beeping sound
- Try with audio signal
- Try with audio signal
- Try without a beeping sound

In the first stage of the test, the response time of the subject is measured in a simple click of a full square on the screen. In the second stage, the response time of the same visual alarm is measured upon hearing the sound of the signal before the square appears. The subject hits the right keyboard key upon hearing the audio signal and before the box fully appears.

The duration of the test: The test took a maximum of six minutes excluding the exercise phase.

Statistical Analysis: In the analysis of the results two types of z-value are calculated as shown in the following:

- An alert value for mental alertness (without sound signal) by averaging all reactions without the sound signal (intrinsic alertness).
- An alert value for mental alertness (sound signal) by calculating the average of all reactions by the sound signal (phasic alertness).

The mental alertness test also measures the following data:

- Measuring the average reaction time and speed process, as it is considered that the slowdown in performance below the normal level (z-value 2-, 3-) may be due to mental stress.
- The level of performance is measured from changes in reaction time, as well as the high degree of standard deviation (SD) indicates a low level of normal excitement status of the subject.
- Delay in response and prolonged reaction refer to the speed of mental stress in the subject, which reduces active mental responses.

A Chi-square test was used to differentiate between each two players (first and second), (first and third), and

(second and third). To determine the validity of the results, the distance between each of the two players was obtained by subtracting the raw values between the tree comparisons.

Results

Mental Alertness:

Without the Sound Signal: The results of the mental alertness without the sound signal are shown in table (1).

Table 1: The results of the mental alertness without the sound signal.

Player	Response	Response time	Response SD	Z-value	Significance
1	332	334	32	31	0
2	275	256	55	13	0
3	286	279	56	12	0
Significance level	0.046	0.004	0.021	0.002	0
Chi sq. value	6.143	11.09	7.688	12.25	0

Table 2: The results of the mental alertness distances between players without the sound signal.

Variables	Comparisons	Distances	Chi sq	Freedom degrees	Significance level
Response	First and second	57	5.352554	1	0.020692
	First and third	46	3.423948	1	0.064257
	Second and third	-11	0.215686	1	0.642347
Response time	First and second	78	10.31186	1	0.001322
	First and third	55	4.934747	1	0.026322
	Second and third	-23	0.988785	1	0.32004
Response SD	First and second	-23	6.08046	1	0.013669
	First and third	-24	6.545455	1	0.010515
	Second and third	-1	0.009009	1	0.924382
Z-value	First and second	18	7.55814	1	0.005974
	First and third	19	27.4	1	0.00000165
	Second and third	1	8.227273	1	0.004127

In table (1), we find that the results of the three players are significant and for all variables, so there are differences between the players, and for the purpose of identifying the order of players, Chi-square value was calculated for each two players as in tables, and the results found that player 1 is the best.

In table (2), we show the distances between the players to indicate the best parameters of each one of them and via the results of the Chi-square test, as the distance between the first and second player in the reaction variable was (57) which is greater than the that from the comparisons, first and third and the second and third, (46) and (-11), respectively, and thus the preference is for the first player.

In the case of reaction time, the distance between the first and second player was the largest (78); however, the distances of the comparisons, first and third and the second and third, (55) and (-23), respectively. According to that, the preference was for the first player.

As for the SD of the reaction variable, the distance between the first and second players was (-23). The preference is for the first player because it has less SD than that from the second player. The distances between the first and third players was (-24), and between the second and third was (-1).

With the sound signal:

Table 3: The results of the mental alertness with the sound signal.

Player	Response	Response time	Response SD	Z-value	Significance
1	343	333	34	92	0
2	292	288	73	44	0
3	253	246	41	36	0
Significance Level	0.001	0.001	0.000156	0.000000113	0
Chi sq. value	13.76	13.1	17.52703	32	0

Table 4: The results of the mental alertness distances between players with the sound signal.

Variables	Comparisons	Distances	Chi sq	Freedom degrees	Significance level
Response	First and second	51	6.916	1	0.008542
	First and third	90	19.63	1	0.00000937
	Second and third	39	15.15	1	0.0000992
Response time	First and second	45	6.544	1	0.010524
	First and third	87	17.97	1	0.0000225
	Second and third	42	15.03	1	0.000106
Response SD	First and second	-39	14.21	1	0.000163
	First and third	-7	0.653	1	0.418923
	Second and third	32	8.982	1	0.002726
Z-value	First and second	48	16.94	1	0.0000386
	First and third	56	67.4	1	1.63E-16
	Second and third	8	18.5	1	0.000017

In Table (3), we find that the results of the three players are significant and for all variables, so there are differences between the players, and for the purpose of identifying the order of players, Chi-square value was calculated for each two players as in tables, and the results found that player 1 is the best.

In table (4), we show the distances between the players to indicate the best parameters of each one of them and via the results of the Chi-square test, as the distance between the first and second player in the reaction variable was (51) which is greater than the that from the comparisons, first and third and the second and third, (90) and (39), respectively, and thus the preference is for the first player.

In the case of reaction time, the distance between the first and second player was the largest (45); however, the distances of the comparisons, first and third and the second and third, (87) and (42), respectively. According to that, the preference was for the first player.

As for the SD of the reaction variable, the distance between the first and second players was (-39). The

preference is for the first player because it has less SD than that from the second player. The distances between the first and third players was (-7), and between the second and third was (32).

Discussion

The results revealed that the reaction variable played a big role in the psychological aspect as it is the basis of alertness and through which a player is prepared for the game. It turns out that the player who was attentive had a high reaction that enables him to make a quick and correct decision. In addition, the right alertness also allowed him to take the right position that enabled the player to respond to the action of the opponent (computer, here), and this is similar to the real life of performing the table-tennis game. It is not possible to get the best playing performance without a high-speed reaction because of the small playing field and the high-speed moving ball which requires high alertness using different senses especially eyesight that induces eye nerve-brain stimulation and responses. The response after brain-analyzing the image may not exceed one

second. This response and its time are determined according to the level of alertness^(9,10).

Hence, the psychological model that should be chosen for table tennis players must be a level of vigilance which is up to a rate of more than 332 (milliseconds) to match the conditions of the game, as one of the most important requirements of the table-tennis player is to be characterized by a high reaction for obtaining the best game scores. This is due to the high-speed optical stimuli that occurs in a small field, three meter, with the high-speed, 100km/hr, moving ball, and this is why a table-tennis player must have high degree of alertness^(11–15).

Conclusion

There are variations in the levels of alertness among the three players according to the ten levels. The profile of the first player is better than that from the other players. Moreover, the profile of the second player is better than that from the third player.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq.

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References

1. Biernat E, Buchholtz S, Krzepota J. Eye on the Ball: Table Tennis as a Pro-Health Form of Leisure-Time Physical Activity. *Int J Environ Res Public Health* [Internet]. 2018 [cited 2019 Aug 26];15(4). Available from: <http://www.ncbi.nlm.nih.gov/pubmed/29649160>
2. Liu Y-C, Wang M-Y, Hsu C-Y. Competition Field Perceptions of Table-tennis Athletes and their Performance. *J Hum Kinet* [Internet]. 2018 Mar [cited 2019 Aug 26];61:241–7. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/29599876>
3. Kondrič M, Zagatto AM, Sekulić D. The Physiological Demands of Table Tennis: A Review. *J Sports Sci Med* [Internet]. 2013 [cited 2019 Aug 26];12(3):362. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3772576/>
4. Milioni F, Leite JV de M, Beneke R, de Poli RAB, Papoti M, Zagatto AM. Table tennis playing styles require specific energy systems demands. *PLoS One* [Internet]. 2018 [cited 2019 Aug 26];13(7):e0199985. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/30020946>
5. Leite JV de M, Barbieri FA, Miyagi W, Malta E de S, Zagatto AM. Influence of Game Evolution and the Phase of Competition on Temporal Game Structure in High-Level Table Tennis Tournaments. *J Hum Kinet* [Internet]. 2017 Jan 1 [cited 2019 Aug 26];55:55–63. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/28210338>
6. Van Biesen D, Mactavish J, Kerremans J, Vanlandewijck YC. Cognitive Predictors of Performance in Well-Trained Table Tennis Players With Intellectual Disability. *Adapt Phys Act Q* [Internet]. 2016 Oct [cited 2019 Aug 26];33(4):324–37. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/27874301>
7. Liu W, Zhou C, Ji L, Watson JC, II. The Effect of Goal Setting Difficulty on Serving Success in Table Tennis and the Mediating Mechanism of Self-regulation. *J Hum Kinet* [Internet]. 2012 Jun [cited 2019 Aug 26];33:173–85. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/23487526>
8. Lim T-H, Jang C-Y, O'Sullivan D, Oh H. Applications of psychological skills training for Paralympic table tennis athletes. *J Exerc Rehabil* [Internet]. 2018 Jun [cited 2019 Aug 26];14(3):367–74. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/30018920>
9. Wolf S, Brölz E, Scholz D, Ramos-Murguialday A, Keune PM, Hautzinger M, et al. Winning the game: brain processes in expert, young elite and amateur table tennis players. *Front Behav Neurosci* [Internet]. 2014 [cited 2019 Aug 26];8:370. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/25386126>
10. Guo Z, Li A, Yu L. "Neural Efficiency " of Athletes' Brain during Visuo-Spatial Task: An fMRI Study on Table Tennis Players. *Front Behav Neurosci* [Internet]. 2017 [cited 2019 Aug 26];11:72. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/28491026>
11. Hung C-H. A Study of Automatic and Real-Time Table Tennis Fault Serve Detection System. *Sport (Basel, Switzerland)* [Internet]. 2018 Nov 28 [cited 2019 Aug 26];6(4). Available from: <http://www.ncbi.nlm.nih.gov/pubmed/30487405>

12. Santos DPR, Barbosa RN, Vieira LHP, Santiago PRP, Zagatto AM, Gomes MM. Training Level Does Not Affect Auditory Perception of The Magnitude of Ball Spin in Table Tennis. *J Hum Kinet* [Internet]. 2017 Jan 1 [cited 2019 Aug 26];55:19–27. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/28210335>
13. Inaba Y, Tamaki S, Ikebukuro H, Yamada K, Ozaki H, Yoshida K. Effect of Changing Table Tennis Ball Material from Celluloid to Plastic on the Post-Collision Ball Trajectory. *J Hum Kinet* [Internet]. 2017 Jan 1 [cited 2019 Aug 26];55:29–38. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/28210336>
14. Wang M, Fu L, Gu Y, Mei Q, Fu F, Fernandez J. Comparative Study of Kinematics and Muscle Activity Between Elite and Amateur Table Tennis Players During Topspin Loop Against Backspin Movements. *J Hum Kinet* [Internet]. 2018 Sep [cited 2019 Aug 26];64:25–33. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/30429896>
15. Iino Y, Kojima T. Kinematics of table tennis topspin forehands: effects of performance level and ball spin. *J Sports Sci* [Internet]. 2009 Oct [cited 2019 Aug 26];27(12):1311–21. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/19746298>

Role of VAC a and CAG a Genes in Detection and Identification of Helicobacter Pylori

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Abstract

A total of (130) samples of stomach ulcer were collected from patients suffering from peptic ulcer who visited three different hospitals in Baghdad. The results showed that after bacterial culturing on the MacConkey agar and Columbia agar and selective media of *Helicobacter Pylori* bacteria under (5% O₂, 10% CO₂, and 85% N₂), detected that 45 isolate were belong *Helicobacter pylori* that represent (35%). After testing the sensitivity test against *Helicobacter pylori* against 10 antibiotics, the sensitivity test for 10 antibiotics demonstrated the efficacy of the antibiotic cephotoxim and rifampicin in the elimination of the bacteria. The resistance ratio was 10%. The tetracycline and duxacycline antibiotic were 10% 20% and were resistant to erythromycin and chlarthromycin 30%, while the resistance to amoxicillin was 100% and the resistance ratio was 80% for both metronidazole and sprofluxacin, while gentamycin had a resistance ratio of 50%.

Keywords: *Helicobacter pylori*, PCR, 16SrRNA.

Introduction

Helicobacter pylori infection, a highly prevalent pathogen, is a major cause of chronic gastritis and peptic ulcer and a risk factor for gastric malignancies, antibiotics-based *Helicobacter pylori* eradication treatment is 90% effective, however, it is expensive and causes side effects and antibiotic resistance⁽¹⁾. Wounds of stomach related framework is considered as the most famous infections around the world, which are identified with poor nourishment, thriving and sanitation conditions and additionally hereditary and natural effects. Ulcers as irresistible maladies, which taint stomach related framework, had been found by⁽²⁾ and viewed as another period with respect to the ideas and treatment of gastro duodenal. It was observed that *Helicobacter pylori* to be the fundamental driver of gastritis, peptic ulcers and gastric disease. *Helicobacter pylori* is considered as an effective pathogenic bacterium that instigates gastritis in all discovered tainted patients and perceived as class-I cancer-causing agent that especially colonizes the gastric epithelial cells of human⁽³⁾. The contamination caused by *Helicobacter pylori* is typically happen in the early youth and continues long lasting if not treated with antimicrobial operators⁽⁴⁾. *Helicobacter pylori* is a standout amongst the most well-

known bacterial pathogens that taints human around the world⁽⁵⁾. Two of the virulence factors that have been implicated in this process are cytotoxin-associated gene A (*CagA*) and vacuolating cytotoxin A (*VacA*), which are cytotoxins that are injected and secreted by *Helicobacter pylori*, respectively. Both of these virulence factors are polymorphic and affect a multitude of host cellular pathways. These combined facts could easily contribute to differences in disease severity across the population as various *CagA* and *VacA* alleles differentially target some pathways⁽⁶⁾.

Materials and Method

Stomach Ulcer Sample Collection: A total of 130 stomach ulcer biopsy samples from male and female were collected for survey from (May 2017 to May 2018) from different hospitals in Baghdad governorate, Alkadimya Hospital, Center of Digestive Tract and Liver disease, Alyarmoq Hospital. Age of patient range from (19-73) year. All samples were placed in separate sterile cotton swab with transport media to prevent contamination and were immediately transported to the laboratory in a cool box with ice packs, and transported to the laboratory within 30 minutes of collection.

Identification of Helicobacter Pylori: Microscopic Examination of *Helicobacter pylori*:

A loopfull of *Helicobacter pylori* isolates was fixed on a microscopic slide, then stained by gram stain to examine cells shape, grouping, reaction and non-spore forming⁽⁷⁾.

Cultural Characteristic of Helicobacter pylori isolates: In order to isolate *Helicobacter pylori* from samples that may contain different varieties of bacteria, selective media should be used to inhibit the growth of the more rapidly growing components of the enteric bacterial flora because *Helicobacter pylori* isolates multiply much more slowly than other enteric bacteria⁽⁸⁾.

Biochemical Tests of Helicobacter pylori isolates: One presumptive *Helicobacter pylori* colony from each selective agar plate was sub cultured and tested by standard microbiological and biochemical procedures, differentiated at species level by Gram stain, oxidase and catalase test, hydrogen sulfide production and susceptibility to nalidixic acid by using a commercially available species differentiation kit API CAMPY (bioMérieux, Marcy-'Etoile, France).

Api CAMPI Identification for Helicobacter pylori Isolates: Identification was carried out by sub culturing of selected colonies grown on selective medium agar (Columbia agar with supplement) into CAMPI microtubes gallery. This system is designed for the performance of more than 20 standard biochemical tests from a single colony grown on plating medium. Inoculation of the galleries was done with sterile pasture pipette and five ml of tap water dispensed into tray provide a humid atmosphere then incubated under micro aerophilic condition for 24 hr. After that reagent added for reading the galleries, each positive reaction was given a value 1,2 or 4 according to the position of the test in its group, so a value from 0 to 7 digit observed was then looked up in the index and the identification is determined .

Sensitivity of Helicobacter pylori to Antibiotic: Ten ml of nutrient broth were inoculated by each

bacterial isolate, then incubated under micro aerophilic condition for 24 hr. to log phase (OD₆₀₀ about 0.35) giving (1*10⁸) cell/ml of broth. After that, 0.1 ml of the inoculated broth was transferred and spread by sterile cotton swab on Muller-Hinton agar plates surface in three different planes (by rotating the plate approximately 60° each time to obtain an even distribution of the inoculums). The inoculated plates were then placed at room temperature for 30 minutes to allow absorption of excess moisture. With a sterile forceps the selected antibiotic disks were placed on the inoculated plates and incubated under micro aerophilic condition for 18 hr in an inverted position. After incubation, the diameter of inhibition zones was measured by a ruler (mm). Results were determined and compared according to the National Committee for Laboratory Standards⁽⁹⁾. Also, DNA Extraction of *Helicobacter pylori* isolates explain in details in⁽¹⁰⁾.

PCR of genes targeted a 16SrRNA and virulence genes (CagA & VacA): The DNA from all isolates was amplified by PCR as a control for DNA extraction *Helicobacter pylori* species confirmation by analysis of the 16SrRNA and (Cag & Vac) genes, Amplification of these genes were carried out in a master mix volume of 25ul containing (5ul Taq PCR Premix G _SPIN kit) and 10 picomols/μ(1ul) Forward primer and 10 picomols/μ(1ul) Reverse primer DNA (1.5μl), Distill water (16.5μl) table(1). The primers were lyophilized, they were dissolved in the free ddH₂O to give a final concentration of 100 pmol/μl as stock solution and keep a stock at -20.

Analyses Sequence of *Helicobacter pylori* isolates were done, the 1500bp fragment of 10 isolates of *Helicobacter pylori* 16SrRNA gene was sequenced. Sequence alignment using Blast and Bio edit was used to sequence and the results were compared with data obtained from gene bank which is available at NCBI online .as in table(1) show the optimum condition of detection (16SrRNA genes) and Cag and Vac of *Helicobacter pylori*.

Table 1: The specific primer of genes (16SrRNA) and virulence factor of Helicobacter pylori

Gene	Primer	Sequence	Tm (°C)	GC (%)	Product size
16Srna	Forward	5'-TTG ATC CTG GCT CAG AGT-3	52.8	50.0%	1500bp
	Reverse	5'-TTC ACC CCA GTC GCT GAT-3	54.6	43.2%	
Cag	Forward	5'-CCTTGTGATGCAAGCAAT-'3	52.2	47.4%	370 bp
	Reverse	5'- AACTCCATTTGCTTTCTG-'3	50.6	2.1%	
Vac	Forward	5'-CAGAAAGCAAATGGAGTGTT-'3	51.1	40.0%	620 bp
	Reverse	5'-AGCTAAAAGCGGTGGAGTAT-'3	53.7	45.0%	

Results and Discussion

Isolation and Identification of Helicobacter pylori: One hundred and thirty stomach ulcers samples, chronic gastritis ulcer, duodenal, duodenitis, gastric cancer were collected from patients suffering from symptoms referred as stomach ulcers infection, of whom 46 were female and 84 male were (15-73) years old. After the patients were subjected to a periscope examination, the prevalence of chronic gastric inflammation was observed at 36%, the stomach ulcer observed by 29%, while the duodenal ulcer, duodenitis appeared at 14.5%, 12.5% respectively and the percentage of gastric cancer appear as 4.5%, as shown in table (2).

Table 2: Clinical cases that included in the specimen collection for identification of Helicobacter pylori

No.	Clinical cases	No.	Percentage %
1	gastritisChronic	47	36%
2	Gastric ulcer	38	29%
3	Duodenal ulcer	19	14.5%
4	Duodenitis	16	12.5%
5	Gastric cancer	6	4.5%
6	Normal Case	4	3%
	Total no.	130	100%

Identification of Helicobacter pylori: The forty five isolation was diagnosed based on the tests used for this purpose, which is the form of colonies, the color of a grams stain, the urease enzyme test and the enzyme test, oxidase and catalase and motility test and obtained (20) isolates were subjected to other tests as well as previous tests, which included test the growth at 25°C and 42°C and the sensitivity test of the antibiotics cephalotoxin and nalidixic acid. CAMPY test and molecular diagnosis were made to 10 isolates of pathogenic bacteria.

Cultural Characteristics of Helicobacter pylori: *Helicobacter pylori* bacteria colonies appeared after the incubation period (3-4 days) in low-air conditions (5% O₂, 10% CO₂, and 85% N₂) at 37°C; small, circular convex in diameter (2-1ml), looks like to a drop of water or grey. That is, the form of colonies corresponds to the diagnostic description of the bacteria^(11, 12).

Biochemical test of Helicobacter pylori: Several biochemical tests were done for characterize

Helicobacter pylori which can be summarized as urease, oxidase, catalase, motility tests. All 20 isolates gave gram negativesmall convex circle pale in color, motile and urease, oxidase, catalase positive result.

Sensitivity Test of Helicobacter pylori for antibiotics: The emergence of prevalence of antibiotic resistance strain is considered as a major therapeutic problem that could be explained by several hypothesis such as, the influence of excessive and/or in appropriate antibiotic use⁽¹³⁾, transmission of resistant isolates, among people, consumption of food from animals that had received antibiotics, and greater mobility of individual worldwide have also contributed to the extension of antibiotic resistance⁽¹⁴⁾. The results indicated that the local isolation of the *Helicobacter pylori* was 100% resistant for amoxicillin and 10% for antibiotics, rifampicin and cephotaxim, and 20% resistance to tetracyclin and doxycycline, six isolates resistant to erthromycin and clarthromycin 30%

resistance, antibiotic resistance ratio gantamycin is 50%, and the resistance to ciprofloxacin is equal to 80%. Moreover, results indicated in table (3) show the frequency of resistance *Helicobacter pylori* isolates to used antibiotics.

Table 3: Frequency of antibiotic resistance of *Helicobacter pylori* isolates.

Antibiotic	Symbol	Resistant isolates	
		Number	Percentage (%)
–β-lactam penicillin			
Amoxicillin	AMX	20	100%
–Cephalosporins			
Cephotaxim	CTX	2	10%
– Aminoglycosides			
Gentamycin	GM	9	50%
– Tetracyclines			
Tetracycline	TE	4	20%
– Quinolons			
Ciprofloxacin	CIP	16	80%
– Others			
Metroidazole	MT	16	80%
Clarthromycin	CLR	6	30%
Rifampcin	RA	2	10%
Arythromycin	E	6	30%
Ducoxy cycline	Do	4	20%

CAMPI Api for characterization of *Helicobacter pylori*: During incubation (in microaerobic conditions), metabolism produces color changes that are either spontaneous or revealed by the addition of reagents. The second part of the strip (assimilation or inhibition tests) is inoculated with a minimal medium and incubated in micro aerophilic conditions. The bacteria grow if they are capable of utilizing the corresponding substrate or if they are resistant to the antibiotic tested. The reactions are read according to the Reading Table. The identification software can also be used⁽¹⁵⁾.

Detection of 16SrRNA, Cag A, VacA genes: Ten *Helicobacter pylori* isolates from current study were subjected to molecular analysis by PCR for confirmation of the microbiology results, we used PCR to detect the presence or absence of *16srRNA* and virulence-associated genes in the *Helicobacter pylori* isolates however this technique does not evaluate gene function, and does not give information about expression levels, nor does it describe deletions or insertions in the gene sequence, all of which may contribute to virulence that associated with clinical signs patient who sever from stomach ulcer. Primers were used in current study target to amplify the

(*16SrRNA*) *16srRNA* gene was the first genes tested in current study for diagnosis of *Helicobacter pylori* isolate because it has considerable length (1,500bp), and it is ubiquitous in members of the *Helicobacter pylori*⁽¹⁶⁾, and has been utilized extensively for rapid detection and identification of *Helicobacter pylori* species. The product size of *16srRNA* gene was 900 bp as shown in figure (1) in all bacterial isolates our data contribute to previous discussions by⁽¹⁷⁾ who conclude that it is not possible to differentiate between the species on basis of *16srRNA*. The second gene detected was cytotoxin associated gene (*Cag A*) associated gene. cytotoxin associated gene (*Cag A*) is widely distributed among Gram-negative bacteria and it best characteristic of the toxins produced by *Helicobacter pylori* isolates, It had been described as an important virulence factor of this pathogen that are related with more prominent aggravation and expanded danger of ulcers and malignancy in people, figure(2) among *Helicobacter pylori* isolates all 10 isolate possess the gene for *CagA, VacA* they all express this gene due to point mutations and deletions and the levels of expressed toxin activities are strain-dependent, this supported and reported by⁽¹⁸⁾, our data also contribute to former studies that concluded the mutation in these gene, could reduce

the adhesion and invasion of the bacteria, or could be attributed to the immune status of the host and the number of infective organisms that affecting virulence associated gene.

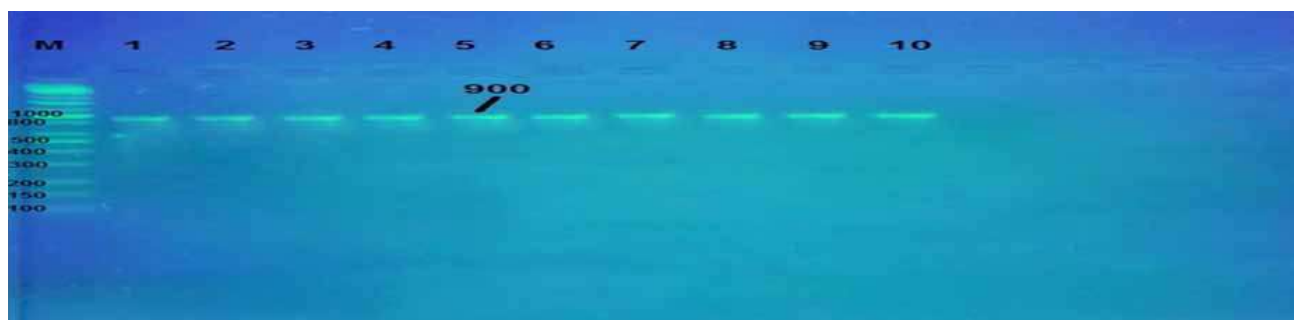


Figure 1: PCR product the band size 900 bp of *Helicobacter pylori* 16S ribosomal RNA gene The product was electrophoresis on 1.5% agarose at 5 volt/cm². 1x TBE buffer for 1:30 hours. N: DNA ladder (100)



Figure 2: PCR product the band size 498 bp. of *Helicobacter pylori* Cytotoxin associated gene A (CagA) gene The product was electrophoresis on 1.5% agarose at 5 volt/cm². 1x TBE buffer for 1:30 hours. N: DNA ladder (100)

Conclusion

According to the results of the sensitivity test, one of the isolates of the *Helicobacter pylori* 4(HpG 4) was chosen for being resistant to all antibiotics (except amoxicillin). Primers were designed to diagnose both *Helicobacter pylori* a gene which were detected and diagnosed by the presence of a *16SrRNA* gene. Genetic primers were designed to detect the virulence genes of *Helicobacter pylori*, *Cag* and *Vac* gene. The genes in ten isolates of *Helicobacter pylori* were investigated.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

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References

1. Solnick JV, Schauer DB. Emergence of diverse *Helicobacter* species in the pathogenesis of gastric and enterohepatic diseases. *Clin Microbiol Rev.*2016;14:59–97.
2. Braden, R. E. *Helicobacter pylori* and non ulcer dyspepsia to treat or no treat *Am. J. Gastroentrol.* 2012, 95 (2): 1 (Editorial).
3. Backert, S.; Clyne, M. and Tegtmeyer, N. Molecular mechanisms of gastric epithelial cell adhesion and injection of CagA by *Helicobacter pylori*. *Cell Commun Signal*,2016,9: 28.
4. McGee T, Yoshiyama H, Nakazawa T. Urease-independent chemotactic responses of *Helicobacter pylori* to urea, urease inhibitors, and sodium bicarbonate. *Infect Immun.* 2015;65:1519–1521.
5. Blaser, M.J. *Helicobacter pylori* and Related Species, 2285. In G. L. Mandell, J. E. Bennett, and

- R. Dolin (eds.), Mandell, Douglas, and Bennett's principles and practice of infectious diseases, vol. 2, 5th ed. Churchill Livingstone, Philadelphia, PA 2012, p. 2276.
6. Falush, D.; Wirth, T.; Linz, B.; Pritchard, J. K.; Stephens, M.; Kidd, M.; Blaser, M. J.; Graham, D. Y.; Vacher, S.; Perez-Perez, G. I.; Yamaoka, Y.; Megraud, F.; Otto, K.; Reichard, U.; Katzowitsch, E.; Wang, X.; Achtman, M. and Suerbaum, S. Traces of human migrations in *Helicobacter pylori* populations. *Science* 2003, 299: 1582- 1585.
 7. Atlas, R. M.; Brown, A. E.; Parks, L. C. Laboratory Manual of Experimental Microbiology. (1st ed). Mosby. Inc. Missouri. Contreras, B. G. L.; Vuyst, L.; Devreese, B.; Busanyova, K.; Raymaeckers, J.; Bosman, F.; Sablon, E. and Vandamme, E. J. (1991). Isolation, purification and amino acid sequence of lactobin A, one of the two bacteriocins produced by *Lactobacillus amylovorus* LMGP. 13139. *Appl. Environ. Microbiol.*, 1995, 63 (1): 13-20.
 8. Allos, B. M., and Taylor, D. N. *Helicobacter* Infections, In A. S. Evans and P. S. Brachman (eds.), *Bacterial infections of humans: epidemiology and control*, 3rd ed. Plenum Medical Book Company, New York, NY. 1998, pp. 169 -191.
 9. NCCLS. Method for dilution antimicrobial susceptibility testing on bacteria that grew aerobically. In *Approved Standard M7-A5.*, 5th ed. National Committee for Clinical Laboratory Standards. 2000.
 10. Denis, M. V.; Rose, A.; Huneau-Salaün, L.; Balaine, and Salvat, G. Diversity of pulsed-field gel electrophoresis profiles of *Helicobacter pylori* and *Campylobacter coli* from broiler chickens in France. *Poult. Sci.* 2008, 87: 1662-1671.
 11. Guerrero S, Pires I, Fernandes E. et al. *Helicobacter pylori* and bacteriological detection: evaluation of a transport medium *Potagerm pylori* (abstract). *Am J Gastroenterol* 1999; 89: 1287.
 12. Bergey's Manual of Determinative Bacteriology. Ninth Edition. Williams and Wilkins, Co., Baltimore, MD. 2009.
 13. Sotto, A.; Boever, C. M.; Fabbro-peray, P.; Gouby, A.; Sirot, D. and Jourdan, J. Risk factors for antibiotic-resistance *Escherichia coli* isolated from hospitalized patients with urinary tract infections: a prospective study. *J. Clin. Microbiol.* 2001, 39 (2): 438-444.
 14. Barret, S. P.; Savage, M. A.; Robec, M. P.; Guyot, A. and Shrimpton, S. B. Antibiotic sensitivity of bacteria associated with community-acquired UTI in Britain. *J. Antimicrob. Agents chemother.* 1999, 44: 359-365.
 15. Holt, J. G. Krieg, N. R., Staley, J. T. and Williams, S. T. Group 2 aerobic/microaerophilic motile Helical/vibroid gram negative bacteria In: *Bergey's manual of determination Bacteriology*, Pp. 42 - 48 19th edition Williams & Wilkins, USA. 2004.
 16. Clarridge, J. E.,. Impact of 16srRNA gene sequence analysis for identification of bacteria on clinical microbiology and infectious diseases. *Clin. Microbiol. Rev.* 2004, 17: 840-862.
 17. Palframan, C.E and Sanders GW Occurrence of thermotolerant *Helicobacter pylori* in fresh vegetables sold at farmers' outdoor markets and supermarkets. *Can J Microbiol* 2012, 38: 313-316.
 18. Abuoun M, Manning G, Cawthraw SA, Ridley A, Ahmed IH, Wassenaar TM & Newell DG Cytotoxic distending toxin (CDT)-negative *Helicobacter pylori* strains and anti-CDT neutralizing antibodies are induced during human infection but not during colonization in chickens. *Infect Immun* 2005, 73: 3053-3062.

A Comparative Study of the Physical Abilities of Children Born Full and Incomplete Pregnancies of Students Aged 8-9 Years

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Abstract

The importance of the research is that it looks for the most precise constraints of the selection process and gives indicators for the teacher and sports educator to take all the details regarding the driver and examine them carefully, some may be a defect or strength during the discovery of talent and hence came this study, which is the first nationwide and looking at the duration of the student The researchers used the descriptive method in the method of comparisons to suit the research problem. The sample of the research was chosen by the researcher, (54) students divided into (27) students with incomplete pregnancy and (27) students with full pregnancy, the main findings showed that students with full pregnancy they overcame pupils with incomplete pregnancies in both muscle strength and speed.

Keywords: *Physical capacity, full load and incomplete pregnancy.*

Introduction

The scientific acceleration and development in all specialties and the associated cognitive superiority has become necessary to interest in education on the use of modern educational method and new technologies in line with this development and scientific progress.

Therefore, the physical education is looking at the particles that will discover the talents and avoid the obstacles. Perhaps the topic of selection is looking at the most accurate details, including the subject of the birth of an embryo of incomplete pregnancy (premature birth), which is the occurrence of contractions in the uterus regular and continuous enough to occur before the birth of growth Fetus for the week 37, starting from the period of fetal capacity to life outside the uterus, which is within 20 weeks, and 20 weeks ago is an abortion and not premature birth, and between 20 - 32 weeks, the term premature birth, accounting for about 5.5% of total births, But at the same time lead to 50% of deaths In newborns.¹ Despite the importance of the subject of physical abilities in sport, this subject has not been researched and studied to the extent that it is reflected in sports at the age of 8-9 years.” Although the physical

level of students is close but we notice differences in growth and Education is due to the pre-school stage, and there are differences that emerge as a result of students playing sports and sports.² For example, we see speed is a component of physical abilities that reflect the extent and compatibility of the mechanism in which the neuron works. Unusual, here we see all two elements associated with some where speed is One of the basic components of motor performance in most sports activities are linked to force because the power status is one of the most important components of motor performance if not the most important because each movement depends on the strength of power to lose the human movement, and affect the strength in some physical qualities such as speed and rotation and hence we find that training Physical fitness in general is to do all muscle work leading to the upgrading and improvement of fitness and development to a high degree under the conditions of conditions appropriate to the scientific stage.³

The importance of the research as it looks for the most precise obstacles to the selection process and gives indicators for the teacher and sports educator to take all the details concerning the driver and examine

them carefully, some may be a defect or strength during the discovery of talent and hence this study, which is the first nationwide and looking at the duration of the student Do they have physical connections.

Research Aim: Identify the differences in physical abilities between children born full and incomplete pregnancy of students aged (8-9) years.

Hypothesis: There are statistically significant differences in physical abilities among children born to complete and incomplete pregnancies for students aged 8-9 years.

Research methodology and field procedures:

Research Methodology: The researchers used the descriptive approach in the method of comparisons as appropriate to solve the research problem.

Community and sample search: The researchers identified their research community from primary school students in the third grade at the age of 8-9 years in the academic year 2018-2019 in Dhi Qar Governorate. The total number of students is 495 students and students from nine schools (Barada Boys School, Al Batha School for Boys, School of Confrontation, Sheikh Al Batha School, Qutaiba School, Jabal Al Sabr School, Al Ezz School).

The sample of the research was chosen by the third-grade students aged 8-9, with 54 students divided into 27 with incomplete pregnancies and 27 with full pregnancy. The percentage of the sample was 10.90%) And Tables (2.1) show the distribution and homogeneity of the sample.

Table (1). Shows the distribution of the sample

Gender	School Name	Total Number	Sample	Percentage
Boys	Sheikh Al Bathaa School	61	6	9.83
	Al Batha School	72	8	11.11
	Barda Boys School	67	8	11.94
	Al - Rawdatain School	43	2	4.65
	Al - Batha Martyrs School	55	6	10.90
	Al Qatif School	67	6	8.95
	El Ezz School	54	8	14.81
	Qutaiba School	32	4	12.5
	School confrontation	44	6	13.63
Total		495	54	%10.90

Table (2). Shows the homogeneity of the sample

Gender	Variables	Units	Mean	Median	SD	Skewness
Male	Length	Cm	128.6	129	4.73	-0.95
	Mass	Kg	26.48	26	5.34	0.81

Table (2) shows that the values of the splicing coefficient were between ± 1 , indicating the homogeneity of the research sample.

Identification of physical abilities and tests: The physical abilities of the subject and their tests were determined by distributing the questionnaire (1) to a group of experts and specialists, where the abilities that were obtained (80%) and above were neglected and the minimum was neglected. (75%) and more of the

opinion of the arbitrators.⁴ The research then asks to conduct the tests for each physical capacity under study, which was chosen through the use of previous studies and was presented to the same experts and obtained their approval by 100% The virtual honesty of the tests, despite the use of tests in the Arab and Iraqi environment and that m The researchers conducted an exploratory experiment on Wednesday, 14/11/2018 on a sample of non-research sample and the community of origin. They are 8 students aged 8-9 years. The aim of the exploratory

experiment was to identify the obstacles that Testing and disposal of the tests, finding out the suitability and efficiency of the instruments and devices during the tests used, knowing the compatibility of the tests with the level and abilities of the students, knowing the length of time taken for each test, the knowledge of the efficiency of the auxiliary team and checking the stability of the tests through the application of tests and the correlation coefficients between them. The correlation coefficients were high, which achieved consistency and objectivity, and Table (3) shows that.

Table (3). Shows stability and objectivity coefficients

Tests	Stability coefficient	Subjectivity coefficient
Jump wide of constancy	0.83	0.92
Jogging 30 meters	0.80	0.91
Jogging between characters	0.81	0.96

Specification tests:

Explosive power test:⁵

Name of test: Wide jump of stability for maximum distance (1) meter.

Objective of the test: measure the explosive force of the two men.

Tools used: flat ground does not expose the individual to slide, measuring tape, line drawn on the ground (starting line).

The method of performance: The laboratory stands behind the starting line and feet slightly spaced, swing the arms in the bottom downwards with the knees bend half and tilt the trunk until they reach the start of the start of swimming, from this situation swinging the arms firmly with the extension of the two legs along the trunk and push the ground Feet firmly in an attempt to jump as far as possible

Registration: The jump distance is measured from the starting line (the inner edge) until the last trace of the laboratory left near the starting line, or when the heel touches the ground, and the laboratory has two attempts to register the best.

The speed test:⁶ Name of test: the enemy for a distance of 30 meters (2).

Objective of the test: Measure the maximum speed in the run

Tools used: a track or a space sports area of not less than 50 m and display at least 5 m, stop time number 2.

Performance method: We draw 3 parallel lines on the ground and the distance between the first line and the second 20 m, between the second line and the third 30 m, the laboratory stands behind the starting line, and from the high start at the signal, the laboratory running up to a maximum of up to the second start line and ends at the end of the line the third.

Registration: The laboratory records the time taken from the beginning of the second line until the moment of passing the finish line in the second and parts, and allows the laboratory to perform two attempts after giving a standard rest to record the best

Fitness test:⁷ Name of test: Running the zigzag between the barriers (jogging between the characters) (in numbers) (3).

Purpose of the test: measure agility:

Tools used: four-track athletics, stopwatch:

Method of performance: The four barriers are placed on a single line so that the distance between each barrier and another 180 cm and the distance between the first barrier and the starting line 360 cm Note that the starting line parallel to the barriers and length of 180 cm and painted on the ground next to the barriers numbers, the laboratory stands at the starting point and then run immediately When you hear the start signal using the route that is set to continue to run in this method (30) continuous seconds and at the end of (30) seconds record the number of place where time ends with the calculation of the number of full cycles of the test and displayed by number.

Research Procedures: The researchers went to the targeted schools for the purpose of conducting the research for the period from 2/12 to 26/12/2018. After meeting with the principals of schools and physical education teachers in these schools and after explaining the research procedures and meeting the students from the target boys, 2) on the students and asked them how to answer them and how to fill the information in them, and set a specific period of three days for the purpose of receiving information, and after collecting all forms from schools have emptied the information and categories according to the duration of the pupils of the boys and researchers have derived from this information Of those with full pregnancy.

Results

Table (4). Shows the computational and standard deviations and the value t calculated for the physical abilities tests of students with full and incomplete pregnancies

Test	Units	Complete pregnancy n = 27		Pregnancy is incomplete n = 27		Value (t) calculated*	Statistical Significance
		Mean	SD	Mean	SD		
Wide jump of stability for maximum distance	Cm	112.31	7.93	107.2	6.88	2.13	Sig.
Enemy for 30 meters	Sec.	6.44	0.66	7.14	0.25	5.05	Sig.
Running down the barriers	Sec.	7.5	1.03	7.20	0.88	0.81	Non sig.

* The value (t) of the table is equal to (2.01) degree of freedom (52) and the level of significance (0.05)

Table (4) shows that the value of the arithmetic mean of the students from the full load in the wide jump test, the enemy for 30 m, the zigzag run respectively (112.31 cm, 6.44 seconds, 7.5 seconds) and standard deviation respectively (7.93, 0.66, 1.03) The value of the computational mean of the students from the full load in the same tests was respectively 107.2 cm, 7.14 seconds, 7.20 seconds, and standard deviation respectively (6.88, 0.25, 0.88). The calculated value (t) was respectively (2.13, 5.05, 0.81). It is clear that the value of t calculated in the wide jump and enemy tests for 30 m is greater than the tabular value of (2.01) and the degree of freedom (52) (0.05). This indicates that there are significant differences in the tests of explosive force and speed between the students born of full and incomplete pregnancy and for the benefit of full pregnancy students, while it was found that the value of t calculated in the running test between the barriers less than the value of (t) (2.01) with a degree of freedom (52) and a significance level (0.05). This indicates that there were no significant differences in the fitness test among students born of full and incomplete pregnancy.

Discussion of Results

Table 4 shows the superiority of students born from full pregnancy in terms of muscle strength and speed, as well as the absence of significant differences between students with full and incomplete pregnancies.⁸ The researchers attribute these differences to the fact that the strength and speed classes of abilities, The physiological organs of the human body in terms of the physiological section of the muscle and the number of motor units as well as the type of muscle fibers fast and slow (red and white) and therefore there is a strong correlation between these two levels, Muscle strength plays a

large role in the level of speed, Where the results of practical and scientific experiments indicate that there is a significant correlation between the two elements of strength and speed,⁹ the muscle or muscle group cannot contract quickly if it does not have sufficient strength for this performance, and that pupils born from incomplete pregnancy show symptoms of non-growth, Therefore, the premature birth of a child implies that his or her physical development is not yet complete, which makes the premature child vulnerable to health problems and complications at higher rates than those of normal-born children such as growth and development problems, lung disease, weak immunity, vision problems, Hearing and physical weakness make the child more vulnerable to childbirth.¹⁰

The researchers also see that the two types of muscle strength and speed of inherited abilities that move with the child from birth and that most of the children born early may show them in the structure of physical and mental in the long term, while we see that the fitness characteristic of the motor capacity acquired from the ocean did not There is a significant difference between those who have full and incomplete pregnancies. Kinetic abilities develop through the ocean, which comes from practice and continuous and repeated training.¹¹

Conclusions

1. Students with full pregnancy outperformed students with incomplete pregnancy in both muscle strength and speed.
2. The differences were not significant between students with full pregnancy and pupils with incomplete pregnancy in fitness.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq.

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References

1. Mattson SN, Riley EP, Gramling L, Delis DC, Jones KL. Neuropsychological comparison of alcohol-exposed children with or without physical features of fetal alcohol syndrome. *Neuropsychology*. 1998 Jan;12(1):146.
2. Welsh L, Kirkby J, Lum S, Odendaal D, Marlow N, Derrick G, Stocks J. The EPICure study: maximal exercise and physical activity in school children born extremely preterm. *Thorax*. 2010 Feb 1;65(2):165-72.
3. Saigal S, Stoskopf B, Boyle M, Paneth N, Pinelli J, Streiner D, Goddeeris J. Comparison of current health, functional limitations, and health care use of young adults who were born with extremely low birth weight and normal birth weight. *Pediatrics*. 2007 Mar 1;119(3):e562-73.
4. Goodman A, Joyce R, Smith JP. The long shadow cast by childhood physical and mental problems on adult life. *Proceedings of the National Academy of Sciences*. 2011 Apr 12;108(15):6032-7.
5. Rose SA. Relation between physical growth and information processing in infants born in India. *Child development*. 1994 Jun;65(3):889-902.
6. Alsayigh HA, Athab NA, Firas M. Journal of Global Pharma Technology The Study of Electrical Activity of the Triceps Brachia Muscle according to the Chemical Changes of Water Loss during Spike in Volleyball. 2017;57-62.
7. Al-Mashhad RAA. The Impact of the Plan and PDEODE Strategies in Developing Awareness of Cognitive Processes and Reducing Psychological Pollution Among Students of the Faculty of Physical Education and Sports Sciences. 2018;928-35.
8. Alsayigh HA, Athab NA. The Study of Rectus Femoris Activity after Knee Joint Rehabilitation. 2016;9(9):360-5.
9. Jumaah H, Ktaiman A, Abdul N, Athab K, Mohammed A. The Effect of Using Pain Management Techniques in the Rehabilitation of Chronic Lower Back Injury in Athletes and Non-Athletes. :108-12.
10. Athab NA, Hussein WR, Ali AA. A Comparative Study for Movement of Sword Fencing Stabbed According to the Technical Programming in the Game of Fencing Wheelchairs Class B. *Indian Journal of Public Health Research & Development*. 2019;10(5):1344-7.
11. Athab NA. An Analytical Study of Cervical Spine Pain According to the Mechanical Indicators of the Administrative Work Staff. *Indian Journal of Public Health Research & Development*. 2019; 10(5):1348-54.

Effect of Salpingectomy Versus Fallopian Tubes Cauterization for Management of Hydrosalpinx on the Future Females' Ovarian Reserve

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Abstract

Background: Injury to the distal end of the fallopian tube (ampulla), and its fimbria, causes the end of the tube to close. Glands within the tube produce a watery fluid that collects within the tube, producing hydrosalpinx which should be blocked surgically before starting in vitro fertilization by salpingectomy, clumping or cauterization in two sites that may influence the vascularity of the adjacent ovarian tissue affecting the IVF results later on.

Aim of Study: To compare between the effect of salpingectomy and cauterization of the fallopian tubes on the ovarian reserve and ovarian vascularity in females undergoing tubal surgeries for hydrosalpinx.

Subjects Materials and Method: The present study was done on 30 infertile females with history of primary or secondary infertility who were diagnosed as having bilateral or unilateral hydrosalpinx by hysterosalpingogram (HSG). These females were divided into two groups, the first group (n=15) were subjected to laparoscopic tubal ligation using cauterization in two sites for each tube, while the other group (n=15) were undergone more aggressive method which is salpingectomy (severed and sealed).

An assessment of their antral follicle count (AFC), anti-Müllerian hormone (AMH) and calculating the ovarian artery pulsatility index (PI) and Doppler index of vascular resistance in the ovarian vessels (resistant index of stromal blood flow - RI) was done for all females before and after surgery.

Results: The results of age, AFC, AMH level, RI, and PI was recorded before and after doing their surgeries in both groups. The statistical analysis recorded no significant difference ($p>0.05$) in all these parameters before and after subjecting to surgeries, but when these parameters were compared within each group only resistance index showed significant difference ($p<0.05$) in the group underwent tubal cauterization while in the other group who underwent salpingectomy a significant difference ($p<0.05$) was recorded in AFC and highly significant difference ($p<0.01$) in AMH level.

Conclusions: The negative effect of salpingectomy on ovarian reserve is more than that of tubal cauterization.

Keyword: Tubal cauterization, salpingectomy, ovarian reserve, pulsatility index, resistant index.

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Introduction

One of the most common causes of female infertility is hydrosalpinx. It may interfere with fertility through lowering implantation and pregnancy rates after in-vitro fertilization. This may be due to mechanical factors, toxicity of the hydrosalpingeal fluid, and receptivity dysfunction⁽¹⁾.

Salpingectomy (removing part of a fallopian tube) is done to improve in vitro fertilization (IVF) success rate and preferred over salpingostomy. Hydrosalpinx may half the IVF success rate⁽²⁾. This led the United Kingdom's National Institute of Health and Clinical Excellence guidelines (NICE) to recommend laparoscopic salpingectomy before assisted reproductive technologies (ART) when hydrosalpinx was diagnosed through hysterosalpingography (HSG) and by ultrasound⁽³⁾.

These Guidelines are also supported by data analyzed in a recent Cochrane review emphasizing a superior pregnancy rate when patients with tubal disease underwent laparoscopic salpingectomy (or at least tubal occlusion) prior to IVF treatments especially if enlarged enough to be visible on ultrasound and in particular for those affected bilaterally^(4, 5). These studies have resulted in the Cochrane library recommendation of salpingectomy for hydrosalpinges^(6,7).

It is generally believed that the fluid holds a key position in impairing the implantation potential. However, aggressive tubal surgery may impact fertility and ovarian reserve because of its effects on ovarian tissue of the same side⁽⁸⁾.

Subjects Materials and Method: The present study was done on 30 infertile females attending high institute of infertility diagnosis and ART during the period from 2016-2018. These females were diagnosed as having bilateral tubal obstruction with unilateral or bilateral hydrosalpinx as diagnosed by hysterosalpingogram and ultrasound for presence of tubal dilatation. An ultrasound assessment of their AFC and day 3 AMH was measured by electro chemiluminescence immunoassay (ECLIA).

Doppler ultrasound assessment: All patients underwent single transvaginal color imaging, as well as pulsed Doppler spectral analysis by the same physician in a quiet and comfortable location; with an empty bladder to normalize blood pressure and pulse rate between the 3rd and 8th days of the menstrual cycle to avoid changes in blood flow due to ovulation and corpus luteum. The number of antral follicles in both ovaries, visualization of the ovarian arteries and the blood vessels within the ovarian stroma was done for all patients.

The ovarian artery located lateral to the upper pole of the ovary, near the infundibulopelvic ligament. The stromal vessels of the ovary were identified as color signals within the ovarian stroma. A pulsed Doppler range gate was placed across each vessel, aiming for

an angle of insonation close to 0° between the Doppler beam and the vessel. Then two blood flow indices were automatically calculated: the pulsatility index (PI); the resistance index (RI) of the bilateral ovarian vessels. The normal resistant index and pulsatility index is (0.62±0.04, 0.97±0.04) respectively⁽⁹⁾.

These patients acceptance for undergoing a laparoscopic tubal occlusion was signed. At least 2 months post- surgery reassessment of the same patients for the same parameters was done including AFC, AMH, PI and RI.

Findings: This prospective comparative study was done between two groups of females. The first group (n=15) underwent tubal cauterization in two sites while the other group underwent tubal blockage by salpingectomy (severed and sealed) (n=15). The age of females, type of infertility, antral follicle count, antimullarian hormone, ovarian vessels pulsatility index and stromal blood flow resistant index were recorded for all infertile females included in the present study (table-1).

A comparison was done for age, AFC, AMH level, ovarian vessels PI and stromal blood flow RI between the group who underwent salpingectomy and those who underwent tubal cauterization before doing their operations. The results showed no significant difference ($p>0.05$) for all these parameters (table - 2).

Within each group comparison was done between the results of AFC, AMH level, ovarian vessels PI and stroma blood flow RI before and after doing the operation. In the group who underwent tubal cauterization; the results recorded no significant difference ($P>0.05$) in AFC, AMH and PI while significant difference ($p<0.05$) was recorded in RI of ovarian stroma (table-3).

While in the second group who underwent salpingectomy; the same parameters were compared before and after doing surgery and showed significant difference ($p<0.05$) in AFC, highly significant difference ($p<0.01$) in AMH level but no significant difference ($p>0.05$) in both PI and RI of ovarian blood flow (table-4).

A comparison was done for AFC, AMH, RI and PI between the group of females who were subjected to tubal cauterization and those who underwent salpingectomy after surgeries. The results showed no significant difference in all parameters (table-5).

Discussion

Tubal ligation may reduce the ovarian blood flow and lead to tissue damage to the ovary that may result in a significant decrease of the total follicular pool. It was suspected to induce several adverse effects such as irregular menstrual cycles, dysmenorrhea, and climacteric symptoms^(10, 11).

In the present study all females included were having normal ovarian reserve before subjecting to surgeries as documented by having AFC and AMH to be within normal range.

Age was documented previously as being one of the most predicting markers for fertility assessment⁽¹²⁾. In the present study, it was found that there was no significant difference in the mean age between the group who underwent tubal cauterization and those who underwent salpingectomy. This finding indicated that both groups had comparable age which is important to eliminate any variable that may affect the results of the procedure type on ovarian reserve as the recent studies have shown that poor ovarian response is a first sign of ovarian ageing (early ovarian failure or early menopause)⁽¹³⁾.

Many markers of ovarian reserve have been considered in the last few decades, but an ultimate marker still has not been proven. Response prediction through ovarian reserve testing is superior to that through chronological age alone. The antral follicle count (AFC) and anti-Müllerian hormone (AMH) are currently considered to have the best sensitivity and specificity to predict the ovarian response, despite them having 10–20% false-positive rates⁽¹⁴⁾, so these parameters were also recorded for both groups and found to be within normal range and no significant difference was found between the two groups indicating that the groups were comparable regarding their ovarian reserve.

The previous studies showed that prophylactic bilateral salpingectomy in some patients with ultrasound-visible bilateral hydrosalpinges improved the IVF outcome. In addition to pregnancy rate, ongoing pregnancy and live birth rate were increased with laparoscopic salpingectomy for hydrosalpinges prior to IVF⁽⁶⁾. But one of the problems caused by salpingectomy is the possibility of impairing the ovarian function after the procedure. The most important blood supply to the Fallopian tube is the medial tubal artery, which originates at the same point as the median ovarian artery. If the salpingectomy procedure is not

properly performed close to the tube, it may disrupt the normal blood flow to the ovary. So in the present study pulsatility index and resistance index were measured by color Doppler ultrasound which showed no significant difference between the two groups.

For the group of females who were subjected to fallopian tubes cauterization the results showed no significant difference in antral follicles count, early follicular AMH and ovarian artery pulsatility index which indicated that this procedure has minimal effect on ovarian vascularity and consequently on their function. These results were in accordance with that of Ercan et al 2012⁽¹⁵⁾. Only resistance index was significantly less after operation this may be due to development of collateral vascular circulation that may resolve the ischemic effect of the procedure as discussed in previous studies^(16, 17).

In the present study the other group who were subjected to more aggressive procedure which is salpingectomy showed significant decrease in antral follicle count (AFC) and highly significant decrease in the early follicular AMH level that indicates the development of poor ovarian reserve which negatively affect IVF result later. This may be explained to be the result of tubal sterilization procedure which could destroy the vascular structures adjacent to fallopian tubes, such as the tubal branch or ovarian branch of the uterine artery in the mesosalpinx, causing an altered blood supply to the ovaries. The diminution of blood flow could affect the ovarian reserve due to possible ischemia in the ovary. As a result ovarian response to gonadotropin signaling may decrease after this relative ischemic effect causing subsequent impairment of follicular growth^(18, 19). Relative ischemia in the ovaries created by the destruction of the vascular mesosalpinx may first affect the preantral and small antral follicles, resulting in a decrease in AMH levels. This effect might also reduce the number of cyclically recruited follicles, causing a decrease in AFCs. These results did not agree with previous studies of Findley et al., 2013. But it agree with that of Goynumer et al., 2009^(20, 21).

Regarding the Doppler study of this group before and after salpingectomy there was no significant difference between them and this agree with previous studies of Kelekci et al., 2005 and 2004^(22, 23). But in other studies an elevation in pulsatility and resistance indices were reported. The authors explained these elevations by the increase in local vascular resistance after tubal sterilization⁽¹⁶⁾.

Table (1): Patients’ general clinical parameters

Parameters		Values
Age (Years)		31.18±1.15 (mean±SER) Range 19-40
Type of infertility	Primary infertility (%)	40.91%
	Secondary infertility (%)	59.09%
Antral follicle count		14.63±0.74 (mean±SER)
Antimullarian hormone level		2.23±0.31 (mean±SER)
Ovarian artery pulsatility index		1.62±0.45 (mean±SER)
Ovarian stromal vessels resistance index		0.87±0.07 (mean±SER)

Table (2): A comparison of all parameters between the group who underwent salpingectomy and those who underwent tubal cauterization before surgeries.

Parameters	Tubal cauterization group	Salpingectomy group	p-value
Age (years)	29±2.02	32.33±1.59	0.34 ^{NS}
Antral follicle count	15±1.36	14.4±1.2	0.78 ^{NS}
Antimullarian hormone level	2.81±0.65	2.1±0.29	0.46 ^{NS}
Ovarian artery pulsatility index	1.76±0.15	1.56±0.17	0.27 ^{NS}
Ovarian stromal vessels resistance index	0.97±0.16	0.85±0.13	0.64 ^{NS}

NS: No significant difference (p>0.05)

Table 3: Acomparison of ovarian reserve parameters before and after surgery within the group who underwent tubal cauterization.

Parameters	Tubal cauterization group before surgery	Tubal cauterization group after surgery	p-value
Antral follicle count	15±1.36	15.2±0.84	0.13 ^{NS}
Antimullarian hormone level	2.81±0.65	2.8±0.44	0.06 ^{NS}
Ovarian artery pulsatility index	1.76±0.15	1.76±0.11	0.39 ^{NS}
Ovarian stromal vessels resistance index	0.97±0.16	0.8±0.11	0.03*

*significant difference (p<0.05). NS: No significant difference (p>0.05)

Table 4: Comparison of ovarian reserve parameters after surgery between the group who underwent tubal cauterization and those who underwent salpingectomy.

Parameters	salpingectomy group before surgery	Salpingectomy group after surgery	p-value
Antral follicle count	14.4±1.2	12±0.95	0.04*
Antimullarian hormone level	2.1±0.29	1.4±0.27	0.001**
Ovarian artery pulsatility index	1.56±0.17	1.42±0.15	0.5 ^{NS}
Ovarian stromal vessels resistance index	0.85±0.13	0.9±0.05	0.6 ^{NS}

*Significant difference (p<0.05). ** Highly significant difference (p<0.01). NS: No significant difference (p>0.05)

Table (5): Comparison of all parameters between the group who underwent salpingectomy and those who underwent tubal cauterization after surgeries.

Parameters	Tubal cauterization group after surgery	Salpingectomy group after surgery	p-value
Antral follicle count	15.2±0.84	12±0.95	0.07 ^{NS}
Antimullarian hormone level	2.8±0.44	1.4±0.27	0.09 ^{NS}
Ovarian artery pulsatility index	1.76±0.11	1.42±0.15	0.28 ^{NS}
Ovarian stromal vessels resistance index	0.8±0.11	0.9±0.05	0.88 ^{NS}

NS: no significant difference $p > 0.05$

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

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References

- Bontis J, Theodoridis T.D. Laparoscopic Management of Hydrosalpinx. *Women's Health and Disease: Gynecologic, Endocrine, and Reproductive Issues* 2007; Volume 1092, Issue 1. Pages: 199-210
- American Society for Reproductive Medicine and Society of Reproductive Surgeons. Salpingectomy for hydrosalpinx prior to in vitro fertilization. *Fertility and Sterility*, 2008; 90(Suppl 3): S66-S68.
- National Collaborating Centre for Women's and Children's Health (UK) *Fertility: Assessment and Treatment for People with Fertility Problems*. London: Royal College of Obstetricians & Gynaecologists (UK); 2013.
- Johnson N, van Voorst S, Sowter MC, Strandell A, Mol BW. Surgical treatment for tubal disease in women due to undergo in vitro fertilisation. *Cochrane Database Syst Rev*. 2010
- Strandell A, Lindhard A, Waldenström U, Thorburn J, Janson PO, Hamberger L. Hydrosalpinx and IVF outcome: a prospective, randomized multicentre trial in Scandinavia on salpingectomy prior to IVF. *Hum Reprod*. 1999 Nov; 14(11):2762-9.
- Johnson NP, Mak W, Sowter MC. Surgical treatment for tubal disease in women due to undergo in vitro fertilisation. *Cochrane Database Syst Rev*. 2004; (3):CD002125.
- Johnson, N.P., Mak, W. and Sowter, M.C. Laparoscopic salpingectomy for women with hydrosalpinges enhances the success of IVF: a Cochrane review. *Hum. Reprod.*, 2002; 17(3): 543-548.
- Otlyar.AK, Gingold J, Shue S, Falcone T. The Effect of Salpingectomy on Ovarian Function. *Journal of Minimally Invasive Gynecology*. 2017:Volume 24, Issue 4, Pages 563-578
- Moon H J, Ko J K, Ahn Y S, Kim W T, Kim M Y, Shin H J, Seo K. Transvaginal Color Doppler Sonography of the Normal Ovaries According to the Menstrual Cycle. *Journal of Korean Society of Medical Ultrasound* 1998; 17(2): 133-137. Published online: January 1, 2001.
- Mümüšoğlu S, Hacıvelioğlu S, Sökmenşter L.K, Karatayl R, Süzer³, Figen Kaymaz A. The comparison of the degree of apoptosis in ovaries and fallopian tubes between two different surgical interventions for tubal ligation: A rat model. *J Turk Ger Gynecol Assoc* 2018; 19: 11-6
- Daniels K, Daugherty J, Jones J, Mosher W. Current Contraceptive Use and Variation by Selected Characteristics Among Women Aged 15-44: United States, 2011-2013. *Natl Health Stat Report* 2015: 1-14.
- Van Loendersloot LL, Repping S, Bossuy PM, et al. prediction models in in vitro fertilization where are we? Amini review. *Journal of Advanced Research*, 2014; 5: 259-30-1 284.
- Jwad M.A, Abdulmajeed B.A, Al-Kawaz U.M . Effect of Ovarian Stimulation Protocol on Embryo Quality in IVF-ICSI. *Iraqi Journal Of Embryos and Infertility Researches*. 2018; Vol.(8) Issue-1: 55-63.

14. Bessow C, Donato R, de Souza T, Chapon R, Genro V, Cunha-Filho JS. Antral follicle responsiveness assessed by follicular output RaTe(FORT) correlates with follicles diameter. *J Ovarian Res.* 2019; 12 (1):48. Published 2019 May 25.
15. Ercan C.M, Sakinci M, Coksuer H, Keskin U, Tapan S, Ergun A. Ovarian reserve testing before and after laparoscopic tubal bipolar electrodesiccation and transection. *European Journal of Obstetrics & Gynecology and Reproductive Biology.* 2013; 166: 56–60
16. Kelekci S, Yilmaz B, Yakut Y, Yasar L, Savan K, Sonmez S. Hormonal and ovarian stromal blood supply changes after laparoscopic tubal sterilization: a prospective controlled study. *Contraception* 2006; 73: 279–83.
17. Timonen S, Tuominen J, Irjala K, Mañenpañã J. Ovarian function and regulation of the hypothalamic-pituitary-ovarian axis after tubal sterilization. *Journal of Reproductive Medicine* 2002; 47:131–6.
18. Dede FS, Dilbaz B, Akyuz O, Caliskan E, Kurtaran V, Dilbaz S. Changes in menstrual pattern and ovarian function following bipolar electrocauterization of the fallopian tubes for voluntary surgical contraception. *Contraception* 2006; 73:88–91.
19. Cattanach JF, Milne BJ. Post-tubal sterilization problems correlated with ovarian steroidogenesis. *Contraception* 1988;38:541–50
20. Findley A.D, Siedhoff M.T.,Hobbs K.A. .Steege J.F. Christina McCall C.A. .Steiner A.Z. Short-term effects of salpingectomy during laparoscopic hysterectomy on ovarian reserve: a pilot randomized controlled trial *Fertility and Sterility* Volume 100, Issue 6, December 2013, Pages 1704-1708
21. Goynumer G, Kayabasoglu F, Aydogdu S, Wetherilt L. The effect of tubal sterilization through electrocoagulation on the ovarian reserve. *Contraception* 2009;80:90–4.
22. Kelekci S, Yilmaz B, Yasar L, Savan K, Sonmez S, Kart C. Ovarian reserve and ovarian stromal blood supply after tubal ligation by the Pomeroy technique: comparison with controls. *Gynecological Endocrinology* 2005;20: 279–83.
23. Kelekci S, Yorgancioglu Z, Yilmaz B, et al. Effect of tubal ligation on ovarian reserve and the ovarian stromal blood supply. *Australian and New Zealand Journal of Obstetrics and Gynaecology* 2004; 44:449–51.

The Effectiveness of Retaliatory Force Exercises in Developing the Explosive Power of Two Legs and Arms and the Accuracy of the Spike in the Badminton of Young Players Under the Age of 18 Year

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Abstract

The problem of research is that most young players with badminton do not have sufficient muscular strength for the muscles of legs who have a big role in the accuracy of the strike. This was observed through the personal experience of the two former players and interested in badminton and through the interviews that were conducted with Most trainers of the youth category and through the belief of researchers in scientific research as the correct scientific step to solve problems, exercises were designed to refine the explosive capacity of the muscles of the two legs and their impact on improving the accuracy of the strike in the field of badminton for young players 18 years old .

Research aim to prepare exercises regressive force to develop explosive power in the muscles of legs, arms and accuracy spike in the badminton players for young people under 18 years old. The researchers used the pilot approach to experimental design with pre-test and post-test for the two groups (experimental and control) to suit the nature of the research. The research community was determined by the players of the Mahaweel Sports Club with ages (16-18) for the training season 2018-2019 of 14 players. The sample was selected in a comprehensive inventory method and the sample was divided into two groups (experimental and control) with seven players per group. One of the most important conclusions was the positive effect on the development of explosive force of arms and legs using the reactive power exercises of the experimental group and all tests. The reason for the development of the experimental group was the result of the independent variable use of aftershocks for the development of explosive force of the arms and legs, Develop the skills of the precision of the spike in the badminton.

Keywords: Explosive power, legs and spike.

Introduction

It is recognized in sports training that it is an organized process aimed at reaching the individual to achieve the best achievements in the field of specialization and within the limits allowed by his physical, psychological and social abilities. The progress in the levels of achievement of sports events in general and badminton especially because of the high adaptations of the body's clean bodies during the use of different method to train muscle strength because it is one of the main performance factors for most sports games and events,

requiring training in all sports activities, but vary in amounts And differentiated details from one activity to another and may have precedence in a particular activity without another, because force is an important function that the body cannot perform movements without its presence in the muscles.¹

One of the first requirements for badminton is to develop its physical characteristics of the force in its explosive type for the purpose of integrating it with the players "because the development of the base of fitness elements specialized in tennis is important for both

performance and health of the sport, the first concern is on the uses of power to develop muscle capacity for good performance, The basic skills of badminton are explosive power.

In this sense, the importance of research in achieving the goal of developing the explosive force of the two legs and the arms of the players is shown by following the method of strength training exercises used in the development of muscles of the two legs and arms working in the skill of beating overwhelming, which depends on the strength and speed of the muscles of the two legs and the arm of the skill.²

Research Aims:

1. Prepare the exercises of the force of a rebound to develop the explosive capacity of the muscles of legs and arms and the accuracy of the spike in the badminton of young players under 18 years.
2. Identify the effect of aftershocks in the development of the explosive power of the muscles of two legs and arms and the accuracy of the spike in the badminton of young players under 18 years

Hypothesis: There is a positive effect of the exercises of aftershocks in the development of the explosive capacity of the muscles of the legs and arms

and the accuracy of the spike in the badminton of young players under 18 years.

Research methodology and field procedures:

Research Methodology: The researchers used the experimental approach with the pre-test and post-test experimental design of the two groups (experimental and control) to suit the nature of the research.

Community and Sample research: The research community was determined by the players of Al Mahaweel Sports Club at the age of (16-18) years for the training season 2018-2019 of 14 players. The sample was selected in a comprehensive inventory method and the sample was divided into two groups (experimental and control) with seven players per group. Homogeneity and equivalence of the sample:

In order to make the researchers work in the right direction and to emphasize the objectivity of the work, the researchers found the homogeneity and equivalence between the two groups of research in terms of physical measurements (length, mass, training and time) using the appropriate statistical treatments in order to know the truth of the differences between the two groups of research and as shown in Table (1, 2).

Table (1). Shows the homogeneity of the sample

Variables	Units	Test value (Leven)		Level of significance
		Calculated	Standard error	
Age	Year	1.432	0.454	Non sig.
Training age	Year	0.783	0.980	Non sig.
Mass	Kg	0.059	0.564	Non sig.
Length	Cm	1.121	0.320	Non sig.

Table (2). Shows the mean, standard deviations, calculated value (t), and significance of differences in tests examined between the control and experimental groups in the pre test

Variables	Units	Control Group		Experimental Group		(t) Calculated	Mistake percentage	Significance of differences
		Mean	SD	Mean	SD			
The explosive power of the two legs	Cm	30.00	3.37	29.86	4.10	0.071	0.431	Non sig.
The explosive power of the arms	Meter	2.742	0.399	2.671	0.446	0.316	0.331	Non sig.
The accuracy of the spike	Grade	9.897	1.934	9.998	1.754	1.983	0.398	Non sig.

Tests used in Research:

1. **Vertical jump test for Sargent:**³ Purpose of the test: Measure the muscle capacity of the two legs in the vertical jump up.

Tools:

- A panel of wood painted black with a width of 1 m and a length of 1 m, with lines drawn in white and the distance between each line and the other (2) cm.
- Smooth wall not less than the height of the land of 3.60 m.
- A piece of chalk or plaster powder, a piece of cloth to clear plaster marks after reading all attempts by the laboratory.
- The blackboard can be removed with a piece of wood that is installed on the wall.

Measures:

- Fixing the blackboard or a piece of wood on the wall so that the bottom edge is at a height allowing the shortest laboratory to perform the test and make sure that the plate is installed away from the wall with a distance of not less than (15) cm, so as not to contact the wall during the jump up.

Test Instructions:

- Both feet must be pushed from a steady position.
- Before jumping up, the lab swings the arms forward and down to adjust the timing of the movement, to reach the maximum height possible.
- The laboratory is given three to five consecutive attempts and is calculated as a result of the best attempt.
- Measurements are taken for the nearest (1) cm.
- Jump up be feet together from the position of stability and not take a step or upgrade.
- Do not extend the chalk pieces outside the fingers so as not to affect the results.
- The arbitrator is preferred to stand on a table or ladder near the board so that he can read the results of the various attempts clearly.

Calculation of grades: The degree of the laboratory is the number of centimeters between the line that reaches it from the position of the stand and the mark to which it reaches as a result of the jump to the highest

close to the nearest (1) cm, and Figure (7) shows the performance of the test.

2. **Test the throwing of the medical ball weighing (2) kg of hands over the head of the sitting position on the chair:**⁴ Objective of the test: Measure the explosive force of the arms and shoulders.

Possibilities and tools: Medical ball weighing (2) kg, measuring tape and chair with belt and trunk fixed and tight.

Performance Specifications: The laboratory is placed on the chair and the medical ball is held by the hands above the head. The trunk is attached to the edge of the chair. The belt is placed around the lab trunk and is held from the back by an airway to prevent the laboratory from moving forward while throwing the ball in the hands. Three attempts to score his best.

Registration method: The distance between the front edge of the chair and the nearest point the ball places on the ground is calculated.

3. **Test the accuracy of the spike in the badminton:**⁵ Purpose of the test: Measure the accuracy of the spike in the badminton.

Performance Specification: The player is 120 cm from the front line, ready to perform the skill and the gap between the feet is 60 cm or chest width.

The trainer sends a feather to the area where the skill is to be performed and in the form determined by the player in advance and the condition is displayed and performed by the player prior to the execution of the test.

Registration method: The number of attempts is five attempts and the final score is 15 because each attempt score of three (3 - 2 - 1) includes all attempts.

Pre Tests: The researchers conducted the pretests on Sunday, 1/12/2018 at 3:00 pm. After giving the researchers a brief explanation of how the tests were performed and the purpose of the tests, then taking the measurements of length, weight, age and training.

Suggested exercises: The exercises were implemented during the special preparation period as follows:

- The proposed exercises started on 1/12/2018.
- Exercise period in weeks: (8) weeks.

- The total number of training units: (24) training units.
- Number of weekly training units: (3) units.
- Weekly training days: (Sunday - Tuesday - Thursday).
- Total training time: (90) minutes.
- Time of the main section of the module: (30-45) minutes.
- Training method used: high intensity training and repetitive training.

Posttests: After the completion of the implementation of the exercise vocabulary within the prescribed period and then conducting the tests for the research on 5/2/2019 at 3:00 pm in the stadium of Mahaweel Sports Club, the researchers took care to provide conditions similar to pretests in terms of time and place, perform the tests).

- Training intensity used: (85-95%). Of the extreme intensity of the player's performance.

Results

Table (3). Shows the mean difference, standard deviation and the value of (t) and the significance of differences between the results of pre and posttests of the control group in the variables under research

Ests	Units	Pretest		Posttest		(t) Calculated	Mistake percentage	Significance of differences
		Mean	SD	Mean	SD			
The explosive power of the two legs	Cm	30.00	3.37	30.14	3.63	5.213	0.005	Sig.
The explosive power of the arms	Meter	2.742	0.399	3.300	0.432	7.136	0.000	Sig.
The accuracy of the spike	Grade	9.864	1.875	11.435	3.985	4.698	0.003	Sig.

Table (4). The difference in the mean and its standard deviation and the value of (t) and the significance of the differences between the results of the pre-test and the experimental group in the variables in question

Tests	Units	Pretest		Posttest		(t) Calculated	Mistake percentage	Significance of differences
		Mean	SD	Mean	SD			
The explosive power of the two legs	Cm	29.86	4.10	44.71	4.11	3.778	0.004	Sig.
The explosive power of the arms	Meter	2.671	0.446	4.478	0.508	3.897	0.040	Sig.
The accuracy of the spike	Grade	9.896	1.543	13.043	4.985	3.328	0.002	Sig.

Table (5). The value of (t) and the error level and the significance of the differences between the results of the post-test of the control and experimental groups in the variables under consideration

Tests	Units	Control group		Experimental group		(t) Calculated	mistake percentage	Significance of differences
		Mean	SD	Mean	SD			
The explosive power of the two legs	Cm	30.14	3.63	44.71	4.11	5.221	0.007	Sig.
The explosive power of the arms	Meter	3.300	0.432	4.478	0.508	4.762	0.000	Sig.
The accuracy of the spike	Grade	11.435	3.985	13.043	4.985	3.832	0.003	Sig.

Discussion of Results: The results in Table (3, 4 and 5) show significant differences between the pre and post measurements of the experimental and control groups and for the post-test. There are also significant differences between the control group and the experimental group and for the experimental group that used the aftershocks. Several variables interfered with the airstrikes that included explosive power exercises in a new mode of increasing both power and speed, long jumps of stability,⁶ vertical jump, and arm-throwing operations, all of which contributed significantly to the development of force. The weight of the arms and the two legs working and intertwined in the skills of the spike in the badminton through the throwing of medical balls and weight in different situations, which strengthened the load of muscles for longitudinal loads, which in turn developed the adequacy of the relationship of tide and shortness in the muscle and also when the development of strength of the two legs, there is a correlation relationship when the strength of the muscles of the two legs. The results of explosive power expressed by vertical jump.⁷

The common pathway pathways lead to the ability of the plyometric for the possible improvement of neural pathways and neuromuscular cooperation during training, leading to increased strength output through improved muscle group collaboration.⁸

It should be noted that the development of the performance capacity can be obtained by producing the highest possible power in the shortest possible time. This situation is characterized by high strength and relatively low strength repressive exercises, which produces a link between power and speed, An explosive act and that the development of explosive power will be through the implementation of the exercises plyometric, which strengthens the saying that.⁹

The researchers attributed the improvement in the accuracy of the spike to the strength training exercises, which worked to develop the explosive force of the arms and legs and thus positively affected the skill performance of the skill of beating overwhelming because of the close link between the explosive ability of muscles and legs and the accuracy of the spike in the badminton, The ability to detonate the arms and legs of the role of positive and influential in the performance of skill, especially in the skill of the spike because it is the ingredients of the actual performance and the correct skill.¹⁰

Conclusions

1. A positive effect in the development of the explosive force of the arms and legs has been demonstrated by the use of the reactive power exercises of the experimental group and all tests.
2. A positive effect on the accuracy of the spike in the badminton has been demonstrated by the development of explosive force of the arms and legs using the reactive power exercises of the experimental group and all tests.
3. The reason for the development of the experimental group was the result of the use of the independent variable of aftershocks for the development of explosive force of the arms and legs, which effectively affected the development of the skill capabilities of the accuracy of the spike in the badminton.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: The authors declare that they have no conflict of interest.

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References

1. Ooi CH, Tan A, Ahmad A, Kwong KW, Sompong R, Mohd Ghazali KA, Liew SL, Chai WJ, Thompson MW. Physiological characteristics of elite and sub-elite badminton players. *Journal of sports sciences*. 2009 Dec 1;27(14):1591-9.
2. Fuchs M, Faude O, Wegmann M, Meyer T. Critical evaluation of a badminton-specific endurance test. *International journal of sports physiology and performance*. 2014 Mar 1;9(2):249-55.
3. Madsen CM, Højlyng M, Nybo L. Testing of Badminton-Specific Endurance. *Journal of strength and conditioning research*. 2016 Sep 1;30(9):2582-90.
4. Srinivasan M, Saikumar CV. Influence of conventional training programme combined with ladder training on selected physical fitness and skill performance variables of college level badminton players. *The Shield—Research Journal of Physical education & Sport Science*. 2012;12:69-82.
5. OZMEN T, AYDOGMUS M. Effect of plyometric

- training on jumping performance and agility in adolescent badminton players. *Turkish Journal of Sport and Exercise*. 2017;19(2):222-7.
6. Athab NA, Hussein WR, Ali AA. A Comparative Study for Movement of Sword Fencing Stabbed According to the Technical Programming in the Game of Fencing Wheelchairs Class B. *Indian Journal of Public Health Research & Development*. 2019;10(5):1344-7.
 7. Athab NA. An Analytical Study of Cervical Spine Pain According to the Mechanical Indicators of the Administrative Work Staff. *Indian Journal of Public Health Research & Development*. 2019; 10(5):1348-54.
 8. Alsayigh HA, Athab NA. The Study of Rectus Femoris Activity after Knee Joint Rehabilitation. 2016;9(9):360-5.
 9. Jumaah H, Ktaiman A, Abdul N, Athab K, Mohammed A. The Effect of Using Pain Management Techniques in the Rehabilitation of Chronic Lower Back Injury in Athletes and Non-Athletes. :108-12.
 10. Alsayigh HA, Athab NA, Firas M. Journal of Global Pharma Technology The Study of Electrical Activity of the Triceps Brachia Muscle according to the Chemical Changes of Water Loss during Spike in Volleyball. 2017;57-62.

Microscopic Vision of an Experimental Infection Effect with *Candida Glabrata* yeast in the Histological Structure of the Heart and Lungs in Immunosuppressed Male Mice and Other Normal Mice

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Abstract

The research was conducted to study histological structure of heart and lungs in male mice after being experimentally infected with *Candida glabrata* yeast isolated from the patient visitors of Tikrit Teaching Hospital suffering from Invasive Candidiasis (38 males, 25 females) between the ages of 15 and 82 years. The results showed pathological histological changes in both heart and lungs of male mice experimentally infected with the *C. glabrata* inhibitory immunosuppressant, which consisted of sloughing the basal membrane of the endocardium, as well as sarcoplasm degeneration of myocardial cells. In lungs the histological sections showed occurrence of extensive hemorrhage in and around alveoli and emergence of lymphocytes around the bronchioles as well as congestion and bleeding of blood vessels. While the results of the normal mice group (non-immunosuppressant) showed pathological histological changes represented by the local degeneration of heart sarcoplasm muscle, and in lungs have shown severe congestion of blood vessels and capillaries around alveoli as well as emergence of RBCs and desquamation of epithelial cells in the trachea with a local lymphocytic aggregation compared to the control group.

Keywords: Heart; histological structure; Microscopic vision.

Introduction

The genus *Candida* consists of a large number of species reaching up to about 200 species, but the pathogen is only about 20 species which are responsible for Invasive Candidiasis in humans and animals. It is characterized by the presence of ferocity factors that contribute to the invasion and colonization of host tissues⁽¹⁾. Therefore, the degree of infection varies between acute, moderate or chronic. Recently, there has been an interest in Candidiasis fungi due to the widespread of diseases caused by these fungi such as cutaneous skin infections as onychia, paronychia, intertrigo, mucocutaneous infections like oral thrush, vaginitis, and systemic infections such as fungemia, endocarditis, meningitis, pneumonitis, osteomyelitis, etc. (2-5).

Myocarditis-endocarditis or pericarditis by *Candida* is due to the spread through the blood, and then adhesion

to the damaged areas of heart. These yeasts usually settle in the endocardium on the valves as well as the entrance of the left ventricle to the aorta causing endocarditis with the possibility of a hole occurring in the heart valves and thus loss of functional control that may develop to severe heart failure, as well as complications that may be a threat to life if not treated quickly, such as the occurrence of clots that may flow into the arteries feeding the body organs causing infarctions or it may lead to pneumonia, respiratory distress, increased heart rate, severe drop in pressure, or loss of consciousness. The disease occurs as chlamydia diffused throughout the heart muscle in the normal tissue. It occurs at a rate of 50% in people with widespread Candidiasis⁽⁶⁾.

Material and Method

The sample was obtained from the blood (Candidemia) and a number of steps were taken to examine the isolate with diagnosis.

The Brain Heart Infusion Agar/Broth media was used to isolate the yeast and increase the vitality of the isolates before it was used in experiments⁽⁷⁾. It was prepared from brain and heart infusion (37 gm), agar (20 gm), distilled water (1000 ml). The media was incubated at (37°C) for (72) hours followed by microscopic examination and then transplanting on a sabouraud dextrose agar media prepared from the sabouraud dextrose agar (65 gm) and distilled water (1000 ml), incubated at (37°C) for (48) hours for purification and diagnosis of the isolate^(8,9). The morphological characteristics of the colonies represented by color and texture were observed and the isolate was identified and diagnosed depending on that, as well as some chemical examinations, with direct microscopy after pigmentation^(10; 11).

In terms of histological study, male mice of the Balb/c strain were used of (6) weeks in age with weights ranging from (22 to 28)gm. They were divided into four groups with (5) mice in each group, as follows:

- The first group: injected with (0.1 ml) of subcutaneous hydrocortisone drug for four days, and on the fifth day it was injected with (0.3 ml) of *C. glabrata* yeast suspension in the tail.
- The second group: injected with (0.3 ml) of *C. glabrata* yeast suspension in the tail.
- The third group: injected with (0.1 ml) of subcutaneous hydrocortisone for four days.
- The fourth group: injected with (0.1 ml) of distilled water and was considered as a control group.

The mice of the four groups were kept in normal conditions and monitored daily until the symptoms were shown (15) days after the injection. They showed underweight, redness of the ear, severe sweating, hair color changed to pale yellow, as well as one fainting case and two fatalities in the third group (injected with hydrocortisone drug and *C. glabrata* yeast suspension). The reason for injecting the mice with hydrocortisone drug is that it is an immunosuppressant or inhibitor for the purpose of increasing the rate of the experimental infection and comparing it with the normal group injected only by the yeast suspension, and then comparing them with the control group.

Then, slides were made by the sectioning method for heart and lung tissues using method of Scheuer and

Chalk, as well as Evans and Richardson^(12;13) and then examined and photographed under the microscope with different magnification forces.

Results and Discussion

The histological sections of immunosuppressed and non-immunosuppressed male mice infected experimentally with *C. glabrata* yeast showed several histopathological changes in heart and lung compared to the control group.

The histological pathological changes in heart and lungs were:

***The Heart:** The histological sections in the first group of mice showed a number of histological changes represented with appearance of a thickened basement membrane of endocardium and which sloughed from the tunica intima (Fig. 1), with degeneration of sarcoplasm of myocardium cells, particularly near the tunica intima and congestion of the branches of coronary arteries and appearance of RBCs outside the blood vessels (Fig. 2).

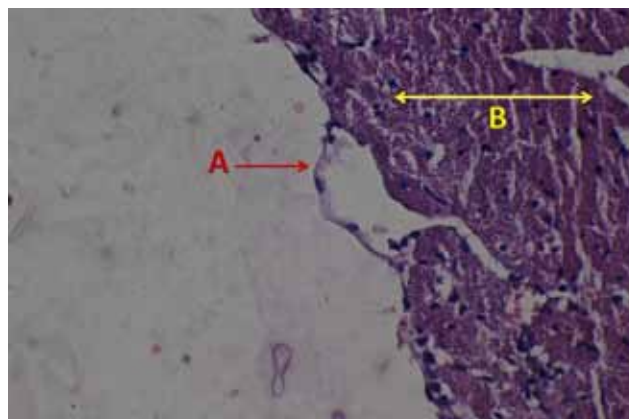


Figure 1: Section in heart of a mouse from the first group showing the sloughing of basement membrane of endocardium (A), as well as appearance myocardium in section (B). Hematoxylin and eosin stain. X40.

While the histological sections of heart in the second group of mice are normal in general in the cardiac muscles, with a number of histological changes represented by a local degeneration of the sarcoplasm and hemorrhage in blood vessels of the coronary arteries, as well as appearance of fibers loosened from each other in a number of heart muscles (Fig. 2).

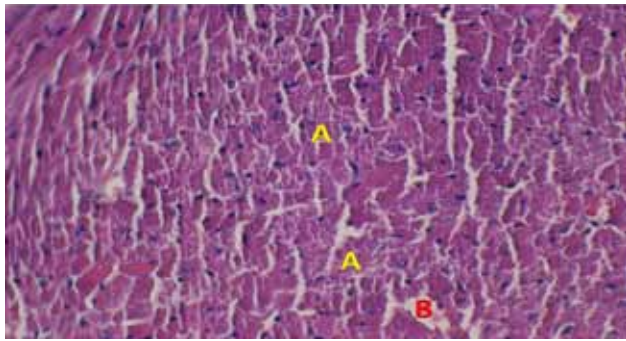


Figure 2: A section in heart of a mouse from the second group in which there is local degeneration of the sarcoplasm of myocardium (A), with hemorrhage in blood vessels of the coronary arteries (B). Hematoxylin and eosin stain. X40.

As for the histological sections of heart in the third group of mice, it appeared normal in the size and shape of the cardiac muscles in general, with a number of histopathological changes represented with loosening of the cardiac muscles and weak interconnections between them (Fig. 3).

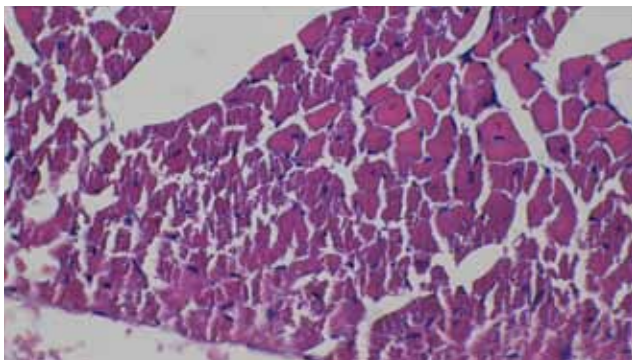


Figure 3: A section in heart of a mouse from the third group detecting the loosening of cardiac muscles, as well as their fibers. Hematoxylin and eosin stain. X40.

* **The Lungs:** The histological sections in the first group of mice showed a number of histological changes represented with occurrence of extensive hemorrhage in and around alveoli (Fig. 4).

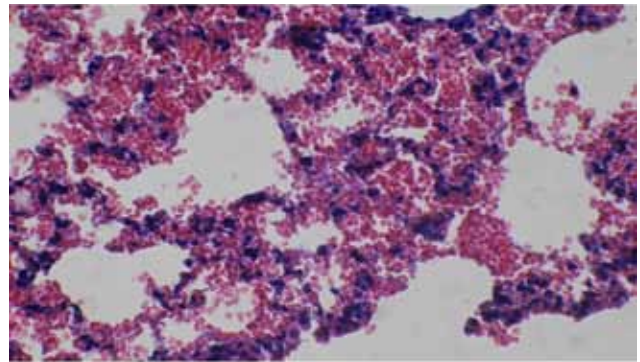


Figure 4: A section from a mouse lung of the first group in which extensive hemorrhage is observed in and around alveoli. Hematoxylin and eosin stain. X40.

While the histological sections of lung in the second group of mice showed a number of histological changes in the form of severe congestion in capillaries in between alveoli, and some of these alveoli consisted of RBCs in their cavities (Fig. 5).

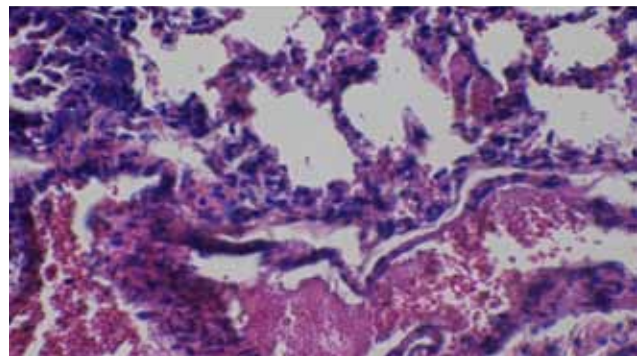


Figure 5: A section from a mouse lung of the second group in which there is a severe congestion of blood vessels and capillaries around alveoli. Hematoxylin and eosin stain. X40.

The histological lung sections of the third group of mice showed a number of histological changes, such as congestion in certain blood vessels in certain areas of the tissue, appearance of RBC outside the blood vessels, and a local aggregation of lymphocytes (Fig. 6). The sections clearly showed alveoli and its walls lined with epithelial cells and surrounded by interstitial connective tissue.

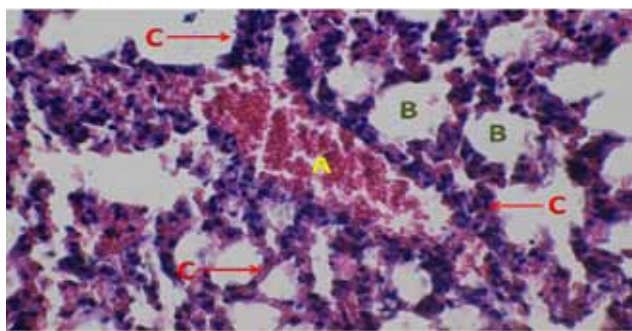


Figure 6: A section from a mouse lung of the third group detecting congestion in blood vessels (A), alveoli (B), and alveolar wall (C). Hematoxylin and eosin stain. X40.

The most important factors of virility of *Candida* genus is the ability of adhesion and penetrating host tissues, the possession of degenerating enzymes, the production of toxins, the ability to withstand different temperatures, the possibility of morphological shift from one form to another, as well as presence of cell wall which is considered the site of adhesion to host cells and then colonizing tissue and secretion of pathogens⁽³⁾.

The two most important physiological barriers for growth of fungi in human tissues are high temperature and redox potential^(14;15).

C. glabrata cell surfaces possess specialized proteins in their cell walls called adhesions⁽¹⁶⁾ similar to those found in *C. albicans*⁽¹⁷⁾. In addition to their normal life roles they work to achieve adhesion with host cells including phagocytes, epithelial and endothelial cells, and thus neutralize host defenses. Thus, it achieves links with host cell membrane proteins and carbohydrates such as fibrinogen, fibronectin, and laminin by forming a fibril layer containing multiple saccharines (i.e., it is of a protein and saccharine nature) on their cell surfaces⁽¹⁸⁾. Its ability to form biofilm helps its survival and is considered a distinguished characteristic and can escape from the host's defenses, as well as increase its resistance to anti-fungal and its ability to withstand the pressure of competition from other microbes^(19;20).

The possession of *Candida* yeast for hemolysin as a blood lyse agent grants it another important ferocity factor for it works to release hemoglobin as an important source of iron, which in turn is an important factor for growth in the body of the host, as well as the lyse of WBCs, especially neutrophils that are active in the resistance to being infected with *Candida* as well as macrophages and, therefore, the process of phagocytosis

becomes inefficient^(21;22).

The ability of *Candida* yeast to produce hydrolytic enzymes (constitutive and inducible) helps it invade the host's tissues by breaking or altering the host cell walls components, leading to rupture membranes of these cells or losing its functions. Although the components of these membranes are mostly lipids and proteins, therefore, these biochemical components were targeted by these enzymes⁽²³⁾, including phospholipase enzyme which analyzes phospholipids, and proteinase enzyme which analyzes the peptide bonds in protein molecules⁽²⁴⁾. In addition, these enzymes enhance the adhesion of *Candida* yeast to host cells, increasing their ferocity in invasion and destruction of its tissues. The seriousness of Candidiasis ranges between Mucosal Candidiasis infection which is a condition often observed in patients with acquired immunodeficiency syndrome (AIDS) and Systemic Candidiasis infections⁽²⁵⁾.

The appearance of histological changes in both heart and lung tissues of the mice experimental groups above mentioned indicates that the *Candida* yeast species have many ferocity factors that enable it to invade and infect host tissues including their adhesion ability⁽²⁶⁾ as well as its ability to produce protein and lipid lyse enzymes since carboxy protease enzymes breakdown Immune globulin IgA while the lyse enzymes of the type aspartyl protease facilitate invasion by breaking keratin and collagen in the basal membrane of the lining of blood vessels⁽²⁷⁾.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: The authors declare that they have no conflict of interest.

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References

1. Al-hussainy A and Kadhim M. Isolation and identification of dermatophytes fungi from under two year children in diaper location, 2014; 19(3): 98–110.
2. Kumar MB and Edwar CK. Robbins and Cotran Review of Pathology, Elsevier, 2014: 6–7.
3. Francois LM, Duncan W and Bernhard H. *Candida albicans* pathogenicity mechanisms, 2013; 4(2): 119–128.

4. Rex J H, Hwalsh TJ, Sobel SG, Filler PG, Pappas WE, Dismukes TW and Edwards JE. Practice guide lines for the treatment of Candidiasis. *Clin. Infect. Dis.*, 2000; 30: 662–678.
5. Coleman DC, Rinald MG and Haynes KA. Importance of *Candida* species other than *Candida albicans* as opportunistic pathogen. *Med. Mycol.*, 1998; 36: 123–128.
6. Vazquez JA and Sobel JD. Candidiasis. Chapter 11 In: *Clinical Mycology*. Dismukes, Ed. W.E. : Pappas, P.G. and Sobel, J.D. Oxford University Press, 2003: 519.
7. Vall JS, Nacente MS and Coll MS. *Handbook of Microbiology culture media*. 5th ed. Williams and Wilkins Philadelphia, 1999.
8. Emmons CW, Binford CH and Utz JP. *Candidiasis. In medical Mycology*. Lea and Fibiger. 2nd ed. Philadelphia, 1974.
9. Davise H L. *Medically important fungi*. 3rd ed. Washington. American Society for Microbiology, 1995.
10. Murray PR, Baron EJ, Pfaller MA, Tenover FC and Tenover RH. *Manual of Clinical Microbiology*. 7th ed. ASM Press. Washington, 1999.
11. Atlas RM. *Principle of Microbiology*. 1st ed. Mosby year book. Inc., 1995: 888.
12. Evans GV and Richardson JC. *Essentials of Medical Mycology*. Churchill Livingstone. Edinburgh, 1985.
13. Scheuer P and Chalk B. *Clinical Tests Histopathology*. Wolf medical publication. Ltd. The Netherlands, 1986.
14. Notario V, Kawai H & Cabib E. Interaction between yeast beta-(1 to 3) glucan synthetase and activating phosphorylated compounds. A kinetic study. *J. Biol. Chem.*, 1982; 257(4): 1902-1905.
15. Douglas L J & Mc Courtie J. Effect of tunicamycin treatment on the adherence of *Candida albicans* to human buccal epithelial cells. *FEMS Microbiol. Lett.*, 1983; 16(2-3): 199-202.
16. De Las A, Pan SJ, Castano I, Alder J, Cregg R and Cormack BP. Virulence-related surface glycoproteins in the yeast pathogen *Candida glabrata* are encoded in subtelomeric clusters and subject to RAPI- and SIR-dependent transcriptional silencing. *Genes Dev.*, 2003; 17: 2245–2258.
17. Cormack B P, Ghori N & Falkow S. An adhesin of the yeast pathogen *Candida glabrata* mediating adherence to human epithelial cells. *Science*, 1999; 285(5427): 578-582.
18. Vazquez JA and Sobel JD. Mucosal Candidiasis. *Infect. Dis. Clin. N. Am.*, 2003; 16: 793–820.
19. Silva S, Henriques M, Oliveira R, Williams D & Azeredo J. In vitro biofilm activity of non-*Candida albicans* *Candida* species. *Curr. Microbiol.*, 2010; 61(6): 534-540.
20. Mezher M A. Histological structure in immune suppression male mice brain and other natural experimentally infected with *Candida glabrata*. *Al-Anbar J. Vet. Sci.*, 2018; 11(2).
21. Berila N, Hyroššová P & Subík J. Oxidative stress response and virulence factors in *Candida glabrata* clinical isolates. *Folia Microbiol. (Praha)*, 2011; 56(2): 116-121.
22. Dupont H, Montraves P, Mohler J and Carbon C. Disparate finding on the role of virulence factors of *Enterococcus faecalis* and *Candida* spp. In mouse and rat models of peritonitis. *Infect. Immun.*, 1998; 66(6): 2570–2575.
23. Beausejour A, Grenier D, Goulet JP and Deslauriers N. Proteolytic activation of the interleukin-1 β precursor by *Candida albicans*. *Infect. Immun.*, 1998; 66: 676–681.
24. Ghannoum M and Abu-ETleen K. Correlative relationship between proteinase production, adherence and pathogenicity of various strains of *Candida albicans*. *J. Med. Vet. Mycol.*, 2000; 24: 204–413.
25. Kalkanci A, Güzel A B, Khalil I I, Aydin M, Ilkit M & Kuştimur S. Yeast vaginitis during pregnancy: susceptibility testing of 13 antifungal drugs and boric acid and the detection of four virulence factors. *Med. Mycol.*, 2012; 50(6): 585-593.
26. Kothavade RJ and Panthaki MH. Evaluation of phospholipase activity of *Candida albicans* pathogenicity in mice. *Med. Microbiol.*, 1998; 47: 99–102.
27. Ruchel R, De Bernardis F, Ray TL, Sullivan PA and Cole GT. *Candida* acid proteinases. *J. Med. Vet. Mycol.*, 1992; 1: 123–132.

Effect of Educational Modules in Learning Some Types of Handball Scoring for Students

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Abstract

The teaching method are no longer meeting the educational requirements that have increased during the current century. The need to expand educational services has multiplied day by day, which requires the development of modern teaching method to meet these challenges facing the educational process.

Therefore, the researchers tended to identify educational leaflets because they help the learner to acquire information in an orderly and intentional manner, and then take into account the link between motor skills and theoretical and emotional information and also link between new information and previous information in the structure of knowledge to reach a holistic view of the situation and the perception of its components, which leads to raise Efficiency of the educational process.

The research objective to: Identify the impact of unit's prepared educational leaflets in learning some types of scoring handball students under research. The research community was represented by students of the second phase, Faculty of Physical Education and Sports Sciences-University of Kerbala for the academic year 2018-2019 and from my division (A, C) where a sample of (40) students was selected in a random stratified manner in an equal manner and by (20) students for each division, where Division (A) represented the experimental group and learned to use educational brochures while Division (C) control group used The method used in the college of explanation and demonstration.

After a statistical analysis of the data, the researchers came to several conclusions. The presence of a positive effect size as a result of teaching using the educational leaflets of the experimental group, as well as the group that learned in the method followed (explanation and presentation) but in varying proportions.

Keywords: Educational, modern teaching; health behavior; modules and learning.

Introduction:

Education is one of the most important areas in the developed societies, where it is indispensable, therefore, the field of education is receiving great attention, especially in our era because of the scientific progress and technological development in various areas of life, especially education.

The educational process, including the challenges of the times, faces many of the problems that have become the focus of study in the field of education. Scientific research is the tool of society to solve its problems, and the strategies of educational systems in the face of these problems may vary according to different educational

reality in the world, and none of these systems can Educational system to overcome its problems without working to renew itself and find a modern system of education that is new in its objectives, content, method and means so that all factors affecting the educational process, and the various self-abilities of the learner, and all the means assigned to education to be subject to The benefit of the educational process so that education comes to fruition desired.¹

The choice of the teacher for the appropriate teaching method has become one of the important pillars on which the success of the educational process is measured, where the effectiveness and success of any

method is measured by the amount of processes used by the learner's abilities to understand what he is learning. Knowledge, and show skills in choosing the appropriate teaching method which helps to have interaction between the teacher and the learner and between the learner and the teaching material.²

Through the experience of researchers and the use of experienced professors and specialists in the teaching of handball course for students of the second phase in the Faculty of Physical Education and Sports Science University of Karbala found that there is difficulty in learning motor skills, in addition to the inability to link between different motor skills in addition to technical performance The skills lack accuracy and good compatibility between the elements of movement and the emergence of many technical errors, which are reflected on the results of students, and thus affect the failure to achieve educational goals at different levels. Handball is a popular team game, for all age groups because of the excitement and excitement as a result of the development of the level of players physically and skillfully.³

Research Hypothesis:

1. There is a positive impact of the educational units using educational brochures, in the level of skill performance of some types of handball for students.

2. There are significant statistical differences between the two groups (experimental and control) in learning the skill level performance of some types of scoring for students and for the experimental group.

Research Methodology: The researchers used the experimental method using the experimental design of two groups, one experimental and the other control, using the pre and post measurement of both groups.

Research community and sample: The research community represented the second stage students/ Faculty of Physical Education and Sport Sciences for the academic year 2018-2019, distributed on four divisions (A, B, C, and D). Division B represented the control group and after the exclusion of a number of students practicing the game of handball and repeaters and thus became the number and the two divisions (40/students) and by (20) students and each group.

Selecting offensive skills under consideration: The researchers identified the offensive skills under consideration by referring to the description of the second stage course in the faculty, namely: scoring of all types (flagellation scoring of stability and movement-scoring high jump and long), then was surveyed for some scientific references in the field of handball, tests and measures to determine a set of tests Attacking skills (under research).

Table (1). Percentage of expert consensus on the most appropriate tests measuring offensive skills (under consideration)

Skills	Tests that measured	Repetition (Number of Approval)	Percentage (%)
Scoring Carbaj stability	Carbajscoring of stability from behind the circle (9) m	13	92.85
	Receiving then scoring of stability	8	57.14
Carbaj scoring of the movement	Dribbling in a straight line and then scoring of the Carbaj movement	11	78.57
	Dribbling in a zigzag and then the scoring of the motion	7	50
High jump scoring	Shooting high jump from a distance of (9) meters	12	85.71
	High jump	8	57.14
Long jump scoring	Continuous jumping then shoot long jump	7	50
	Scroll and receive and then shoot long jump	11	78.57

Distribution of the research plan (for the pilot group) over the program weeks:

- A. The research plan using the educational leaflets included (6) weeks to implement the teaching units and lecture time (90) minutes divided into

(30) minutes to teach the educational aspect, (60) minutes for the applied side, and was applied in the period (6/3/2019) until (23/4/2018), The remaining lectures were devoted to the teaching of the rest of the handball course, and this division is due to the

researcher as the teaching plan in the faculty did not specify a time dedicated to teaching (the educational aspect and another applied).⁴

B. Preparation of educational units using educational leaflets: The educational units were constructed using educational leaflets for some types of scoring in all types (whip of stability and movement - high jump and long) by reference to scientific references such as: Time distribution of the plan of the handball course and by two lectures a week each time (90) minutes for (6) weeks duration The basic experience, then the educational units were presented to the professors experts and specialists in the field of teaching method and handball Appendix (1) and the experts suggested some modifications in the objectives of the educational units have been modified and expressed their approval of the proposed units.⁵

The researcher has followed the following steps when designing educational brochures:

1. Identifying Objectives: The researchers considered that the objectives of the educational units using the educational leaflets are clear in terms of the general

goal, which is translated into behavioral objectives formulated with precision and specific.

2. Educational leaflets: The leaflets were designed according to the steps of media preparation (name of the skill - the sample of the study - the general goal of the brochure procedural behavioral objectives - place - learning time - some important information about the skill learned - the educational progression of the skill).

Pretests: After the completion of the preparation of research tools in terms of scientific transactions (honesty, consistency and objectivity) were conducted pre measurements in the tests of some types of scoring (under research) on the research groups (experimental and control) for the period (4-5/3/2019) and the presence both the researchers, the teacher of Article and the assistant team.

Homogeneity and equivalence: In order to control the variables that affect the accuracy of the results, the researchers used to verify the homogeneity of the research sample of the variables studied as shown in Table (2).

Table (2).Shows the homogeneity of the members of the research sample

Variables	Experimental group N = 20		Control group N = 20		Value (t)
	Mean	SD	Mean	SD	
Weight (kg)	73.65	3.84	71.95	5.63	1.12
Overall body length (cm)	169.5	5.7	172	6.28	1.11
Age (years)	20.94	2.1	21.3	1.95	0.35

* The value of (T) tabular at the level and at the value (0.5) = 2.021

The equivalence of the two research groups:

Table (3).Shows the equivalence of the two research groups (experimental - control) in the study variables

Skills	Tests	Experimental group N = 20		Control group N = 20		Value (t)*	Sig.
		Mean	SD	Mean	SD		
Scoring Carbaj stability	Carbaj scoring of stability from behind the circle (9 m)	19	3.569	20.80	2.526	1.841	0.073
Carbaj scoring of the movement	Bouncing in a straight line and then scoring Carbaj of the movement	3.411	0.352	3.551	0.348	1.266	0.213
High jump scoring	Accurate jumping high jump from a distance of (9) meters	4.050	0.945	4.450	1.356	1.082	0.286
Long jump scoring	Scroll and receive and then scoring long jump	6.333	0.519	6.406	0.421	0.492	0.626

*Tabular value (t) at degrees of freedom (38) and significance level (0.05) = 2.021

Implementation of educational units: The educational units were implemented on the two research groups in the period from (6/3/2019) to (21/4/2019), which is two lectures per week (90) minutes divided into (30) minutes to teach the educational side, (60) minutes for the side Applied for a period of (4) weeks the duration of the basic experiment, according to the timetable of the course of handball, has been teaching to the experimental group using (educational leaflets) and

the control group according to the method used by the teacher.⁶

Posttests: After the completion of the application of the basic experiment was conducted after the tests of the two research groups in the tests of offensive skills (under research) on (22-23/4/2019) and the same conditions of pretest.

Results

Table (4). Mean, standard deviation and value (t) between the pre and post averages of the experimental group in tests of some scoring types (under consideration)

Tests	Pretest		Posttest		Value (t)*	Mean Diff.	SD diff.	Effect size
	Mean	SD	Mean	SD				
Carbaj scoring of stability from behind the circle (9 m)	19	3.569	26.250	5.350	6.211	7.250	5.220	1.389
Bouncing in a straight line and then scoring Carbaj of the movement	3.411	0.352	2.953	0.354	5.414	0.458	0.378	1.211
Accurate jumping high jump from a distance of (9) meters	4.05	0.945	6.150	1.089	8.768	2.100	1.354	1.551
Scroll and receive and then scoring long jump	6.333	0.519	5.817	0.528	7.865	0.516	0.293	1.759

*Tabular value (t) at degrees of freedom (38) and significance level (0.05) = 2.021

Table (5). Mean, standard deviation and the value of (t) between the mean of pre and post measurements of the control group in the tests of some types of scoring (under consideration)

Tests	Pretest		Posttest		Value (t)*	Mean Diff.	SD diff.	Effect size
	Mean	SD	Mean	SD				
Carbaj scoring of stability from behind the circle (9 m)	20.8	2.526	21.450	2.800	1.656	0.650	1.755	0.370
Bouncing in a straight line and then scoring Carbaj of the movement	3.551	0.348	3.435	0.422	2.784	0.116	0.186	0.623
Accurate jumping high jump from a distance of (9) meters	4.450	1.356	4.850	1.424	2.990	0.400	0.598	0.669
Scroll and receive and then scoring long jump	6.406	0.421	6.281	0.445	1.871	0.125	0.299	0.418

* Tabular value (t) at degrees of freedom (38) and significance level (0.05) = 2.021

Table (6). Mean, standard deviation and the value of (t) for experimental and control groups in telemetry scores for tests of some types of scoring (under consideration)

Tests	Experimental group N = 20		Control group N = 20		Value (t)*	Sig.	ETA square
	Mean	SD	Mean	SD			
Carbaj scoring of stability from behind the circle (9 m)	26.250	5.350	21.450	2.800	3.555	0.001	0.250
Bouncing in a straight line and then scoring Carbaj of the movement	2.953	0.354	3.435	0.422	3.913	0.000	0.287
Accurate jumping high jump from a distance of (9) meters	6.150	1.089	4.850	1.424	3.242	0.002	0.217
Scroll and receive and then scoring long jump	5.817	0.528	6.281	0.445	3.005	0.005	0.192

* The value of (t) tabular at the significance level (0.05) = 2.021

Discussions

These results are an indication of the role of the proposed teaching units in accordance with educational levels in the emphasis on linking educational experiences with each other and that previous experience is a guide to new experiences and all this contributed to the achievement of learning objectives in a better manner and continuous and permanent and continuous.⁷

In addition to the consolidation of information in the minds of learners and clarity of the knowledge structure of students, which led to the possibility and ease of recall and application of information in new situations, which shows through the implementation of what students have studied in the theoretical side through the application of skills with a set of individual, even and group exercises that lead to the arrival of students to the stage Good performance in the applied lecture.⁸

The results of the study are consistent with the assertions of meaningful learning is based on what remains in the learner's cognitive structure helps to re-learn any new information similar or similar to the information previously learned, and that in case of forgetting For some information, the basic concepts lose some of its sub-elements, but continue to retain the new meanings it has acquired, and thus continue to be able to facilitate the entry of new information to the cognitive structure of the learner. Added that the speed and effectiveness of learning depends on the learner's ability to make connections between the learning material and the repository of his knowledge structure and to link previous information with new concepts.⁹

This is confirmed by the findings of study which proved that the organization of information related to the learner's cognitive structure is useful in memorization, recall and retrieval processes, and leads to a clearer learning effect. Given the results of the skill tests, it was found that the mean values of the telemetric measurements were higher in all tests, which are important. The researchers refer to these results to present the content of the course of the handball (under research) in a more organized manner where the interaction of expertise, whether emotional dynamics. The material in the framework of the interdependent kidney and the realization of all its components and interconnections, thus the first hypothesis, which states there are statistically significant differences between the mean scores of the pre- and post-measurements of the experimental group in some types of scoring and in

favor of post-measurement is validated.¹⁰

Conclusions

1. The presence of a positive impact as a result of teaching using educational leaflets for the experimental group, and the method used (explanation and presentation) for the control group for some types of handball scoring (under research).
2. The experimental group that was taught using educational leaflets outweigh the control group that was taught by the method followed (explanation and presentation) in the performance level of some types of scoring (under research).
3. The results achieved proved the effectiveness of educational units prepared by researchers through the development of the variables under study.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

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References

1. Duchesne S, Mc Maugh A. Educational psychology for learning and teaching. Cengage AU; 2018 Oct 1.
2. Broek GV, Boen F, Claessens M, Feys J, Ceux T. Comparison of three instructional approaches to enhance tactical knowledge in volleyball among university students. *Journal of Teaching in Physical Education*. 2011 Oct 1; 30(4):375-92.
3. Siedentop DL, Hastie P, Van der Mars H. Complete guide to sport education. *Human Kinetics*; 2019 Feb 28.
4. Roberts SJ, Ryrie A. Socratic case-method teaching in sports coach education: reflections of students and course tutors. *Sport, Education and Society*. 2014 Jan 2;19(1):63-79.
5. Elsisy A. Effect of hybrid learning on student's satisfaction in faculty of physical education. In the 13th Conference Proceeding, Perspectives in physical education and Sport, Constanta 2013 May (Vol. 473).
6. Alsayigh HA, Athab NA, Firas M. *Journal of*

- Global Pharma Technology The Study of Electrical Activity of the Triceps Brachia Muscle according to the Chemical Changes of Water Loss during Spike in Volleyball. 2017;57–62.
7. Alsayigh HA, Athab NA. The Study of Rectus Femoris Activity after Knee Joint Rehabilitation. 2016;9(9):360–5.
 8. Jumaah H, Ktaiman A, Abdul N, Athab K, Mohammed A. The Effect of Using Pain Management Techniques in the Rehabilitation of Chronic Lower Back Injury in Athletes and Non-Athletes.: 108–12.
 9. Athab NA, Hussein WR, Ali AA. A Comparative Study for Movement of Sword Fencing Stabbed According to the Technical Programming in the Game of Fencing Wheelchairs Class B. *Indian Journal of Public Health Research & Development*. 2019;10(5):1344-7.
 10. Athab NA. An Analytical Study of Cervical Spine Pain According to the Mechanical Indicators of the Administrative Work Staff. *Indian Journal of Public Health Research & Development*. 2019; 10(5):1348-54.

Association between Diabetic Retinopathy and (Albumin/Creatinine) Ratio in Diabetic Patients

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Abstract

Introduction: Diabetes mellitus is a quickly upward illnesses in our world and it develop a chief community health problem. Diabetes is a sources of multiple long-term complications that have significant effect on the patients and society, the illness mostly touches peoples in their most creative ages diabetes has multiple systematic complications with macro-vascular and micro-vascular problems. Micro-vascular illness such as retinopathy, neuropathy, nephropathy and cardiovascular illnesses are a common problems of diabetes and it have a significant interrupting on the community & public health. Method: Across sectional study involved 75 patients with diabetes M. done in Al-Emamain Al-Kadhumain medical city from period September 2018 to July 2019, we organized questionnaire involved age of patients, gender, type of DM and duration of illness. Also all patents send for lab. To investigate HbA1c and albumin/creatinine ratio. Examination of fundus done after application of mydriatic eye drops (tropic amid) and used slit limp bio microscope and 90 D lens. Results: 75 patients included in our study, age of patients 51.4 ± 13.7 years old, duration of Diabetes M. 7.1 ± 4.2 years, 47 (63%) male included in our study and 28 (37%) female, also 12 (16%) of patients type 1 DM and 63 (84%) type 2 DM, there is significant association (P-value < 0.05) between degree of retinopathy and (albumin/creatinine) ratio; 29% of patents with microalbuminuria and 16% of patients with macro albuminuria, 9% of patients with ADED have macro albuminuria, 5% of patients with PDR have macro albuminuria, while 16% of patients with NPDR have microalbuminuria, 8% of patients with PDR have microalbuminuria.

Conclusion: Albuminuria/creatinine ratio is linked with theretinopathy in patients who have diabetic. So micro and macro albumin urea may be marker of proliferative retinopathy development so need close follow up.

Keyword: Diabetic retinopathy, HbA1c, (albumin/creatinine) ratio.

Introduction

Diabetes mellitus is a quickly upward illnesses in our world and it develop a chief community health problem. Diabetes is a sources of multiple long-term complications that have significant effect on the patients and society, the illness mostly touches peoples in their most creative ages. diabetes has multiple systematic complications with macro-vascular and micro-vascular problems. Micro-vascular illness such as retinopathy, neuropathy, nephropathy and cardiovascular illnesses are a common problems of diabetes and it have a significant interrupting on the community & public health. Diabetic retinopathy (DR) and nephropathy reflected one of the public reasons of visual damage⁽¹⁾, and end-stage renal illness correspondingly in persons

of both developed and developing civilizations⁽²⁾. Diabetic retinopathy is divided into two stages non-proliferative and proliferative stages. The stage of non-proliferative retinopathy usually appears lately in the first decade or early in the second decade of disease and the early pathologic changes consist of increasing thickness of the basement membrane endothelium and decrease in the pericytes number together with capillary micro aneurysms. Diabetic retinopathy also presented as new vessels formation in optic disc and the retina which proliferated into vitreous and causing eventually increase in fibrous tissue as well as vitreous hemorrhage and retinal tractional detachment^(3,4). It has been shown that individuals with diabetic retinopathy have a 25 times increased chance of losing their sight

comparing to normal individuals⁽⁵⁾. Reduction in visual acuity is moreover connected with proliferative harms or maculopathy. Numerous studies have been approved to discovery the issues that hasty retinopathy such as duration of the hyperglycemia, kind of diabetes, alteration in hormonal level, microalbuminuria, genetics, pregnancy. Some recommend that with the usage of new therapeutic and surgical method for handling diabetic retinopathy, lead to decrease the incidence of blindness up to 90%⁽⁶⁾, yet the available treatment options for the diabetic retinopathy are usually suboptimal in regard to restoring vision and for the prevention of further loss of vision. So it is of great importance to identify the local incidence of diabetic retinopathy, the progression rates and regression with treatment whether medical or surgical, and more importantly the associated risk factors in order to understand the disease and more importantly modifying such factors whenever it is possible that could help in decrease the incidence of diabetic retinopathy or at least slowing the progression of the visual impairment associated with diabetic retinopathy⁽⁷⁾. The aim of study is to find association between degree of retinopathy and level of albumin/creatinine ratio.

Material and Method

Across sectional study involved 75 patients with diabetes M. done in Al-Emamain Al-Kadhumain medical city from period September 2018 to July 2019, we organized questionnaire involved age of patients, gender, type of DM and duration of illness. Also all patents send for lab. To investigate HbA1c and

albumin/creatinine ratio. Normal of HbA1c was 7 so above it mean hyperglycemia. Early morning albumin/creatinine ratio classified to Norm albuminuria less than 30 mg/g, micro 30 – 300 mg/g and > 300 mg/g macro albuminuria⁽⁸⁾. Examination of fundus done after application of mydriatic eye drops (tropic amid) and used slit lamp bio microscope and 90 D lens. Also the degree of retinopathy classified to :

NO = No retinopathy, NPDR= No proliferative Diabetic Retinopathy, PDR = proliferative Diabetic Retinopathy and ADED = advance diabetic eye disease⁽⁸⁾. Analysis of data done by SPSS 22, for analyzed the association between variables used Chi- square for categorical data and spearman correlation for continuous data of HbA1c and albumin/creatinine ratio P- value < 0.05 mean significant association.

Results

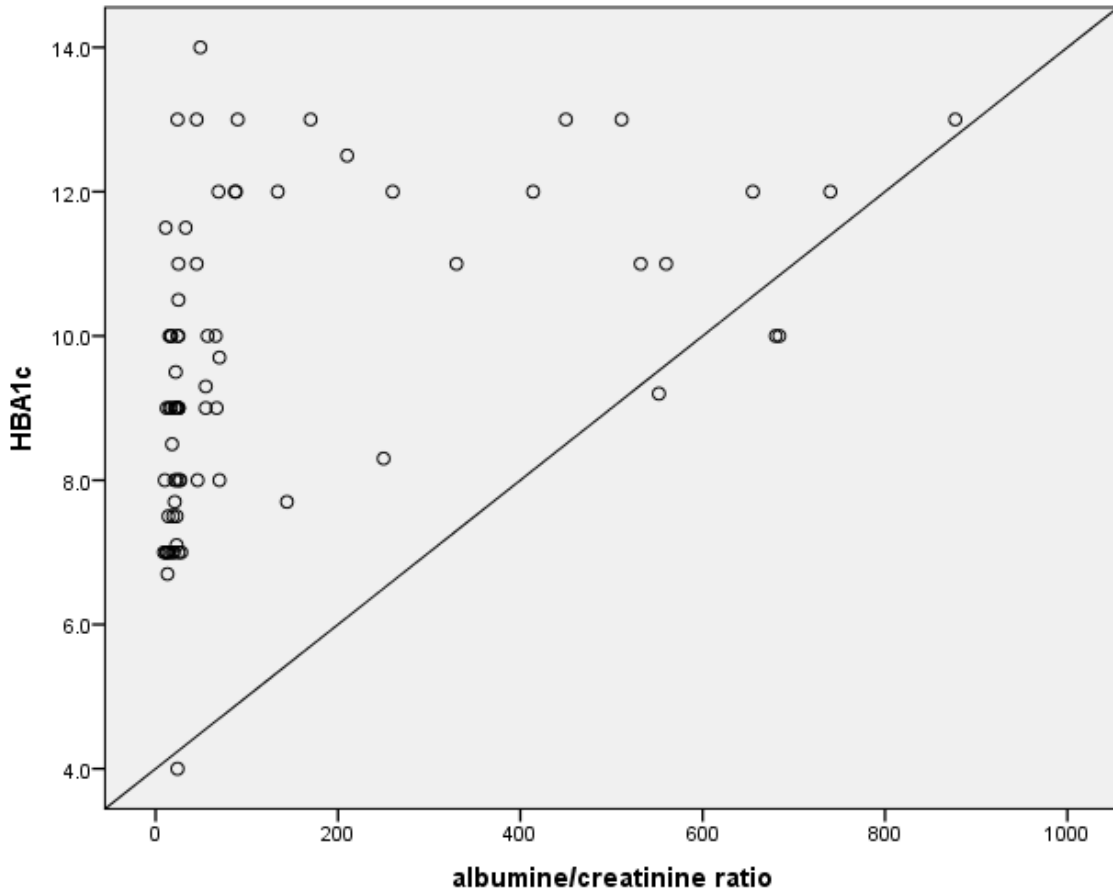
75 patients included in our study, age of patients 51.4±13.7 years old, duration of Diabetes M. 7.1±4.2 years, 47 (63%) male included in our study and 28 (37%) female, also 12 (16%) of patients type 1 DM and 63 (84%) type 2 DM. From table (1); show there is no significant association between age, gender and type of DM with degree of retinopathy, while according to duration of DM (years) there is significant association with positive correlation between it and degree of retinopathy especially after 5-10 years duration 40% of patient with ADED retinopathy.

Table (1): Association between variables and types of retinopathy

Variables	Retinopathy					X ²	P-value
	No	NPDR	PDR	ADED	Total		
Age							
≤30 years	4 (5.3%)	1 (1.3%)	1 (1.4%)	1 (1%)	7 (9%)	0.67	0.89
>30 years	31 (41%)	19 (25%)	10 (13%)	8 (11%)	68 (91%)		
Gender							
Female	21(28%)	14(18.7%)	9 (12%)	3 (4%)	47(62.7%)	5.6	0.13
Male	14(18.7%)	6 (8%)	2 (2.7%)	6 (8%)	28(37.3%)		
Type of DM							
1	6 (8%)	2 (2.7%)	3 (4%)	1 (1.3%)	12 (16%)	1.8	0.6
2	29(38.7%)	18 (24%)	8 (10.7%)	8(10.7%)	63(84%)		
Duration							
<5 years	23 (30.7%)	8(10.7%)	1(1.3%)	0(0.0%)	32(42.7%)	20.78	0.002**
5 –10years	9(12.0%)	7(9.3%)	7(9.3%)	7(9.3%)	30(40.0%)		
>10 years	3(4.0%)	5(6.7%)	3(4.0%)	2(2.7%)	13(17.3%)		

P- value< 0.05 * (significant).

All patients' HbA1c%, mean and SD (9.6±2.1) and about (albumin/creatinine) ratio mean and SD 132.6±212 mg/g. so there is significant positive correlation between HbA1c and (albumin/creatinine) ratio. When increase in HbA1c lead to increase in (albumin/creatinine) ratios show in fig (1).



Correlation Coefficient = 0.61, P-value = 0.0001**

Fig (1): Correlation between HbA1c and (albumin/creatinine) ratio.

In our study there is significant association (P- value <0.05) between degree of retinopathy and (albumin/creatinine) ratio; 29% of patents with microalbuminuria and 16% of patients with macro albuminuria, 9% of patients with ADED have macro albuminuria, 5% of patients with PDR have macro albuminuria, while 16%of patients with NPDR have microalbuminuria, 8% of patients with PDR have microalbuminuria, so when degree of retinopathy become more advance lead to increase (albumin/creatinine) ratio. As show in table (2).

Table (2): Association between types of retinopathy and (albumin/creatinine) ratio.

			Retinopathy				Total
			NO	NPDR	PDR	ADED	
Albumin Creatinine	Below 30 mg/g Norm albuminuria	Count	33	7	1	0	41
		% of Total	44.0%	9.3%	1.3%	0.0%	54.7%
	30 _ 300 mg/g microalbuminuria	Count	2	12	6	2	22
		% of Total	2.7%	16.0%	8.0%	2.7%	29.3%
	above 300 mg/g macro albuminuria	Count	0	1	4	7	12
		% of Total	0.0%	1.3%	5.3%	9.3%	16.0%
Total		Count	35	20	11	9	75
		% of Total	46.7%	26.7%	14.7%	12.0%	100.0%

Pearson Chi-Square = 67.603, P-value = 0.0001**

According to table (3) our study show significant association (P-value <0.05) between HbA1c and degree of retinopathy, so when degree of retinopathy become more advance lead to increase HbA1c, in the table; 85%

of patients with HbA1c more than 7, so 27% of patients with NPDR and have HbA1c>7, 15% of patients with PDR and have HbA1c >7 and 12% of patients with ADED and have HbA1c >7.

Table (3):

			Retinopathy				Total
			NO	NPDR	PDR	ADED	
HbA1c	7 and below	Count	11	0	0	0	11
		% of Total	14.7%	0.0%	0.0%	0.0%	14.7%
	above 7	Count	24	20	11	9	64
		% of Total	32.0%	26.7%	14.7%	12.0%	85.3%
Total		Count	35	20	11	9	75
		% of Total	46.7%	26.7%	14.7%	12.0%	100.0%

Pearson Chi-Square = 14.732, P- value = 0.002**

Discussion

Diabetic retinopathy is visual and a vascular problems related to diabetes M., it is defined as a gradually progressive alterations in the vessels of retina, rise in vascular permeability, retinal hypo perfusion and propagation of retinal vessels. So retinopathy reflected as one of problems of diabetes (9). In this study there is a significant association between duration of diabetes with degree of retinopathy especially NPDR with incidence 26% similar to study done by Kiran; NPDR was higher than PDR in all the patients. A significant association (0.0001)(10-12).

In our study there is positive colleration between HbA1c and (albumin/creatinine) ratio R= 0.61, P-value = 0.0001, similar to study done by U. Anandh; R= 0.14 and P-value 0.001(13).

Numerous studies were approved the occurrence of retinopathy and albuminuria in patients with diabetics, These revisions had diverse rates between 16 to 53.4% for retinopathy (14).this study displayed the occurrence rate of 53% in other study the occurrence rate was 39.3%(8). The used of different approaches in those study lead to difference in the rate, the population and or different in blood sugar level. The incidence rate of our study was 43% while in another study was 22% of microalbuminuria in diabetes patients(8,15) and 154% in study done by(8,16). In this study there is significant association between

the degree of retinopathy and albuminuria/creatinine ratio, similar to study above had the same significant association (14).Our study showed also the significant association between HbA1c and degree of retinopathy and also significant association between duration of illness and degree of retinopathy similar to study done by Masoud R Manaviat had the same significant association due to harm of vessels in retina and kidney(8). Klein et al showing that microalbuminuria may be seen in 29.2% of patients with insulin and 22% of non-insulin patients. So, insulin may have a part in nephropathy (17).Renal harm may hasten retinopathy also positive correlation between microalbuminuria and heart disease(12,13). So albumin in urine may be a mark of kidney illnesses and could be a reflect of vessel injury. In our study also there was significant association between HbA1c and degree of retinopathy (P- value = 0.002**), agreed with this result a study done by Pragati Garg(9), and other studies; a significant association between severity of diabetic retinopathy and HbA1c (p < 0.001)(10,18,19).

Conclusion

Albuminuria/creatinine ratio is related with theretinopathy in diabetic patients. So micro and macro albumin urea may be marker of proliferative retinopathy development so need close follow up.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of

both environmental and health and higher education and scientific research ministries in Iraq.

Conflict of Interest: The authors declare that they have no conflict of interest.

Funding: Self-funding

Reference

- Congdon, N. G., Friedman, D. S. & Lietman, T. Important Causes of Visual Impairment in the World Today. *Journal of the American Medical Association* (2003) 290, 2057–2060.
- Ritz, E., Rychlik, I., Locatelli, F. & Halimi, S. End-stage renal failure in type 2 diabetes: A medical catastrophe of worldwide dimensions. *American Journal of Kidney Diseases* (1999)34, 795–808
- Fong DS, Aiello L, Gardner TW, King GL, Blankenship G, Cavallerano JD, et al. Retinopathy in diabetes. *Diabetes Care*.(2004)1:S84-7..
- Viswanath, K. & McGavin, D. D. M. Diabetic Retinopathy: Clinical Findings and Management. *Community Eye Health* (2003) 16, 21–24.
- Browning, D. J., Stewart, M. W. & Lee, C. Diabetic macular edema: Evidence-based management. *Indian Journal of Ophthalmology* (2018).66, 1736–1750
- Fonseca, V., Munshi, M., Merin, L. M. & Bradford, J. D. Diabetic retinopathy: A review for the primary care physician. *Southern Medical Journal* (1996)89, 839–850.
- Mehanna, C. J. et al. Five-year incidence and progression of diabetic retinopathy in patients with type II diabetes in a tertiary care center in Lebanon. *Journal of Ophthalmology*,(2017)volume 2017, article ID 9805145, 7 pages,.
- Manaviat, M. R., Afkhami, M. & Shoja, M. R. Retinopathy and microalbuminuria in type II diabetic patients. *BMC Ophthalmology* (2004)4, 1–4.
- Karoli, R., Fatima, J., Shukla, V., Garg, P. & Ali, A. Predictors of Diabetic retinopathy in Patients with type 2 Diabetes who have normoalbuminuria. *Annals of Medical and Health Sciences Research* (2013)3, 536.
- Shah, K., Gandhi, A. & Natarajan, S. Diabetic retinopathy awareness and associations with multiple comorbidities: Insights from DIAMOND Study. *Indian Journal of Endocrinology and Metabolism* (2018)22, 30–35.
- De Block, C. E. M., De Leeuw, I. H. & Van Gaal, L. F. Impact of overweight on chronic microvascular complications in type 1 diabetic patients. *Diabetes Care* (2005)28, 1649–1655.
- Zhang, X. et al. Prevalence of diabetic retinopathy in the United States, 2005–2008. *JAMA - Journal of the American Medical Association* (2010)304, 649–656.
- Anandh, U. et al. MON-287 CORRELATION OF HBA1c AND URINE ALBUMIN CREATININE RATIO (UACR) WITH RENAL AND CARDIOVASCULAR HEALTH RISK FACTORS IN PATIENTS WITH DIABETES MELLITUS. *Kidney International Reports* (2019)4, S416–S417.
- Liu, D. P. et al. Retinopathy in a Chinese population with type 2 diabetes: Factors affecting the presence of this complication at diagnosis of diabetes. *Diabetes Research and Clinical Practice* (2002)56, 125–131 .
- Parving, H. H. et al. Prevalence of microalbuminuria, arterial hypertension retinopathy and neuropathy in patients with insulin dependent diabetes. *British Medical Journal (Clinical research ed.)* (1988)296, 156–160.
- Lunetta, M., Infantone, L., Calogero, A. E. & Infantone, E. Increased urinary albumin excretion is a marker of risk for retinopathy and coronary heart disease in patients with type 2 diabetes mellitus. *Diabetes Research and Clinical Practice* (1998).40, 45–51
- Eppens, M. C. et al. Prevalence of diabetes complications in adolescents with type 2 compared with type 1 diabetes. *Diabetes Care* (2006)29, 1300–1306.
- El Demerdash, F., Refaie, W., Allakany, R., Tantawy, S. & Dawood, E. Diabetic retinopathy: A predictor of coronary artery disease. *Egyptian Heart Journal*(2012) 64, 63–68.
- Ajoy Mohan, V., Nithyanandam, S. & Idiculla, J. Microalbuminuria and low hemoglobin as risk factors for the occurrence and increasing severity of diabetic retinopathy. *Indian Journal of Ophthalmology* (2011)59, 207–210.

The Effect of Socioeconomic Level on Dental Caries among Preschool Children in Baghdad City

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Abstract

Background: Dental caries and periodontal disease are the most common oral problems. It may start early in life and if not treated may end with tooth loss. Oral health is influenced by the socioeconomic status in which the socialization of the child takes place.

Aim of the Study: The survey was made to investigate the effect of socioeconomic status on dental caries of preschool children.

Subjects and Method: The total sample composed of 893 children aged (4-5) year selected randomly from different kindergartens in Baghdad governorate. WHO 2013 index was used for assessment of the dental caries experience and questionnaire was send to parents to assess their knowledge and behavior.

Results: Results showed that the prevalence of dental caries was 98% for the total sample, highly significant differences were seen between SES and dental caries experience dmfs of primary teeth, highly significant relation between SES and parents knowledge in all questions except questions concerning tooth decay and crowding of the permanent dentition was no significant while in behavior questions a highly significant relation was seen in all questions except questions concerning the type of bristle of the brush and preferable time for eating sweets was no significant . Conclusion: Preschool children in Baghdad were found to have a high prevalence of dental cariesSES effect on the dental condition. Hence this survey highlighted the need for children to dental health education programs and public and school preventive measures among those children.

Keywords: *Socioeconomic status, Dental caries, Preschool children.*

Introduction

Dental caries most commonly affect children, the impact of the oral conditions on children life include: difficulty with chewing, oral pain, missed school days due to their cumulative dental caries experience and changes in emotional e.g being upset and worrying about being different as well as anxiety or distress about their mouth⁽¹⁾.

The association between social and economic condition and dental caries prevalence has been observed, Inequalities in the distribution of dental caries were observed and socioeconomic factors were found to be strong predictors of the prevalence of oral disease in preschool children, family income, occupational

prestige, and educational attainment are measures of SES that have been found to influence an individuals life opportunities⁽²⁾.

Iraq is one of the developing countries that exhibited an increase of dental caries prevalence and severity. Many of studies found that dental caries prevalence showed low while the other studies was high prevalence^(3,4).many studies conducted to revel the relationship of socioeconomic status with dental caries all these studies depended on one or combination parameters of socioeconomic level, In the economically developing countries the prevalence and severity of dental caries has increased with industrialization and exposure of these populations to western diets. The families with higher

level of education, higher income, better occupation have higher caries experience which is attributed to the reason of consuming more refined sugar and cariogenic foods⁽⁵⁾.

This study was conducted on group of preschool children 4-5 year old living in Baghdad governorate to find out the effect of socioeconomic level on dental condition.

Subjects and Method

A sample of 893 preschool children 4-5 year old were selected randomly from different kindergartens in Baghdad governorate (471 boys and 422 girls) from urban areas in Baghdad city, from different kindergartens distributed in the city. The study received approval from the Research Ethics Committee of the College of Dentistry, University of Baghdad, Iraq.

Knowledge and behavior questions was recorded by 20 questionnaire⁽⁶⁾, which consist of: Question knowledge of parents about the mouth and teeth (Q1. and 2 concerning the number of deciduous and permanent teeth, tooth composition. Q3, 4 and 6 concerning tooth decay. Q5, 8 and 10 concerning crowding of the permanent dentition, and early loss of the primary teeth and thumb sucking habits. Q7 concerning the benefit of fluoride Q9 concerning visit to dentist), Question about the behavior of the parents (Q11, 12, 13, 16 and 19 concerning the frequency of the tooth brushing, brushing technique, use of dental floss and tooth picks, the way that child used to brush his teeth and the type of bristle of the brush respectively. Q14 concerning the preferable time for eating sweets. Q15 concerning the number of visits to the dentist Q17 and 18 concerning with toothache of child and dental decay respectively. Q20 concerning the use of tooth in bad habits).

Intra oral examination of dental caries status was recorded according to WHO 2013⁽⁹⁾ using CPI probe. Dental caries was measured by dmft/s for deciduous teeth.

The statistical data analysis was approached by using statistical package (SPSS) ver. (23.0) in order to analyze and assess the results of this study through application of descriptive data analysis, by frequencies and percentages. Inferential data analysis, these types of analysis were used to test hypotheses by accept or reject it, which include the following; Spearman Rank Correlation test, analysis of variance and significant at $p \geq 0.05$.

Results

Results showed that the prevalence of dental caries was 98% for the total sample. The mean dmfs (13.180).

The highly significant of relation dmfs with the level of SES found p value equal to 0.0000.

Highly Significant differences were seen between knowledge questionnaires and dental caries experience dmfs of primary teeth, some knowledge questions were no significant, the question about concerning crowding of the permanent dentition, and early loss of the primary teeth the dmfs p value=0.172 and the question about tooth decay the dmfs p value=0.985 also the question about thumb sucking habits the dmfs p value=0.150 and the question about visit to dentist the dmfs p value=0.086.

No significant differences were seen between behavior questionnaires and dental caries experience dmfs of primary teeth except the question about use of tooth in bad habits highly significant p value=0.000, and question about way that child used to brush his teeth p value=0.001.

Table (1): Caries Experience (Mean±SE) of Primary Teeth and dmfs in Relation to parents knowledge Questionnaires

	Know-ledge	ds				ms				fs				dmfs			
		mean	SE	T	p	mean	SE	T	p	mean	SE	T	p	mean	SE	T	P
Number of deciduous	Good	10.53	0.32	8.3	0.000	0.83	0.10	1.0	0.315	0.26	0.03	3.2	0.002	11.61	0.35	7.3	0.000
	Poor	15.06	0.44			0.68	0.10			0.11	0.03			15.86	0.46		
Tooth composition	Good	11.37	0.31	4.6	0.000	0.83	0.09	1.2	0.220	0.25	0.03	3.5	0.001	12.45	0.34	3.9	0.000
	Poor	14.09	0.50			0.65	.11			0.10	0.03			14.84	0.52		

	Know-ledge	ds				ms				fs				dmfs			
		mean	SE	T	p	mean	SE	T	p	mean	SE	T	p	mean	SE	T	P
Tooth decay	Good	12.21	0.27	.4	0.707	0.76	0.07	0.8	0.426	0.20	0.02	0.6	0.556	13.18	0.29	.0	0.985
	Poor	11.25	2.45			1.88	1.32			0.13	0.13			13.25	3.51		
Oral health	Good	11.64	0.28	4.9	0.000	0.80	0.08	1.1	0.264	0.23	0.03	6.4	0.000	12.67	0.30	4.2	0.000
	Poor	15.73	0.79			0.60	0.15			0.02	0.02			16.35	0.82		
Decay initiation	Good	11.72	0.30	3.8	0.000	0.77	0.08	0.0	0.964	0.22	0.03	1.3	0.186	12.71	0.32	3.4	0.001
	Poor	14.14	0.57			0.77	0.14			0.14	0.05			15.05	0.60		
Crowding of the permanent dentition	Good	12.16	0.27	1.8	0.106	0.78	0.07	0.7	0.499	0.20	0.02	0.1	0.910	13.14	0.29	1.5	.172
	Poor	15.91	2.10			0.45	0.45			0.18	0.18			16.55	2.30		
Early loss of the primary teeth	Good	11.46	0.31	4.9	0.000	0.76	0.09	0.4	0.698	0.23	0.03	1.9	0.064	12.44	0.34	4.7	0.000
	Poor	14.37	0.51			0.82	0.14			0.14	0.04			15.33	0.52		
Thumb sucking habits	Good	11.99	0.29	2.2	0.031	0.83	0.08	3.5	0.001	0.21	0.03	1.1	0.257	13.03	0.31	1.4	.150
	Poor	13.83	0.79			0.33	0.12			0.13	0.06			14.29	0.81		
Benefit of fluoride	Good	11.67	0.30	4.2	0.000	0.82	0.09	1.5	0.126	0.22	0.03	1.4	0.168	12.70	0.32	3.5	0.000
	Poor	14.40	0.58			0.57	0.14			0.14	0.05			15.12	0.60		
Visit to dentist	Good	12.02	0.28	2.7	0.008	0.82	0.08	5.1	0.000	0.22	0.03	8.6	0.000	13.06	0.30	1.7	.086
	Poor	14.56	0.89			0.15	0.11			0.00	0.00			14.71	0.90		

Not significant at $p \geq 0.05$, * significant $p < 0.05$

Table (2): Level of SES in Relation to behavior Questionnaires

	Socioeconomic Level												Chi-Square	P
	Low				Middle				High					
	Good		Poor		Good		Poor		Good		Poor			
	N.	%	N.	%	N.	%	N.	%	N.	%	N.	%		
Frequency of the tooth brushing	348	40.37	24	77.42	233	27.03	5	16.13	281	32.60	2	6.45	17.649	0.000
Brushing technique	342	40.09	30	75.00	230	26.96	8	20.00	281	32.94	2	5.00	21.284	0.000
Dental floss and tooth picks	358	40.87	14	82.35	236	26.94	2	11.76	282	32.19	1	5.88	11.973	0.003
Way that child used to brush his teeth	275	37.11	97	63.82	198	26.72	40	26.32	268	36.17	15	9.87	49.125	0.000
The type of bristle of the brush	370	41.62	2	50.00	236	26.55	2	50.00	283	31.83	0	.00	2.162	0.339
Preferable time for eating sweets	327	40.77	45	49.45	217	27.06	21	23.08	258	32.17	25	27.47	2.532	0.282
Number of visits to the dentist	324	39.46	48	66.67	224	27.28	14	19.44	273	33.25	10	13.89	21.116	0.000
Toothache of child	338	40.67	34	54.84	220	26.47	18	29.03	273	32.85	10	16.13	8.012	0.018
Dental decay	372	41.66	0	0	238	26.65	0	0	283	31.69	0	0	0	0
Use of tooth in bad habits	219	63.85	153	27.82	89	25.95	149	27.09	35	10.20	248	45.09	147.069	0.000

Not significant at $p \geq 0.05$, * significant $p < 0.05$

Table (3): Caries Experience (Mean±SE) of Primary Teeth and dmfs in Relation to SES

Dental caries	Low SES		Middle SES		High SES		F	p
	Mean	SE	Mean	SE	Mean	SE		
ds	15.04	0.440	12.20	0.490	8.466	0.365	60.94	0.000 HS
ms	0.688	0.104	0.887	0.148	0.788	0.140	0.602	0.548 NS
fs	0.118	0.030	0.294	0.056	0.237	0.042	5.032	0.007 S
dmfs	15.85	0.460	13.38	0.534	9.491	0.420	48.91	0.000 HS

Not significant at $p \geq 0.05$, * significant $p < 0.05$

Discussion

In this study, the prevalence of dental caries was found to be high for primary school (4-5) year children. This percentage was more than study done in Indian⁽⁷⁾ and more than some Iraqi studies^(3,8,9,10). The high caries prevalence recorded by this study may partly be attributed to lower fluoride level in drinking water in Iraq that was ranging between 0.12-0.22⁽¹¹⁾, and may also related to other factors related to the socioeconomic condition and living style of the families⁽¹²⁾. For the diagnosis and recording of caries-experience; dmfs indices was used in present study. This indices allows measurement of the past caries-experience indicated by missing and filled fraction, and the present caries by the decayed fraction. In addition, dmfs index allow the measurement of dental caries by severity. The mean dmfs value was (13.180) compare with other Iraqi studies^(14,15).

This study showed that the mean of ds fraction (12.205) was higher than ms and fs components of dmfs index, which is an indication of a poor dental treatment. Which is mean that even if treatment is present, it is directed toward extraction rather than restoration. This result is in agreement with other studies^(8,13,9).

In this study, the knowledge questionnaire has highly significant difference with SES, may be attributed that low knowledge group compared to children from high SES families. This discrepancy differences in the home learning environment. and in parent beliefs⁽¹⁶⁾, except the question about dental caries and crowding in permanent teeth had no significant difference. Also the study showed that there was highly significant difference

in the relation behavior questionnaires to SES, may be attributed, The relationship between family life events and rates of maternal reports of child behavior and child rearing problems preschool-aged children. Mothers experiencing a large number of life events reported higher rates of child rearing problems⁽¹⁷⁾, except the question about type of bristle and preferable time of eating sweet had no significant difference.

Conclusion

This survey highlighted the need of children to preventive measures and dental health education and improvement of dental knowledge and attitude towards good oral hygiene.

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References

1. Foster Page LA, Thomson WM, Jokovic A, Locker D. Validation of the Child Perceptions Questionnaire (CPQ 11–14). Journal of Dental Research 2005;84(July (7)):649–52.

2. Shubber S, Al-Obaidi W. Oral Health Status among Kindergarten Children in Relation to Socioeconomic Status in Al-Najaf Governorate-Iraq. Master D submitted to the college of Dentistry, University of Baghdad;2014.
3. Diab B. Nutritional Status In Relation To Oral Health Condition among 10 years primary school Iraqi children in the middle region of Iraq. Ph D thesis submitted to the college of Dentistry, University of Baghdad;2003.
4. Abdul Razzaq Q. Oral Health Status Among 15 Year-Old School Students In Sulaimania City-Iraq. Master Thesis Submitted to College of Dentistry, University of Baghdad;2007.
5. Al-Hassnawy A, Socioeconomic and Nutritional Status in Relation to Oral health Status and Treatment needs in Dewanyiah Governorate among 12 years old school students Master Thesis Submitted to College of Dentistry, University of Baghdad;2014.
6. Al-Eissa D, Oral Health Status of Preschool Children aged 3-5 years old and Its Relation to Their Socioeconomic and Parental Knowledge and Behavior and Attitude in Two Different Social area in Baghdad City Master Thesis Submitted to College of Dentistry, University of Baghdad;2004.
7. Martins-Júnior PA, Oliveira M, Marques LS, Ramos-Jorge ML. Untreated dental caries: impact on quality of life of children of low socioeconomic status. *Pediatr Dent.* 2012;34(3):49-52.
8. Alwaheb A and Alhuwaizi A. Assessment of Dental Caries among Internally Displaced Children in Baghdad. *Bagh Coll Dentistry* 2018; 30(3): 28-31
9. AL-Ghalabi S. Oral health status and treatment need in relation to nutritional status among 9-10 year-old School Children in Nassirya City, Iraq. Master thesis submitted to College of Dentistry, University of Baghdad; 2011.
10. Al-Awadi A. Oral Health Status in Relation to Nutritional Status among 9 Years- old School Children in Al-Diwaniyah City, Iraq. Master thesis submitted to College of Dentistry, University of Baghdad;2016.
11. AL-Azawi L. Oral health status and treatment needs among Iraqi five-years old kindergarten children and fifteen-years old students (A national survey) Ph.D. thesis submitted to College of Dentistry, University of Baghdad;2000.
12. Al-Hassnawi A and Alwaheb A. Socioeconomic status in relation to dental caries in Dewanyiah governorate among 12 years old school students. *J Bagh College Dentistry* June 2014; Vol. 26(2),22-26
13. Baram A. Oral health status and treatment needs among primary school children in Sulaimani city. Master thesis submitted to College of Dentistry, University of Baghdad;2007.
14. Al-Ghalebi S. and El-Samarrai S. Oral health status and treatment needs in relation to nutritional status among 9-10 year-old school children in Nassirya City, Iraq. *J Bagh College Dentistry*,2012.
15. -Diab, B.S., 2003. Nutritional status in relation to oral health condition among 6-10 years primary school children in the middle region of Iraq (Doctoral dissertation, PhD thesis, College of Dentistry, University of Baghdad).
16. DeFlorio L and Beliakoff A - Early Education and Development, Taylor & Francis, Socioeconomic status and preschoolers' mathematical knowledge: The contribution of home activities and parent beliefs,26,(3),319-341,2015.
17. Beautrais A L, Fergusson DM, Shannon F T. Family Life Events and Behavioral Problems in Preschool-Aged Children, November 1982, VOLUME 70 .

The Effect of Submucous Dexamethasone Injection on the Post-Operative Sequelae After Impacted Third Molar Surgery

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Abstract

Background: Different methods were attempted by many researchers to reduce postoperative inflammatory response following surgical extraction of lower wisdom teeth because this is a very common procedure and is usually associated with pain, difficulty in mouth opening and swelling. Aims: To assess the effect of sub mucosal injection of 4mg/1ml dexamethasone on reduction of postoperative pain, facial swelling and trismus following the surgical extraction of impacted lower wisdom teeth.

Materials and Method: forty patients were selected to be included in this randomized clinical study with a total number of 42 impacted mandibular third molars, they divided randomly into two groups, control and study group of twenty patients for each, patients in the study group received 4mg/1 ml submucosal injection of dexamethasone, while patients in the control group received placebo (normal saline) five minutes after local anesthesia administration, and surgical removal of impacted teeth was done after further five minutes. Evaluation of mouth opening and swelling was done as a baseline and on the second and seventh postoperative days after surgery, while pain was scored daily until the 7th postoperative day by the patient according to numerical rating scale. Assessment of trismus was done by measuring the maximum interincisal distance swelling was evaluated by measuring the distance between five selected points. Every one of these factors in addition to the time of surgery were compared between the two groups.

Results: Study group showed less limitation in mouth opening than control group but there was no statistically significant difference between them however study group showed a significant reduction in pain scores on the first and the second post-operative days and a significant improvement of swelling compared with the control group at the 48 hour follow up.

Conclusion: Submucosal injection of dexamethasone was effective in minimizing facial swelling, Pain and trismus after surgical extraction of mandibular third molar.

Keywords: *Impacted third molar; corticosteroid therapy, submucosal injection, dexamethasone.*

Introduction

Impacted tooth is defined as a tooth, maintained in

the jaw, beyond its normal time of eruption. Impaction also can be defined as a pathological problem in which a tooth fails to erupt into its correct functioning position⁽¹⁾.

Surgical extraction of lower third molar is one, of the most, common minor oral surgical, procedures practiced on a daily basis, in oral and maxillofacial surgery⁽²⁾. Difficulty of extraction varies from relatively easy to extremely difficult depending on many factors, for example, depth and angulation of the tooth in relation to investing bone and ascending ramus of the mandible, and bone density⁽³⁾ many surgical elements, like the design

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of flap or time of the procedure, can affect postoperative symptoms after lower third molar surgery, though it is frequently associated with symptoms, like pain, and signs, like swelling and trismus⁽⁴⁾. Also these post-operative sequelae varies according to the individual physiologic inflammatory response⁽⁵⁾. understanding the predisposing factors of postoperative morbidity is necessary in determining treatment options and the intellectual preparation of the patients⁽⁶⁾ different method were attempted to reduce postoperative sequelae after lower third molar surgery.⁽⁷⁾ Corticosteroids are one of the most widely employed medications administered to control these complications.⁽⁸⁾

The most widely used type of corticosteroid is Dexamethasone which has a substantial effect on the resolution of inflammation.⁽⁹⁾

However, the use of sub mucosal route of administration of dexamethasone injection in the surgical removal of impacted lower wisdom teeth remains under investigated. but data from many studies suggests that the sub mucosal injection of dexamethasone leads to a reduction in the postoperative signs and symptoms following impacted third molar surgery^(10,11).

Materials and Method: forty patients were selected to be included in this randomized clinical study with a total number of 42 impacted mandibular third molars. They divided randomly into two groups: control and study group of twenty patients for each (A computer-generated random numbers were used for simple randomization of subjects).

The inclusion criteria of the selected patients was No history of any uncontrolled systemic diseases or any recent anti-inflammatory drug intake (1 week) or being under long term treatment with NSAIDs, steroids, or antihistamines.

Pregnant women or any patient with acute infection or patients allergic to corticosteroids were excluded from this study.

A specially designated case sheet was filled. radiographical examination (Orthopantomogram (OPG) and a periapical radiograph) in addition to clinical examination was done for all the patients prior to the surgery after that subjects were informed about the study protocol and a written approval was gained preoperative evaluation of Mouth opening was checked by the researcher by using a sliding caliper and determine the

distance between the incisal edges of the upper left to the lower left central incisor.

At 48 hour and 7th day visit, evaluation of mouth opening was done, by using similar method of preoperative evaluation and by the same examiner. Calculation of the percentage of trismus was done by measurement of preoperative value minus postoperative value divided by preoperative value multiplied by 100.⁽¹²⁾

Swelling was estimated by using The measuring tape to calculate the distance between 3 selected planes: tragus to the outer corner of the mouth, tragus to the soft tissue pogonion and the distance between lateral angle of the eye and angle of the mandible. These measurement are done prior to the surgical removal of the impacted third molar as well as on the second and the seventh postoperative days.

calculation of swelling was done by the sum of the three measurements divided by three and percentage of facial swelling was calculated as preoperative measurement minus postoperative measurement divided by preoperative measurement multiplied by 100.⁽¹²⁾

Pain evaluated by using numeric rating scale.

All surgeries were performed under local anesthesia using lidocaine hydrochloride 2% with adrenaline 1:80,000 (septodent, France) in 2.2 ml glass cartridge (2 carpules).

Five minutes after the application of lingual, inferior alveolar nerve block, and infiltration anaesthesia for long buccal nerve, each patient received a submucosal injection by using insulin syringe of 1 ml dexamethasone or 1 ml placebo based on their group either study or control which was selected randomly (0.5ml in the lower buccal vestibule near the intended area for surgical removal of impacted mandibular molar and 0.5 ml in the retromolar area of the same side). A further 5 min after the application of dexamethasone or placebo, incision was performed and reflection of a mucoperiosteal flap on the buccal side to gain adequate access to the field, overlying bone must be removed for exposure.

bonecutting was done under continuous irrigation with normal saline, and sectioning of the tooth was done when needed. tooth was removed from the socket then inspected for any sharp edges then it was irrigated thoroughly with normal saline. the flap adapted to the underlying, then suturing with 3/0 black silk

The time of the procedure was recorded from the first cut of incision to the end of suturing subtracting the time for any obstacle or delaying issue from the total time

All patients had instructed to take systemic antibiotic which consist of Amoxicillin 875 mg/Clavulanate 125 mg tab. once daily for 5 days, or if the patient allergic to penicillin Azithromycin tab. 500 mg once daily for 5 days

The analgesic was (paracetamol tab 500 mg. for 3 days) and instructed to request additional analgesics tabs of the same type in the event of aggravated pain episodes

Statistical Analysis: The data analyzed using Statistical Package for Social Sciences (SPSS) version 25. The data presented as mean, standard deviation and ranges. Categorical data presented by frequencies and percentages. Independent t-test (two tailed) was used to compare the continuous variables accordingly between study groups. Z-test was used to compare the categorical variables accordingly between study groups. Paired t-test was used to compare the continuous variables preoperatively and in the 1st and 2nd follow up postoperatively. A level of P – value less than 0.05 was

considered significant.

Findings: A total of 40 Iraqipatients were included in this study,patient’s age was ranging from 17 to 40 years with a mean age of 28.85 years .of total 60% were males and 40% were females.

The radiographic analysis of the angulation of the impacted teeth according to winters classification showed that the majority of impacted third molars in this study were mesioangular (50%), (35.7%) were Horizontal, (11.9%)were Vertical, (2.4%)were Distoangular.

Position B was the most frequent depth according to Pell and Gregory classification(64.3%), Position A: (31.0%), Position C: (4.8%).class I(42.9%),class II (57.1%), class III(0%).

At the 1 st follow up (48 hour)percentage of swelling was less in the study group than in the control group and the difference was statistically significant between two groups (P-value = 0.001), but no statistically significant difference was found between two groups on 7thpost-operative day follow up,while for trismus the difference was statistically non-significant at both follow up periods.

Table 1: Comparison of swelling between study and control groups in first and second follow up

Swelling (%)	Group		P- Value
	Control Group Mean±SD	Study Group Mean±SD	
First follow up	6.49±1.11	1.05±0.5	0.001
Second follow up	3.26±0.47	3.01±0.53	0.11

Means of pain scores according to NRS was less in the study group than in control group from the first to the seventh post-operative days but still statistically non-significant, except for the first and the second post-

operative days in which the difference was statistically significant.(5.8 versus 4.28, P= 0.001; and 4.9 versus 3.45, P= 0.001 respectively).

Table 2: Difference by group of NRS for seven postoperative days

Postoperative Pain	Study Group		P- Value
	Control group Mean±SD	Study Group Mean±SD	
Day One	5.8±0.87	4.28±0.71	0.001
Day Two	4.9±0.99	3.45±0.75	0.001
Day Three	3.12±1.26	2.55±0.75	0.093
Day Four	2.21±1.37	1.85±0.81	0.317
Day Five	1.56±0.89	1.3±0.65	0.3
Day Six	0.81±0.54	0.65±0.67	0.416
Day Seven	0.43±0.31	0.2±0.41	0.069

Table 3: Comparison in limitation of mouth opening between study groups in first and second follow up

Mouth opening limitation (%)	Study Group		P- Value
	Group A Mean±SD	Group B Mean±SD	
First follow up	- 41.63±10.02	- 39.65±9.8	0.52
Second follow up	- 9.14±4.55	-7.92±3.8	0.35

Discussion

The surgical removal of impacted third molar is the most common surgical procedure in oral and maxillofacial surgery⁽¹³⁾. Impacted third molar surgery commonly involves elevating the mucoperiosteal layer, guttering the bone adequately, and performing an odontectomy. These procedures cause severe soft tissue and bone damage and inevitably lead to the release of various inflammation mediators, including bradykinin, histamine, and serotonin, which precede pain, swelling, and trismus after third molar surgery.⁽¹⁴⁾

Corticosteroids have potent anti-inflammatory activity and have been used at different dosages and through various routes of administration to lessen the inflammatory effects of third molar surgical removal⁽¹⁵⁾

Dexamethasone has the highest anti-inflammatory potency among synthetic corticosteroids which is 20-30.⁽¹⁶⁾

In 2017, a systematic review and meta-analysis by Chen et al. found a significant effect for the reduction of early and late oedema and early trismus following submucosal dexamethasone administration⁵. No significant result was found for the reduction of late trismus⁽¹⁷⁾ use of dexamethasone to minimize edema is due to the fact that Corticosteroids are known to reduce fluid transudation, and edema. Their anti-inflammatory role is explained by the principle of endogenous protein synthesis which blocks the enzymatic activation of phospholipase A2. This in turn blocks the release of arachidonic acid from components of cell membrane thereby finally inhibiting substances related to thromboxane such as prostaglandins and leukotrienes.⁽¹⁸⁾ pain is a significant postoperative complications, and it mainly arise from inflammatory response.

Several biochemical mediators are involved in the pain process, particularly histamine, bradykinin and prostaglandins, The intensity of postoperative pain ranges from moderate to severe during the first 24 h

after surgery, with the pain peak being within the first 12 h when a medium-acting local anesthetic is used⁽¹⁹⁾ prostaglandin formation is inhibited by corticosteroids, thereby facilitating some analgesic effects⁽²⁰⁾ a systematic review conducted by O'Hare et al. in 2019 concluded that, pain was reduced in terms of the VAS score on days 1, 3, and 7 postoperative in patients who received submucosal dexamethasone compared with placebo or no intervention and the maximal reduction of postoperative pain occurs in the early postoperative period.⁽²¹⁾

Conclusion: in conclusion submucosal administration of dexamethasone is simple and effective method to reduce pain, swelling and trismus after surgical removal of impacted third molar.

Conflict of Interest: There are no conflict of interest for both authors.

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Ethical Clearance: This research was approved by ethics committee at college of dentistry/Baghdad university.

References

1. Pechalova PF, Pavlov, N.V. and Konstantinova, D.A. . Mandibular Third Molars in Southern Bulgaria–A Clinical and Radiological Study of 1518 Patients. J Dent Probl Solut. 2017;4(2):pp.026-30.
2. Chaudhary PD, Rastogi S, Gupta P, Niranjana Prasad Indra B, Thomas R, Choudhury R. Pre-emptive effect of dexamethasone injection and consumption on post-operative swelling, pain, and trismus after third molar surgery. A prospective, double blind and randomized study. Journal of oral biology and craniofacial research. 2015;5(1):21-7.
3. Mistry FK, Hegde ND, Hegde MN. Postsurgical consequences in lower third molar surgical extraction using micromotor and piezosurgery. Annals of maxillofacial surgery. 2016;6(2):251-9.

4. Mobilio N, Vecchiatini R, Vasquez M, Calura G, Catapano S. Effect of flap design and duration of surgery on acute postoperative symptoms and signs after extraction of lower third molars: A randomized prospective study. *Journal of dental research, dental clinics, dental prospects*. 2017;11(3):156-60.
5. Sabhlok S, Kenjale P, Mony D, Khatri I, Kumar P. Randomized Controlled Trial to Evaluate the Efficacy of Oral Dexamethasone and Intramuscular Dexamethasone in Mandibular Third Molar Surgeries. *Journal of clinical and diagnostic research : JCDR*. 2015;9(11):ZC48-ZC51.
6. Rakhshan V. Common risk factors for postoperative pain following the extraction of wisdom teeth. *Journal of the Korean Association of Oral and Maxillofacial Surgeons*. 2015;41(2):59-65.
7. Chukwuneke F, Onyejiaka N. Management of postoperative morbidity after third molar surgery: a review of the literature. *Nigerian journal of medicine : journal of the National Association of Resident Doctors of Nigeria*. 2007;16(2):107-12.
8. Klongnoi B, Kaewpradub P, Boonsiriseth K, Wongsirichat N. Effect of single dose preoperative intramuscular dexamethasone injection on lower impacted third molar surgery. *International journal of oral and maxillofacial surgery*. 2012;41(3):376-9.
9. Bamgbose BO, Akinwande JA, Adeyemo WL, Ladeinde AL, Arotiba GT, Ogunlewe MO. Effects of co-administered dexamethasone and diclofenac potassium on pain, swelling and trismus following third molar surgery. *Head Face Med*. 2005;1:11.
10. Mojsa I, Pokrowiecki R, Lipczyński K, Czerwonka D, Szczeklik K, Zaleska M. Effect of submucosal dexamethasone injection on postoperative pain, oedema, and trismus following mandibular third molar surgery: a prospective, randomized, double-blind clinical trial 2016.
11. Moraschini V, Hidalgo R, Porto Barboza E. Effect of submucosal injection of dexamethasone after third molar surgery: a meta-analysis of randomized controlled trials. *International journal of oral and maxillofacial surgery*. 2016;45(2):232-40.
12. de Santana-Santos T, de Souza-Santos a-A-S, Martins-Filho P-R-S, da Silva L-C-F, de Oliveira E Silva E-D, Gomes A-C-A. Prediction of postoperative facial swelling, pain and trismus following third molar surgery based on preoperative variables. *Medicina oral, patologia oral y cirugia bucal*. 2012;18(1):e65-e70.
13. Ravikumar KK, Narayanan V. Prediction of postoperative outcome in mandibular third molar surgery based on preoperative variables: A Prospective clinical study. *International Journal of Social Rehabilitation*. 2018;3(1):14.
14. Liu S, Zhao H, Wang Y, Zhao H, Ma C. Oral bromelain for the control of facial swelling, trismus and pain after mandibular third molar surgery: a systematic review and meta-analysis. *Journal of Oral and Maxillofacial Surgery*. 2019.
15. Latt MM, Kiattavorncharoen S, Boonsiriseth K, Pairuchvej V, Wongsirichat N. The efficacy of dexamethasone injection on postoperative pain in lower third molar surgery. *Journal of dental anesthesia and pain medicine*. 2016;16(2):95-102.
16. Al Katheeri N, Wasfi I, Lambert M, Saeed A. Pharmacokinetics and pharmacodynamics of dexamethasone after intravenous administration in camels: effect of dose. *Veterinary research communications*. 2004;28(6):525-42.
17. Chen Q, Chen J, Hu B, Feng G, Song J. Submucosal injection of dexamethasone reduces postoperative discomfort after third-molar extraction: A systematic review and meta-analysis. *The Journal of the American Dental Association*. 2017;148(2):81-91.
18. Syed KB, AlQahtani FHK, Mohammad AHA, Abdullah IM, Qahtani HSH, Hameed MS. Assessment of pain, swelling and trismus following impacted third molar surgery using injection dexamethasone submucosally: A prospective, randomized, crossover clinical study. *Journal of International Oral Health*. 2017;9(3):116.
19. Martins L-D, Rezende M, Loguercio AD, Bortoluzzi M-C, Reis A. Analgesic efficacy of ketorolac associated with a tramadol/acetaminophen combination after third molar surgery-a randomized, triple-blind clinical trial. *Medicina oral, patologia oral y cirugia bucal*. 2019;24(1):e96-e102.
20. Larsen MK, Kofod T, Starch-Jensen T. Therapeutic efficacy of cryotherapy on facial swelling, pain, trismus and quality of life after surgical removal of mandibular third molars: a systematic review. *Journal of oral rehabilitation*. 2019;46(6):563-73.
21. O'Hare PE, Wilson BJ, Loga MG, Ariyawardana A. Effect of submucosal dexamethasone injections in the prevention of postoperative pain, trismus, and oedema associated with mandibular third molar surgery: a systematic review and meta-analysis. *International journal of oral and maxillofacial surgery*. 2019.

Hypothyroidism, Prolactin and Function of the Pituitary-Gonadal Axis in Iraqi Patients with Chronic Kidney Disease

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Abstract

The present study was aimed to examine the associations among chronic kidney disease (CKD) and hormonal status by evaluation levels of: Luteinizing hormone (LH) and Follicle-stimulating hormone (FSH), Prolactin, Estrogen (E2) and Progesterone (P4) for females and Testosterone for males along with thyroid hormones (TSH, T3, and T4) in CKD patients. The study included 50 patients who are diagnosed to have CKD stage-5, their ages ranged between 20-50 years (25 males and 25 females) who attended the Nephrology and Transplant Center in Medical City of Baghdad- Iraq from April 2018 to July 2018, and 20 matched apparently healthy as control, their ages ranged between 20-48 years (10 males and 10 females). The study showed a highly significant ($P < 0.01$) increase in LH, FSH levels in CKD patients compared to the control group. Highly significant ($P < 0.01$) increase in Prolactin level as compared to healthy individuals and highly significant ($P < 0.01$) decrease in E2 level in CKD female patients compared to the control group, while there was non-significant ($P > 0.05$) decrease in P4 level in CKD female patients compared to the control group. On the other hand there is significant ($P < 0.05$) decrease in Testosterone level in CKD male patients compared to the control group. In parallel TSH was recorded a highly significant ($P < 0.01$) increase in CKD patients in comparison with control. While T3 and T4 levels highly significant ($P < 0.01$) decrease in CKD patients in comparison with control.

Keywords: CKD, Hypothyroidism, Prolactin, LH, FSH, E2, P4, Testosterone.

Introduction

Chronic kidney disease (CKD) is a progressive deterioration in kidney function that is normally a result of disease or injury to the glomerular or tubular structures within the nephron and advances until the kidneys cannot maintain homeostatic [1]. Hormonal dysfunction in CKD is clinically accompanied by sexual dysfunction that influences the life quality of these patients. In advanced stages of CKD, these sexual dysfunctions can be more evident, several changes in hormone levels have been

demonstrated, these changes can be because of decreased renal excretion and disturbance of the endocrine system because of uremic effects [2]. Thyroid hormones are necessary for growth and development of the kidney and for the maintenance of water and electrolyte homeostasis, CKD upsets thyroid function in many ways, including low circulating thyroid hormone concentration, insufficient binding to carrier proteins and altered iodine storage in the thyroid gland, low T3 is the hallmark of main disturbance [3]. Prolactin is a hormone secreted by the pituitary gland and is involved in the lactation, it is normally considered as an inhibitor of gonadotropin releasing hormone (GnRH) [4]. Probably both the decline of renal prolactin clearance and increased production rate (caused by the inadequate dopaminergic inhibition of prolactin release) contribute to hyperprolactinemia in patients with CKD [5]. Prolactin accumulation causes the inhibition of pulsatile secretion of GnRH as well as the decrement in the testosterone synthesis, which results

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in worsening of sexual functions and infertility^[1,6]. In CKD patient, level of Luteinizing hormone (LH) and Follicle-stimulating hormone (FSH) rise up ^[7]. Due to high level of gonadotropins (LH and FSH) and low level of gonads hormones Estrogen (E2) and Progesterone (P4) in female, Testosterone in male result in a situation which is called hypergonadotrophichypogonadism but this increase is not enough to reverse hypogonadism and it means that there is a problem in GnRH^[4,7]. In uremic patients, GnRH releasing from the hypothalamus and GnRH-LH signal are impaired. In these patients, bioactivity of LH changes and then a series of function inhibitors of LH are made ^[4].

Material and Method

The study was carried out at Nephrology and Transplant Center in Medical City of Baghdad- Iraq from April 2018 to July 2018. This study included two groups, patients and control group. The study included 50 patients are diagnosed to have CKD stage 5, their ages ranged between 20-50 years (25 males and 25 females) and 20 control their ages ranged between 20-48 years (10 males and 10 females). Blood samples were collected from all groups for estimation of (LH, FSH, Prolactin, E2, P4, Testosterone, TSH, T3, and T4). All biomarkers were estimated in serum of all subjects by using an automated quantitative COBAS e411 test (from Roche, Germany).

Results

In this study the level of LH (7.10±0. 57) was highly significant increased (P<0.01) in comparison with control (3.62±0.45). Also, the level of FSH showed high significant increase (P<0.01) in patients group (8.01±0.50) when compared with control group (4.79±0.55), Table (1).

Table 1: Comparison between patients and control in level of LH, and FSH.

Group	Mean±SE	
	LH mIU/ml	FSH mIU/ml
Patients	7.10±0. 57	8.01±0.50
Control	3.62±0.45	4.79±0.55
T-Test	1.897 **	1.732 **
P-value	0.0005	0.0004
** (P<0.01): Highly Significant		

On the other hand Prolactin level in patients group (19.85±1.96) highly significant increase (P<0.01) in

comparison with control group (8.93±2.56) as shown in Table (2).

Table 2: Comparison between patients and control in level of Prolactin

Group	Mean±SE of Prolactin ng/ml
Patients	19.85±1.96
Control	8.93±2.56
T-Test	27.001 **
P-value	0.0047
** (P<0.01): Highly Significant	

The mean of serum E2 and P4 levels in the females of the study groups are summarized in Table (3). E2 level (7.89±1.17) in patients group observed highly significant decrease (P<0.01) in comparison with control group (20.80±5.04), while P4 levels showed non-significant decrease (0.407±0.06) in patients compared to control group (0.408±0.10) .

Table 3: Compare between patients and control (Female) in E2 and P4.

Group	Mean±SE	
	E2 Pg/ml	P4 ng/ml
Patients	7.89±1.17	0.407±0.06
Control	20.80±5.04	0.408±0.10
T-Test	7.318 **	0.249 NS
P-value	0.0008	0.997
** (P<0.01): Highly Significant; NS: Non-Significant.		

The present study displayed, significant decrease (P<0.05) in Testosterone level in male patients with CKD (1.57±0.25) in comparison with healthy control group (2.73±0.58). as shown in Table (4).

Table 4: Compare between patients and control (Male) in level of Testosterone.

Group	Mean±SE of Testosterone ng/ml
Patients	1.57±0.25
Control	2.73±0.58
T-Test	1.097 *
P-value	0.0387
* (P<0.05): Significant	

On the other hand, in this study, as shown in Table (5) TSH level in patients group (12.12±1.97) revealed high significant elevation (P<0.01) in comparison with control (1.73±0.24), while T3 level (0.970±0.05) revealed high significant (P<0.01) decrease in patients

group in comparison with control (1.43±0.11), also high significant (P<0.01) decrease in T4 (6.81±0.32) in patients group when compared with control group (9.21±0.25).

Table 5: Comparison between patients and control in TSH, T3 and T4.

Group	Mean±SE		
	TSH mu/ml	T3 ng/ml	T4 mg/dl
Patients	12.12±1.97	0.970±0.05	6.81±0.32
Control	1.73±0.24	1.43±0.11	9.21±0.25
T-Test	6.256 **	0.229 **	1.059 **
P-value	0.0015	0.0001	0.0001
** (P<0.01): Highly Significant			

Statistically, the finding in Table (6) indicate a correlation coefficient between thyroid hormone and other parameter in this study. As showed there is a highly significant (P<0.01) positive correlation between TSH with FSH and significant (P<0.05) positive correlation between TSH with LH. There is non-significant positive correlation between TSH with Prolactin, while there is significant (P<0.05) negative correlation between TSH with E2 and non-significant negative correlation between TSH with P4, and Testosterone. On the other hand, there is non-significant positive correlation between T3 with E2, P4 and Testosterone. And there is high significant (P<0.01) negative correlation between T3 with FSH and non-significant negative correlation between T3 with LH, and Prolactin. Also, this study showed high significant (P<0.01) positive correlation between T4 with E2, non-significant positive correlation between T4 with P4 and Testosterone. And highly significant (P<0.01) negative correlation between T4 with LH, and FSH. While there is non-significant negative correlation between T4 with Prolactin.

Table 6: Correlation coefficient between TSH, T3, T4 with other parameters of patients.

Parameters	Correlation coefficient-r and Level of significant		
	TSH	T3	T4
LH	0.27*	-0.20 NS	-0.33**
FSH	0.51**	-0.42**	-0.57**
Prolactin	0.19 NS	-0.06 NS	-0.20 NS
E2	-0.26 *	0.19 NS	0.39 **
P4	-0.06 NS	0.10 NS	0.12 NS
Testosterone	-0.17 NS	0.10 NS	0.14 NS
* (P<0.05), ** (P<0.01), NS: Non-Significant.			

Discussion

Several changes in hormone levels have been demonstrated in patients with end stage renal disease (ESRD), these changes can be because of decreased renal excretion and disturbance of the hypothalamic pituitary gonadal axis because of uremic effects [2,8]. There are many studies in the world that have been dealt with LH and FSH levels in CKD patients one of these, is a study which has come in supporting results of this study has been stated by Anatharama and Schmidt [9], who they found that changes in pulsatile release of GnRH and LH reduce feedback inhibition of LH production (because of low levels of testosterone) contribute to high serum LH levels, FSH secretion is also increased in CKD patients. With ESRD there was a significant increase in LH and FSH and development of pattern of hyper gonadotropic hypogonadism, which indicates that uremic metabolite tend to increase CKD effect on testes and ovaries more than hypothalamic or pituitary function [10].

Previous studies go in agreement with the results of this study which reported high elevation in levels of prolactin among occurrence CKD patients [11-13]. A study done by Hylander and Lehtihet [10], on young and middle aged men with CKD, showed that 30% of patients had hyperprolactinemia and this go in agreement with results of this study. Edey [14], found that the endocrine complications of hyperprolactinemia are manifest through disruption of pulsatile GnRH and this leads in turn to hypergonadotrophic hypogonadism.

The results of this study agree with those that have been found with previous studies [4,6,12], who showed that low concentration of E2 has been seen in uremic patients, nevertheless it has insufficient concentration in the puberty, while in the second half of menstrual cycle serum P4 concentrations are decreased due to the defective follicle luteinization. In this study P4 levels are slightly decreased with no significance compared to the control group, many other authors also approved this result who found that mean P4 levels in patients were not significantly different from those of control subjects [11,15]

In the current study, the results of testosterone in male patients indicated significant decrease (P<0.05) in CKD patients, and this result was also approved by many other authors as testosterone which is normally reduced in CKD patients and when LH level is arise in response to low levels of testosterone, so that the hypothalamic pituitary axis in CKD is reset in such a way that it is more sensitive to the negative

feedback inhibition of testosterone^[9,10,16,17]. Rathi and Ramachandren.^[18], showed that low testosterone is due to decreased production, increased metabolic and dialytic clearance, alteration in testosterone binding capacity^[19,20].

This study showed that gonadotropin hormones LH and FSH, have positive correlation with serum TSH and negative correlation with T3,T4 in men and women with CKD. This result was in agreement with Saran *et al.*^[21], which found that serum level of FSH and LH are significantly high in cases of high TSH and low T3, T4. In another study Haponet *al.*^[22] have shown that change in thyroid hormones does not influence the classical preovulatory patterns of LH and FSH secretion in rats, and this finding disagrees with the results of this study. The finding of this study is in agreement with the findings of a study done by GoswamiBinita *et al.*^[23] and Fupareet *al.*^[24], whom they found that patients with elevated TSH and low levels of T3,T4 had hyperprolactinemia. Kumkumet *al.*^[25], in their study they found a positive correlation between low T3, T4 and elevated levels of TSH with prolactin. AffiaTasneemet *al.*^[26], in their study they measured serum Prolactin and TSH levels in 1365 patients (46 males, 1319 females), They found 33% had low levels of T3,T4, in hyperprolactinemic patients. A previous study demonstrated positive correlation between TSH and Prolactin in hypothyroid women^[27].

In this study, E2 hormone was positively correlated with serum T3, T4 and negatively with TSH, and this result was in agreement with Saran *et al.*^[21] and Santinet *al.*^[28], which reported that E2 decrease secretion of TSH and increases secretion of both T4 and T3, and they revealed that E2 is directly stimulating the thyroid gland to produce more thyroid hormone, which will also contribute to lowering TSH. Current study showed a negative non-significant correlation between TSH and P4, and positive non-significant correlation between T3, T4 and P4. The results of this study showed a negative non-significant correlation between TSH and testosterone and positive non-significant correlation between T3,T4 and testosterone. The correlation between thyroid hormone and testosterone demonstrated by Donnelly and White^[29], which reported that men with low levels of T3, T4 and high levels of TSH have an affliction that is known to disturb normal gonadal function.

Conclusion

This study confirms the noxious role of CKD in hormonal disruption and sexual function.

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References

1. Terrill B. Renal nursing : a guide to practice, Abingdon, Radcliffe Medical Press. 2002.
2. Palmer B.F. Sexual dysfunction in men and women with chronic kidney disease and end-stage kidney disease. *Adv Ren Replace Ther* 2003;10: 48-60.
3. Singh S, Verma A, Aryal A, Thapa S, Khakurel S, Shrestha K. Thyroid hormone profile in patients with chronic kidney disease: a single centrestudy J Nepal Health Res Counc 2016;14(34): 197-201.
4. Asadi R. Endocrine disorders in chronic kidney disease. *International Journal of Children and Adolescents* 2016; 2(3):1-5.
5. Ros S, Carrero J.J. Endocrine alterations and cardiovascular risk in CKD: Is there a link? *Nefrologia* 2013;33: 87-181.
6. Kuczera P, Adamczak M, Wiecek A. Endocrine abnormalities in patients with chronic kidney diseases. *Sec. of Med. Sci* 2015; 2: 1-18.
7. Handelsman D.J. Hypothalamic-pituitary gonadal dysfunction in renal failure, dialysis and renal transplantation. *Endocr Rev* 1985;6(1):151-182.
8. Eckersten D, Giwercman A, Bruun L, Christensson A. Anti-Müllerian hormone, a Sertoli cell-derived marker, is decreased in plasma of male patients in all stages of chronic kidney disease. *Andrology* 2015; 3: 1160-1164.
9. Anantharaman P, Schmidt R.J. Sexual function in chronic kidney disease. *Adv Chronic Kidney Dis* 2007;14(2): 119-125.
10. Hylander B, Lehtihet M. Testosterone and gonadotropins but not SHBG vary with CKD stages in young and middle aged men *Basic and Clinical. Andrology* 2015;25:9.

11. El-Assaly N.M, El-Ashry N.I, Waked E, El-Damarawy M. Gonadal Dysfunction in Chronic Renal Failure. *Australian Journal of Basic and Applied Sciences* 2008; 2(3): 481-487.
12. Ahmed S.B, Ramesh S. Sex hormones in women with kidney disease. *Nephrol Dial Transplant* 2016;31:1787-1795.
13. Fugl-Meyer K.S, Nilsson M, Hylander B. Lehtihet M. Sexual function and Testosterone Level in Men With Conservatively Treated Chronic Kidney. Disease *American Journal of Men's Health* 2017; 11(4): 1069-1076.
14. Edey M.M. Male Sexual Dysfunction and Chronic Kidney Disease. *Front. Med* 2017); 4(32):4-32
15. Joven J, Villabona J, Rubiés-Prat E, Espinel and Galard R. Hormonal profile and serum zinc levels in uraemic men with gonadal dysfunction undergoinghaemodialysis. *ClinChimActa* 1985; 148(3):45-239.
16. Daniell H.W. Erythropoietin resistance during androgen deficiency. *Archives of Internal Medicine* 2006; 166(17):1923-1925.
17. Papadopoulou E, Varouktsi A, Lazaridis A, Boutari C, Doumas M. Erectile dysfunction in chronic kidney disease: From pathophysiology to management. *World J Nephrol* 2015; 4(3):379-387.
18. Rathi M, Ramachandran R. Sexual and gonadal dysfunction in chronic kidney disease: Pathophysiology. *Indian J EndocrinolMetab* 2012;16 (2):9-214.
19. Keerthana B.L, Kumar T.A. Study of Thyroid and Lipid Profile in Chronic Kidney Disease. *International Journal of Medical and Health Research* 2016; 2(3):6-9.
20. Zoccali C, Tripepi G, Cutrupi S, Pizzini P, Mallamaci F. Low triiodothyronine: A new facet of inflammation in end-stage kidney disease. *J Am SocNephrol* 2005; 16:2789-2795.
21. Saran S, Gupta B.S, Philip R. Effect of hypothyroidism on female reproductive hormones. *Indian J EndocrinolMetab* 2016;20(1):13-108.
22. Hapon M.B, Gamarra-Luques C, Jahn G.A. Short term hypothyroidism affects ovarian function in the cycling rat. *Reprod Biol Endocrinol* 2010; 8:14.
23. Goswami B, Patel S, Chaterjee M, Koner B.C, Saxena A. Correlation of prolactin and thyroid hormone concentration with menstrual patterns in infertile women. *J ReprodInfertil* 2009; 10(3):12-207.
24. Fupare S, Gadhiya B.M, Jambhulkar R.K, Tale A. Correlation of Thyroid Hormones with FSH, LH and Prolactin in Infertility in the Reproductive Age. *International Journal of Clinical Biochemistry and Research* 2015; 2(4):216-222.
25. Kumkum A, Kaur J, Gupta S, Narang P.A. Hyperprolactinemia and its correlation with hypothyroidism in infertile woman. *Obstetrics and Gynecology of India* 2005;56:68-71.
26. Affia T, Ismat F, Adeela A, Nasir M, Muhammad K.A. The incidence of hyperprolactinaemia and associated hypothyroidism: local experience from Lahore. *PJNM* 2011; 1:49-55.
27. Binita G, Suprava P, Mainak C, Koner B.C, Alpana S. Correlation of prolactin and thyroid hormone concentration with menstrual patterns in infertile women. *J ReprodInfertil* 2009; 10:12-207.
28. Santin, A.P, Furlanetto T.W. Role of estrogen in thyroid function and growth regulation. *Journal of thyroid research*2011: 875125.
29. Donnelly P, White C. Testicular dysfunction in men with primary hypothyroidism; reversal of hypogonadotrophichypogonadism with replacement thyroxine. *Clinical endocrinology* 2001; 52 (2):197.

Mood Disorders in Rheumatoid Arthritis

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Abstract

The mood disorder refers to a sequence of mood episodes. Mood disorder are further classified as depressive (major depressive or bipolar) The course of this disorder is characterized as unipolar or bipolar. The aim of the study is to show the relationship between the mood disorder and rheumatoid arthritis and to classify some of the relationship between etiology, symptoms and underlying biochemical processes. Method :Use in this study Three appendix to asses the cases A cohort study composes of 50 patient suffering from rheumatoid arthritis with repeated mood disorders the samples was chosen from both outpatient in Rheumatology unit in IMAM- Al -Sadek teaching hospital and Margin teaching hospital the study was carry out during the period from the first Oct. 2018 through the first April 2019 for each patient critical interview was done by sociodemographic data was recorded according to- appendix A-. The interview was based on national institute of mental health diagnostic interview schedule (NIMH-DIS). Quetionnare designed t0 assess Mood Disorders which include question specific for the diagnosis of depression (72-99) and for mania (100-117) where used to confirm the diagnosis- appendix B-. and proposed 2007 Revised American Rheumatism Association criteria for Rheumatoid Arthritis -appendix C-3. The Result of study revealed the following result the feature of the mood disorder in rheumatoid arthritis where studied in 50 patient a total of 40% meat criteria for mood disorders based on (NIMH-DIS) it's This slightly more in females and more in married patients

Conclusion: This study proved that most of the mood symptoms in rheumatoid arthritis case appeared to be of mild severity and more often showed symptoms of fatigability work retardation, sadness and less suicidal feeling.

Keywords: *Rheumatoid Arthritis; Mood Disorders.*

Introduction

Mood refers to the internal emotional state of an individual and it is also defined as a pervasive and sustained emotion that in the extreme markedly colors one's perception of the world⁽¹⁾Affect refers to the external expression of emotional contents . Affect and emotion are commonly used interchangeably .

In mood (affective) disorders, the fundamental disturbance is a change in mood or affect usually to depression (with or without anxiety) or to elation. This mood is normally accompanied by a change in the overall level of activity, and most other symptoms are either secondary to, or easily understood in the context of such changes. Most of mood disorders tend to be recurrent

There are some of the terms have been used in the DSM-IV-TR as follows:

- Mood syndrome: is a group of mood and other symptoms occurring together for a minimum period of time (specified as two weeks for a depressive and a “distinct period” for a manic episode). A mood syndrome can occur in a schizoaffective disorder or an organic mental disorder, as well as an affective disorder ⁽⁹⁾
- Mood episode: is a term restricted to mood syndromes occurring in the absence of either an organic disorder or a ‘non – mood’ psychiatric disorder (that is schizophrenia, schizoaffective disorder, or delusional disorder) ⁽⁴⁾
- Mood disorder: is a term refers to a sequence of mood episodes. Mood disorders are further classified

as depressive (major depression) or bipolar. The course of disorder is characterized as unipolar or bipolar.

In summary, the classification of mood disorders in ICD - 10 is quite complicated, and makes provision for a wide range of detailed distinctions, but is singularly free of assumption about disease entities and causation⁽⁸⁾

Classification in (DSM-IV-TR), differs only in minor ways from its predecessor. The detailed criteria for a major depressive episode are different and now make it possible for the diagnosis to be made in the absence of a depressed mood, provided there is anhedonia. The criteria for melancholia² are also changed, with diagnostic weight now is given to a good previous response to antidepressants or ECT and to full recovery from a previous episode. There is also a new set of criteria for seasonal mood disorder ⁽³⁾ Mood (affective) disorders periodically disable many people over the world. Although manic disorders are comparatively rare, depression is, quite possibly, the most widespread serious and costly psychiatric disease afflicting humankind today. It is at least ten times as prevalent as schizophrenia. Severe depression affects fully 2 - 3% of the world's population⁽⁶⁾.

The life time expectancy of developing unipolar depression is approximately 20% in women and 10% in men, the onset can occur from childhood through senescence, but 50% of the patients have the onset between ages 20 and 50, the mean age being about 40. In general, more often in divorced or separated individuals. There is no correlation between social class and unipolar depression ⁽²⁾

The life time expectancy of developing bipolar disorder is about 1% in both men and women. The mean age of onset is earlier than that of unipolar disorder, the range begins from childhood to 50 years. It may be more common in divorced and single individuals than among married persons. Bipolar disorders are more frequent in the upper social class ⁽⁵⁾ a group of individuals who experience their symptoms in response to an identifiable

life event and whose depression remits rapidly and often spontaneously. This may account for up to half the depressed individuals in the community. Second, there is a group of depressed individuals whose depression lasts longer and recur more frequently. Third, there is a group of chronically depressed individuals, many of whom might be regarded as having a personality disorder ⁽³⁾.

The frequency of episodes and the pattern of remissions and relapses are both very variable, though remission tend to get shorter as time goes on and depression to become commoner and longer lasting after middle age⁽⁸⁾. Most of mood disorders tend to be recurrent and the onset of the individual episode is often related to stressful events ⁽⁸⁾.

to appendix a. The interview was based on national institute of mental health diagnostic interview schedule (NIMH-DIA). question specific for the diagnosis of depression (72-99) and for mania (100-117) were used to confirm the diagnosis appendix b. 3. Result study revealed the following result the feature of the mood disorder in rheumatoid arthritis where studied in 50 patient a total of 40% met criteria for mood disorders based on (NIMH-DIS) it's This slightly more in females and more in married patient.

Conclusion this study proved that most of the mood symptoms in rheumatoid arthritis cases appeared to be of mild severity and more often showed symptoms of fatigability work retardation, sadness and less suicidal feeling.

Table 1: Mood disorder among patients with rheumatoid arthritis in comparison with non-rheumatoid chronic medical disease, Z-Test =2.3, P.Value =0.05

Mood disorders		Total number of the patients	Illness
%	Number		
40	20	50	Rheumatoid arthritis
38	19	50	Non- rheumatoid chronic medical disease

**Table 2: Sex variation in mood disorder in rheumatoid and non- rheumatoid patients Z-Test =6.8
P.Value=0.001**

Mood disorders		Total number of the patients	Sex	Illness
%	Number			
40	16	37	F	Rheumatoid arthritis
36	4	13	M	
35	14	37	F	Non- rheumatoid chronic medical disease
32	6	13	M	

**Table 3: Mood disorder according to the age among patients with rheumatoid arthritis Z-Test=3.3,P.
Value=0.007**

Mood disorder		Total number	Age
%	Number		
25	5	14	20-29
35	7	16	30-39
40	8	20	40-45

**Table 4: Mood disorder according to marital status in patients with rheumatoid arthritis Z-Test=4.9,P.
Value=0.001**

Mood Disorder		Total	Marital status
%	Number		
37	15	40	Married patients
50	5	10	Single patients

Table 5: Recent life event (R.L.E) and previous psychiatric history in mood disorders with rheumatoid arthritis and non- rheumatoid chronic medical patient,Z-Test=7.5 P.Value=0.0001

%	Psychiatric history	%	R.L.E	Number of mood disorder patient	Illness
10	2	30	6	20	Rheumatoid arthritis
6	1	28	4	18	Non rheumatoid medical disease

Table 6: The symptom rating of patients with mood disorders table-6- Z-Test =3.91 P.Value =0.001

Symptom ratings	R. A	Non-R.A
Sadness	0.87	1.1
Pessimism and hopelessness	0.68	0.78
Helplessness	0.65	0.57
Fatigability	1.55	1.12
Work retardation	1.47	1.21
Sense of failure	0.55	0.33
Suicidal thinking	0.28	0.18
Anorexia	0.63	0.51
Indecisiveness	0.71	0.84
Guilty feeling	0.01	0.21
Dissatisfaction	0.50	0.63
Concerning for other	0.47	0.54
Body image change	0.39	0.39

R.A. = Rheumatoid Arthritis

Result

The 50 patients with rheumatoid arthritis screened by (NIMH-DIS) national institute of mental health diagnostic interview schedule question specific for the diagnosis of depression (72-99) and for mania (100-117) were used to conform the diagnosis the NIMH-DIS is a fully structure interview designed to enable physicians to make accurate psychiatric diagnosis according to three diagnostic system DSM, FEIGHNER CRITRIA and RESEARCH DIAGNOSTIC CRITRIA so they meet the predetermined criteria for mood disorder, while in non- rheumatoid patient among fifty patient screening 38% reach as in table 1 among female patient with rheumatoid arthritis screened 80% where mood disorder while it was 35% among males as in table 2. The rheumatoid patients divided into 3 age group the distribution of mood disorder according to these groups is shown in table 3. mood disorder among 40 married patient and ten single patient is shown in table 4. About 10% of mood disorder rheumatoid patient had received psychiatric treatment previously as shown in table 5. The predominant depressive symptoms in rheumatoid and non- rheumatoid chronic medical patients were nearly similar, apart from more fatigability than work retardation in R. A, the reverse in non-rheumatoid patients as in table -6- Discussion: R.A pain lead to depression, depression may worsen pain perception. Depression and pain are akin to the proverbial chicken and the egg. chronic pain can lead to depression, and feeling down in the dumps can worsen the perception of pain. The researchers asked 56 people with R.A to complete questionnaire designed to assess their Depression and anxiety levels. A year later during follow up, researchers found a strong association between the Number of sore joints and scores on how participant were feeling in general⁽¹⁵⁾. This study comparable with our study which proved the association between the pain and the mood disorders the above results have shown that mood disorders are common phenomena among rheumatoid & other chronic medical patient.

That are 40% among rheumatoid and 38% among non-rheumatoid patient as in table 1 by application of chi -square test and Z-Test we noticed that there is no significant difference in distribution of mood disorders among rheumatoid and non-rheumatoid patient. This prevalence of mood disorder among rheumatoid patients is consistent with that in other studies. A study investigating 50 adult female patients with rheumatoid

arthritis, control cases where 50 patients admitted in the same hospital. 29% revealed distinct mood disorders⁽¹⁰⁾. A 15 years follow up study of 74 female patients with classic rheumatoid arthritis was performed with special emphasis on overt psychopathology during the clinical course of the illness 40% had mood disorders⁽¹⁴⁾ Several studies have demonstrated that post stroke mood disorders are frequent sequel of cerebrovascular disease occurring in up to 50% of stroke patients⁽⁹⁾. mood disorder increase with age as shown as in table -3 -this maybe related to the fact that psychological mechanism which permitted coping with stress at an earlier may have diminish gradually, as well as chronicity of illness may play the same role. There is more mood disorder in married patient than single as in table-4- this may be due to the lowering of self-esteem, the possible loss of love and admiration of the husband or wife and the fear of being not wanted physically here too chronicity may play the same rule. A study examine the relationship between the health status of rheumatoid arthritis wife it was found that higher mood disorder were associated with lower family cohesiveness, functioning and higher conflict in subjects, less expressiveness in spouse⁽¹³⁾. The mood disorders referred to variety of psychiatric facilities in New Haven reported as 3 times as many events in six month before the onset as much as control from surrounding population as in table-5-⁽¹¹⁾. Work retardation and fatigability may reflect real incapacity and disability of the patients due to physical illness⁽¹⁾. The study of mood disorders in medical patients, found that when compare with mood disorders in psychiatric unit, suicidal thinking and guilty feeling were found little but more likely to manifest pessimism, agitation, helplessness, anxiety, and retardation⁽¹¹⁾. Rate of Depression, Anxiety, and Bipolar Disorders are higher in people with R.A. Researcher in Manitoba –Canada, studied more than 60,000 people with R.A and Healthy-Individual. The incidence of Depression was 45 percent higher, and Bipolar Disorder was 20 percent more common⁽¹⁶⁾.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

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References

1. Kaplan HI and Sadock BJ. Synopsis of psychiatry. 11th edition by Michael G. Fisher, Wilkin, Baltimore, Maryland, USA, 2014; P350
2. Donald W. Psychiatric Diagnosis 2018; 7th.ed, New York/Oxford P.50
3. Kendell RE . Affective (mood) Disorder. In companion to psychiatry studies. Edited by R.E Kendell, A .K.Z eally. 8th .Ed. PP 421-443 churchill living stone Edinburg,2010.
4. Louis Ap. 2nd.ed. Affective (mood) Disorders. In postgraduate psychiatry PP,2001; 186-193.
5. Theodore A. mood disorders, psychiatry update PP,2000; 103-126.
6. Patridge AJ. psychosocial aspect of the rheumatic diseases, 1988; 307 Primer on the Rheumatic diseases, 9th, ed. Arthritis Foundation. Atlanta G.A by Schumach and Klippel, 7.
7. World Health Organization . Tenth Revision of international classification of diseases,1992; (ICD-10),P 112.
8. Gelder M, Gated, Mayour. OXFORD textbook of psychiatry, 2018;7th. ed P231.
9. Starkstein S . and Robinsom R . Affective disorders & cerebral vascular disease, Brit. J.Psych. 1989;154,(170-182).
10. Silverman A J. Rheumatoid Arthritis section 10, Comprehensive text book of psychiatric, 1985.
11. Pakel ES,Myers JK,Dienelt MN et al., life event and depression: control study.Archives of Genaral Psychiatry,1969; 21:753.
12. Newman S.P, Fitzpatrick R, Lamb R. The origin of depression mood in R .A,1989.
13. Barbara W. The relationship of family dynamics to health status in R.A American arthritis & Rheumatism,1985;.28 No.4
14. Rimon R. and Loakso R L. Over Psychopathology in R.A psychiatric section 32 1984; 51/915-Astudy published on line in April- 2016 inBMC Muscular Skeletal Disorders.
15. Carol Hitchon, MD,an associate professor of medicine at the University of Manitoba,2004. Canada 10.
16. Margaretten M, Julian L, Katz P, Yelin E. Depression in patients with rheumatoid arthritis: description, causes and mechanisms. Int J Clin Rheumtol. 2011;6(6):617–623.

Pattern of Mechanical Intestinal Obstruction in Al-Yarmouk Teaching Hospital

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Abstract

Background: The effective treatment of patients with intestinal obstruction is essential and requires initial rapid diagnosis and therapeutic intervention.

Aim of Study: To determine the causes, the accuracy of preoperative diagnosis, and other epidemiological characteristics of intestinal obstruction in Al-Yarmouk Teaching Hospital in Baghdad, Iraq.

Patients and Method: A prospective study was conducted in the Surgical Department of Al-Yarmouk Teaching Hospital for a period of two years (from Jan 1999 to the end of Dec 2000) and included 178 patients admitted and proved to be diagnosed with mechanical intestinal obstruction.

Results: Of the 178 patients enrolled in this study; maximum incidence was seen in patients aged between 40-59 years with male predominance (62.4%). Abdominal pain and constipation, were presenting in majority of cases (87.6% and 83.1% respectively). Common causes were hernias, adhesions and bands (35.4% and 28.6% respectively). Small bowel was involved in 69.7% cases and large bowel in 30.3%. Laparotomy was the main option for management (69.1%). The mortality rate was 9.5% and death is associated significantly with aging and volvulus and intussusception as causes of intestinal obstruction.

Conclusion: Acute intestinal obstruction still a major cause of morbidity and mortality which was associated with aging, compound volvulus and intussusception. Hernias and adhesions were the leading causes of intestinal obstruction. Abdominal pain and distension, and constipation were seen in majority of cases. Laparotomy was the most common method of intestinal obstruction management in our institute.

Keywords: *Intestinal obstruction, mechanical, small bowel, large bowel, Iraq.*

Introduction

Intestinal obstruction (IO) is defined as obstruction of the passage of the intestine for its contents⁽¹⁾. It is a commonly encountered problem in gastrointestinal

surgery all over the world⁽²⁾. Despite advances in surgery, bowel obstruction remains a difficult problem with significant morbidity and mortality due to disrupted gastrointestinal flow. Consequently, IO is associated with considerable clinical burdens, major financial expenditure, frequent emergency room visits and economic loss from time spent away from duties⁽³⁾. In the last century, significant changes in etiological factors of IO have occurred from changes in epidemiologic and environment factors, health services provision and education⁽³⁾. It may occur in both small and large intestines. However, obstruction in the small bowel is more prevalent⁽⁴⁾. Of all IO, mechanical IO forms an important part of pathologies that necessitate emergency

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surgical interventions⁽⁵⁾ and is a significant cause of morbidity and mortality, especially when associated with bowel gangrene or perforation⁽⁶⁾. The clinical signs and symptoms which could be helpful in diagnosis of IO are usually abdominal pain, vomiting, abdominal distention, and absence of flatus or feces passage⁽⁷⁾. There are several causes of IO and their relative incidence varies in different populations, between countries and has also changed over the last decades. Several factors are described to be responsible for these differences. Socioeconomic factors and diet have mostly been incriminated to be responsible for the observed difference⁽⁸⁾. The most important risk factor for mechanical small bowel obstruction is prior abdominal surgery causing postoperative adhesions usually⁽⁹⁾. Patients with a history of prior abdominal or pelvic surgery, and particularly colorectal surgery, appendectomy, gynecologic surgery, prior adhesiolysis, and resection of malignancy are prone to adhesive small bowel obstruction^(10,11). Optimal outcomes at the end of life rely upon a careful analysis of the patient, their pathology, and the likely benefits to be gained from intervention, be they psychological, social, or to enable further adjunctive treatment⁽¹²⁾. Considering the importance of IO and its life-threatening complications, learning about the epidemiological characteristics of the disease and determining its prevalence can be effective in management of this disease and providing essential sources for its early diagnosis. The present study aims to determine the most important and frequent causes, the accuracy of preoperative diagnosis, and other epidemiological characteristics of IO by using the data that was collected from single institute during the last two years.

Patients and Method

Study design, setting and sample size: A prospective study was conducted in the Surgical Department of Al-Yarmouk Teaching Hospital for a period of two years (from Jan 1999 to the end of Dec 2000) and included 178 patients admitted and proved to be diagnosed with mechanical IO.

Diagnosis of IO was based on the history, physical examination, supported by radiological evidence of obstruction (Plain x-ray of the abdomen). Physical findings which usually present in cases of complicated

IO were put in mind including (Abdominal tenderness, rebound tenderness or muscle guarding, tachycardia > 100 beats/min, fever > 38 C°, pain suggestive of strangulation, palpable abdominal mass or irreducible hernia, and shock). Patients with incomplete records or with functional causes of IO were excluded.

Patients first admitted to the surgical causality unit, necessary resuscitation done for the patients including intravenous administration of at least one liter of ringer lactate or normal saline solution, antibiotic administered and measures for associated diseases. Laboratory investigations were done including (complete blood count, blood group and Rh, serum electrolytes, blood urea, and random blood sugar).

Data collection tools: A questionnaire had been applied to all patients to collect the needed information, the questionnaire was filled by the researcher through direct interview with the study patients. It included questions to gather information on certain socio – demographic variables (age and gender), site and cause of IO, time between presentation and surgery, preoperative provisional diagnosis, clinical findings suggesting strangulation and complications).

Statistical Analysis: The data analyzed using Statistical Package for Social Sciences (SPSS) version 25. The data presented as mean, standard deviation and ranges. Categorical data presented by frequencies and percentages. Chi square test was used to assess the association between mortality rate and certain information. A level of P – value less than 0.05 was considered significant.

Results

In this study, 200 couples were enrolled. The age was ranging from 10 to 90 years with a mean of 40.2±10.8 years and the mainly affected age was from 40 – 59 years (35.5%). Regarding gender, proportion of males was higher than females (62.4% versus 37.6%) with a male to female ratio of 1.65:1. The highest incidence of IO occurred in small bowel (69.7%), the most prevalent presenting symptoms were abdominal pain (87.6%) and constipation (83.1%), and the most common cause of IO was hernia (35.4%) as shown in table (1).

Table 1: Distribution of study patients by general information

Variable	No. (n=178)	Percentage (%)
Age (Years)		
<20	16	9.0
20 - 39	44	24.5
40 - 59	63	35.5
≥ 60	55	31.0
Gender		
Male	111	62.4
Female	67	37.6
Etiology of IO		
Hernia	63	35.4
Adhesions and bands	51	28.6
Neoplasms	32	17.9
Fecal impaction	12	6.8
Volvulus	8	4.5
Intussusception	4	2.3
Miscellaneous	8	4.5
Site of IO		
SMALL Bowel Obstruction (SBO)	124	69.7
LARGE Bowel Obstruction (LBO)	54	30.3
Clinical presentation		
Abdominal pain	156	87.6
Constipation	148	83.1
Abdominal distension	124	69.7
Vomiting	112	62.9
Bowel sound	46	25.8

More details about the causes of IO is shown in table (2). Inguinal hernias constituted the largest no. of hernia cases (55.9%). Regarding cause of adhesions and bands,

appendectomy was the most common condition that causing adhesions and bands (35.4%). Sigmoid colon neoplasms represented more than third of neoplasm that cause IO (37.5%).

Table 2: Distribution of study patients by certain details of IO causes

Variable	Number	Percentage (%)
Type of hernia n= 63		
Inguinal	34	55.9
Para-umbilical	15	23.8
Incisional	8	12.7
Femoral	4	6.4
Internal	2	3.2
Cause of adhesions and bands n= 51		
Appendectomy	18	35.4
Gynecological surgery	12	23.5
Laparotomy for trauma	10	19.6
Previous IO	4	7.8
Elective laparotomy	3	5.8
Congenital bands	4	7.9
Site of neoplasm		
Small bowel lymphoma	1	3.2
Right colon	2	6.3
Left colon	6	18.7
Sigmoid colon	12	37.5
Recto-sigmoid	8	25.0
Rectal	3	9.3

Of the 178 patients, 69.1% were operated while 30.9% responded to conservative management as shown in figure (1).

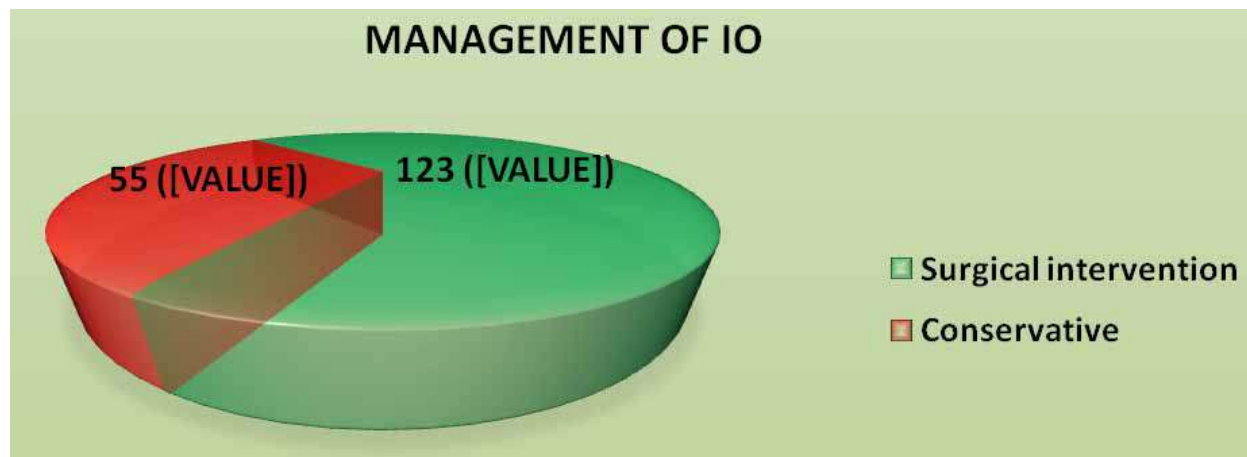


Figure 1: Distribution of study patients by type of management of IO

Among 123 patients who underwent surgical operation, we noticed that all cases with hernia or volvulus were operated within the 1st 24 hrs., one case was operated in the 4th day and other case was operated in the 5th day; these two cases were diagnosed with neoplasm as shown in table (3).

Table 3: Time between admission and operation according to cause of IO

Cause of IO	Time between admission and operation					Total (%) n= 123
	1 st 24 hrs. (%) n= 108	2 nd day (%) n= 8	3 rd day n= 5	4 th day n= 1	6 th day n= 1	
Hernia	63	0	0	0	0	63
Adhesion and band	16	3	2	0	0	21
Neoplasm	13	4	2	1	1	21
volvulus	8	0	0	0	0	8
Intussusception	3	1	0	0	0	4
Fecal impaction & Others	5	0	1	0	0	6

In this study, from those 123 patients who undergone surgical operation, 19 (15.4%) patients found to have complicated (ischemic) IO. From those 19 patients, 17 patients were diagnosed preoperatively as complicated.

The sensitivity of preoperative diagnosis was 89.4%, specificity was 94.2%, positive predictive value was 73.9%, negative predictive value was 98%, and accuracy rate was 93.5% as demonstrated in table (4).

Table 4: Sensitivity, specificity, and accuracy of preoperative diagnosis

Preoperative Diagnosis	Operative finding		Total (%) n= 123
	Complicated	Simple	
Complicated	17	6	23
Simple	2	98	100
Total	19	104	123

As shown in table (5), the mortality rate in this study was 9.5% (17 patients). The highest prevalence of death was seen among elderly patients (21.8%) and in patients

presented with intussusception (75%) with a significant association between prevalence of death and both of age (P= 0.002) and cause of IO (P= 0.001).

Table 5: Association between mortality rate and certain information

Variable	Mortality		Total (%) n= 178	P - Value
	Yes (%) n= 17	No (%) n= 161		
Age (Years)				
< 20	1 (6.3)	15 (93.8)	16 (9)	0.002
20 - 39	2 (4.5)	42 (95.5)	44 (24.7)	
40 - 59	2 (3.2)	61 (96.8)	63 (35.4)	
≥ 60	12 (21.8)	43 (78.2)	55 (31.0)	
Gender				
Male	11 (9.9)	100 (90.1)	111 (62.4)	0.833
Female	6 (9.0)	61 (91.0)	67 (37.6)	

Variable	Mortality		Total (%) n= 178	P - Value
	Yes (%) n= 17	No (%) n= 161		
Etiology of IO				
Hernia	3 (4.8)	60 (95.2)	63 (35.4)	0.001
Adhesions and bands	1 (2.0)	50 (98.0)	51 (28.6)	
Neoplasms	6 (18.8)	26 (81.2)	32 (17.9)	
Fecal impaction	0 (0)	12 (100.0)	12 (6.8)	
Volvulus	3 (37.5)	5 (62.5)	8 (4.5)	
Intussusception	3 (75.0)	1 (25.0)	4 (2.3)	
Miscellaneous	1 (12.5)	7 (87.5)	8 (4.5)	

Discussion

Bowel obstructions till one of the most common surgical emergencies worldwide⁽¹³⁾, management of which requires quick, appropriate diagnosis and, rational and proper treatment⁽¹⁴⁾. In this study, the mean age was 40.2±10.8 years with a male predominance (62.4%). This results are consistent with other published studies as studies conducted by Souvik A et al in 2010⁽¹⁵⁾, and Doumi EB et al in 2008⁽¹⁶⁾ when they reporting mean ages between 39 and 42 years, and male predominance rates of 60 - 70%. Significant regional variation in the causes of IO has been noticed among various studies as this study showed that the most common cause of IO was hernia (35.4%) and adhesions and bands (28.6%) similar to a studies conducted by Mohamed A et al, 2017 (Hernia 31.4% and adhesions 25.2%)⁽¹⁷⁾, and by Thampi D et al, 2014 (Hernia 30% and adhesions 40%)⁽¹⁸⁾ while a study conducted by Manafi A et al, 2009 showed that the common causes of IO were mostly due to volvulus (76%) and neoplasm (15%)⁽¹⁹⁾, and the most common underlying cause of IO in Saudi study 2010 was found to be adhesive obstruction⁽¹³⁾. In Iraqi community, it was believed that due to poverty, lack of education, and general fear of surgery, patients were reluctant for elective surgery of hernias and this might lead to a large number of hernias presenting as obstructed/strangulated bowel obstruction. There is also a parallel increase in the number of laparotomies, and this has raised the incidence of adhesive obstruction in our institute. In this study, the small bowel was more preferred site for obstruction than large bowel (69.7%). Similar studies also reported that SBO was the most common type of IO whereas LBO was relatively less common^(1, 13, 20).

This fact may help us to know that socio-economic factors and diet might be responsible for the causes of IO in some developing countries. The most presenting

features in this study were abdominal pain (87.6%), constipation (83.1%), and abdominal distension (69.7%). It was comparable to various studies done by Thampi D et al⁽¹⁸⁾, Malik AM et al⁽¹³⁾ and Mohamed A et al⁽¹⁷⁾. The minor differences noted maybe due to the difference in time of presentation to hospital invarious setups. The mortality rate in this study was 9.5% which is comparable with various studies by Souvik et al (7.35%)⁽¹⁵⁾, Viji G (9%)⁽²¹⁾, and Madziga AG et al (9.14%)⁽²²⁾. Poor outcomes have been noted in elderly patients and those with early development of bowel gangrene like compound volvulus and intussusception and acute mesenteric ischaemia and also in cases of malignancies.

In conclusion, acute IO still a major cause of morbidity and mortality. Aging and compound volvulus and intussusception are the most important associated factors for mortality. Hernias and adhesions were the leading causes of IO. Abdominal pain and distension, and constipation were seen in majority of cases. Small bowel obstruction was more prevalent than large bowel obstruction. Laparotomy was the most common method of IO management in our institute.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq.

Conflict of Interest: The authors declare that they have no conflict of interest.

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References

1. Soressa U, Mamo A, Hiko D, Fentahun N. Prevalence, causes and management outcome of intestinal obstruction in Adama Hospital, Ethiopia.

- BMC surgery. 2016;16(1):38.
2. Kapan M, Onder A, Polat S, Aliosmanoglu I, Arikanoglu Z, Taskesen F, et al. Mechanical bowel obstruction and related risk factors on morbidity and mortality. *Journal of Current surgery*. 2012; 2(2):55-61.
 3. Ogunrinde TJ, Dosumu OO, Shaba OP, Akeredolu PA, Ajayi MD. The influence of the design of mandibular major connectors on gingival health. *Afr J Med Med Sci*. 2014;43(1):29-33.
 4. Markogiannakis H, Messaris E, Dardamanis D, Pararas N, Tzertzemelis D, Giannopoulos P, et al. Acute mechanical bowel obstruction: clinical presentation, etiology, management and outcome. *World journal of gastroenterology: WJG*. 2007;13(3):432.
 5. Shaikh M, Dholia K. Current Spectrum of Acute Intestinal obstruction at CMC Larkana. *Medical Channel*. 2010;16(2):74-8.
 6. Eren T, Boluk S, Bayraktar B, Ozemir IA, Yildirim Boluk S, Tombalak E, et al. Surgical indicators for the operative treatment of acute mechanical intestinal obstruction due to adhesions. *Annals of surgical treatment and research*. 2015;88(6):325-33.
 7. Akrami M, Ghaeini Hesarooieih A, Barfei M, Zangouri V, Alborzi Z. Clinical Characteristics of Bowel Obstruction in Southern Iran; Results of a Single Center Experience. *Bull Emerg Trauma*. 2015;3(1):22-6.
 8. Moalim AM, Fiqi AO, Dalmar AA, Ankarali H, Karaman MI, Alimoglu O. Factors Associated with Intestinal Obstructions among Adults in Keysaney Hospital, Mogadishu-Somalia. *International Journal of Human and Health Sciences (IJHHS)*. 2018;1(2):70-8.
 9. Ten Broek RP, Issa Y, van Santbrink EJ, Bouvy ND, Kruitwagen RF, Jeekel J, et al. Burden of adhesions in abdominal and pelvic surgery: systematic review and meta-analysis. *Bmj*. 2013;347:f5588.
 10. Barmparas G, Branco BC, Schnüriger B, Oliver M, Konstantinidis A, Lustenberger T, et al. In-hospital small bowel obstruction after exploratory laparotomy for trauma. *Journal of Trauma and Acute Care Surgery*. 2011;71(2):486-90.
 11. Khatri JN, Khatri R. Role of CT Scan in evaluation and management of Intestinal Obstruction. *Indian Journal of Basic and Applied Medical Research*. 2018;7(2):189-93.
 12. Tuca A, Guell E, Martinez-Losada E, Codorniu N. Malignant bowel obstruction in advanced cancer patients: epidemiology, management, and factors influencing spontaneous resolution. *Cancer management and research*. 2012;4:159.
 13. Malik AM, Shah M, Pathan R, Sufi K. Pattern of acute intestinal obstruction: is there a change in the underlying etiology? *Saudi journal of gastroenterology: official journal of the Saudi Gastroenterology Association*. 2010;16(4):272.
 14. Ntakiyiruta G, Mukarugwiro B. The pattern of intestinal obstruction at Kibogola Hospital, a Rural Hospital in Rwanda. *East and central African journal of surgery*. 2009;14(2):103-8.
 15. Souvik A, Hossein MZ, Amitabha D, Nilanjan M, Udipta R. Etiology and outcome of acute intestinal obstruction: A review of 367 patients in Eastern India. *Saudi journal of gastroenterology: official journal of the Saudi Gastroenterology Association*. 2010;16(4):285.
 16. Doumi EBA, Mohammed MI. Acute Intestinal Obstruction in El Obeid Hospital, Western Sudan. *Sudan Journal of Medical Sciences*. 2008; 3(3):191-6.
 17. Mohamed A, Sahoo N, Das SK, Das BB, Pradhan SK, Gouda PK. Profile of operated acute intestinal obstruction patients at a tertiary health care institution. *J Evolution Med Dent Sci* 2017; 6 (15): 1215. 2017;1219.
 18. Thampi D, Tukka VN, Bhalki N, Sreekantha RS. A clinical study of surgical management of acute intestinal obstruction. *Int J Res Health Sci*. 2014;2(1):299-308.
 19. Manafi A, Lotfi M, Amini M. Volvulus Talks Louder than Colon Cancer in Iranian Patients with Acute Large Bowel Obstruction. *Middle East Journal of Digestive Diseases (MEJDD)*. 2009;1(1):7-11.
 20. Bhange S, Jadhav S, Naik A. A prospective study of intestinal obstruction in a rural hospital in India. *Indian J Appl Res*. 2011;1(12):166-8.
 21. Viji G. A prospective clinical study of dynamic intestinal obstruction in a tertiary care centre. *Indian Journal of Applied Research*. 2016;6(5):111-3.
 22. Madziga A, Nuhu A. Causes and treatment outcome of mechanical bowel obstruction in north eastern Nigeria. *West African journal of medicine*. 2008;27(2):101-5.

Infection Rate of Trichomoniasis among Women in AL Hilla City

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Abstract

Trichomoniasis is a very common parasitic disease transmitted sexually in the world. The infection caused by unicellular, flagellated parasite *Trichomonas vaginalis*. The present study was conducted from January to April 2019 to investigate the infective rate of trichomoniasis in women attending family planning unit in maternity and children hospital in Al-Hilla city. A total of 255 women of different ages (>20-50)yr. were enrolled in this study. All of them were screened for trichomoniasis by wet mount preparation. A consent was taken from all participants which included (age, area of residence, marital status, pregnancy status, use of contraceptive) in addition to the symptoms. Out of 255 women, 67 (26.27%) revealed positive results for trichomoniasis. According to age groups the results showed the highest rate of infection (39.6%) in (21-30) yr. age group. The infection rate was high among women lived in rural areas (67.45%) than women lived in urban areas (32.54%). Non-Pregnant women showed higher infective rate of trichomoniasis than pregnant women (65.86% and 43.13%), respectively. The infection rate in married women was (62.74%) and unmarried women was (37.25%). The present study showed high rate of trichomoniasis (67.84%) in women that use contraceptive, while the lower rate of infection with trichomoniasis (32.54%) in women that non-using contraceptive. The present study showed there were significant differences ($p < 0.05$) correlation between trichomoniasis in women with (age, residency, marital status, pregnancy status and using or non-using of contraceptive).

Keywords: *Trichomoniasis, women, infection rate, pregnant, contraceptive.*

Introduction:

Urogenital trichomoniasis is one of the most common diseases transmitted by sexual intercourse and distributed worldwide, the disease spread usually in females more than males, and caused by infection with a flagellated unicellular parasite *Trichomonas vaginalis* and cause inflammatory reactions, vaginal discharge and vulvar itching for infected women [1]. Man is the only known best host of parasite transmitted during sex, and occasionally by fomites [2]. Infected individuals without any clinical features are responsible for spreading the infection to other healthy individuals. Trichomoniasis in women inhabits the lower genital tract of the body and most commonly infect (vagina, urethra or vulva) while in men, the most common infection is found in the prostate, urethra or epididymis causing prostatitis and urethritis [3]. Transmission of *Trichomonas vaginalis* to neonates via passage of infected birth canal is also

imaginable in pregnant women [4] trichomoniasis in women causes profuse vaginal discharge, vulvar burning, irritation and itching, of the genital tract, dysuria, or profuse discharge with unusual bad smell that may be yellow, white or green in color and sometimes frothy vaginal discharge [5]. The World Health Organization estimated the prevalence, ranges about sixty to eighty percent based on wet mount microscopy [6]. Demonstration of source of this infection is challenging because of numerous pathogens can cause vaginal infection and many other infections. Useful tests for diagnosis trichomonas include analysis of vaginal fluid, wet mount technique, culture media and Gram stain [7]. Direct examination of wet mount examination of women, vaginal swabs is less expensive technique and most rapid, for demonstration. *Trichomonas vaginalis* [8]. Trichomoniasis may increase the danger of acquiring or spreading other infection that transmitted sexually. Some studies showed that trichomonas

infection can increase the susceptibility to other co-infection like bacterial infection and urogenital irritation that increases the endangering of viral infections, or to pass the viral pathogens into a sex partner [9]. High rate of trichomoniasis ranging from 21 to 42.6 present in the general population especially in pregnant women. The infection rate of trichomoniasis has been occurs vary depending to place of living or community setting, marital status and age [10].

Subjects and Method

The present study was aimed to evaluate the infection rate of trichomoniasis and its relationships with epidemiological and demographic factors among women attending the family planning unit in maternity and children hospital in Al-Hilla city during the period from January to April 2019. Initially, an informed consent was taken from the contributor then, the information were recoded (age, marital, pregnancy and residency status, use of contraceptive) in addition to clinical symptoms (vaginal discharge, itching, burning, dysuria). Vaginal discharge swab was obtained from posterior vaginal fornix after putting a woman at lithotomic position in non-pregnant women while press secretion and discharge were sweep from the passage of the vulva and modicum deep in vagina with sterilized cotton swabs in pregnant women. The swabs obscure in a tube with one ml of a sterile normal saline, then the suspension was used to prepare wet mount slides and they were immediately examined microscopically at 40x, 100x power according to [11] for demonstrate the parasite oval shaped, jerky motile, flagellated trichomonas vaginalis. Then results were tabulated and analyzed.

Statistical Analysis: Statistical data analysis were done by using the SPP program software, version (17), and chi square analysis test (x2) with (P) value <0.05 for statistical analysis of the results of this study.

Results

Table 1: Infection rate of trichomoniasis according to age groups

Age groups	No. of exam	%	No. of infected	%
>20	25	9.803	9	13.43
21 - 30	101	39.6	31	46.26
31 -40	94	36.8	20	29.85
41 - 50	35	13.72	7	10.44
Total	255	%100	67	%100

P. value <0.05 is statistically significant

In the present study (255) women from (> 20 -50) yr. were arranged in to four categories .the result recorded higher infection rate(46.26%)and (29.85%) among the age groups (21-30),(31-40)respectively while the lower infection rate (10.44%) among the age group(41-50)as show in table 1 .

Table 2: Infection rate of trichomoniasis according the residency status

Residency Status	No. of exam	%	No. of infected	%
Rural	172	67.45	47	70.14
Urban	83	32.54	20	29.85
Total	255	%	67	%

P. value <0.05 is statistically significant

The present study showed higher infective rate Trichomoniasis among women lived in rural areas (70.41%) as compared with women lived in urban areas (29.85%) .the result reveals significant differences (p<0.05) between them as show in table 2.

Table 3: Infection rate of trichomoniasis according the pregnancy status

Pregnancy Status	No. of exam	%	No. of infected	%
Pregnant	110	43.13	21	31.34
Non-Pregnant	145	56.86	46	68.65
Total	255	%	67	%

P. value <0.05 is statistically significant

The results of present study found that high rate of infection were observed in non-pregnant women(68.65%) than pregnant women (31.34%). The results showed statistically significant as in table3.

Table 4: Infection rate of Trichomoniasis according the marital status

Marital Status	No. of exam	%	No. of infected	%
Married	160	62.74	55	82.08
Unmarried	95	37.25	12	17.91
Total	255	%	67	%

P. value <0.05 is statistically significant

The infective rate with Trichomoniasis in married and unmarried was (82.08%) and (17.91%) respectively statistically differences (P<0.05) between the infective rate in two status as reported in table 4.

Table 5: Infection rate of trichomoniasis according the contraceptive using

Contraceptive	No. of exam	%	No. of infected	%
Users	173	67.84	44	65.67
Non-users	82	32.15	65.67	34.32
Total	255	%	23	%

P. value<0.05 is statistically significant

Infection rate of Trichomoniasis was more common between women who using contraceptive (65.67%) than those did not using contraceptive (34.32%) as in table 5.

Discussion

In the present study, 255 women from (>20 to 50) yr. old were arranged in to four categories. 67 (26.27%) revealed positive results for trichomoniasis. According to the age group the result recorded high infection rate(46.26%) of trichomoniasis among the age group (31-40) yr. which in agreement with similar studies in Baghdad,Iraq^[12,13]and ^[14] in Dohok,Iraq . Also in agreement with ^[15]who demonstrated that the infection rate is high in the young age and risk than other age, on the other hands this finding disagreement with some studies done by ^[16,17] and study in Kirkuk,Iraq^[18]. This suggests that greater sexual activity responsible for high rate of infection of this age group. The present study showed a lower infection rate of trichomoniasis among women lived in urban areas (29.85%) as compared with women lived in rural areas (70.41%) this finding may be due to the scope and quality of health care, socioeconomic conditions, life style and educational status of the women setting in rural areas, the results agreement with the study of ^[19]in Tikrit,Iraq also agreement with study done in India ^[20]. The present study reveals the high infection rate of trichomoniasis was (68.65%) in non-pregnant women compared with pregnant women was (31.34%) this finding may be due to the variation in sample size of pregnant and non-pregnant women examined in present study or because of that pregnant women make attend antenatal clinics where they check out and treated in bureaucracy antenatal clinics. This results agree with study done by ^[21] in Iraq who indicated that the infective rate in non-pregnant women (20.0%) higher than in pregnant women was (9.09%) while the results of present study disagree with some study done by ^[22-24] reported that the pregnant women more insecure to infection with trichomoniasis than non-pregnant women. The

observation of present study is reveal that the infection rate of trichomoniasis varied with the marital status of the women, the highest infection rate among the married women (82.08%) and less among the unmarried women (17.91%). One of the reasons for the lower infection rate of Trichomoniasis in unmarried women that is a disease fundamentally transmitted sexually. ^[25] reported that two to three million of trichomoniasis with clinical symptoms occur mainly among sexually active women. The results of present study is agree with similar studies that showed high rate of trichomoniasis among married women in compare with unmarried women^[26-28]. Regarding to use of contraceptive the present study was recorded more frequently of trichomoniasis (65.67%) in women that were contraceptive users than in women that did not use contraceptive (34.32%) . This result was also recorded by ^[29]. The effect of contraceptive may create suitable condition that is good hospitable for parasite because of the contraceptives changes the normal condition of the genital tract and alter the usual lubricant secretions then causes damage to the epithelial lining of vagina through which sexually transmitted pathogenic organisms such as *Trichomonas vaginalis* may invade the urogenital tract easily^[30,31].

Conclusion

Trichomoniasis the most common disease spread among women during sexually active age. The studies on it relatively scanty in Iraq, Also there is a very poor awareness about trichomoniasis among women with high risk to infection such as married and urban lived women. Thus, we need plans which aims to improve the knowledge about the disease in populations, Also future epidemiological studies in various areas of country are required to promote understand the prevalence of trichomoniasis

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: The authors declare that they have no conflict of interest.

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References

1. Vander PB. Trichomonas vaginalis infection, the most prevalent non-viral sexually transmitted

- infection receives the least public health attention. *Clin Infect Dis.* 2007; 44(1): 23-5.
2. Harp DF, Chowdhury I. Trichomoniasis: evaluation to execution. *Eur J Obstet Gynecol Reprod Biol.* 2011;157(1):3-9.
 3. Krieger JN. Trichomoniasis in men: old issues and new data. *Sex Transm Dis.* 1995; 22(2): 83-96.
 4. Jawetz E, Melnick G, Adel bery E. *Medical Microbiology*. 22nd ed. LANGE Geo F Brooks. 2001;563-566.
 5. Pastorek JG, Cotch MF, Martin D, Eschenbach DA. Clinical and Microbiological correlates of vaginal trichomoniasis during pregnancy. *Clin Infect Dis.* 1996; 23:1075–1080. [PubMed] [Google Scholar]
 6. WHO. Global prevalence and incidence of selected curable sexually transmitted infections: overviews and estimates. WHO/HIV_AIDS/2001.02. Geneva: World Health Organization. 2001.
 7. Hogniberg BM, Burgess E. *Trichomonas* of importance in human medicine including *Dientamoeba fragilis* In: Kreier JP. *Parasitic Protozoa*. 1994; 2th ed. San Diego Acad Press, 1–57. [Google Scholar]
 8. Rezaeian M, Vatanshenassan M, Rezaie S, . Prevalence of *Trichomonas vaginalis* Using Parasitological Method in Tehran. *Iran J Parasitol.* 2009;4(4):43–7. 2009.
 9. Magnus M, Clark R, Myers L, Farley T, Kissinger PJ. *Trichomonas vaginalis* among HIV— infected women: are immune status or protease inhibitor use associated with subsequent *T. vaginalis* positivity. *Sex Transm Dis.* 2003; 30(11):839-43. 2003.
 10. Shuter J, Bell D, Graham D, Holbrook KA, Bellin EY.. Rates of and risk factors for trichomoniasis among pregnant inmates in New York City. *Sex Transm Dis.* 1998; 25(6):303-7.
 11. Nasir JA, Najam J, Tahir F, Asghar MN and Iqbal J. *Trichomonas vaginalis* in vaginal smears of women using Intrauterine Contraceptive Device. *Pak J Med Res.* 2005; 44(3):144-116.
 12. Al- Samarra'ie HF. Comparative study of *Trichomonas vagina/is* and bacteria coexistence in vaginal infection in pregnant and nonpregnant women. *MSC thesis College of Medicine Baghdad University.* 2002.
 13. Khalil HI, Al-Kuraishi AH, Al-Naimi UAM, Al-Naimi SA. *Trichomoniasis vaginalis* in women attending planning unit in Al-Liqa'a hospital. *Iraqi J of Sci.* 2012; 53: 746-753.
 14. Al-Saeed, .Detection of *Trichomonas vaginalis* by different method in women from Dohok province. *Eastern Mediterranean Health J.* 2011; 17 (9): 706–709. View at Google Scholar
 15. Guidance F, Guidance B. The management of women of reproductive age attending nongenitourinary medicine settings complaining of vaginal discharge. *J FamPlann Reprod Health Care.* 2006; 32(1): 33-42.
 16. Sorvillo F, Smith L, Kerndt P. *Trichomonas vaginalis* and HIV in African Americans. *Emerg Inf Dis.* 2001; 7: 927–932.
 17. Moshfe AA, Hosseini S. Comparison of clinical and microscopic diagnosis of trichomoniasis referred to the Yasuj women clinic. *Arma Danesh.* 2004; 33: 71-82.
 18. Salman YJ, Esraa AK. Detection of *Trichomonas vaginalis* among females attending Private Gynaecological clinics in Kirkuk province using different laboratory method. *Jof Kirkuk Medical College.* 2013; 1(2): 1-8.
 19. Al-Somaeday EG. Study on the prevalence of trichomoniasis in married women intended Tikrit teaching hospital and the effect of some plant extracts on the parasite. M.Sc. Thesis, College of Education for Girls, University of Tikrit. 2006.
 20. Franceschi S, Rajkumar R, Snijders PJF, Arslan I A, Mahe C, Plummer M, Sankaranarayanan R, Cherian J, Meijer CJLM, Weiderpass E. Papillomavirus infection in rural women in southern India. *BrJ Cancer.* 2005; 92(3): 601-606.
 21. Al- Kaisi A.A.R. *Trichomoniasis* among females with vaginal discharge in Baghdad Medical City. *J. Fac. Med. Baghdad.* 2008; 50 :37- 41.
 22. Kadir M.A., Salehy A.M.S. and Hammad E.F. Studies on *Trichomonas vagina/is* 'in Erbil Teaching Hospital. *I. Fac. Med.* 1988;30: 83-88.
 23. Aboyeji AP, Nwabuisi C. Prevalence of sexually transmitted diseases among pregnant women in Ilorin, Nigeria. *J Obstet Gynecol.* 2003; 23(6): 637-639.
 24. Mahdi NK. Urogenital trichomoniasis in an Iraqi population. *Eastern Mediterranean J.* 1996; 2 (3): 501- 505.

25. Abdol-Samad M, Gavgani I, Asiye N, Ardavan G, Sakineh A, Fahimeh S, Sakineh R, Afsaneh D. Prevalence and risk factors of trichomoniasis among women in Tabriz. Iran. *J. Clin. Inf. Dis.* 2008; 3(2):67-71.
26. Buv'e A, Weiss HA, Laga M, Van Dyck E, Musonda R, Zekeng L. The epidemiology of trichomoniasis in women in four African Cities. *AIDS.* 2001; 15: 589-96.
27. Azambakhtiar A, Nikmanesh B, Rezaeian M, Dashti N, Safari F, and Zarebavani E. The prevalence of trichomoniasis in women referred to clinical centers in south of Tehran, Iran during 2015-2016. *Iranian J of Parasitol.* 2018; 13(1) 108–113. View at Google Scholar.
28. Arbabi M, Fakhrieh Z, Delavari M, and Abdoli A. Prevalence of *Trichomonas vaginalis* infection in Kashan City, Iran (2012-2013). *Iranian J of Rep Med.* 2014; 12(7) 507–512. View at Google Scholar.
29. Whitaker AK, Johnson LM, Harwood B, Chiappetta L, Creinin MD, Gold MA. Adolescent and young adult women's knowledge of and attitudes toward the intrauterine device. *Contraception.* 2008; 78(3):211–7. [PubMed] [Google Scholar]
30. Nizami D, Gülnaz Ç, Ali U, Arif G. The Investigation of the Association Between the Frequency of *Trichomonas Vaginalis* and Using Intrauterine Contraceptive Device. *Trakya Univ Tip Fak Derg.* 2009; 26(3):197-202.
31. Agboola A. Vaginal Discharge: In the Textbook of Obstetrics and Gynecology for Medical Students. 2nd ed Heinemann Educational Books. (Nigeria) plc 548pp. 2006.

Genotyping of Epstein-Barr Virus in EBV-Positive Burkett's Lymphoma in Anbar Province (Western of Iraq)

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Abstract

Background: Epstein-Barr virus (EBV) is the first identified human virus with a proven association with the pathogenesis of cancer including Burkitt's lymphoma (BL). Two subtypes of EBV, type A and B have been identified based on divergence in the nuclear protein genes (EBNA) 2, 3, 4 and 6.

Objectives: This study aimed to determine the genotype of EBV in BL cases in Anbar province (Western of Iraq).

Materials and Method: This study was conducted at Anbar Medical college-Ramadi city, Iraq and the molecular analyses were carried out at private laboratories in Baghdad city during the period from January 2017 to December 2019. The expression of EBV-to-EBV-encoded small RNA in BL cases was detected by the in situ hybridization technique (EBER- RISH). EBV DNA was extracted from formalin-fixed, paraffin-embedded tumor blocks of BL cases. One-stage polymerase chain reaction (PCR) and two-stage (nested) PCR assays were performed with the primers common for both EBV genotypes and the primers specific for EBV types 1 and 2, respectively. PCR reaction was employed for EBV Genotyping using sets of primers flanking the EBNA-2.

Results: EBV genomes were detected in all BL, and EBV type 1 virus (EBV type A) infected the majority of EBV-positive BL cases (85/90) (94.44%), while EBV type two (EBV type B) was detected in five cases only (5.56%).

Conclusion: Predominant of EBV Type 1(EBV type A) in the Iraqi positive BL cases.

Keywords: *EBV, Burkett's lymphoma, genotyping, PCR.*

Introduction

Epstein-Barr virus (EBV) also called human herpesvirus 4 (HHV-4) affecting more than 90% of individuals worldwide¹. Most primary EBV infections are asymptomatic^{2,3}. Reactivated EBV infections are associated with serious complications such as lymphoproliferative disorders and malignancy^{1,3-6}.

Epstein-Barr nuclear antigen 1 (EBNA-1) and the two small noncoding Epstein-Barr RNAs (EBERs) (latency I) have been generally thought to be the only EBV genes expressed in Burkitt's lymphoma (BL)^{3,6,7}. Variations in the EBV genome made it possible to distinguish two (02) subtypes of the virus: EBV-1 and EBV-2 (or EBV-A and EBV-B types)^{3,8,9,10,11,12}.

There are three subtypes of BL: endemic BL, sporadic or non-endemic BL, and immunodeficiency-associated BL¹¹. Endemic BL commonly seen in children aged 4–9 years affecting the facial skeleton involve the maxilla or mandible and Jaw tumors^{4,11,14,15,16,17}. Sporadic BL, affecting mainly abdominal viscera¹⁴ typically seen in patients less than 35 years of age^{7,17}. Immunodeficiency-associated BL occurring in association with the HIV infection¹⁶.

In Iraq, there are not enough data are available for the EBV genotypes in EBV positive BL cases. This study aimed to determine the genotype of EBV in BL cases in Anbar province (Western of Iraq).

Materials and Method

Study Setting: The study was a retrospective cross-sectional design to investigate the presence of the DNA and genotypes of EBV from primary archives tissue samples of the pathologist Dr. Arkan AL Essawi, in AL-Anbar medical college during period from January 2017 to December 2019, and the molecular analyses were carried out at private laboratories in Baghdad city.

Ninety cases previously diagnosed as BL were retrieved from the archives. Hematoxylin and eosin stained slides of 90 biopsies from 64 patients were reviewed for confirmation and classification according to the criteria from the WHO-proposed list of lymphoid neoplasms¹⁷ by pathologist Dr. Arkan AL Essawi. Archived slides were reviewed by two pathologists for confirmation of diagnosis and tissue adequacy for extracting of DNA. Detection of EBV in BL cases were done in the previous study¹⁸.

The demographic data of these patients' biopsies were obtained from an information sheet volunteered by the clinicians. Statistical analyses were based on non-parametric method and a P value <0.05 was considered significant. The study was retrospective, so informed consent not taken from the patients. This study was approved by the Microbiology Department, Anbar medical College, University of Anbar, Ramadi city, Iraq.

Method

In Situ Hybridization: The expression of EBV-

to-EBV-encoded small RNA in Burkitt's lymphoma (BL) cases was detected by the in situ hybridization technique (EBER-RISH) were performed according to the manufacturer's instructions.

PCR Amplification:

DNA extraction: EBV DNA was extracted from formalin fixed paraffin-embedded tumor blocks of (BL) cases according to procedure describe previously¹⁹.

Detection of EBV DNA: Detection of EBV DNA in BL cases according to the manufacturer's instructions (Merck, Darmstadt, Germany). The amount and purity of DNA were determined by spectrophotometer. DNA was stored at 80° C until use. The supernatant containing DNA was used directly for PCR amplification.

Genotyping of EBV: EBV Genotyping was carried out when the virus was detected by in situ hybridizations. Genotyping was carried out when the virus was detected by PCR. A nested PCR procedure was performed as previously described²⁰. Amplification of the EBNA-2 gene was performed according to a nested PCR procedure by using the two primer pairs as showed in table 1. These primer pairs generated products of 300 bp for type 1 (type A), and 250 bp for type 2 (type B) of EBV (Fig 1). The reaction products were examined by direct visualization using Ethidium bromide stain as a fluorescent dye in agarose gels (2%) under UV transilluminator.

Table (1): Primers used for EBV genotyping

Primers	Sequence (5'-3')	Use in the PCR reaction EBNA-2
EBNA-2F	5' TTT CAC CAA TAC ATG AAC 3'	1st reaction sense
EBNA-2I	5' TGG CAA AGT GCT GAG AGC AA 3')	1st reaction Antisense
EBNA-2C	5' CAA TAC ATG AAC CRG AGT CC 3'	Nested reactive sense
EBNA-2G	5' AAG TGC TGA GAG CAA CCG GC 3'	Nested reaction antisense type-1
EBNA-2B	5' TTGAAGAGTATGTCCTAAGG3'	Nested reaction antisense type-2

Results

All Burkett's lymphoma biopsies were EBV-positive using in situ hybridization (ISH) technique.

A total of 90 EBV-positive BL biopsies belong to 60 males and 30 females, for a male to female ratio of 2:1. The main sites of presentation are the gum and maxilla

41/90, (42.55%) and lymph nodes 26/90, (28.88%). Other common sites included the abdominal viscera 10(11.11%), 3/90 (3.33%) for each of testes and ovary, tonsil, Nose and brain 1/90, (1.12%). The remaining three (3.33%) biopsies were taken from other sites (orbit, bone marrow, the soft tissue of the neck, upper thigh, and the infra-spinal region) (Tab 2).

PCR amplification of the EBNA-2 gene to determine the type of EBV was successful all of the 90 EBV-positive BL cases (Tab 2). In 85 of the 90 cases (94.44%), a 300-bp product was identified by PCR consistent with type A EBV (EBV Type 1), whereas in five of the 90 cases (5.56%), a 250-bp product was consistent with type B

EBV (EBV Type 2). No case demonstrated both EBV subtypes in the same sample (Tab 2).

Among the EBV-positive cases, 53 of 90(58.88%) belonged to children younger than 17 years with median age 6 years, 37 of 90 (41.12%) were adults with Median age 28 years. (Tab 1).



Figure (1): Shows the results of EBV types 1(types A) (300 bp) and EBV types 2 (types B) (250 bp) detection in EBV-positive Burkett’s lymphoma cases

Table (2): Demographic Characteristics, Localization of Tissue Site and genotyping of EBV among the EBV-positive Burkett’s lymphoma cases

Characteristic	Total No. 90
Sex	
Male	53 (58.88%)
Female	37 (41.12%)
Median age (Years)	
Younger than 17 year	6. years
Adults	28 years
Localization	
Gum and maxilla	41/90 (42.55%)
Lymph nodes	26/90 (28.88%)

Characteristic	Total No. 90
Abdominal viscera	10/90 (11.11%)
Tests and ovary	3/90 (3.33%)
Tonsil	3/90 (3.33%)
Nose	3/90 (3.33%)
Brain	1/90 (1.11%)
Others	
Orbit, bone marrow, the soft tissue of the neck, upper thigh, and the infra-spinal region	3/90 (3.33%)
Genotyping of EBV	
EBV type 1	85 (94.44%)
EBV type 2	5 (5.56%)

Discussion

In the current study, Among the EBV-positive BL cases, 53 of 90(58.88%) belonged to children younger than 17 years with median age 6 year, 37 of 90 (41.12%) belonged to adults with median age 28 year (Tab.2) and these results is in accordance with several authors^{5, 13, 15} who showed that the majority of EBV-positive BL of pediatric cases in ages ranging from 5 to 9 years, whereas in the United States it is slightly higher,10 years^{7,13}. it was in contrast to the previous studies among children from North America where the median ages 19.2 years¹⁷.

Results regarding the medium age of adults who EBV-positive BL in present study were consistent with previous reports that showed sporadic BL is typically seen in patients less than 35 years of age^{18,24}, whereas it was the difference from the previous study in North America^{7,17} that showed a mean age occurring in the 19.2 years.

Regarding gender distribution of EBV- positive BL biopsies in current study (Tab 2) were consistent with previous reports that showed BL was more frequent in males in low-risk areas like Europe^{19, 5,23}, conversely to other studies females were more affected than males,²³, contrary to early African reports where males and females were almost equally affected^{15, 25}.

In the present study, type A EBV (EBV Type 1) was the most common genotype detected in 94.44% (85/90) of the EBV+ BL cases whereas five of the 90 (5.56%) EBV+ BL cases were type B EBV (EBV Type 2) (Tab 2). These findings were in agreement with Robaina et al.⁸ and Naresh⁹, Hassan et al. in Brazil¹⁴ who found the overwhelming majority of EBV infections were due to genotype A. Similar results from developing countries^{12,7,11}, Egyptian and Turkey studies^{26,27}, Western and Asian countries²⁴, whereas other studies found that both types A and B EBV have been identified at high frequency in equatorial Africa and Central West region^{10,28}.

It is unknown why BL was rarely associated with EBV-2 (type B virus)^{1,11}. The ability for transformation to the EBNA2B genotype is stronger in immuno compromised patients, such as those with HIV infection and in an individual as low cellular immunity is postulated to enhance the expression of genotype B^{9,19, 28}. In Australia, genotype B infections were reportedly six-fold higher in HIV-infected patients than in the general community^{1,9}, whereas other studies report the dominance of Epstein Barr virus genotype A in HIV-

infected patients¹⁶. The explanation for this result may be due to EBV-1 is more efficient to transform and immortalize infected B lymphocytes in vitro; whereas, EBV-2 is reported to be a weaker transformer¹⁶.

Using of EBER-RNA in situ hybridization is the standard for EBV diagnosis in BL biopsies as described previously while PCR procedures are used for EBV typing^{29, 30}. PCR-based method are used for strain determination (type-1 or 2)²⁹.

Regarding the positivity of all BL biopsies for EBV using in situ hybridization (ISH) technique, These findings are in agreement with several studies in tropical Africa^{5,4,16}, South America²⁸, Northeast of Brazil (~80%)³⁰. Conversely, in sporadic BL in developed countries, and EBV association has been demonstrated in 15 to 30% of cases^{1,8,11}, and a lower association in patients from Argentina and Chile³¹. However, recent works suggest that low socioeconomic status and an early EBV infection can be associated with a higher prevalence of EBV+ BL in low-incidence areas.

Regarding the main sites of BL biopsies at the presentation in our patients, was more consistent with the endemic variety of BL as in North African patients^{11,16,28} that show a facial or jaw tumor at the same time an abdominal mass similar to finding that observed in other parts of the Middle East^{14,19, 11,16}. Finally, detection and genotyping of EBV in pathology samples is relevant since its high prevalence in some cancers makes the virus a promising target of specific therapies.

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Conflict of Interest: The authors declare that they have no conflict of interest.

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References

1. Santpere, G. et al. Genome-wide analysis of wild-type Epstein-Barr virus genomes derived from

- healthy individuals of the 1000 Genomes Project. *Genome Biol. Evol.*(2014).6, 846–860
2. Lieberman, P. M. Epstein-Barr virus turns 50. *Science (80-.)*.(2014).343, 1323–1325
 3. Palma, I. et al. Detection of Epstein-Barr virus and genotyping based on EBNA2 protein in Mexican patients With Hodgkin lymphoma: a comparative study in children and adults. *Clin. Lymphoma Myeloma Leuk.*(2013).13, 266–272
 4. Young, L. S. & Rickinson, A. B. Epstein-Barr virus: 40 years on. *Nat. Rev. Cancer*(2004).4, 757
 5. Yao, Y. et al. Genome-wide analysis of Epstein-Barr virus identifies variants and genes associated with gastric carcinoma and population structure. *Tumor Biol.*39, 1010428317714195 (2017).
 6. Lay, M.-L. J. et al. Epstein-Barr virus genotypes and strains in central nervous system demyelinating disease and Epstein-Barr virus-related illnesses in Australia. *Intervirology*(2012)55, 372–379.
 7. Pannone, G. et al. The role of EBV in the pathogenesis of Burkitt's Lymphoma: an Italian hospital based survey. *Infect. Agent. Cancer*(2014).9, 34
 8. Robaina, T. F. et al. Polymerase chain reaction genotyping of Epstein-Barr virus in scraping samples of the tongue lateral border in HIV-1 seropositive patients. *Mem. Inst. Oswaldo Cruz*(2008)103, 326–331.
 9. Naresh, K. N. et al. Diagnosis of Burkitt lymphoma using an algorithmic approach—applicable in both resource-poor and resource-rich countries. *Br. J. Haematol.*(2011).154, 770–776
 10. Chang, C. M., Kelly, J. Y., Mbulaiteye, S. M., Hildesheim, A. & Bhatia, K. The extent of genetic diversity of Epstein-Barr virus and its geographic and disease patterns: a need for reappraisal. *Virus Res.*(2009)143, 209–221.
 11. Van den Bosch, C. A. Is endemic Burkitt's lymphoma an alliance between three infections and a tumour promoter? *Lancet Oncol.*(2004).5, 738–746
 12. Otieno, J. et al. Human and Epstein-Barr Virus miRNA Profiling as Predictive Biomarkers for Endemic Burkitt Lymphoma. *Front. Microbiol.* (2017).8, 1–13
 13. Magrath, I. Epidemiology: clues to the pathogenesis of Burkitt lymphoma. *Br. J. Haematol.*(2012).156, 744–756
 14. Hassan, R. et al. Clinical and demographic characteristics of Epstein-Barr virus-associated childhood Burkitt's lymphoma in Southeastern Brazil: epidemiological insights from an intermediate risk region. *Haematologica* (2008).93, 780–783
 15. Sant, M. et al. Incidence of hematologic malignancies in Europe by morphologic subtype: results of the HAEMACARE project. *Blood*(2010)116, 3724–3734.
 16. Traore, L. et al. EBV and HHV-6 circulating subtypes in People Living with HIV in Burkina Faso, impact on CD4 T cell count and HIV viral load. *Mediterr. J. Hematol. Infect. Dis.*9, (2017).
 17. Diebold J, Raphael M, Jaffe ES, W. R. In World Health Organization classification of tumours, pathology and genetics of haemopoietic and lymphoid tissues, Burkitt lymphoma. IARC Press. Lyon(2001).1181–4
 18. Al-Fahdawi, K. A. Z., Al-Zobae, M. A. K. & Al-Esawi, A. O. J. Association Between Epstein-Barr Virus and Burkitt's lymphoma in Western Iraq. (A molecular case-control study. *Al-Anbar Med. J.*(2016)13, 114–124.
 19. Green, M. R. & Sambrook, J. Chapter I, Isolation and Quantification of DNA. *Molecular cloning, A laboratory manual*1, (2012).
 20. van Baarle, D. et al. Direct Epstein-Barr virus (EBV) typing on peripheral blood mononuclear cells: no association between EBV type 2 infection or superinfection and the development of acquired immunodeficiency syndrome-related non-Hodgkin's lymphoma. *Blood* (1999)93, 3949–3955.
 21. Boerma, E. G. et al. Gender and age-related differences in Burkitt lymphoma—epidemiological and clinical data from The Netherlands. *Eur. J. Cancer*(2004).40, 2781–2787
 22. Michelow, P., Wright, C. & Pantanowitz, L. A review of the cytomorphology of Epstein-Barr virus-associated malignancies. *Acta Cytol.* (2012).56, 1–14
 23. Ogwang, M. D., Bhatia, K., Biggar, R. J. & Mbulaiteye, S. M. Incidence and geographic distribution of endemic Burkitt lymphoma in northern Uganda revisited. *Int. J. cancer*(2008)123, 2658–2663.

24. Lucchesi, W. et al. Differential gene regulation by Epstein-Barr virus type 1 and type 2 EBNA2. *J. Virol.*(2008).82, 7456–7466
25. Anwar, N. et al. The investigation of Epstein-Barr viral sequences in 41 cases of Burkitt's lymphoma from Egypt. *Epidemiologic correlations. Cancer*(1995)76, 1245–1252.
26. Cavdar, A. O. et al. Burkitt's lymphoma between African and American types in Turkish children: clinical, viral (EBV), and molecular studies. *Med. Pediatr. Oncol.*(1993).21, 36–42
27. Kabyemera, R. et al. Relationship between Non-Hodgkin's lymphoma and blood levels of Epstein-Barr Virus in children in north-western Tanzania: a case control study. *BMC Pediatr.*(2013)13, 4.
28. Minnicelli, C. et al. Relationship of Epstein-Barr virus and interleukin 10 promoter polymorphisms with the risk and clinical outcome of childhood Burkitt lymphoma. *PLoS One*(2012)7, e46005.
29. Gatto, F. et al. A multiplex calibrated real-time PCR assay for quantitation of DNA of EBV-1 and 2. *J. Virol. Method*(2011).178, 98–105
30. Kelly, G. L. & Rickinson, A. B. Burkitt lymphoma: revisiting the pathogenesis of a virus-associated malignancy. *ASH Educ. Progr. B.*2007, 277–284 (2007).
31. Chabay, P. A. et al. Assessment of Epstein-Barr virus association with pediatric non-Hodgkin lymphoma in immunocompetent and in immunocompromised patients in Argentina. *Arch. Pathol. Lab. Med.* (2002). 126, 331–335

Study Effect of Pills and Alcoholic Extract of Rue Plant on the Histological Structure of Ovary in Adult Rabbit Females

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Abstract

The study was conducted on a group of adult female white rabbits aged between 5-10 months and weights ranging between 700-1500g, the groups included one male and two female adult rabbits, a group of which was orally administered oral contraceptives at a concentration of 30mg/28kg of body weight per day for a period of 28 days while a group of 40 mg was injected group a concentration of 40 mg/kg of body weight per day and for the same duration of the extract of the rue plant. Animals were treated comparatively with distilled water. The results of the histological study also showed satisfactory changes in the tissue of rabbit ovaries dosed with pill. Pregnancy where hyperplasia has been observed and a decrease in the numbers of mature primary and secondary follicles. Atresia follicle has been observed. The histological study also revealed the occurrence of graafian follicular oocyte degradation and shrinkage, and the occurrence of thickening in the follicular cells and bleeding and blood congestion in the interstitial space and hyaline follicles in the cortical layer, but in the medulla region was observed rupture and necrosis and dissolution and disaggregation of stroma cells, and the occurrence of inflammatory cells and the occurrence of degeneration (fatty and hyaline and hydropic). Not for the occurrence of necrosis of fibrous and cellular integration as observed expansion vasodilation of blood vessels. The study also showed a thickening of follicular cell nuclei. For the injected group at a concentration of 40 mg/kg body weight has reduced/decreased the number of mature follicles. The small size of the egg in the follicles of Krav, and the emergence of glass degeneration and the emergence of follicular follicles, while maintaining the number of primary and secondary follicles similar to the control group, also did not notice the occurrence of rabbits injected plant extract.

Keywords: *Rutagraveolens, Estrogen, Pills, Progesterone, Follicles, FSH.*

Introduction

Herbal remedies are well-known in the Iraqi society and are well-known among his sons, for their confidence in the effectiveness of these plants in the treatment of diseases¹. The use of these plants may be due to their appropriate price and very low or no toxicity compared to other chemical drugs². These natural substances have

proven effective in treating and healing many diseases, especially infectious diseases³. Chemical treatments, such as birth control pills that contain both the estrogen hormone that is in the form of Ethinylestradiol and Progesterone. These hormones work to prevent pregnancy by inhibiting the pituitary gland and hypothalamus, which inhibits the release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH). As progesterone injections and other drugs negatively affect the near and long term on a woman's body and fetal health, it has been noted⁴. These drugs cause thrombosis, mesenteric vein thrombosis, artery occlusion, gastrointestinal disorders etc⁵. One natural herb that has been used to prevent pregnancy is Rutagraveolen Proteins s, known as Rue, a perennial herbaceous plant. It belongs to the Rutaceae family, and the medical and therapeutic importance

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of Ruta is attributed to its possession of many active (Alkaloids, Coumariens, Phenolic, Proteins, Tannins, Resines, Glycosides, Volatile oil) The most important compounds of the plant are Rutin and Quercetin⁶. Proteins, Tannins, Resines, Glycosides, Volatile oil). The most important compounds of the plant are Rutin and Quercetin⁶. This inhibits the secretion of pituitary hormones FSH, LH and hypothalamus, which affects the growth and maturation of ovarian vesicles and the formation of the luteal body⁷. As well as its effect on smooth muscles of the uterus causing increased mobility which prevents the implantation of the fetus⁸. That inhibit the secretion of pituitary hormones FSH The plant is also used to treat diarrhea and skeletal disorders and as an antibiotic against various bacteria and fungi and in the treatment of nerve tumors. The aim of this study is to influence the contraceptive pills and the alcoholic extract of the pulling plant on the histological structure of adult rabbit ovaries.

Materials and Method

Preparation of hot alcoholic extract of the rue plant: Continuous extraction apparatus (Soxhlet Apparatus) was used according to the method described by⁹ (Soaked ground samples were soaked in saxolite for 24 hours using 70% methyl alcohol solvent (60-80°C) and 250 ml or 10 g/100 ml. After completing the process that took (8-10) hours and until the disappearance of the green solvent color in the Batch, then concentrated the solutions to the dry stage under pressure rarefied by using the rotary evaporator device kept the plant in sterile sealed tubes until used in subsequent experiments as well as the process of separation And diagnosis.

Animals: Six white rabbits were collected from the Institute of Embryology and Infertility Research/ Al-Nahrain University. Their weight ranged between 700-1500 g and their ages were between 5-10 months. It was adapted and reared at the Animal House of the College of Veterinary Medicine, University of Diyala for one month before conducting experiments where Brushed with sawdust and cages were sterilized and cleaned during the experiment period, provided with water and appropriate ration, which consisted of dried bread, vegetables and barley and provided the appropriate environmental conditions of temperature and ventilation. Animals were randomly grouped and rabbits were marked with different colors to distinguish between them. Each color indicated a concentration of injected or dosed concentration. Then the adult rabbits

used in this study were randomly divided into 3 groups comprising each group (2) female rabbits with an adult male rabbit. Females were injected with birth control pills and injected with alcoholic extract for 28 days. The first group: (control group) dosed physiological solution, Group 2: Orally administered oral contraceptive pills dissolved in water at a concentration of 30 mg. Group III: injected subcutaneously with alcoholic extract of the extracting plant at a concentration of 40 mg.

Results and Discussion

Histological changes of the ovarian rabbit dosed with birth control pills: The results of the present study showed that there were many histopathological changes in the tissue of rabbit ovaries administered to the pill at a concentration of 30 mg.kg⁻¹ Changes were seen in the cortex and medulla regions, where pathological changes in the cortical layer included hyperplasia of the ovary A decrease in the number of Oocyte and secondary follicle cells was also observed. In contrast, atresia follicle was formed compared to the control group females as shown in Figure (1).



Fig. 1 Cross-sectional section of the ovary of a female rabbit inoculated with COCP at a concentration of 30 mg.kg⁻¹ for 28 days. Cellular hyperplasia (HYP), primary follicles (PF), secondary follicle (SF), corpus luteum (CL), follicular follicles (AF). (40x H & E).

This is due to the effect of negative contraceptive pills on both the pituitary and hypothalamus. FSH is less secreted by the gland, the hormone responsible for follicular growth, which negatively affects the size of the follicles. This increases the thickness and thickening of the coated layer of cystic follicles and natural follicles¹⁰. This may be due to the effect of birth control pills on the hypothalamus (especially hypothalamus), especially synthetic progesterone, in disrupting pituitary secretions. GnRH hormones, which secrete FSH in less than normal, and inhibit FSHRNA secretion and thus

inhibit hormone receptors on the surface of the ovary by its effect on Protein secreted by the pituitary gland thus affects egg cell formation and division process, inhibits maturation and egg cell formation and reduces the number of primary follicles or atrophy in the ovary¹¹. Histological sections also indicated vasodilation with hemorrhage and congestion. Clearly in the area of the cortex as it was noted that the thickening of the nuclei of the warp cells (pyknosis) and the death of some cells (cell dead) according to Figure (2).

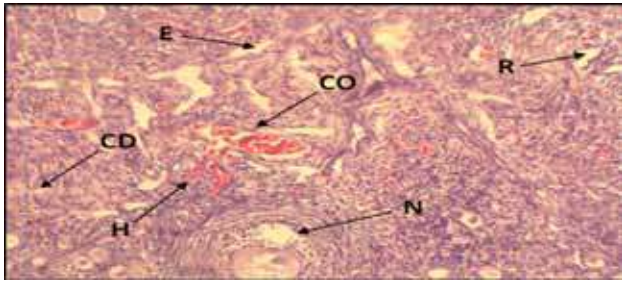


Figure (2) Cross-section in the ovary of the rabbit female vaccinated with a drug (COCP) at a concentration of 30 mg.Kg⁻¹. The section explains: hemorrhage (H), congestion (CO), thickening (P), cell death (CD), rupture (R), necrosis (N), edema (E) (40x H & E).

Suhail *et al.* (2014)¹² have confirmed that low-dose progesterone hormone indirectly affects the function of hormones secreted by the pituitary gland and thus inhibits the development of follicles and may inhibit ovulation. This is due to the inability of the cells of the ovary tissue to adapt to the changes caused by the negative impact of synthetic hormones, thus occurs the nuclei (Pyknosis) in the cells of the layer of the medulla and cortical layer of the ovary, which is a phase of cell death. Perhaps the reason for the negative COCP effect and the pressure it causes on the walls of blood vessels leading to the expansion of blood vessels in the pulp and cortical area of the ovary, as a result of response to pressure and an increase in Rapid flow of blood leading to dilatation of the artery (Artriole resulting from neurological consultation and thus generating greater pressure on the sphincter before the capillaries (Prebloodcapillary Constrictor). The resulting accumulation of blood in the ovarian capillaries results in an increase in the speed of the bloodstream in dilated veins^{13,14}. The appearance of the edema, which represents the first stage of the occurrence of inflammation. Vascular filtration increases, followed by arterial dilatation and an increase in the speed and flow of blood volume in the arteries leading to an increase in hydrostatic pressure. Intravascular fluid

resulting in an increase in the movement of fluid from within the capillary blood vessels towards tissues, which is represented by physiological fluids (Transudates)¹⁵. The combined oral contraceptive pills (Hemorrhage) between the stroma cells of the endodortic layer in the ovaries administered by hormone-induced rabbits may be due to rupture. In the vascular walls represented by a basement membrane causing the red blood cells (RBC) to break out and spread within the tissues of the pulp layer of the affected ovary¹⁶.

Histological changes of rabbit ovaries injected with plant extract: Histological sections of female ovaries injected with a dose of 40 mg.kg⁻¹b.w. showed that the effect of the extract was Reduce the number of mature follicles and mature follicles without eggs and the emergence of hyaline degeneration within the vesicles. Mature with the preservation of the cortex stock of primary and secondary follicles in numbers parallel to the control group but a decrease in the number of corpus luteum of the ovary and the occurrence of necrosis and degeneration in corpus luteum and also the presence of follicular follicles but in small numbers in the cortical layer of the ovary as shown in Figure (3, 4, 5)

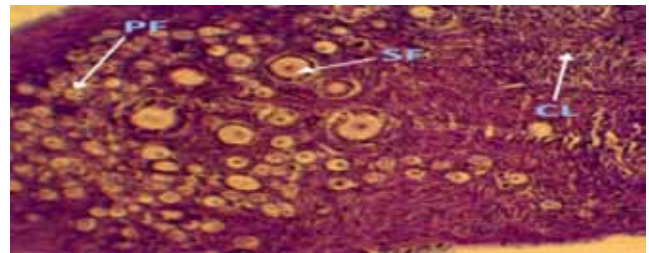


Figure (3) Cross-section of bleached tissue treated with alcoholic extract of the extracting plant at a concentration of 40 mg.kg⁻¹. The section illustrates: primary follicles (PF) and secondary (SF) corpus luteum (CL)(40x H & E).

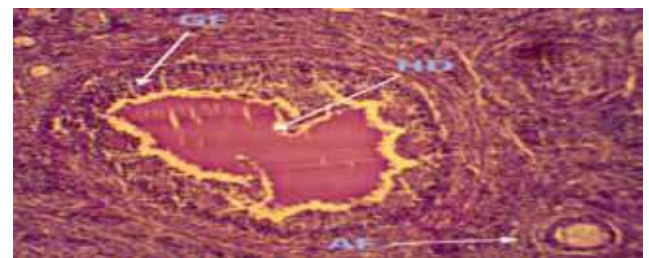


Figure (4) Cross-section of bleached tissue treated with alcoholic extract of the extracting plant at a concentration of 40 mg.kg⁻¹. The section illustrates: atristle follicles (GF) graffian follicles (GF) hyaline degeneration (HYD) (40x H & E).

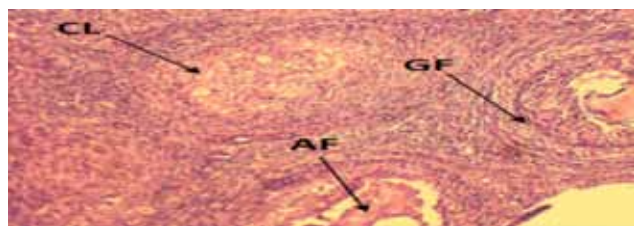


Figure (5) Cross-section of bleached tissue treated with alcoholic extract of the extracting plant at a concentration of 40 mg.day. The section illustrates: corpus luteum (CL), Antral follicles (AF) Graafian follicles (GF) (40x H & E).

The decrease in the development of bleached follicles may be attributed to the effectiveness of the alcoholic extract of the Rue plant in reducing the secretion of follicle-stimulating hormones and luteinizing hormones¹⁷. In his study, the leaves of the Rue plant have a role in inhibition of the pituitary gland leading to a decrease in the numbers of primary and secondary follicles and mature follicles, while the study of researchers¹⁸ (The alcoholic extract of the succulent plant may cause a change in the hormonal balance resulting in an increase in the length of the pre-estrus cycle. As a result of an increase in the level of estrogen (estrogen), which adversely affects the growth and development of follicles at different stages as a result of negative feedback As noted in the present study, there is little yellow corpus luteum in ovarian tissue This is due to the high levels of the hormone prolactin, which causes an increase in the rate of irregular menstrual cycle and therefore a decline in growth of the yellow body accompanied by a decrease in the concentration of hormone LH and FSH¹⁹. Hyaline degeneration in rabbit ovarian tissue in granular layer of graafian follicles and vitreous degeneration within the interstitial spaces of the stroma the cause of vitreous degeneration is due to the deposition and accumulation of protein in the cell cytoplasm as a result of the dissolution of amino acids. The²⁰ study also confirmed when treated with quercetin mice at 10 mg.kg⁻¹ per day isolated from a succulent plant; there was a significant reduction in the number of primary and secondary follicles. Which may be follicular follicles in the ovary resulting in depletion of ovarian reserve and failure of ovarian function and also cause a 70% decrease in pregnancy in mice This can be explained by the effect of quansin, which inhibits the action of TG2, the enzyme responsible for inhibiting ovarian action and the division and proliferation of fertilized egg cells^{1,21}.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: The authors declare that they have no conflict of interest.

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References

1. Al-Douri NA. Some Important Medical Plants in Iraq. *AS International Journal of Advances in Herbal and Alternative Medicine (IAHAM)*. 2014;2(1):10-20, August 16. www.academiascholarlyjournal.org/ijaham/index_ijaham.htm
2. Odeyemi S. and Bradley G. Medicinal Plants Used for the Traditional Management of Diabetes in the Eastern Cape, South Africa: Pharmacology and Toxicology. *Molecules*. 2018; 23(11). Article Number 2759, 19 pages.
3. Aziz TAT, and Ghali MA. Effect of hot aqueous extract of seeds and leaves of fenugreek (*Trigonella foenum-graceum*) on embryonic development in Swiss albino mice. *Baghdad Journal of Science*. 2017;(1)14:11-21.
4. Kamanda MI and Mathenge MI. Simultaneous occurrence of five prothrombotic induced vaso-occlusive phenomena and focal nodular hyperplasia due to prolonged use of combined oral contraceptive pills. *The British Journal of Radiology Case Report*. 2018; 4(3), 20170070.
5. Rawla P, Raj JP, Thandra KC and Bandaru SS. Superior Mesenteric Vein Thrombosis in a Patient on Oral Contraceptive Pills. *Gastroenterology Research*. 2017;10(6):380-382.
6. Selvaraj G, Kaliamurthi S, Thirungnasambandam R, Vivekanandan L and Thangavel B. Anti-Nociceptive Effect in Mice of Thillai Flavonoid Rutin. *Biomedical and Environmental Sciences*. 2014;27(4):295-299.
7. Orlanda JFF. and Nascimento AR. Chemical composition and antibacterial activity of *Rutagraveolens* L. (Rutaceae) volatile oils, from São Luís, Maranhão, Brazil. *South African Journal of Botany*. 2015;99:103-106. July. <https://doi.org/10.1016/j.sajb.2015.03.198>
8. Beazley KE and Nurminskaya M. Effects of dietary quercetin on female fertility in mice: implication

- of transglutaminase 2. *Reproduction, Fertility and Development*. 2016;28(7):974–981. June.
9. AL-Daody AC. Chemical study on some Iraqi plant. 1998.Ph.D.Thesis, Collage of Science, Mosul University.
 10. Williams C J and Erickson GF. Morphology and physiology of the ovary. In *Endocrinology of Female Reproduction* (R. Rebar, ed.). 2014. Accessed January 14, from Endotext website: <http://www.endotext.org/chapter/morphology-and-physiology-of-the-ovary>.
 11. Chen Y and Shi X. Repeated use of mifepristone and levonorgestrel and their effect on the ovarian function in mice. *The Journal of Obstetrics and Gynaecology Research*. 2016;42(11):1519-1524.
 12. Suhail AI. Effect of contraceptive pills on some physiological and biochemical parameters in a sample of women in Baghdad. 2014. Master Thesis, University of Baghdad, College of Education for Pure Sciences (Ibn al-Haytham), Department of Biological Sciences/Zoology/Physiology.
 13. Soroush A, Farshchian N, Komasi S, Izadi N, Amirifard N and Shahmohammadi A. The Role of Oral Contraceptive Pills on Increased Risk of Breast Cancer in Iranian Populations: A Meta-analysis. *Journal of Cancer Prevention*. 2016;21(4):294-301. December
 14. Matyanga CMJ and Dzingirai B. Clinical Pharmacology of Hormonal Emergency Contraceptive Pills. *International Journal of Reproductive Medicine*. 2018;Article ID 2785839, 5 pages.
 15. Madendag Y, Acmaz G, Atas M, Sahin E, Tayyar AT, Madendag IÇ, Özdemir F and Senol V. The Effect of Oral Contraceptive Pills on the Macula, the Retinal Nerve Fiber Layer, and Choroidal Thickness. *Medical Science Monitor*. 2017;23:5657-5661. November 27.
 16. Klaus H. and Cortés ME. Psychological, social, and spiritual effects of contraceptive steroid hormones. *The Linacre Quarterly*. 2017;82(3):283–300
 17. Al-Shaibani, S. and Wissam O. Study of reproductive and physiological changes caused by *Dacuscarota L.* carrot seed extract in egg laboratory rats. 2011. Master Thesis, University of Kufa, Faculty of Science, Department of Life Sciences/Zoology.
 18. Richardson JSM, Sethi G, Lee GS and Malek SN. Chalepin: isolated from *Ruta angustifolia L.* Pers induces mitochondrial mediated apoptosis in lung carcinoma cells. *BMC Complementary and Alternative Medicine*. 2016;16(389):1-27.
 19. Al-ShahriNJ. and Saleh RA. The role of broccoli (*Brassica oleracea*) in the treatment of induced cystic syndrome in *Rattus norvegicus*. *Ibn al-Haytham Journal of Pure and Applied Sciences*. 2015;28 (3):286-301.
 20. Kappel VD, Zanatta L, Postal BG and Silva FRMB. Rutin potentiates calcium uptake via voltage-dependent calcium channel 3 associated with stimulation of glucose uptake in skeletal muscle. *Archives of Biochemistry and Biophysics*. 2013;532(2):55-60. April 15.
 21. El-Gerbed MSA. Histopathological and ultrastructural effects of methyl parathion on rat testis and protection by selenium. *Journal of Applied Pharmaceutical Science*. 2013;3(8):S53-S63. DOI: 10.7324/JAPS.2013.38.S9.

Molecular Detection of Human Cytomegalovirus and Immunohistochemical Expression of BCL2 in Lymph Nodes from Hodgkin's Lymphoma

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Abstract

Background: A lifelong persistence of latent human cytomegalovirus (hCMV) infection may result and/or associated with Hodgkin's lymphoma (HL). The B-cell lymphoma-2 (BCL2) is an anti-apoptotic molecule expressed in non-neoplastic lymphoid tissue (hyperplastic lymph node) while down-regulated in normal germinal center B cells.

Objective: Is to analyze the concordant impact of BCL2 expression and hCMV infection on tissues from a group of patients with Hodgkin's lymphoma.

Patients and Method: Eighty formalin-fixed, paraffin-embedded lymph node tissue-biopsies enrolled in this study; 40 from HL and 40 with unremarkable pathological changes. Detection of hCMV was done by chromogenic in situ hybridization (CISH) technique while immunohistochemistry (IHC) was used for the BCL2 protein expression.

Results: In HL, the hCMV-positive CISH and the BCL2-positive IHC reactions were detected in 35% and 42.5% of tissues, respectively. The correlation between hCMV and BCL2 was highly significant ($P=0.002$).

Conclusions: The significant co-expression of BCL2 and hCMV genes in HL tissues could point for their possible role in either lymph node pathogenesis or carcinogenesis.

Keyword: hCMV, Hodgkin's lymphoma, BCL2, CISH, IHC.

Introduction

Hodgkin lymphoma (HL) and Non-Hodgkin's lymphomas (NHL) are two lymph nodes (LN) malignancies, where NHL is comprising approximately 85% of cases and 15% for HL.¹ Human cytomegalovirus (hCMV) is double-stranded DNA virus, encodes more than 200 protein products,² and may persist lifelong following asymptomatic primary infections, entering in a latency phase.³ The virus is an opportunistic for a variety of cases having an impaired cellular immunity.⁴ Reactivation of CMV can arise in immunosuppression states, either iatrogenic or secondary to systemic medical conditions.⁵ Subsets of genes, including immediate early

genes, has an important role to reactivate the latency state.⁶ A poly-cistronic locus (UL133-UL138) contains genes involved in regulating latency, viral immune escape and cell tropism.⁷ It is estimated that more than 90% of population in the developing countries are infected with hCMV.⁸ Although hCMV is not a recognized oncogenic virus, observations have demonstrated that this virus has been correlated with gastric cancer and T-cell lymphoma⁹ and might be associated with Hodgkin and NHLs.^{10,11} Also, hCMV is an important cause of morbidity and mortality in leukemic patients. However, the incidence of hCMV in patients with lymphoma is not known.¹²

The BCL2 is a human proto-oncoprotein located in the membranes of the nuclear envelope, endoplasmic reticulum, and in the outer membrane of mitochondria.¹³ It can occur as BCL2 alpha (active and membrane bound) or BCL2 beta (an inactive cytosolic, contributing to the survival activity of BCL2).¹⁴ The BCL2 protein expression is found in follicular lymphoma and some cases of diffuse large B-cell lymphoma.¹⁵ The BCL2 expression in HL is frequently observed, almost 54% of classical HL cases revealed a variable proportion Hodgkin RS BCL2-positive cells.^{16,17} The rise of BCL2 expression has a bad prognosis and is associated with relapses in young patients with classical HL.^{18,19}

This study was done to unravel the rate as well as impact of either hCMV or BCL2 in a group of Iraqi patients with HL.

Materials and Method

A retrospective case-control study recruited 80 formalin fixed, paraffin-embedded LN tissue blocks, among them 40 tissue biopsies from HL with different grades as well as 40 LNs with unremarkable pathological changes used as an apparently healthy controls (AHC). The diagnosis of these tissue blocks were based on their accompanied records. One section was mounted on ordinary glass slide and stained with hematoxylin and eosin and a consultant pathologist reexamined all these tissues for further confirmation of their diagnosis, while other section were mounted on charged slides to be used for CISH and IHC.

The detection of hCMV by CISH kit (Zyto Vision GmbH, Fischkai, Bremerhaven, Germany) was performed on 4µm-paraffin-embedded tissue sections.

The CISH technique was applied according to the kit manufacture instructions. Positive CISH reaction for hCMV stains (blue) using digoxigenin-labeled hCMV probes and counter stains (red) by Nuclear Fast Red.

The IHC/Detection system (Abcam, England) was used to demonstrate the BCL2 protein expression in cells using primary biotinylated anti-BCL2 protein antibodies. The bound primary antibody is then detected by secondary antibody which contains specific peroxidase-labeled polymer conjugated to goat anti-mouse immunoglobulin. The chromogen solution (substrate) 3,3'-Diaminobenzidine produces a brown-color precipitate at the antigen site in these tissues as positive reaction and counter-stained by Mayer's Hematoxylin (Blue).

Positive cells were determined as the average percentage of positive cells counted in 10 different fields of 100 cells for each sample. A scale of 0-3 was used for relative intensity with 0 corresponding to no detectable IHC reaction, and 1, 2, 3 equivalents to weak, moderate, and strong intensity of reaction, respectively. Cases were assigned to one of the following percentage score categories: 1%-25% (score 1; low), 26%-50% (score 2; moderate) or > 50% (score 3; high).²⁰

Statistical analyses were done by SPSS program, version 21. Chi square test was used for testing relationships between categorical variables. Spearman's rho was used to test the correlations between different variables. *P*-value <0.05 was considered significant.

Results

The highest percentage of HL patients was seen in grade I (45%) followed by grade II (30%) and the lowest was in grade III (25%).

hCMV-CISH expression in HL patients: Fourteen out of forty (35%) LN tissue biopsies with HL showed positive CISH reactions for hCMV-DNA (Figure 1). The AHC tissues revealed 5% (2/40) positive signals. The comparison between the percentage of hCMV-CISH reaction in AHC group and patients group showed highly significant statistical difference, *P*=0.002 (Table 1).

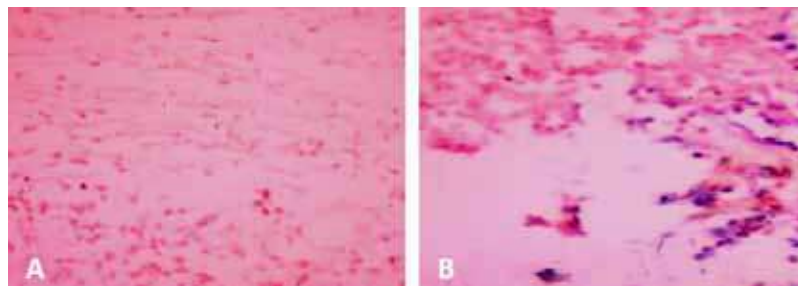


Figure 1 Lymph node sections in Hodgkin Lymphoma: CISH reaction for hCMV detection ×40. (A) Negative reaction; (B) positive reaction with low score and strong signal intensity.

Table 1: CISH reaction on LN biopsy sections to hCMV in patients with HL.

hCMV	HL (no.=40)	%	AHC (no.=40)	%	P-value (Z test)
Negative	26	65%	38	95	0.002
Positive	14	35%	2	5	

A. Positive hCMV-CISH signal scoring: The highest percentage of hCMV score signaling (17.5%; 7/40) was found in the high score (Score III), whereas (10%; 4/40) and (7.5%; 3/40) were found within

moderate (Score II) and low (Score I) scores, respectively (Table 2). There was statistically significant difference among them ($P=0.02$).

B. Signal intensity of hCMV-CISH testing: The percentage of hCMV-infected cells that were evaluated for the intensity of hCMV-CISH reactions showed moderate signal intensity in 15% (6/40), weak signal intensity in 12.5% (5/40) and strong signal intensity in 7.5% (3/40). The statistical analysis showed significant difference ($P=0.03$).

Table 2 Distribution of hCMV signal scoring and intensity associated with HL by using CISH technique

P-value (χ^2 test)	Hodgkin lymphoma (n=40)			hCMV-CISH	
	% out of 14	% out of 40	No.		
0.02		65	26	Negative	
		35	14	Positive	
	21.4	7.5	3	I	Signal Score
28.6	10	4	II		
50	17.5	7	III		
0.03	35.7	12.5	5	Weak	Signal Intensity
	42.9	15	6	Moderate	
	21.4	7.5	3	Strong	

BCL2-IHC expression in patients with HL: Among the 40 Hodgkin lymphomatous tissues, 42.5% (17/40) exhibited positive BCL2-IHC reaction (Figure 2).

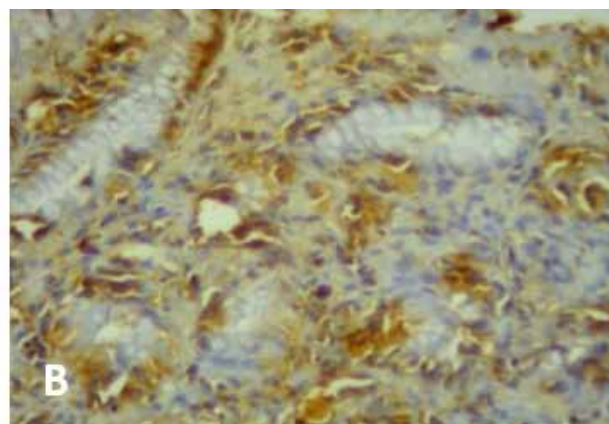
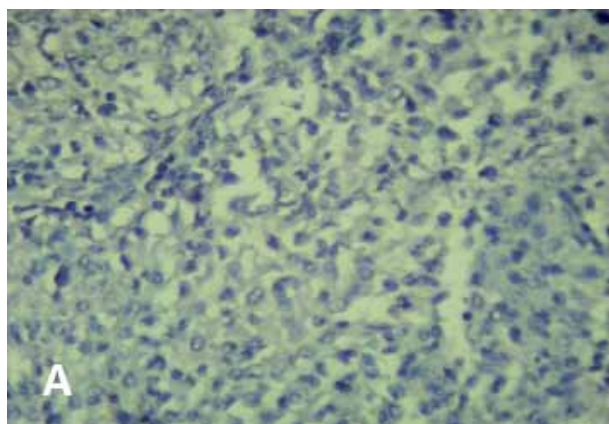


Figure 2: LN sections in HL: IHC staining of BCL2 protein $\times 40$. (A) Negative reaction, (B) Positive reaction

A. BCL2-IHC score signal in HL: The signal scores were as follows: 20% (8/40) score I followed by 15% (6/40) and 7.5% (3/40) in score II and score III, respectively (Table 3). Statistically significant difference was noticed between low, moderate and high BCL2 scoring of tissues, ($P=0.01$).

B. BCL2-IHC intensity signal in HL: The intensity signals were weak (Intensity I) in 22.5%, followed by 15% moderate (Intensity II), and 5% strong (Intensity III). There was statistically significant difference, ($P<0.03$), between various intensities of tissues in HL group (Table 3).

Table 3 The percentage of BCL2-IHC score and intensity signaling in HL

P-value (χ^2 test)	Hodgkin lymphoma (n=40)			BCL2-IHC	
	% out of 17	% out of 40	No.		
		57.5	23	Negative	
		42.5	17	Positive	
0.01	47.1	20	8	I	Signal Score
	35.3	15	6	II	
	17.6	7.5	3	III	
0.03	52.9	22.5	9	Weak	Signal Intensity
	35.3	15	6	Moderate	
	11.8	5	2	Strong	

Correlations between the grades, hCMV and, BCL2 in LN tissues from HL patients: A highly significant correlation was found between hCMV and BCL2 markers in HL ($P=0.002$). Similarly, there is a

strong positive relationship between BCL2 and grade of HL ($P=0.007$). However, there are no significant correlations among hCMV and other markers (Table 4).

Table 4: Spearman’s rho statistical testing of age, grade, hCMV-CISH and BCL2-IHC to evaluate the studied markers in HL.

Spearman’s rho		Age Groups (Years)	Grade	hCMV	BCL2
Grade	r	-0.125			
	P	0.442			
hCMV	r	0.030	0.133		
	P	0.855	0.412		
BCL2	r	0.152	0.419	0.483	
	P	0.350	0.007*	0.002*	

*Correlation is highly significant ($P<0.01$).

Discussion

The highest percentage of HL patients were seen in grade I (45%) followed by grade II (30%) and the lowest was in grade III (25%). Although grade I is the most prevalent in Iraq but it is much less than reported in western studies (54.5%).^{21,22} This could mark for more frequent intermediate and high-grade lymphomas in Iraqi patients than expected worldwide. This variation is probably attributed to the small number of patients in this study or patients are attending lately at medical care centers when the low grade have evolved into higher grades.

hCMV pp65is found to be involved in numerous

significant events in the tumor progression and is the most abundant viral protein during active infection has been detected in biopsies of patients with NHL and HLs (57% and 49%), respectively.²³In Iraq, and up to our best knowledge no research study on hCMV in HL tissues was done.

BCL2 over expression plays an important role in lymphomagenesis and extension of survival of malignant cells for the apoptosis process blocking or slowing down.²⁴ The BCL2 over expression in HL is a predictor of poor outcome and shorter survival.^{16,25}It had a prognostic significance for development of primary refractory HL.²⁶

In this research, 42.5% of HL group showed positive BCL2-IHC detection signals. This result is broadly consistent with those done by other studies (62.5%, 42.9%, 54%, and 54%, respectively).²⁷ Jakovica *et al.*²⁸ found that 31% of HL patients exhibited BCL2-protein overexpression was associated with worse outcome. The altered expression of BCL2 and apoptosis regulators proteins in HL may prevent apoptosis and as such confers a worse prognosis. This is supported by studies done by Rassidakis *et al.*²⁵ and Montalban *et al.*²⁹ However, Koh *et al.*³⁰ study revealed that BCL2 protein was found in only 14% of patients with Hodgkin/Reed-Sternberg (HRS) cells, and was not associated with overall survival and event-free survival. In this respect, Kim *et al.*¹⁶ stated that the genetic mechanism, behind BCL2 overexpression in HRS cells, is unknown.

In our study, a high percentage 52.9% of HL group were found to have weak BCL2 signal intensity, while the moderate intensity was represented in 35.1%, followed by the strong signal intensity in 11.8%. Comparable results were found by LeBrunet *et al.*³⁴ who reported a presence of BCL2 expression in Hodgkin cells in 63% tissues. However, strong staining was present in only 7 cases (22%) and weak staining in 41%. Also, our results are consistent with those of Rassidakis *et al.*²⁵ who found that BCL2 is expressed in HRS cells in 61% of patients with HL. In BCL2-positive HL, the majority of HRS cells express BCL2 but the intensity of expression is variable. The strong staining intensity was (25%). However, there was a variation in weak staining intensity (36%) whereas, in present study it was (5%). Immunohistochemical stain intensity is frequently interpreted as being proportional to the protein that interacts with the primary antibody. However, the relationship between the stain intensity and amount of protein is not always so simple. However, it was found that some positive BCL2 IHC staining can occur in the absence of BCL2 mutation and some mutations in BCL2 do not result in positive IHC staining.

In conclusion, the detection of hCMV along with BCL2 overexpression in HL patients supports the hypothesis of an important role for CMV along with mutated and/or defected *BCL2* gene in HL development.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: The authors declare that they have no conflict of interest.

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References

1. Habibian A, Makvandi M, Samarbafzadeh A, Neisi N, Ranjbari N. Epstein-Barr Virus DNA frequency in paraffin embedded tissues of Non-Hodgkin lymphoma patients from Ahvaz, Iran. *Jentashapir J Health Res* 2013;4:315-320.
2. Nakase H, Herfarth H. Cytomegalovirus colitis, cytomegalovirus hepatitis and systemic cytomegalovirus infection: common features and differences. *Inflamm Intest Dis*. 2016;1:15-23.
3. do Carmo AM, Santos FM, Ortiz-Agostinho CL, *et al.* Cytomegalovirus infection in inflammatory bowel disease is not associated with worsening of intestinal inflammatory activity. *PLoS One*. 2014; 9:e111574.
4. La Rosa C and Diamond DJ. The immune response to human CMV. *Future Virol*. 2012;7(3):279-293. doi: 10.2217/fvl.12.8.
5. Plosa EJ, Esbenshade JC, Fuller MP, *et al.* Cytomegalovirus infection. *Pediatr Rev*. 2012;33:156-163.
6. Harwardt T, Lukas S, Zenger M, *et al.* Human cytomegalovirus immediate-early 1 protein rewires upstream STAT3 to downstream STAT1 signaling switching an IL6-type to an IFN γ -like response. *PLoS Pathog*. 2016;12:e1005748.
7. Petrucelli A, Umashankar M, Zagallo P, *et al.* Interactions between proteins encoded within the human cytomegalovirus UL133-UL138 locus. *J Virol*. 2012;86:8653-8662.
8. Lanzieri TM, Dollard SC, Bialek SR, *et al.* Systematic review of the birth prevalence of congenital cytomegalovirus infection in developing countries. *Int J Infect Dis*. 2014;22:44-48.
9. Jin J, Hu C, Wang P, *et al.* Latent infection of human cytomegalovirus is associated with the development of gastric cancer. *Oncol Lett*. 2014;4:898-904.
10. Tafvizi F, Fard ZT. Detection of human cytomegalovirus in patients with colorectal cancer by nested-PCR. *Asian Pac J Cancer Prev*. 2014;15:1453-1457.
11. Kadry DY, Khorshed AM, Rashed RA, *et al.* Association of viral infections with risk of human

- lymphomas, Egypt. Asian Pac J Cancer Prev 2016;17:1705-1712.
12. Manna A, Cordani S, Canessa P, Pronzato P. CMV infection and pneumonia in hematological malignancies. J Infect Chemother. 2003;9:265-267.
 13. Tulalamba W and Janvilisri T. Nasopharyngeal carcinoma signaling pathway: an update on molecular biomarkers. International Journal of Cell Biology; 2012.
doi.org/10.1155/2012/594681.
 14. Igaki T and Miura M. Role of Bcl-2 family members in invertebrates. Biochimica et Biophysica Acta 2004;1644:73-81.
 15. Deng M, *et al.* An integrated probabilistic model for functional prediction of proteins. J Comput Biol 2004;11(2-3):463-475.
 16. Kim LH, Nadarajah VS, Peh SC, Poppema S. Expression of Bcl-2 family members and presence of Epstein-Barr virus in the regulation of cell growth and death in classical Hodgkin's lymphoma. Histopathology 2004;44(3):257-267.
 17. Sup SJ, Alemañy CA, Pohlman B, Elson P, Malhi S, Thakkar S, Steinle R, Hsi ED. Expression of bcl-2 in classical Hodgkin's lymphoma: an independent predictor of poor outcome. J Clin Oncol 2005;23(16):3773-3779.
 18. Pileri SA, Zinzani PL, Went P, Pileri AJr, Bendandi M. Indolent lymphoma: the pathologist's viewpoint. Ann Oncol 2004;15(1):12-18.
 19. Tzankov A, Zimpfer A, Went P, Maurer R, Pileri SA, Geley S, Dirnhofer S. Aberrant expression of cell cycle regulators in Hodgkin and Reed-Sternberg cells of classical Hodgkin's Lymphoma. Mod Pathol 2005;18(1):90-96.
 20. Cinatl, J., Vogel, Ju., Kotchetkov, R. Oncomodulatory signal by regulatory proteins encoded by human cytomegalovirus: a novel role for viral infection in tumor progression. FEMS Microbial Rev. 2004;28:59-77.
 21. Hashemi M, Parwaresh MR. A study of lymphomas in selected centers in Tehran, based on the updated Kiel classification. Arch Iran Med 2001;4:59-66.
 22. Al-Lebawy NS, Al-Alwany SHM, Tarrad JK. Nuclear co-localization of expressional products of CDK4 & CDK6 and human T cell lymphotropic virus type-1- genes: an *in situ* hybridization and immunohistochemical study of Hodgkin's lymphoma tissues from a group of Iraqi patients. Journal of Global Pharma Technology 2017;10(9):438-447.
 23. Jacopo M, Francesco M, Francesco S, *et al.* Impact of cytomegalovirus replication and cytomegalovirus serostatus on the outcome of patients with B cell lymphoma after allogeneic stem cell transplantation. Biol Blood Marrow Transplant 2014;20:885-890.
 24. Pileri SA, Gaidano G, Zinzani PL, Falini B, Gaulard P, Zucca E, *et al.* Primary mediastinal B-cell lymphoma. High frequency of BCL-6 mutations and consistent expression of the transcription factors OCT-2, BOB.1, and PU.1 in the absence of immunoglobulins. Am J Pathol 2003;162(1):243-253.
 25. Rassidakis GZ, Medeiros LJ, Vassilakopoulos TP, Viviani S, Bonfante V, Nadali G, *et al.* BCL-2 expression in Hodgkin and Reed-Sternberg cells of classical Hodgkin disease predicts a poorer prognosis in patients treated with ABVD or equivalent regimens. Blood 2002;100(12):3935-3941.
 26. Benharroch D, Pilosof S, Gopas J, Levi I. Primary refractory and relapsed classical Hodgkin Lymphoma – significance of differential CD15 expression in Hodgkin-Reed-Sternberg cells. Journal of Cancer 2012;3:322-327. doi: 10.7150/jca.4716.
 27. Hussein MR, Al-Sabae TM, Georgis MN. Analysis of the Bcl-2 and p53 protein expression in the lymphoproliferative lesions in the Upper Egypt. Cancer Biology & Therapy 2005;4(3):324-328.
 28. Jakovica LR, Mihaljevic BS, Jovanovic MD, Bogdanovic AD, Andjelic BM, Bumbasirevic VZ. Prognostic significance of Bcl-2, tumor-associated macrophages, and total neoplastic and inflammatory lymph node involvement in advanced stage classical Hodgkin's Lymphoma. Onkologie 2012;35(12):733-739.
 29. Montalban C, Garcia JF, Abaira V, Gonzalez-Camacho L, Morente MM, Bello JL, *et al.* Influence of biologic markers on the outcome of Hodgkin's lymphoma: a study by the Spanish Hodgkin's Lymphoma Study Group. Journal of Clinical Oncology 2004;22:1664-1673.
 30. LeBrun DP, Warnke RA, Cleary ML. Expression of bcl-2 in fetal tissues suggests a role in morphogenesis. Am J Pathol 1993;142(3):743-753.

Normal Anatomical Variants of the Paranasal Sinuses at Computed Tomography Scanning

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Abstract

Background: Recognition of PNS (Paranasal sinus) anatomic variants is particularly important in preoperative workup of patients with sinonasal pathology. CT (computed tomography) scanning can give exquisite details on sinus anatomy and pathology and is the main modality used to image the paranasal sinuses so the aim of the study is to evaluate certain anatomic variants of the paranasal sinuses in patients referred to the CT unit in Al-Immamain Al-Kadhymain Medical City. **Patients and Method:** We retrospectively analyzed the CT scans of the paranasal sinuses for patients referred to the CT unit in Al-Immamain Al-Kadhymain Medical City/Baghdad, Iraq for a period of 12 months. All the patients included in the study underwent standard CT scan of the PNS. **Results:** A net sample size of 188 was analyzed by the current study. Female: Male ratio was (1.26:1). The incidence of septal deviation in the study sample was (51.06%) slightly more cases were deviated to the right (51.4%) than to the left (48.95%). Paradoxical middle turbinate's were observed in (18.6%), middle turbinate aeration was observed in (58.5%) on the right and (53.1%) on the left. The incidence of variant air cells were as follows: Onodi (24.4%), Haller (11.1%), and Agger nasi (87.7%). **Conclusion:** The percent of most of the anatomical variants in our study sample was approximate to the percent published in the literature with the most common anatomic variants encountered being septal deviation followed by aerated middle turbinate's whether unilateral or bilateral. The most frequent air cell was Agger nasi present in 87.7%.

Keywords: PNS, anatomic variants, CT scan, septal deviation, variant air cells.

Introduction

The paranasal sinuses are subject to variation between individuals and between sides in the same individual with regards to size (aeration) and bony septations⁽¹⁾. The most common variation of the nasal septum is deviation. The septum is usually deviated out of the midline to some degree in 20% to 79% of the population⁽²⁾. It is usually deviated in its inferior portion nearby the chondrovomer junction and can also accept an S-shaped arrangement with an rolling deviation onto both sides of the midline⁽²⁾. Septal pneumatization, additional described variant, may occur anteriorly from the crista galli or posteriorly from the sphenoid sinus⁽²⁾. Septal spurs are seen in connotation with septal deviation and may be bonded with the together turbinate's⁽³⁾. The middle turbinate is focus to variations in size and form. The turbinate is regularly pneumatized the so-called 'concha bullosa'. This pneumatization can be in

anterior or posterior, or both⁽⁴⁾. The turbinate may be paradoxically curved which refers to an infer medially curved turbinate edge with the concave surface against the nasal septum and usually occurs bilaterally⁽⁵⁾. The Agger Nasi Air Cell (ANC) is the greatest continuous and anterior of the ethmoidal air cells. The grade of ANC pneumatization varies and has an important outcome on both the size of the frontal sinus ostium and the form of the recess⁽⁶⁾. Infraorbital (Haller) Air Cells are situated inferior to the ethmoidal bulla and growing into the floor of the orbit. They may narrow the maxillary ostium, particularly if infected. The reported frequencies of Haller cells vary in the literature (up to 45%)^(7,8). Onodi cells are posterior ethmoidal cells extending into the sphenoid bone adjacent to the optic nerve. The nerve is at risk when surgical excision of these cells is performed⁽⁹⁾. Focal small corticated faults in the lamina papyracea are found in more than 0.5% to 10% of the population

and are not clinically important⁽¹⁰⁾. This study aims to evaluate the frequency of certain anatomical variants of the paranasal sinuses in patients referred to the CT unit in our hospital.

Material and Method

This retrospective cross sectional study was undertaken in Al-Immamain Al- Kadhymian Medical City for a period of 12 months from August 2017 to August 2018. Included in the study were all CT scan exams of the paranasal sinuses in the CT unit of Al-Immamain Medical City requested for evaluation of certain pathological conditions or for planning prior to surgery. We excluded patient with extensive sinonasal pathology e.g. polyposis, extensive sinusitis, malignancy, trauma or any disease that obscure the visualization of normal anatomical structures. Patients under 13-year old were also excluded from the study. Data collection: Two hundred and fifty one patients were recruited for the study, of these patients 31 were excluded (27 patients had extensive sinonasal polyposis, 28 patients had marked pansinusitis, and 8 were < 13-year old) so the net results were based on 188 patients. Examination procedure: The CT examination was performed using the 256 slice MDCT(Multidetector CT) scanner Somatom Definition Edge (Siemens medical systems, Erlangen, Germany), the following parameters were utilized: variable Kv(Kilovolt) (100-120), variable mAs(Milliamperage second) (30-45), 0.6 mm slice thickness with image reconstruction into the coronal plane from axial image dataset. Total DLP(Dose length product) approximately 60-70 mGycm. Image interpretation: The CT examination of eligible patients was reviewed and evaluated by a specialist radiologist. We evaluated the anatomic variants of nasal septum (deviation side, single or double curve, septal spur, aeration..), variants of the nasal turbinates (aeration, paradoxical turbinate, hypoplastic, aplastic ...), abnormalities within the PNSs (separte within maxillary sinus, aplasia of the frontal sinus), variant air cells (Onodi, Aggernasi,Haller), and lamina papyracea dehiscence. Statistical analysis: Data were analyzed using the commercially available software statistical package for social sciences (SPSS). The presentation of data was in the form of frequency and percent in tables and cross tables.

Results

A total of 188 CT scans were analyzed. Of these 83 (44.1%) were male and 105 (55.9%) females as

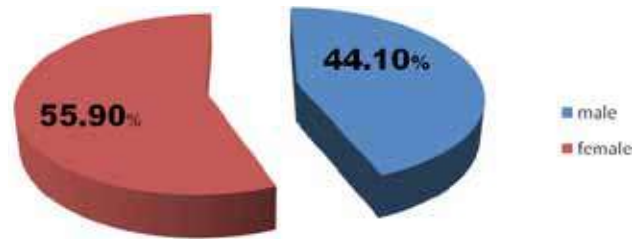


Fig. (1): Gender distribution.

The age range of the study sample was 13y - 72y (mean age was 30 years). Deviation was found in 96 (51.06%) cases, of these cases 49 (51.04%) were deviated to the right and 47 (48.95%) of them were deviated to the left. The majority of deviated nasal septa in females were to the left side while in males most deviated nasal septa were to the right there was no difference between male and female in septal deviation as in table(1).

Table (1): Septal deviation according to gender

		Septal			Total
		Left	Right		
Gender	Female	Count	29	23	52
		% of Total	30.2%	24.0%	54.2%
	Male	Count	18	26	44
		% of Total	18.8%	27.1%	45.8%
Total		Count	47	49	96
		% of Total	49.0%	51.0%	100.0%

CHI square (Fisher’s Exact Test) = 2.106, P value = 0.15 > 0.05 (not significant).

Also, there is an association between septal deviation and middle turbinate size see (table 2). Also 75 out of 96 cases of nasal septal deviation (78.1%) had a single curve and 21 (21.87%) of them had double (S-shaped) curve. Regarding the septal spur it was present in 57 of the cases, 30 (52.6%) of them had left sided spur, figure 1(A) and 27(47.3%) of them had right sided spur figure 1(B).

Table(2): Middle turbinate according to gender

			Middle Turbinate		Total
			Left Middle Turbinate	Right Middle Turbinate	
Gender	Left Septal Deviation	Count	16	27	43
		% of Total	16.3%	27.6%	43.9%
	Right Septal Deviation	Count	30	25	55
		% of Total	30.6%	25.5%	56.1%
Total		Count	46	52	98
		% of Total	46.9%	53.1%	100.0%

CHI square (Fisher’s Exact Test) = 2.912, P value = 0.1 > 0.05 (not significant).

Septal aeration: Out of 188 cases, 141(75%) had septal aeration and all of these aerated septa had their aeration from the sphenoid sinus, Superior turbinate: Out of the 188 cases evaluated, 174 patients (92.5%) had both superior turbinate’s present, in 11 out of 188 (5.8%) cases were both absent and in 2(1.06%) case only the right was present and 1(0.53%) case only the left present (figure 2). Regarding superior turbinate aeration 66 cases had aeration, 12(18.1%) had right sided aeration,

21 (31.8%) of them had left sided aeration and 33 (50%) of them had bilateral superior turbinate aeration and in all of them (66 cases) the source of aeration was the ethmoid air cells.

Greater number of patients with left septal deviation had right middle turbinate aeration while patients with right septal deviation had left middle turbinate aeration (table 3).

(Table 3): Paradoxical middle turbinate

		Septal				Total	
		Left Large	Left Small	Right Large	Right Small		
Left septal deviation	Count	2	9	12	0	23	
	% of Total	5.4%	24.3%	32.4%	0.0%	62.2%	
Right septal deviation	Count	9	1	0	4	14	
	% of Total	24.3%	2.7%	0.0%	10.8%	37.8%	
Total		Count	11	10	12	4	37
		% of Total	29.7%	27.0%	32.4%	10.8%	100.0%

CHI square = 26.217, P value = 0.0001** < 0.05 (significant).

Paradoxical middle turbinates were found in 35 out of 188 cases (18.6%). Of these 12 were bilateral (34.2%) see (figure 3). Frontal sinus: regarding frontal sinus size, small sinus was seen in 64 cases (25%), large sinus in 47(35.04%) and the frontal sinus was absent (figure 10) in 7 cases (3.7%), fig 4. Haller cell : In 21 of cases Haller cells were present, 9(4.7%) were right sided, 8(4.2%) were left sided and only 4(2.1%) was bilateral (figure

5). Inferior turbinate aeration: was present in only 1 case (figure 14). laminapapyracea dehiscence: was present in only 1 case (figure 6).

From table 4 in our study air cells consist of 3 types of cells; onodi RT 8.5%, and left 70.5%, while other type; haller consist of RT 4.7% and left 4.2% and last type agger; RT 1.06% and left 0.053%.

Table 4: Air cell distribution according to type

Types	Right	Left	Bilateral	Total
Onodi	16 (8.5%)	14 (7.5%)	16 (8.5%)	46 (24.5%)
Haller	9 (4.7%)	8 (4.2%)	4 (2.1%)	21 (11%)
Agger	2 (1.06%)	1 (0.53%)	0 (0%)	3 (2.1%)

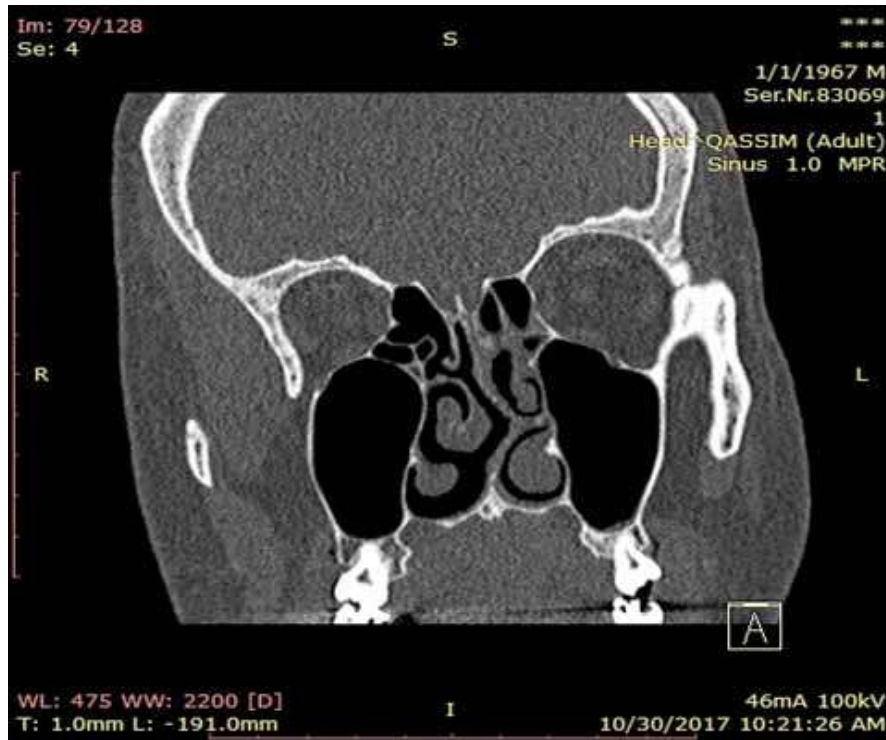


Figure 1: (A) right septal spur without septal deviation, (B) left septal deviation with septal spur fused to the lateral nasal wall



Figure 2: Note there are bilateral superior turbinate which show complete aeration. Left septal deviation is noted with septal spur



Figure 3: Bilateral paradoxical turbinate

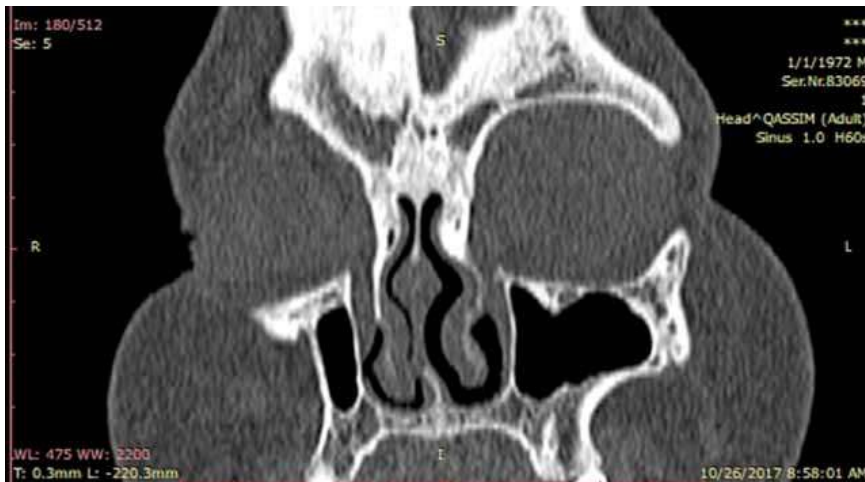


Figure 4: The frontal sinuses are aplastic.

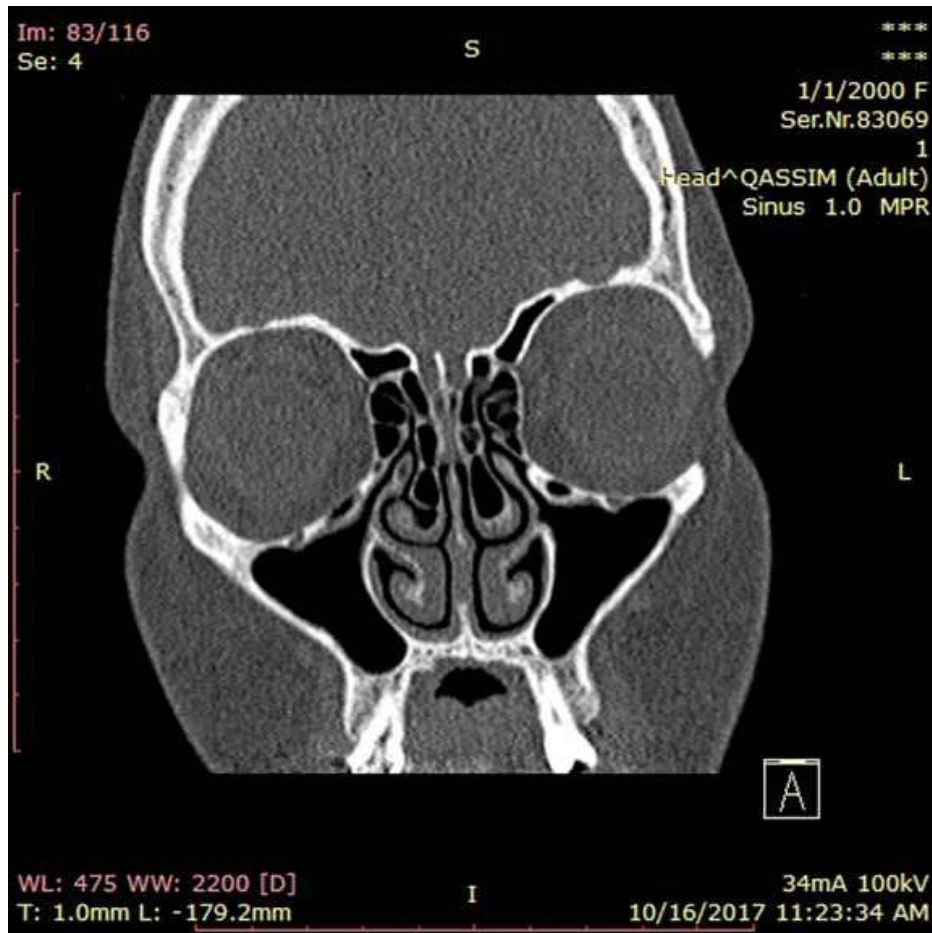


Figure 5: Bilateral Haller cells. Aerated middle turbinates are noted.



Figure 6: Partial aeration of left inferior turbinate is seen.

Discussion:

Anatomic structural variations of the paranasal sinuses have a practical significance during surgical procedures conducted on the sinuses by ENT (Ear, Nose and Throat) surgeons. Preoperative detection of

the clinically significant variations has dramatically improved owing to the improvement in modern imaging techniques utilized for evaluating the sinuses namely computed tomography (CT) scanning. 1: Nasal septum: Septal deviation: In this study, septal deviation was observed in 51.06% (96 out of 188). Of these cases, 49

(51.04%) were deviated to the right and 47 (48.95%) were deviated to left, 75 (78.1%) of them were single curve and 7 (21.8%) of them were double curve (S-shaped). Nearly similar to our results, Earwaker⁽¹¹⁾, found that 44.25% of his study sample had septal deviation (354 out of 800). Of these, 185 cases (52.3%) were deviated to the right and 169 cases (47.7%) were deviated to the left. Double curve septal deviation was observed in 21 (21.87%). In another study⁽¹²⁾, it was found that 23(20.91%) out of 110 cases evaluated had septal deviation. Septal spur: We observed that out of the 96 cases with septal deviation, 57 (59.3%) had septal spur. Of these cases 30 (52.6%) of the cases had left sided spur and 27 (47.3%) of them had right sided spur. We observed single case with right septal spur but no septal deviation. This percent is higher than that seen in previous studies. Earwaker found that 34% of patients with septal deviation had septal spur and unlike our results found left sided spurs twice as common as right sided ones⁽¹¹⁾. Shpilberg et al have documented septal spur in 32.3% of patients with septal deviation⁽¹³⁾. Superior turbinate: The superior turbinates were both present in 174 out of 188 cases (92.5%), both absent in 11(5.8%) cases and in 2(1.06%) case only the right was present and 1(0.53%) case only the left present regarding superior turbinate aeration 66 (35.1%) cases had aeration, 12(18.1%) had right sided aeration, 21 (31.8%) of them had left sided aeration and 33 (50%) of them had bilateral superior turbinate aeration and in all of them (66 cases) the source of aeration was the ethmoid air cells. Onwuchekwa and Alazigha found superior turbinate pneumatization in 6.36% and absence of both superior turbinates was observed in 0.91% of cases⁽¹²⁾. Earwaker found that superior turbinate aeration was present in 12.3% (98 case) of which 34.7% (34 case) were bilateral⁽¹¹⁾. Paradoxical middle turbinate: Paradoxical turbinates were observed in 35 patients (18.6%), 65.7% of these were unilateral (13 right sided and 10 left sided) and 34.2% bilateral. Al-Abri et al reported an incidence of paradoxical middle turbinates approximate to our results (13%)⁽¹⁴⁾. Earwaker found higher percent of paradoxical turbinates 40.3% (323 out of 800) of these 69.3% were unilateral and 30.7% bilateral⁽¹¹⁾. On the other hand Onwuchekwa and Alazigha found that only 1.82% had Paradoxical middle turbinate⁽¹²⁾. Frontal sinus :In the current study, 35.04% of patients had small frontal sinus and in 3.7% the sinus was absent. Earwaker found out of 800 cases⁽¹¹⁾, 4% of cases had small sinus and 5% had absent sinus. Also Onwuchekwa and Alazigha reported 4% incidence of frontal sinus hypoplasia with no reference in his study to

aplasia of the sinus⁽¹²⁾. About air cells consist of 3 types: Onodi cell In this study, the overall percent of Onodi cell was 24.4%. This percent of Onodi cells was higher than that previously reported by several studies. In Al-Abri et al⁽¹⁴⁾ study, the percent of Onodi cells was 7.5%(27 out of 360 cases), also another study by Onwuchekwa and Alazigha⁽¹²⁾ observed Onodi cells in 7.27% (8 out of 110 cases). Haller cell: The percent of Haller cells in the evaluated sample was 11.17% which is lower than that observed by the researcher in Al-Abri et al study which found that the percent of patients who had Haller cells was (24%)⁽¹⁴⁾, a percent which is approximate to that reported by Onwuchekwa and Alazigha (20.91%)⁽¹²⁾. Aggernasi: these were present in 165(87.7%) out of 188 cases it was absent in 20(10.6%) cases, 2(1.06%) cases only the right present and in 1(0.53%) case the left was present although the reported incidence of Aggernasi cells is variable according to the definition used. Several previous studies reported very high incidence of Aggernasi cells in the range of 96-98.5%^(11,8).

Conclusions: The percent of most of the anatomical variants in our study sample was approximate to the percent published in the literature with the most common anatomic variants encountered being septal deviation followed by aerated middle turbinate's whether unilateral or bilateral. The most frequent air cell was Aggernasi present in 87.7%.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: The authors declare that they have no conflict of interest.

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References

1. Korkmaz H, Korkmaz M. Total aplasia of the paranasal sinuses. *Allergy Rhinol.* 2013;4 (2): e105-9.
2. Sarna A, Hayman LA, Laine FJ, Taber KH: Coronal imaging of the ostiomeatal unit: anatomy of 24 variants. *J Comput Assist Tomogr.* 2002; 26(1):153-7.
3. Wormald PJ. Endoscopic sinus surgery: anatomy, three-dimensional reconstruction and surgical technique. 3rd edition. New York: Thieme Medical Publishers; 2013

4. Youngs R, Evans K, Watson M. THE PARANASAL SINUSES: A HANDBOOK OF APPLIED SURGICAL ANATOMY. LONDON: Taylor and Francis; 2005:34-39.
5. Kasper KA. Nasofrontal connection. A study based on one hundred consecutive dissections. *Arch Otolaryngol.* 1936;23(3):322-343
6. Bruner E, Jacobs JB, Lebowitz RA, Shpizner BA: Role of the aggerasi air cell in chronic frontal sinusitis. *Ann OtolRhinolLaryngol.* 1996;105(9):694-700.
7. Stammberger H, Wolf G: Headaches and sinus disease: the endoscopic approach. *Ann OtolRhinolLaryngol Suppl.* 1988;134:3-23
8. Bolger WE, Butzin CA, Parsons DS: Paranasal sinus bony anatomic variations and mucosal abnormalities: CT analysis for endoscopic sinus surgery. *Laryngoscope.* 1991;101(1 Pt 1):56-64.
9. Stammberger HR, Kennedy DW, Anatomic Terminology Group. Paranasal sinus: Anatomic terminology and nomenclature. *Ann OtolRhinolLaryngol Suppl.* 1995 Oct;167:7-16.
10. Vaid S, Vaid N, Rawat S, Ahuja AT. An imaging checklist for pre-FESS CT: framing a surgically relevant report. *ClinRadiol.* 2011;66(5):459-70.
11. Earwaker JN. Anatomic variants in sinonasal CT. *Radiographics* 1993;13:381-415.
12. R.C. Onwuchekwa, N. Alazigha. Computed tomography anatomy of the paranasal sinuses and anatomical variants of clinical relevance in Nigerian adults. *Egyptian Journal of Ear, Nose, Throat and Allied Sciences* 18 (2017) 31–38
13. Shpilberg K. A, Daniel S. C, CT of Anatomic Variants of the Paranasal Sinuses and Nasal Cavity: Poor Correlation With Radiologically Significant Rhinosinusitis but Importance in Surgical Planning. *AJR* 2015; (204):1255–1260
14. Al-Abri R, Deepa B, Al-Bassam W, Al-Badaai Y, Sawhney S. Clinically Significant Anatomical Variants of the Paranasal Sinuses. *Oman Medical Journal* 2014;29 (2):110-113

The Relationship between Malondialdehyde, Uric Acid and CRP in GDM Pregnant Women During Different Trimesters

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Abstract

GDM Common medical complication of pregnancy, it's increasing enormously worldwide in the recent decades especially in developing countries, the onset of GDM occurred, due to islet β cell function defect. There are a close relationship between the GDM, OS, antioxidants and inflammation. The aim of this study was the assessment to oxidative stress factor changes, UA and CRP in pregnant women with GDM in Misan province. The study included (30) GDM pregnant women, (25 -35) years. The study has during Nov.2018 to Feb. 2019. Diagnosed parameters done by ELISA, and mindray (BS -230). Our results revealed all parameters increased during pregnancy, highest increase in the third trimesters, it is increased significantly ($p \leq 0.05$) in comparison with the first and second trimesters.

Keywords: GDM, oxidative stress, uric acid, CRP. *Introduction:*

Introduction

Gestational diabetes mellitus (GDM): It is a common medical complication of pregnancy, the prevalence of GDM differs depending on the regions and the country, about half of women with a history of GDM develop type 2 diabetes out of 25% pregnancies develop GDM⁽¹⁾. GDM defined as any degree of glucose intolerance with onset or first recognition during gravidity, it is impaired glucose tolerance and IR with first onset during pregnancy⁽²⁻³⁾. Various risk factors associated with development of GDM such as developing type 2 DM, maternal obesity⁽⁴⁾, and low-grade inflammation⁽⁵⁾. GDM caused an elevation in OS occurred by more ROS production in mitochondria⁽⁶⁾.

Oxidative stress (OS): Defined as a state characterized by an imbalance between pro-oxidant molecules, and antioxidant defenses, OS result of overproduction of reactive oxygen species (ROS) in relation to antioxidant defense levels, excessive ROS production and resulting OS may contribute to aging and several diseased states affecting female reproduction⁽⁷⁾. OS increased during pregnancy due to some changes in such biomarkers (TC, TG, LDL and UA), these changes were demonstrated by a rise in lipid peroxidation⁽⁸⁾.

Malondialdehyde (MDA), and 8-iso-prostaglandin F₂ α (8-iso-PGF) best marker to OS⁽⁹⁾. MDA is the product of polyunsaturated fatty acid peroxidation, this aldehyde is a highly toxic molecule and should be considered as more than just a marker of lipid peroxidation, its interaction with DNA and proteins has often been referred to as potentially mutagenic and atherogenic⁽¹⁰⁾.

Uric acid (UA): It is the final product of purine metabolism⁽¹¹⁾. It is considered as a powerful scavenger of singlet oxygen, peroxy radicals and hydroxyl radicals⁽¹²⁾. Moreover, UA can become a pro-oxidant by forming radicals in reactions with other oxidants, these radicals seem to target predominantly lipids (LDL and membranes) rather than other cellular components, at the same time, the hydrophobic environment created by lipids is unfavorable for the antioxidant effects of UA⁽¹²⁻¹³⁾, and oxidized lipids can even convert UA into an oxidant⁽¹⁴⁾. Study in (2017) considered the UA as one of the diabetogenic factors during pregnancy via their IR effect and this relationship occurred due to two proposed mechanisms: 1. UA causes endothelial dysfunction and decreases endothelial NO production leads to decreased glucose uptake and development of IR⁽¹⁵⁻¹⁶⁻¹⁷⁾. 2. UA may induce IR and causes inflammation and OS in

adipocytes, which is a contributor to the development of metabolic syndrome⁽¹⁸⁾. On the other hand, high level of UA in early pregnancy indicated that metabolic state may affect adversely pregnancy outcomes, it is possible that of the women who develop GDM, those with elevated first-trimester UA are the women who are at risk to develop type 2 diabetes, thus, we postulate that elevated first-trimester sUA helps in the prediction of GDM and developing type 2 DM⁽¹⁵⁾.

C-reactive protein (CRP): It is a protein produced in response to inflammation to control it via activating the complementary immune system⁽¹⁹⁾, it's considered as a sensitive marker of chronic inflammation and a risk factor for diabetes and mortality⁽²⁰⁻²¹⁾. Study in (2018) showed the relationship between the CRP and insulin resistance, IR was elevated with high CRP levels in both men and women⁽²²⁾. In pregnancy many studies indicated that an early CRP determination may help in the prediction of adverse pregnancy outcome, preeclampsia and GDM⁽²³⁻²⁴⁾. CRP elevated in GDM, these elevation increases with gestational weeks during pregnancy from 5 to 20 weeks and from 28 to 32 weeks, and modest elevation in CRP later in pregnancy may be expected to occur and reflects the immune adaptations during pregnancy⁽²⁵⁾. In addition, the maternal immune system is also altered during pregnancy creating a state of balance between enhanced immune response in the form of increased circulating levels of CRP⁽²⁶⁾. Besides that, higher level of CRP in women who developed GDM growing evidence implies inflammation in the pathogenesis of type II diabetes which is directly correlated with IR⁽²⁷⁻²⁸⁾. Study in (2016) showed the glucose intolerance and GWG, that affected on CRP levels⁽²⁹⁾.

Material and Method

Subjects : Our study has been done at al - Sadr educational hospital, child and birth governmental hospital, golden medical clinic, altayf laboratory, sample selected according to the following criteria :

- Fasting plasma glucose (5.1–6.9 mmol/L) (92–125 mg/dL) .
- 1-hour plasma glucose (10.0 mmol/L) (180 mg/dL) following a 75 g oral glucose load .
- 2-hour plasma glucose (8.5–11.0 mmol/L) (153–199 mg/dL) following a 75 g oral glucose load (30).

Blood Samples: Five milliliters of venous blood samples were drawn, and left at room temperature for 10 minutes for clotting, centrifuged 3000 rpm for 5 minutes, then serum was separated and transported for storage. MDA diagnosed by myobiosource (USA) ELISA human kit, CRP and UA by mindray (BS -230).

Statistical analysis : Statistical analysis was performed by SPSS (23) .It was performed ANOVA, followed by LSD at ($p \leq 0.05$) significant level.

Results

The concentration of MDA in different trimesters: The MDA concentration in the second trimester (6.600 ± 0.722 ng/ml) increased ($p < 0.05$) in comparison with the first trimester (4.750 ± 0.672 ng/ml) .In the third trimester (7.110 ± 0.810 ng/ml) increased ($p < 0.05$) in comparison with the first trimester, but have no significant difference with the second trimester . (Table 1, Figure 1) .

The levels of uric acid in different trimesters: The UA in the second trimester (5.176 ± 0.913 mg/dl) increased ($p < 0.05$) in comparison with the first trimester (4.716 ± 0.800 mg/dl) .In the third trimester (5.990 ± 0.935 mg/dl) increased ($p < 0.05$) in comparison with the first and second trimesters . (Table 1, Figure1) .

The levels of CRP in different trimesters: The CRP level in the second trimester (8.790 ± 0.290 mg/l) have no significant difference in comparison with the first trimester (8.560 ± 0.189 mg/l) .

In the third trimester (12.66 ± 0.576 mg/l) increased ($p < 0.05$) in comparison with the first and second trimesters . (Table 1, Figure1) .

Discussion

Our results revealed the OS factors increased during gestation that's due to the elevation metabolic rate of the placenta causes increased generation of ROS, MDA concentration increase, in GDM pregnant because the oxygen free radicals and lipid peroxidation products increase in GDM (excessive production of free radicals observed in group of study), its insufficient removal results in damage to cellular proteins, membrane lipids, and nucleic acids, the presence of high levels of MDA in the present study may relate to the glycemic control, that's lined with other studies⁽³¹⁻³²⁾ .

Table (1): The concentration of MDA (ng/ml) and levels of uric acid (mg/dl) and CRP (mg/l) during different trimesters in GDM pregnant women .

Trimester Parameters	1st	2nd	3rd
MDA	4.750±0.672 ^A	6.600±0.722 ^B	7.11±0.810 ^B
Uric Acid	4.716±0.800 ^A	5.176±0.913 ^B	5.990±0.935 ^C
CRP	8.560±0.290 ^A	8.790±0.341 ^A	12.660±0.576 ^B

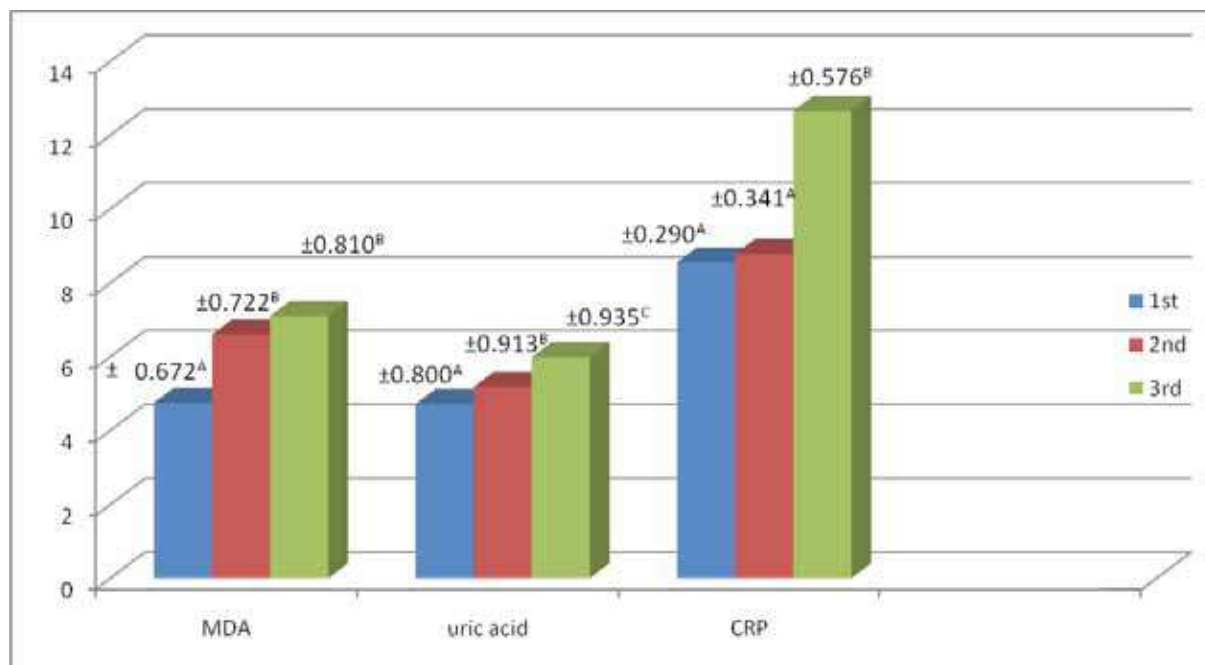


Figure (1): The concentration of MDA (ng/ml), uric acid (mg/dl),and CRP (mg/l) levels during different trimesters in GDM pregnant women .

The values represent the mean±SD.

Similar capital letters represent no significant difference between trimesters .

Different capital letters represent a significant difference (p<0.05) between trimester .

In the other hand, our results of UA levels improved fact, the antioxidant system was stronger than peroxidation during pregnancy, that’s confirm the antioxidant role for uric acid, that’s agreement with other studies⁽³³⁻³⁴⁾ . UA levels increase, because the placenta leads to overproduction of UA which serves as a marker of the disease,hyperuricemia may predate proteinuria by several weeks⁽³⁵⁻³⁶⁾ . This elevation predicate a GDM as our results show,furthermore it is considered a risk factor for development GDM because the correlation between UA and IR, probably because hyperisulinemia would cause lower renal UA excretion, and different role for the UA it is an antioxidant role in the GDM group^(37-38-39 -40-41) .Besides that these increase suggesting excessive free radical production evokes a

response to combat OS because different role for UA an antioxidant property, our result in oxidative factor confirms that, and that lined with other study⁽⁴²⁾ . CRP levels increased (p≤0.05) in trimesters, that’s due to the CRP may excessive with GWG,and IR. That suggest a decrease ability of pregnant women with GDM to compensate for OS which manifested as increased IR, reduced insulin sensitivity,and β-cell dysfunction, that’s lined with other research⁽²⁴⁾. Inflammatory and stress responses mediate IR, and inflammatory mediators play an important role in the development and progression of GDM,the elevation of CRP levels have been associated with abnormalmetabolic conditions such as IR, hyperglycemia, and type 2 DM, that’s lined with other study⁽⁴³⁾.

Conclusion

In summary, our observational study provides the important role of placenta, it's increase OS markers and uric acid, moreover the GWG increase CRP all these increases occurred in GDM pregnant.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: The authors declare that they have no conflict of interest.

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References

1. Tamrakar, P. Prevalence of GDM and its associated risk indicators: A hospital based study in Nepal (Master's thesis).2014.
2. Lowe, L. P., Metzger, B. E., Lowe Jr, W. L., Dyer, A. R., McDade, & HAPO Study Cooperative Research Group. Inflammatory mediators and glucose in pregnancy: results from a subset of the hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study. *JCEM*. 2010; 95(12), 5427-5434.
3. Abariga, S. A., & Whitcomb, B. W. Periodontitis and GDM : a systematic review and meta-analysis of observational studies. *BMC pregnancy and childbirth*.2016; 16(1), 344 .
4. Metzger, B. E. Long-term outcomes in mothers diagnosed with GDM and their offspring . *Clinical obstetrics and gynecology*. 2007; 50(4), 972-979
5. Lappas, M., Jinks, D., Ugoni, A., & Georgiou, H. M. Post-partum plasma C-peptide and ghrelin concentrations are predictive of type 2 diabetes in women with previous GDM .*Journal of diabetes*. 2015; 7(4), 506-511.
6. Toljic, M., Egic, A., Munjas, J., Orlic, N. K., Milovanovic, A., & Joksic, I. Increased OS and cytokinesis-block micronucleus cytome assay parameters in pregnant women with GDM and gestational arterial hypertension . *Reproductive Toxicology*.2017;71, 55-62 .
7. Agarwal, A., Aponte-Mellado, A., Premkumar, B. J.,... & Gupta, S. The effects of OS on female reproduction : a review. *Reproductive biology and endocrinology*.2012; 10(1), 49 .
8. Toescu V, Nuttall SL, Martin U, Kendall MJ, Dunne F. OS and normal pregnancy . *Clin Endocrinol* 2002; 57: 609– 613 .
9. Vessby, J., Basu, S., Mohsen, R., Berne, C., & Vessby, B. OS and antioxidant status in type 1 DM. *JIM*.2002;251(1), 69-76.
10. Del Rio, D., Stewart, A. J., & Pellegrini, N. A review of recent studies on malondialdehyde as toxic molecule and biological marker of OS. *NMCD*.2005;15(4), 316-328 .
11. Niraula, A., Lamsal, M., Majhi, S., Khan, S. A., & Basnet, P. Significance of serum UA in pregnancy induced hypertension .*NMA*.2017; 109(3), 198-202 .
12. Sautin, Y. Y., & Johnson, R. J. UA: the oxidant-antioxidant paradox. *Nucleosides, Nucleotides, and Nucleic Acids*, (2008); 27(6-7), 608-619 .
13. Muraoka, S., & Miura, T. Inhibition by UA of free radicals that damage biological molecules. *JPT*. 2003;93(6), 284-289.
14. Bagnatib, M., Perugini, C., Cristiana, C. A. U., Bordone, R., Albano, E., & Bellomo, G. When and why a water-soluble antioxidant becomes pro-oxidant during copper-induced LDL oxidation: a study using UA. *Biochemical Journal*.1999;340(1), 143-152
15. Ramalakshmi, S., & Arumugaselvi, B. Role of First-Trimester UA Level in Prediction of GDM .*IJSR*|.2017; July 2018 | Vol 6 | Issue 4.
16. Nakagawa, T. Uncoupling of the VEGF-endothelial NO axis in diabetic nephropathy : an explanation for the paradoxical effects of VEGF in renal disease. *AJP- Renal Physiology*.2007; 292(6), F1665-F1672 .
17. Cooke, J. P. NO and angiogenesis. *Atherosclerosis Supplements*, 4(4), 53-60 .
18. Furukawa, S., Fujita, T., Shimabukuro, M., Iwaki,... & Shimomura, I. Increased OS in obesity and its impact on metabolic syndrome. *The JCI*.2004;114(12), 1752-1761 .
19. Al-ofi, E. A. Implications of inflammation and IR in obese pregnant women with GDM : A case study. *SAGE Open Medical Case Reports*, (2019). 7, 2050313X19843737 .
20. Britton, K. A., & Fox, C. S. Ectopic fat depots and CV disease. *Circulation*.(2011); 124(24), e837-e841.
21. Franceschi, C., & Campisi, J. chronic inflammation (inflammaging) and its potential contribution to

- age-associated diseases. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences*.2014; 69(Suppl_1), S4-S9.
22. Shahid, R. Examination of the Cross-Sectional Association between IR (HOMAIR) and an Inflammatory Marker (CRP) in a Representative Canadian Non-Diabetic Population .(Doctoral dissertation, University of Saskatchewan) .2018.
 23. Hawkins, M., Pekow, P., & Chasan-Taber, L.. Physical activity, sedentary behavior, and C-reactive protein in pregnancy. *Medicine and science in sports and exercise*. 2014; 46(2), 284-292.
 24. Kumari, R., & Singh, H. The prevalence of elevated high-sensitivity CRP in normal pregnancy and GDM.*JFMPC*.2017; 6(2), 259 .
 25. Mei, Z., Li, H., Serdula, M. K., Flores-Ayala, R. C., & Grummer-Strawn, L. M. C-reactive protein increases with gestational age during pregnancy among Chinese women .*AJHB*. 2016; 28(4), 574-579 .
 26. Schmatz, M., Madan, J., Marino, T., & Davis, J. Maternal obesity: the interplay between inflammation, mother and fetus. *Journal of Perinatology*.(2010); 30(7), 441.
 27. Festa, A., D'Agostino Jr, R., Howard, G., Mykkanen, L., Tracy, R. P., & Haffner, S. M. Chronic subclinical inflammation as part of the IR syndrome: the Insulin Resistance Atherosclerosis Study (IRAS). *Circulation*, (2000) . 102(1), 42-47 .
 28. Maged, A. M., Moety, G. A. F., Mostafa, W. A., & Hamed, D. A. Comparative study between different biomarkers for early prediction of GDM. *The Journal of Maternal-Fetal & Neonatal Medicine*.2014; 27(11), 1108-1112 .
 29. Haidari, F., Jalali, M. T., Shahbazian, N., Haghizadeh, M. H., & Azadegan, E. Comparison of serum levels of vitamin D and inflammatory markers between women with GDM and healthy pregnant control .*JFRH*.2016; 10(1), 1 .
 30. World health organizer . GDM criteria . 2013.
 31. Kamath, U., Rao, G., Raghobama, C., Rai, L., & Rao, P. Erythrocyte indicators of OS in GDM. *Acta Paediatrica*. (1998); 87(6), 676-679 .
 32. Kharb, S., Gulati, N., Singh, V., & Singh, G. P. (1998). Lipid Peroxidation and Vitamin E Levels in Preeclampsia. *Gynecologic and obstetric investigation*.(1998); 46(4), 238-240 .
 33. Uotila, J., Tuimala, R., Aarnio, T., Pyykkö, K., & Ahotupa, M. Lipid peroxidation products, selenium-dependent glutathione peroxidase and vitamin E in normal pregnancy. *EJOG*.(1991).;42(2), 95-100.
 34. Yaseen, H. A., & Hussein, B. H. Selected salivary antioxidants and gingival health condition among a group of obese females aged 20-22 years in Baghdad, Iraq. *Mustansiria Dental Journal*.2017; 14(1), 65-71.
 35. Ishimoto, T., Lanaspas, M. A., Le, M. T., Garcia, G. E., Diggle, C. P., MacLean, P. S., & Rivard, C. J. Opposing effects of fructokinase C and A isoforms on fructose-induced metabolic syndrome in mice . *PNAS*.2012; 109(11), 4320-4325.
 36. Lanaspas, M. A., Sanchez-Lozada, L. G., Choi, Y. J., Cicerchi, C., & Schreiner, G. UA induces hepatic steatosis by generation of mitochondrial OS potential role in fructose-dependent and-independent fatty liver. *JBC*.2012; 287(48), 40732-40744 .
 37. Yoo, T. W., Sung, K. C., Shin, H. S., Kim, B. J., Kim, B. S., Kang, J. H., & Lee, W. Y. Relationship between serum UA concentration and IR and metabolic syndrome. *Circulation Journal*, (2005). 69(8), 928-933.
 38. Fawzy, M. M., Mohamed, M. E. M., Hassanin, A. S., & Ghally, M. N. The Association between Hyperuricemia in First Trimester and the Development of GDM. *JFIV Reprod Med Genet*.2017; 5(2), 1-8.
 39. Ali, O. A. S., Al Sawy, I. R., Salah, M. A., & Kattaria, M. K. . Predictive Value of First Trimester UA in Development of GDM. *EJHM*.2019; 74(7), 1675-1679 .
 40. Valle, M., Martos, R., Cañete, M. D., Valle, R., & Cañete, R. Association of serum UA levels to inflammation biomarkers and endothelial dysfunction in obese prepubertal children . *Pediatric diabetes*.(2015); 16(6), 441-447 .
 41. Liu, S., & Mauvais-Jarvis, F. Minireview: estrogenic protection of β -cell failure in metabolic diseases *Endocrinology*. 2009; 151(3),859-864 .
 42. Jaya, B., Devi, R. M., Saikumar, P., & Karthikeyan, E. A comparative study of OS among GDM and normal pregnancy. *National Journal of Physiology, Pharmacy and Pharmacology*.2019; 9(1), 86-89.
 43. Pickup, J. C. (2004). Inflammation and activated innate immunity in the pathogenesis of type 2 diabetes. *Diabetes care*, 27(3), 813-823.

The Effect of Teaching in Educational Complexes Using Harmonic Exercises to Improve Motor Compatibility and Some Basketball Offensive Skills

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Abstract

The research included the introduction, the importance of the research and the goal of the research:

- Identify the effect of using teaching in educational complexes according to harmonic exercises to improve motor compatibility.
- Recognize the impact of the use of teaching in educational complexes according to harmonic exercises to improve some offensive skills basketball.

The researchers used the experimental method as well as the research sample, the students of the preparatory stage in Al-Khadra School (30) divided into two equal experimental and control groups and included a number of educational units (7) units applied to the research sample where teaching was used in educational complexes. Using harmonic exercises on the experimental group.

The research reached the most important results of them:

- The results showed that the experimental group that used teaching in the educational complexes and harmonic exercises in improving the motor compatibility and learning some skills in basketball (long hand over the shoulder and the freshman and scoring from the free throw line) over the control group.
- The results showed that the control group that used the teaching followed by the teacher in learning some skills and motor compatibility in basketball.

Keywords: Complexes exercises, harmonic, offensive and basketball.

Introduction

In light of the great scientific and cognitive advancement in the fields of life, information is now being published at the time of its birth, and the field has

expanded for all those who have a bright idea and a good opinion to publish it via the internet to be the subject of research in an international seminar. In this scene, the groups of teachers should take advantage of this reality to advance the educational process at all levels of its educational institutions. It has become obligatory for the teacher of physical education at various stages of study from kindergarten to university care and development towards the correct performance of sports skills as much as given to take care of the level of achievement and development.

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In general, the role of the teacher and teacher in the past limited to the delivery of information and transfer

of knowledge to students, but today with the new developments and with the challenges of the modern era has become its role is changed and renewed by modern preparation curricula in line with the challenges of this era of factors affecting the development of physical education lesson are teaching method The method of learning, which have witnessed a clear expansion in recent years, because of their importance in the education of students to raise their motivations and needs cognitive, physical and skill.¹

This is what has been overlooked by many researches, which is the care of the physical education teacher for the direction of the correctness of the technical performance and the level of achievement of students who need the so-called teaching complexes. Teaching in the educational complexes works to “raise the level of individual management for himself and his environment, and awareness of his ambitions and problems combined, and this requires him to be able to analyze and understand not only through educational stages, but continuously expected to go through the individual educated.

All sports require a special degree of motor compatibility rates and conditions vary according to the type of sport practice and skill required and almost no type of sports of that compatibility, including basketball, which is one of the most widespread games in the world and practice by both sexes and includes a range of defensive and offensive skills And the vehicle, which requires a set of physical and motor abilities and thus it is natural compatibility between the organs of the body in order to perceive and bring out the skill properly and high accuracy and the fact that the ability of compatibility is one of the basic pillars in building the performance of the motor and skills right Curse in all overlooked cases.²

Research Hypotheses:

1. There are statistically significant differences between the results of pretest and posttest tests of the experimental group and the control group in improving the motor compatibility and learning some skills in basketball.
2. There are statistically significant differences between the results of the experimental group and the control group in the motor compatibility and learning some skills in basketball and for the benefit of the experimental group.

Research Methodology: The researchers used the experimental method.

The Research Sample: The research sample is represented by the fourth grade literary students in Al-Khadraa for boys in Baghdad/Al-Karkh governorate for the academic year 2017-2018. A student where the proportion of (60%) and they are divided into two divisions, Division A and Division (B) If the Division (A) was chosen to be the experimental group and Division (B) to be the control group.

Homogenization of the sample: The researchers performed homogeneity in some growth rates (height, age and weight) as shown in Table (1).

Table (1). Shows sample homogeneity

Variables	Mean	SD	Median	Skewness
Age (Year)	15.20	0.33	15.00	2.44
Weight (Kg)	64.90	6.00	65.00	0.20
Length (cm)	169.20	5.40	169	0.30

The table shows that the skewness coefficient in growth rates is confined to the real boundary (± 3) and thus the sample is homogeneous.

Research tools and means of gathering information:

- Legal basketball balls.
- Legal basketball court.
- Tape measure.
- Medical balance.
- Electronic stopwatch.
- Hand calculator type SONY.
- Glove number 4.
- Persons-adhesive tape.

Tests used in research:

1. **Test name: throw and receive balls:**³
 - Purpose of the test: to measure the compatibility between the eye and arm
2. **(test high dribblefor a distance of 20 m dominant arm):**⁴
 - Purpose of the selection: measure the speed of the high bandwidth.
3. **Choose one-handed passing over the shoulder (long):**⁵

- Purpose of the selection: Measure the accuracy of one-handed scrolling over the shoulder on the target.
- The maximum score is 30 degrees.

4. Free throw test:⁶

- Purpose of the test: To measure the accuracy of the free throw scoring from behind the free throw line.

Pilot Study: The researchers carried out the exploratory experiment on a sample of the students who were excluded from the main experiment (10) on Sunday

19/11/2017 and the experiment was repeated seven days later on 26/11/2017.

- Knowledge of the efficiency of the tools and the team working assistant and know the time required to explain the tests and their application.

The tests used in the research have scientific bases and have been applied to the Iraqi environment and obtained the scientific bases, but the researchers deliberately conducted the scientific bases as shown in table (2).

Table (2). Shows validity, stability and objectivity

Variables	Validity	Stability	Objectivity
Compatibility	0.90	0.81	0.94
The dribble	0.92	0.85	0.95
Handling over the shoulder	0.94	0.88	0.96
Scoring from the free throw line	0.94	0.89	0.96

Tribal Tests: When the researchers to conduct pre-tests on 27-28/11/2017.

The main experiment is the introduction of teaching in educational complexes and harmonic exercises: Researchers have introduced the teaching in the educational complexes in the curriculum of the Directorate of Education Baghdad - Department of Technical Affairs/Curricula and books for the preparatory stage and also prepared and prepared educational units including harmonic exercises * and inserted within the curriculum, which amounted to (7) educational units and

began to apply from (3/12/2017) (To (24/24/2017) The last educational unit was divided into (2) educational units for long-handling over the shoulder (2) educational units for the tomato and (3) educational units for scoring from the free throw line and he introduced the harmonic exercises in the units Dedicated to selected skills which lasted for 4 weeks (2) teaching units per week and the time of the educational unit (45 Min.) and took the total time of the units (315 Min.).

Posttest Tests: The post-test was conducted on 26-27 December 2017.

Results

Presenting, analyzing and discussing the results of the pre- and post-tests of the experimental and control groups for compatibility and basketball skills:

Table (3). Shows the arithmetic media, standard deviations and the calculated and tabular (t) value in the pre- and post-tests of compatibility and basketball skills of the two groups

Abilities and skills	Groups	Pretest		Posttest		(t) calculated	(t) tabulated	Type of significance
		Mean	SD	Mean	SD			
Compatibility	Experimental	3.46	0.46	8.04	0.59	24.35	1.76	Sig.
	Control	3.44	0.56	6.25	0.64	13.40		Sig.
Long passing over the shoulder	Experimental	11.15	1.30	19.20	0.85	19.0		Sig.
	Control	10.90	1.40	15.60	0.96	8.01		Sig.
Dribble	Experimental	13.70	1.90	10.90	1.23	6.21		Sig.
	Control	13.73	1.88	11.91	1.91	2.60		Sig.
Scoring from the free throw line	Experimental	3.70	0.97	7.14	1.05	7.60		Sig.
	Control	3.30	1.0	4.80	0.85	5.12		Sig.

Table (3) shows that the first and second experimental group advanced the tests of compatibility and long handling over the shoulder, drum and scoring from the free throw line and for the benefit of the post-test. The researcher attributes this to the use of teaching in educational complexes and the introduction within the curriculum, which depends on learning Self-making makes learners more positive and makes it more adoption of the same bug in the learning process and works to give the freedom of the learner in the choice to achieve the objectives set and the teacher works on guidance and guidance and provide feedback (Provide that every individual is characterized in the background and speed of learning as well as teaching method and how to activate the cycle in the process so that it becomes the learner’s learning process axis at the time to be a teacher as a mentor and assistant to the learner .⁷

As well as worked to give a good opportunity for learners from the optimal use of time allocated and not wasting and that the harmonic exercises that have a clear impact on the progress of the experimental group in all variables, where prepared appropriately with the research sample in terms of estimating the situation of orientation ability for time and space and control the movement of the body in space and time The perception of the status of the body and changes for the stadium and movement and the ability to link motor coordination and this gives the quality of harmonic exercises prepared by the researcher, ⁸which focused on improving the compatibility between the body parts and skills in basketball that developed free movement Training of the umbilical response exercises and kinetic linkage between movements within the rhythm will lead to the development of motor speed of the body and show through the movement of the body as a whole or in the movements of the upper limbs.⁹

Table (4). Shows the arithmetic and standard deviations for the two posttests of the experimental and control groups of motor and skill basketball

Abilities and skills	Experimentalgroup		Controlgroup		(t) calculated	(t) tabulated	Type of significance
	Mean	SD	Mean	SD			
Compatibility	8.04	0.59	6.25	0.48	10.29	1.70	Sig.
Long passing over the shoulder	19.20	0.85	15.60	0.96	9.95		Sig.
Dribble	10.90	1.21	11.91	1.91	1.89		Sig.
Scoring from the free throw line	7.14	1.05	4.80	0.85	8.90		Sig.

Table (4) shows that there are significant differences between the experimental groups and the control group in the results of the post test of the motor compatibility and basketball skills. As shown in the test of long handling over the shoulder we find that the value of (t) calculated (9.95), which is greater than the value of (t) tabular and this confirms the presence Significant differences between the two groups in this test for the benefit of the experimental group In the skill of (Dribble) we find that the value of (t) calculated (1.89), which is greater than the value (t) spreadsheet adult and this confirms the existence of significant differences between the two groups in this test and for the benefit of the experimental group. The calculated value of (t) was (8,90), which is greater than the value of (t) tabular adult and this confirms the existence of significant differences between the two groups in this test and for the benefit of the experimental group.¹⁰

We note from Table (4) that the experimental group that was introduced teaching in educational complexes curriculum was more influential in the improvement and development of motor compatibility and skills basketball and this confirms the effectiveness of teaching in educational complexes according to harmonic exercises, which was implicitly consistent with learning skills and has played an effective role for progress The experimental group and where the educational complex is an educational unit includes a specific subject and contains elements of learning that may be different and multiple primary objective of increasing student interaction and active participation in the various activities that provide the educational complex to reach the educational goal To a specific unit of educational and powerfully high (teaching that gives a sense of educational complexes student achievement that the value achieved in accordance with a particular

focus of the goal expert defined in specific and short) period of time.¹¹

The organization of educational units for teaching in the educational complexes of the variables under study, where the activities are designed according to the needs of the subject and the specific goal and taking into account the sequence in the presentation of the content of skills and take into account the individual differences between learners as well as developed a set of exercises that allow learners an opportunity to practice and perform the duty in educational situations The teaching in the educational complexes is characterized by it provides flexibility in the choice of activities and learning according to its own speed and self-ability in learning and provide the conditions that give the learner a positive role in each educational situation in a run.¹²

The researchers believe that the improvement and development of kinetic compatibility comes through the implementation of exercises introduced to the curriculum followed by the learners, which was necessary and necessary to improve the compatibility and skills of basketball (that kinetic differentiation and reaction are the most important harmonic abilities and therefore can be considered that harmonic exercises Target those abilities and complement educational or training courses and improve the learning process). The progress achieved on the experimental group and the skills of long hand over shoulder, and the skill of Dribble and scoring from the free throw line because the skills require compatibility between the arm and sight and arm and the rest of the limbs and members of the body and require the compatibility of neurological and muscular where appropriate exercises have been selected To serve the requirements of the selected skills, which are carefully designed and highly planned to achieve the goal (Planning is the important means that works to determine the goal set in the plan accurately and prevents dependence on dispersion).¹³

Conclusions

1. The results showed that the experimental group that used teaching in the educational complexes and harmonic exercises in improving the motor compatibility and learning some skills in basketball (long hand over the shoulder and the freshman and scoring from the free throw line) over the control group.
2. The results showed that the control group that used

the teaching followed by the teacher in learning some skills and motor compatibility in basketball.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

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References

1. MacPherson AC, Collins D, Obhi SS. The importance of temporal structure and rhythm for the optimum performance of motor skills: A new focus for practitioners of sport psychology. *Journal of Applied Sport Psychology*. 2009 May 12;21(S1):S48-61.
2. Berk RA. Multimedia teaching with video clips: TV, movies, YouTube, and mtvU in the college classroom. *International Journal of Technology in Teaching & Learning*. 2009 Jun 1;5(1).
3. Khoran H, Khoran Z, Bakhshi EA. Effect of music on learning of hand fine movement skills in mental retarded children. *Procedia-Social and Behavioral Sciences*. 2012;12:324-7.
4. Karageorghis CI, Terry PC, Lane AM. Development and initial validation of an instrument to assess the motivational qualities of music in exercise and sport: The Brunel Music Rating Inventory. *Journal of sports sciences*. 1999 Jan 1;17(9):713-24.
5. Berk RA. Music and music technology in college teaching: Classical to hip hop across the curriculum. *International Journal of Technology in Teaching and Learning*. 2008;4(1):45-67.
6. Alsayigh HA, Athab NA, Firas M. Journal of Global Pharma Technology The Study of Electrical Activity of the Triceps Brachia Muscle according to the Chemical Changes of Water Loss during Spike in Volleyball. 2017;57-62.
7. Alsayigh HA, Athab NA. The Study of Rectus Femoris Activity after Knee Joint Rehabilitation. 2016;9(9):360-5.
8. Jumaah H, Ktaiman A, Abdul N, Athab K, Mohammed A. The Effect of Using Pain Management Techniques in the Rehabilitation of Chronic Lower Back Injury in Athletes and Non-Athletes. :108-12.

9. Athab NA, Hussein WR, Ali AA. A Comparative Study for Movement of Sword Fencing Stabbed According to the Technical Programming in the Game of Fencing Wheelchairs Class B. *Indian Journal of Public Health Research & Development*. 2019;10(5):1344-7.
10. Athab NA. An Analytical Study of Cervical Spine Pain According to the Mechanical Indicators of the Administrative Work Staff. *Indian Journal of Public Health Research & Development*. 2019; 10(5):1348-54.
11. Cahn D. The effects of varying ratios of physical and mental practice, and task difficulty on performance of a tonal pattern. *Psychology of Music*. 2008 Apr;36(2):179-91.
12. González-Villora S, Sierra-Díaz MJ, Pastor-Vicedo JC, Contreras-Jordán OR. The way to increase the motor and sport competence among children: the contextualized sport alphabetization model. *Frontiers in physiology*. 2019 May 16;10:569.
13. Roters TT. Physical improvement of students during interactive physical and aesthetic education. *Physical education of students*. 2013 Aug 28;17(4):72-6.

The Impact of Qualitative Exercises in the Development of Some Basic Skills in Football for the Cubs

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Abstract

Football has witnessed a significant development in the levels reached by the players, especially their physical, motor and skill levels. This is what we see today through what they offer while playing in world tournaments. Training programs often emphasize the physical and skill aspects of the players and not focusing on the aspects related to motor skills.

It has emerged in recent years and unquestionably a great development in football events where it is one of the games that require a high physical effort and skill to play the ball strongly impulsive, with coordinated movements where the player can perform the kinetic duty with minimal effort and high accuracy that economize on the use His physical and psychological abilities are balanced, as this leads to the fact that if two players with the same skill level and planning, the player with a physical level, motor and psychological high will be able to control the course of the game, so the skill side plays a big role in the game of football.

The problem of research was reflected in the skills weakness of the Cubs of football, especially passing and scoring, and this is attributed to the lack of motor programs in this category, and this causes a weak performance in the skills of many of the qualitative skills of the game. Here, the researcher considered that the development of specific exercises aimed at developing some of the basic skills of Cub football through the combination of motor and skill training to serve the goal of research.

Keywords: *Qualitative exercises; qualitative exercises; basic skills and weakness Health.*

Introduction

Football has witnessed a significant development in the levels reached by the players, especially their physical, motor and skill levels. This is what we see today through what they offer while playing in world tournaments. Training programs often emphasize the physical and skill aspects of the players and not focusing on the aspects related to motor skills¹⁻³.

It has emerged in recent years and unquestionably a great development in football events where it is one of the games that require a high physical effort and skill to play the ball strongly impulsive, with coordinated movements where the player can perform the kinetic duty with minimal effort and high accuracy that economize on the use His physical and psychological

abilities are balanced, as this leads to the fact that if two players with the same skill level and planning, the player with a physical level, motor and psychological high will be able to control the course of the game, so the skill side plays a big role in the game of football^{2,4,5}. The problem of research was reflected in the skills weakness of the Cubs of football, especially passing and scoring, and this is attributed to the lack of motor programs in this category, and this causes a weak performance in the skills of many of the qualitative skills of the game⁶.

Here, the researcher considered that the development of specific exercises aimed at developing some of the basic skills of Cub football through the combination of motor and skill training to serve the goal of research.

The research aims to:

- Preparation of qualitative exercises to develop the development of some basic skills of football cubs.
- Identify the impact of qualitative exercises to develop some basic skills of football cubs.

From the research objectives, the research hypothesis

- There is a positive impact of qualitative exercises to develop some basic skills of football cubs and for the benefit of the experimental group.

Research methodology and field procedures

Research Methodology: The researcher used the descriptive method of the survey method and the experimental method with two equal groups to suit the nature of the research.

Research community and sample: The research community included the players of Babylon Clubs for the season 2018-2019 and the number of 32 players are divided into four clubs, the club of Babylon, Hilla, Baladi and Mahaweel, where they were divided randomly (lottery) into two control and experimental groups (20) players for each group (10) players.

Data collection tools, means and devices used: Scientific sources. Resolution. the interview. Observation and experimentation. Testing and measurement. Legal stadium (1). Colored strips, 1 metric tape and 2.5 cm red tape. Computer type (Dell) 5040) number (1). A Japanese-made digital camera (Nikon). Chinese Medical Balance. Balls (24). Digital stopwatch. Colored signs (red, blue, yellow, green) 12 training collars (10). Agility ladder (6). Educational objectives (1 m).

Field research procedures

Identify research variables: Researcher's field experience in the field of football training has a role in determining the variables of the research under study namely passing and scoring for the Cubs of football, but the researchers worked to take the opinion of many experts and specialists.

Identify skill tests: The skill tests under study were determined by the expertise of researchers as well as from scientific consultations with experts and specialists.

1. Test the accuracy of football passing:

Test Name: Receipt and delivery.

Objective of the test: To measure the accuracy of the performance of passing football.

The Tools Used: A legal football field, 5 legal football balls, a tape measure, small targets with a width of 1 meter and a height of 0.5 meters, a pre-prepared evaluation form.

Performance Specifications: Standing (5) players in a straight line and the distance between the player (2meters), and the players in front of the five goals away from them (30) meters stand the player tested in the middle between the player (1) and goal (1) and when you hear a signal Start The player receives the ball from the player number (1) and then the rapid rotation within the specified distance (2) located in the middle of the distance between the five goals and the line cross, and then passing the ball towards goal (1) and thus repeated the attempt with his teammates.

Method of registration: Calculated two degrees for each injury, and one score if you touch one of the officials, and does not count any score in the absence of injury to the target, the total score of the test (10) degrees.

2. Test the accuracy of football scoring performance:

Test Name: Scoring towards the goal divided into boxes.

The objective of the test: To measure the accuracy of the performance of scoring football.

Tools Used: a legal football field, a number of legal football (5), a tape to identify the scoring area, a form of assessment prepared in advance.

Performance Specifications: (5) balls are placed on the penalty line, which is (18) yards from the goal line and the distance between the ball and another (1) yards, as the player scoring in the areas indicated by the test and according to their importance and difficulty and sequentially the ball after another to be tested Of jogging mode.

Method of scoring: Calculates the number of injuries entering the specified goals from both sides so that the scores of each of the five balls are calculated as follows:

1. (5) Grades when the ball enters the zone number (5).
2. (4) Degrees are given when the ball enters area No. (4).

3. Gives (3) degrees when the ball enters area No. (3).
4. (2) Is given two degrees when the ball enters the zone No. (2).
5. Is given a score when the ball enters (1) the goalkeeper's place.
6. Zero grades shall be given in case of extending the boundaries of the five numbered areas.
7. In the case of touching the ball of the tape is calculated for the highest area according to the numbered areas.
8. The total score test (25) degree.

Specify specific exercises: Through the technical expertise of the researcher in the field of training, he designed (12) special exercises between physical, motor and skills, and nevertheless, the researcher presented them to specialists in the sports field and then all of them (100%) agreed to these exercises.

Pilot Study: The researcher conducted a pilot experiment on four cubs of football on Monday 10/12/2018.

Scientific bases of research variables: The researchers used to extract the objective test passing and scoring for the eye and man as it depends on the time has reached (0.95), as well as extracting the coefficient of stability through the test and returned, the results came as in the table following:

Table (1). Shows the stability parameters of the motor tests under study

S	Tests	Stability
1	Passing	0.94
2	Scoring	0.93

Pretests: The researchers conducted a pre-test on the variables under study on Monday, 17/12/2018.

Homogeneity and equivalence: The researchers made homogeneity and equivalence among the members of the research sample, as in Table (1)

Table (2). Values (F) and (t) for homogeneity and equivalence

Independent Samples Test							
Research variables	Levene's Test for Equality of Variances		t-test for Equality of Means				
	F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference
Passing	0.507	0.486	0.318	18	0.754	0.20	0.62893
Scoring	0.201	0.660	0.355	18	0.726	0.198	0.55705

From the values of (Sig.) Of (F) in table (2) of more than (0.05) in all variables we infer from this as a homogeneity process exists, and through the values of (Sig.) Of (t) of more than (0.05) This means that there is no significant difference for all variables and this will give the researcher initiation on one starting line.

Perform specific exercises: After conducting the pre-tests of the research groups, the specific exercises were carried out during (8) weeks (3) training units per week (Sunday, Tuesday, Thursday), with a total of (24) training units where (5) exercises were put to the training unit where the time was The training unit (60) minutes and took (40) minutes from the time of

the training unit, which is the main section, which was the implementation of exercises, has been implemented during the preparation period for the training method of high intensity and repetitive training as these exercises aimed to develop passing and scoring for the Cubs of football. Develop these exercises appropriately for the current study as it worked this exercise Reduce boredom and the desire to repeat more of the repetitions applied to the experimental group.

Posttest tests: After completing the twenty-four training modules, the researcher conducted the post-tests of the research variables under study for both groups on Saturday 16/2/2019.

Results

View the results of the passing, scoring and ground strike tests of the Cubs of football and the experimental and control groups

Table (3). Shows the mean of the experimental group scores, standard deviations and the value of (t) in the pretest-post test of the research variables under study

Paired Samples Test							
Research variables		Paired Differences			t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean			
Passing	Pre-Post	7	1.41421	0.44721	15.652	9	0.000
Scoring	Pre-Post	1.057	1.10203	0.34849	3.033	9	0.014

Table (4). Shows the mean of control group scores, standard deviations and the value of (t) in the pre-posttest of the research variables under study

Paired Samples Test							
Research variables		Paired Differences			t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean			
Passing	Pre-Post	5.3	1.94651	0.61554	8.610	9	0.000
Scoring	Pre-Post	0.582	.52837	0.16708	3.483	9	0.007

Discuss the results of the two research groups:

Through the values of (Sig.) For all the variables in the previous two tables of less than (0.05) for all variables and for the control and experimental groups and this

shows that both groups have evolved, and this confirms the effectiveness of the exercises used by the researcher to develop passing and scoring, so that we can know which groups Evolved by a larger revision table (5).

Table (5). Shows the mean of the experimental and control group scores and their standard deviation and the value of (t) in the post-posttest of the research variables under study

Independent Samples Test					
Research variables	t-test for Equality of Means				
	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference
Passing	4.881	18	0.000	1.5	0.30732
Scoring	2.304	18	0.033	0.67300	0.29215

Through Table (5) which shows the values of (Sig.), Which is less than (0.05) for passing skill and more for scoring; here we can know here that the evolution occurred for both groups and that the great development that came in favor of the experimental group and the researcher attributes that development to exercise⁷⁻¹⁰. The quality applied to the experimental group, which was codified according to the scientific equations studied and calculated to suit the levels of players to change from the training routine, and create a new training atmosphere, and the desire to repeat a greater number of iterations, as

evidenced by the findings of the researcher^{10,11}.

Here we see that it is no secret to anyone today has become the majority of trainers keep pace with scientific development at the sports level because of the availability of all means to raise their scientific and practical levels and the best evidence of this is to inform them on the training curricula for global teams, whether at the level of group games or individual, and therefore we found the development of the control group By close to the evolution of the experimental group⁸⁻¹⁰.

Conclusions

In the light of the findings of the researchers through the field experiment and using the appropriate statistical method concluded the following:

1. Qualitative exercises have been instrumental in the development of passing and scoring in football cubs.
2. The use of qualitative exercises and save effort and time for the coach and the player in the development of passing and scoring for the Cubs of football well and is suitable for training this category of ages.
3. The use of qualitative exercises has a positive impact on the interaction of players during the exercise and attendance and the desire to repeat a greater number of repetitions.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: The authors declare that they have no conflict of interest.

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References

1. Lune H, Berg BL. Qualitative research method for the social sciences. Pearson Higher Ed; 2016 Nov 21.
2. Weinberg RS, Gould D. Foundations of Sport and Exercise Psychology, 7E. Human Kinetics; 2018 Nov 16.
3. Gill DL, Williams L, Reifsteck EJ. Psychological dynamics of sport and exercise. Human Kinetics; 2017 Jun 23.
4. Weinberg RS, Gould DS. Foundations of sport and exercise psychology. Human Kinetics; 2014 Nov 11.
5. Vealey RS. Smocks and jocks outside the box: The paradigmatic evolution of sport and exercise psychology. Quest. 2006 Feb 1;58(1):128-59.
6. Zakrajsek RA, Blanton JE. Evaluation of psychological interventions in sport and exercise settings. InOxford Research Encyclopedia of Psychology 2017 Aug 22.
7. Mulvihill C, Rivers K, Aggleton P. A qualitative study investigating the views of primary-age children and parents on physical activity. Health Education Journal. 2000 Jun;59(2):166-79.
8. Gallucci NT. Sport psychology: Performance enhancement, performance inhibition, individuals, and teams. Psychology press; 2013 Dec 4.
9. Wenner LA. Media, sports, and society: The research agenda. Media, sports, and society. 1989:13-48.
10. Athab NA, Hussein WR, Ali AA. A Comparative Study for Movement of Sword Fencing Stabbed According to the Technical Programming in the Game of Fencing Wheelchairs Class B. Indian Journal of Public Health Research & Development. 2019;10(5):1344-7.
11. Athab NA. An Analytical Study of Cervical Spine Pain According to the Mechanical Indicators of the Administrative Work Staff. Indian Journal of Public Health Research & Development. 2019;10(5):1348-54.

Assessment of the Antimicrobial Resistance of Urinary Escherichia Coli and Some Factors Related to Urinary Tract Infection in Karbala Patients

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Abstract

Background: Urinary tract infection is one of the most common type of infectious disease encountered in the practice of medicine. Antimicrobial resistance is huge problem cause of a great concern throughout the world.

This study was carried out to assess the antimicrobial resistance of urinary *E. coli* and some factors related to urinary tract infection.

Results: Out of the 100 patients studied, the urine samples of 49 patients were found to have culture positive; and out of these, the urine samples of 28 patients were positive for urinary *E. coli*. Thus the prevalence was 57.1% for *E. coli*, and 42.9% for other type of bacteria such as *Staphylococcus aureus*, *Hemolytic streptococci*, *Klebsiella spp.*, *Proteus spp.*, *Enterococcus spp.* and *Pseudomonas aeruginosa*.

The results of sensitivity tests showed that the resistance of *E. coli* was about 10 times higher for nitrofurantoin, ceftazidime and ceftriaxone; relative to amikacin, ampicillin and imipenem.

Aim of the study: Assessment of the antimicrobial resistance of urinary *E. coli* and some factors related to urinary tract infection in Karbala patients .

Conclusions: *Escherichia coli* remains the most common pathogens isolated from urine samples of patients with urinary tract infection . The resistance of uropathogenic *E. coli* to antimicrobial drugs has been gradually increasing for commonly used drugs.

Keywords: Karbala patients; *Escherichia coli*; antimicrobial resistance; factors.

Introduction

UTIs are most common bacterial infection account for significant morbidity and health care costs. [1].

UTI is predominantly a disease of females due to anatomic and physiologic differences after age of 50years [2] after age of 50years,UTI most common in male than female due to prostatic hypertrophy in men.[3].

Most UTIs are caused by single bacterium that mainly lived in bowel and rarely they may be due to viral or fungal infection.[4]

Escherichia coli is a Gram-negative bacterium. There are many serotype of this organism, only a few of these are responsible for infections uropathogenic *E. coli* (UPEC) [5].

Aging is associated with an increased in the susceptibility to UTI due to alteration in the vaginal and periurethral flora and reduction in the estrogen level from menopause in women [6] .

UTI in more frequent and more sever diabetic patient because of glucose in the urine which promotes bacterial growth and impairs leukocytes functions [7].

The incidence of acute clinical pyelonephritis is about 25% to 35% in untreated bacteriuric women [8].

Obstruction to urine flow at all anatomic level caused by stone is a key factor increasing susceptibility to UTI [9],[10].

Urinary catheterized increases the risk UTIs, longer time catheterization associated with bacterial growth [11].

Bactericidal antibiotic are superior to bacteriostatic agent in treating in relapsing infection. [12] antibiotics are considered the most effective method of treatment for bacterial infections [13,14].

The prevalence of antibiotic resistance stems primarily from the promiscuous nature of bacteria, as susceptible bacteria may acquire resistance genes from plasmids and other horizontally transferred genetic material, resulting in evolution by leaps [15,16]

Aim of the study: Assessment of the antimicrobial resistance of urinary *E. coli* and some factors related to urinary tract infection in Karbala patients .

Patients and Method

Patients selection:

The study retrospective,cross sectional was conducted at outpatient urology department in Al-Hussein teaching hospital in Karbala city, from august 2012 to October 2012.

A total number of 100 patients (78 male and 22 female) were randomly selected included in study, all of them lived in Karbala city. The patients ages were 25-65 years. All patients were clinically diagnosed and examined by urologists for signs and symptoms of urinary tract infections.

Ethical approvals were obtained from the local research ethical committee in Karbala health care office according to the proposal format for research project protocol from WHO. All patients gave verbal informed consent to participate in the research.

Inclusion criteria/Exclusion criteria: Inclusion criteria: All patients that not used antibiotics previously and had the signs and symptoms of urinary tract infections and have positive results in the urine culture test for *E. coli* were included in the study. They were 28 patients out of the 100 patients visited the urology department for UTIs.

Exclusion criteria: All patients that had negative results for urine culture (51 patients) and patients that had negative results for *E. coli* but positive for other types of bacteria (21 patients) were excluded from the study.

Results

Distribution of uropathogens in patients:

Out of total of 100 patients, 51 patients had negative results of urine culture (-ve). The remaining 49 patients had positive results (+ve). From these positive results, only 28 patient had *E. coli* in the culture test, the number of females were 22 patients (78.51%) while males were 6 patients (21.49%). While 21 patients had other types of bacteria.

Table (1)show the distribution of urinary tract pathogens and the prevalence in percentage.

Table (1): Distribution of isolated urinary tract pathogens and the prevalence in percentage (N=49 patients).

No.	Organism isolated	No. of patients	Prevalence (%)
1	Escherichia coli	28	57.1%
2	Staphylococcus aureus	6	12.2%
3	other Staphylococcus spp.	4	8.1%
4	Hemolytic streptococci	3	6.1%
5	Klebsiella spp.	3	6.1%
6	Proteus spp.	2	4.1%
7	Enterococcus spp.	2	4.1%
8	Pseudomonas aeruginosa	1	2%

Alteration in some parameters of urinalysis in patients with urinary tract infection caused by *E. coli*:

The alteration in some urinalysis parameters in patients with urinary *E. coli* infections from the normal level are presented in table (2).

Table (2): Alteration in some parameters of urinalysis in patients with urinary *E. coli* (N=28 patients).

No.	Parameters of urinalysis	Prevalence of alteration from the normal level (%)
1	Pus cell	100%
2	Bacteria	100%
3	Red blood cells (R.B.Cs)	20%

Antimicrobial resistance in the urine culture of patients with urinary tract infection caused by *E. coli*:

The results of sensitivity tests in the urine culture of patients with urinary *E. coli* are presented in table (3). It is obvious from this table that *E. coli* is highly resistant to Nitrofurantoin. Whereas, on the other extreme, the lowest resistance of *E. coli* was for Ampicillin and Imipenem.

Table (3): Antimicrobial resistance in the urine culture of patients with urinary *E. coli* (N=28 patients).

No.	Antimicrobial agent	Resistance (%)
1	Nitrofurantoin	35.7%
2	Ceftazidime	28.6%
3	Ceftriaxone	28.6%
4	Co-amoxiclavate	25%
5	Ciprofloxacin	25%
6	Gentamicin	21.4%
7	Trimethoprim-sulfamethoxazole	20%
8	Amikacin	10.7%
9	Ampicillin	3.6%
10	Imipenem	3.6%

Discussion

E. coli was isolated in (57.1%) cases in this study. While (59%) was the isolation of *E. coli* has been reported in many other studies in India [21]. The difference in the prevalence rate of *E. coli* in this study and other studies is low. [22].

Staphylococcus aureus was the second most common uropathogens appeared in this study (12.2%). There is small difference between the present results and (17%) was the result of other study conducted in Iraq [23]. The high percentage of *Staphylococcus spp.* is the main bacteria that cause skin infection and easily to cause contamination and infection of urinary tract [24].

The other bacteria found in the patients urine of this study was *hemolytic streptococci* with percentage of (6.1%) that more than in the result (1.8%) of study in Canada [38]. And *proteus spp.* contribute to (4.1%), which resemble to the finding other study that was (4.1%) [25]. However, the percentages of other pathogens such as *enterococcus spp.* and *pseudomonasaeruginosa* were (4.1%) and (2%) respectively, that differ from results of other studies were (14%) for *enterococcus spp.* and (3.4%) for *pseudomonasaeruginosa* [25]. This may be due

to demographic variation, drug use between different communities that lead to some pathogens to be more predominant than others.

In the present study, high percentage of *E. coli* infection was found in females which was (78.5%), while in males was (21.5%). These percentage is more than the result of other studies that was (77.4%) in females and (22.6) in males [26] which may be due to difference in the age of marriage, the number of deliveries, contraception and health care education between the communities. The oral contraceptive use has also increased risk of UTIs which appear to be related to the alteration in vaginal flora that allow for the bacterial over growth and subsequent infection [27].

The signs and symptoms had great prevalence rates with values (73.3%), (73.3%), (66.7%) and (53.3%), respectively. This may be considered as the typical symptoms of lower UTI [28]. On the other hand, fever was (46.7%), nausea (33.3), diarrhea (20%) and vomiting (13.3%). These signs are mainly associated with upper UTI [29].

The risk factors for UTI. Including recurrent infections (46.7%) and elderly (33.3%). These values are higher than in other study [30] which were (17%) for recurrent infection and (15%) for elderly. The higher percentage found in this study is probably due to the fact that the patients in Iraqi community do not visit hospitals until the disease become big problem and effect on the patient's life, especially in elderly who are associated with more medical problem and lower health care.

The changes of urinalysis parameters were pus cell (100%) and bacteria seen (100%). These results indicate the presence of bacteriuria in the patients studied. Which highly specific for UTIs. Red blood cells (R.B.Cs) were (20%). This may indicate presence of renal stone that cause irritation and bleeding in the urinary tract [31].

The resistance rate for nitrofurantoin was (35.7%). This value is greater than the resistance rates found in previous studies which were (6.7%) in Canada [25] and (1.9%) in USA [32]. This high difference between the results of the present study and other studies may be due to highest antibiotics consumption rate in Iraq which has been identified as strongest risk factors for antimicrobial resistance, especially nitrofurantoin [33].

The other antibiotics tested in this study was ceftriaxone which also showed large value of resistance

(28.6%), in comparison with other studies which were (4.4%) [32] and (2.3%) [34]. This variation in observation was expected and may be a result of increasing excessive use particularly to ceftriaxone which are used in large quantities in both hospitals and the outpatient settings.

For co-amoxiclavate and ciprofloxacin the resistance found in this study was 25% which is different than other study [33] which was (17.1%) for ciprofloxacin and (5.3%) for co-amoxiclavate. These results differ from the study in Iraq is probably due to the fact that these two drugs are considered as widest drugs used for empirical therapy of UTI.

For gentamicin and trimethoprim-sulfamethoxazole (TMP-SMX), the results of resistance distribution found in this study were (21.4%) and (20%), respectively. However, in comparison with other studies were (7.5%) and (4.6%) for gentamicin, and for TMP-SMX were (22.1) and (39.3%) [32], [35]. These justifications are also applied for trimethoprim-sulfamethoxazole (TMP-SMX), as in the Outpatient isolates of *E coli* in the United States show resistance rates ranging from 15% in the upper Midwest to greater than 40% in the southwest and south-central United States [36].

The result of resistance for amikacin found in this study was (10.7%) which is less than the result reported from other study which was (27,8%) [37]. This may be due to restriction in use for treatment of UTI.

For ampicillin and Imipenem, the resistance observed in the present study was (3.6%), while in other study, the resistance rate was (56%) for ampicillin [34]. This great difference may result from the fact that ampicillin is limited or not used for UTI recently in Iraq and therefore lesser resistance development. Another study revealed that Imipenem sensitivity to urinary *E. coli* was (100%) [32]. The explanation for this result may be due to Imipenem use in Iraq is associated some times without regarding the limitations for prescribing. [38].

Conclusion *Escherichia coli* remains the most common pathogens isolated from urine samples of patients with urinary tract infection. Urinalysis is helpful as a mean of excluding bacteriuria. The resistance of uropathogenic *E. coli* to antimicrobial drugs has been gradually increasing for commonly used drugs. Thus, the knowledge of antimicrobial resistance among uropathogenes is essential to provide appropriate cost effective therapy.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: The authors declare that they have no conflict of interest.

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References

1. Tanagho E, McAninch J. Smith's general urology. 17th ed. Lange medical book, San Francisco 2008;13:203-209.
2. Foxman B et al: Urinary tract infection among women aged 40 to 65: Behavioral and sexual factors. Clin Epidemiol 2001;54:710.
3. Williams DH, Schaeffer AJ. Current concept in urinary tract infection . Minerva Urol Nefrol 2004;56(1):15.
3. Ronald A. The etiology of urinary tract infection: traditional and emerging pathogens. Am J Med 2002;113:14.
4. Karlowsky et al . Genetic relatedness of multidrug-resistant *Escherichia coli* cultured from geographically diverse outpatient, midstream urine specimens. Diagn Microbiol Infect Dis 2007; 58:283–287.
5. Nicolle LE. Urinary tract infection in geriatric and institutionalized patient . Curr Opin Urol 2002;12:51.
6. Ramzan M et al . Risk factors in urinary tract infection. Gomal J Med Sci. 2004; 2: 1- 4.
7. McLaughlin SP et al .Urinary tract infections in women. Med Clin North Am 2004;88:417.
8. Arslan H et al. Risk factors for ciprofloxacin resistance among *Escherichia coli* strains isolated from community-acquired urinary tract infections in Turkey. J Antimicrob Chemother 2005; 56(5):914-8.
9. Griebing TL . Urologic diseases in America project :trends in resource use of for urinary tract infections in men . J U 2005;173(4):1281-7.
10. Hooton TM et al. Diagnosis, prevention and treatment of catheter-associated urinary tract infection in adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America. Clin Infect Dis

- 2010;50(5):625-63.
11. Wolverson S . Comprehensive dermatologic drug therapy.2ed ed. Elsevier, Philadelphia 2007.p:40-60.
 12. Llor C., Bjerrum L. Antimicrobial resistance: Risk associated with antibiotic overuse and initiatives to reduce the problem. *Ther. Adv. Drug Saf.* 2014;5:229–241. doi: 10.1177/2042098614554919.
 13. Laxminarayan R., Duse A., Wattal C., Zaidi A.K., Wertheim H.F., Sumpradit N., Vlieghe E., Hara G.L., Gould I.M., Goossens H., et al. Antibiotic resistance—The need for global solutions. *Lancet Infect. Dis.* 2013;13:1057–1098. doi: 10.1016/S1473-3099(13)70318-14.
 15. Higgins C.F. Multiple molecular mechanisms for multidrug resistance transporters. *Nature.* 2007;446:749–757. doi: 10.1038/nature05630.
 16. Krizova L., Nemecek A. A 63 kb genomic resistance island found in a multidrug-resistant *Acinetobacter baumannii* isolate of European clone I from 1977. *J. Antimicrob. Chemother.* 2010;65:1915–1918.
 17. Jawetz et al. *Medical microbiology* 25th ed. Lange basic science 2011.
 18. Richard V. Goering et al. *Mims's medical microbiology*.4th ed. Mosby Elsevier, Philadelphia 2008;20:254-256.
 19. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing: 20th Informational Supplement 2010.M100-S20. CLSI, Wayne,PA .
 20. Levinson W. Review of medical microbiology and immunology.9th ed. Lange medical book, New York 2006;11:85-93
 21. Akram M. et al . Etiology and antibiotic resistance patterns of community-acquired urinary tract infections in JNMC Hospital Aligarh, India. *Ann Clin Microbiol Antimicrob* 2007; 6:4
 22. Mulvey MA :Adhesion and entry of uropathogenic *Escherichia coli*. *Cell Microbiol* 2002;4:257-271.
 23. Aamal GM. Isolation & identification of aerobic bacteria Causing urinary Tract Infection in pregnant women in Al-Diwaniya city and its sensitivity to some antibiotics. *Al-Qadisiyah Medical Journal* 2009;1:14.
 24. Jackson SL et al .Predictors of urinary tract infection after menopause :a prospective study . *Am J Med* 2004;117(12).903-11.
 25. Karlowsky J et al . Antimicrobial resistance in urinary tract pathogens In Canada from 2007-2009:CANWARD surveillance study. *Antimicrob agents chemother* 2011;55(7):3169-3175.
 26. Gupta K, Sahm D. Antimicrobial Resistance among uropathogens that cause community –acquired urinary tract infections in women. Department of medicine,division of allergy and infectious diseases,university of Washington school of medicine . *Clin Infect Dis* 2001;33(1):89-94.
 27. Handley MA et al . Incidence of acute urinary tract infection in young women and use of male condoms with and without nonoxynol-9 spermicides. *Epidemiology*2002;13:431.
 28. Sobel JD et al. Principle and practice of infectious diseases .6th ed. Churchill Livingstone, New York 2006;p.875.
 29. Ramakishnan K et al. Diagnosis and management of acute pyelonephritis in adults. *Am Fam Physicin* 2005;81:83.
 30. Sotto A et al. Risk factors for antibiotic-resistant *Escherichia coli* isolated from hospitalized patients with urinary tract infections: a prospective study. *J Clin Microbiol* 2001;39(2):438–44:
 31. Nicolle LE et al .Infectious diseases society of America .Guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adult . *Clin Infect Dis* 2005;40:643-654.
 32. Guillermo V et al . In vitro antimicrobial resistance of urinary *Escherichia coli* isolates among U.S. outpatients from 2000 to 2010. *Antimicrob Agents Chemother* 2012; 56(4):2181.
 33. Nicolas chanoine et al . Intercontinental emergence of *Escherichia coli* clone O25:H4-ST131producing CTX-M-15. *J Antimicrob chemother* 2008;61:273-281.
 34. Peirano G et al . High prevalence of ST131 isolates producing CTXM- 15 and CTX-M-14 among extended spectrum-lactamase-producing *Escherichia coli* isolates from Canada. *Antimicrob. Agents Chemother* 2010; 54: 1327–1330.
 35. McCarty et al . A randomized trial of short-course ciprofloxacin and trimethoprim-sulfamethoxazole for the treatment of acute urinary tract infection in women. *J Med* 1999;106:292-299.
 36. Zhanel GG et al. Antibiotic resistance in *Escherichia coli* outpatient urinary isolates: final

- results from the North American urinary tract infection collaborative alliance (NAUTICA). *Int J Antimicrob* 2006 . Agents 27:468–475.
37. Kahlmeter G et al . Non-hospital antimicrobial usage and resistance in community-acquired *Escherichia coli* urinary tract infection. *J Antimicrob Chemother* 2003;52(6):1005–10.
 38. Alos JI et al . Antibiotic resistance of *Escherichia coli* from community-acquired urinary tract infections in relation to demographic and clinical data. *Clin Microbiol Infect* 2005;11(3):199–203.

Inhibitory Effects of Carbonyl Cyanide 3-Chlorophenylhydrazone (CCCP) and Ciprofloxacin on the Gene Expression of Nor a Efflux Pump and Reduce Antibiotic Resistance in *Staphylococcus Aureus*

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Abstract

One of the important pathogen with increasing resistance rate in hospitalized patients is *Staphylococcus aureus*. The useful results for antimicrobial activity of CCCP made it a proper candidate to enhance the inhibitory effect of some certain antibiotics like Ciprofloxacin. The aim of this study was to investigate the Inhibitory effects of CCCP on the gene expression of *norA* efflux pump and decrease Ciprofloxacin resistance in *Staphylococcus aureus*. Thirty isolates of *S. aureus* were acquired from different clinical specimens at the Baquba teaching hospital. Susceptibility test to ciprofloxacin was done by disk diffusion test and broth dilution method. Activity of the efflux pump was recognized using CCCP as a chemical efflux pump inhibitor. MIC of CCCP was evaluated with Muller Hinton Broth dilution method. Bacterial culture was performed and *norA* gene expression was examined by Taqman qRT-PCR by one-step and .The expression of *norA* was significantly decreased in these isolates when were treated with CCCP & Cip. Our results showed that CCCP can increase ciprofloxacin susceptibility through inhibition of the *norA* efflux pump. Combination of CCCP with ciprofloxacin can reduce the antibiotic resistance.

Keywords: *Staphylococcus aureus*, CCCP, Antibiotic Resistance, Efflux Pump Inhibitor, *norA*.

Introduction

In recent years, several studies have supported drug efflux as a player in the emergence of resistance toward antibiotics and other antimicrobials in *S. aureus* [1],[2]. One of several contributing mechanisms to bacterial is the action of membrane-based efflux proteins with broad substrate profiles, known as multidrug resistance efflux pumps (MDR-EPs). In bacteria there are six distinct families of transporter proteins: the Small Multidrug Resistance (SMR) family, the Major

Facilitator Superfamily (MFS), the Multidrug and Toxic Compound Extrusion (MATE) superfamily, the ATP (adenosine triphosphate)-Binding Cassette (ABC) superfamily and the Resistance Nodulation Division (RND) family [3]. Recently, a sixth bacterial efflux pump group was described, namely the Proteobacterial Antimicrobial Compound Efflux (PACE) superfamily [4]. The MFS is a large family of secondary-active transporters. They use the proton motive force (PMF) as energy source [5],[6]. The most extensively studied efflux pumps in *S. aureus* are those belonging to the MFS family, with NorA as a representative example [7]. One of the important Inhibitor compound is (CCCP) was used as efflux pump inhibitor [8]. This compound destroys oxidative phosphorylation and concentration gradient of cell membranes and inhibits the activity of efflux pump in bacteria and the procedure of this method

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is similar to MIC test^[9]. Efflux Pumps Inhibitors (EPIs), which are compounds targeting the efflux activity and/or pump components, have been identified as promising therapeutic agents, as they may restore the activity of standard antibiotics^[10].

Material and Method

Bacterial Isolates: Thirty isolates of *S. aureus* were acquired from different clinical samples at the Baquba teaching hospital; these samples including nasal, wound, blood, ear, burn, UTI infection. Samples taken and right away transported to the microbiology laboratory. The *S. aureus* identification was done according to standard procedures^[11]. Bacteria were stored at -80°C as 20% glycerol stocks and subculture on mannitol salt agar at 37°C before testing^[12].

Susceptibility determination: Disk diffusion method was used on Muller- Hinton agar to determine resistance or susceptibility to ciprofloxacin, conforming to clinical laboratory standards institute ^[13]. Ciprofloxacin disc (Cip: 5µg). Plates incubation at 37°C for 24 hours. Results have been record and bacterial sensitivity was obtained through measure the diameter of the inhibition zones according to ^[13].

Minimum Inhibitory Concentration (MIC): We were re-examined all of the strains by disk diffusion method, through Muller Hinton broth dilution method based on [13]. Stock solution of Ciprofloxacin was prepared at final concentration of 10 mg/ml by dissolving

500 gm of Ciprofloxacin in 4.1 ml distilled water and the volume was completed to 10 ml and prepared a serial dilution of Ciprofloxacin between (1-2048) µg/ml according to [13]. The presence of active efflux pump inhibitor system, (CCCP) was used. Stock solution of CCCP was prepared at final concentration of 25 µg/ml by dissolving 0.5 gm of CCCP in 9.5 ml of 50% ethanol and prepared a serial dilution between (1-2048) µg/ml according to ^[13].

Identification of norA in S. aureus by PCR: Eighteen of *S. aureus* was determined by the presence of the *norA* gene by PCR as described by^[14]. *S. aureus* isolates were tested for the presence of the 620-bp PCR product of the *norA* gene using the primer: forward, TTCACCAAGCCATCAAAAAG and reverse, CTTGCCTTTCTCCAGCAATA. PCR was performed with an initial denaturation at 95°C for 5 min by one cycle, followed by 30 cycles of denaturation at 94°C for 30 Sec, annealing at 60°C for 15 Sec and elongation at 72°C for 1 min. The final elongation step was at 72°C for 7 min by one cycle.

RNA Extraction: The RNA was extracted from the *S. aureus*, isolates using a commercial TRIzol extraction kit (promega, USA) according to the manufacturer’s instructions.

Primers and Probes preparation: The *norA* primers, housekeeping gene *gmk* and probe for the *S. aureus* were supplied by promega Company. The name and sequence of primer and probe are listed in table (1).

Table (1): Primer, probe and housekeeping gene are used in the gene expression in this study

Primer Name	Primer sequences 5’3’	Reference	Annealing Tem
norA-F	TTTGTTTCAGTGCAGAATTTATGTTG	This study	55
norA-R	GGCTTGGTGAAATATCAGCTATTAAC		
gmk-R	ATC GTT TTA TCG GGA CCA TC	[15]	55
gmk-F	TCA TTA ACT ACA ACG TAA TCG TA		
norA-p	6FAM*- AGGCATAACCATAACCAGCACTCATACCACC-BHQ1*	This study	

*6FAM, 6-carboxyfluorescein; *BHQ, black hole quencher/p, probe

qRT-PCR program: The qRT-PCR program to detect the gene expression of the *norA*, gene was set; thus, the following qRT-PCR program was adopted in table (2).

Table (2): RT-PCR program

Extension	Annealing	Denaturation	Initial Denaturation	RT. Enzyme Activation	Amplified gene
72°C/30 sec	55°C/30 sec	95°C/30 sec	95°C/10 min	37°C/15 min	<i>norA</i>
40 cycle	40 cycle	40 cycle	One cycle	One cycle	

The ΔC_t between the target gene and the reference gene is calculated in the following equation:

$$\Delta C_t = C_t \text{ target gene} - C_t \text{ reference gene}$$

Then the difference between the ΔC_t of the unknown and the ΔC_t of the calibrator is calculated, giving the $\Delta\Delta C_t$ value, as the following :

$\Delta\Delta C_t = (C_t \text{ target} - C_t \text{ reference}) \text{ sample} - (C_t \text{ target} - C_t \text{ reference}) \text{ calibrator}$ The normalized target amount in the sample is then equal to $2^{-\Delta\Delta C_t}$ [16].

Results

Susceptibility Determination: Among 30 isolated of *S. aureus*, that tested by disc diffusion method, 18 of them were ciprofloxacin resistance (60%). Between ciprofloxacin resistant isolates, 18 of them had the activated efflux pump according to CCCP results. The effect of pump Inhibitor on the treatment of efflux pump shown in table (3).

Table(3): Effect of efflux pump inhibitors on MIC of Ciprofloxacin in clinical isolates

MIC $\mu\text{g/ml}$ of CIP+CCCP	MIC $\mu\text{g/ml}$ of CCCP	MIC $\mu\text{g/ml}$ of CIP	Isolate. N
4(x)	512	8	SA1
16(2x)	512	64	SA2
64(x)	512	128	SA3
128(x)	1024	256	SA4
16(3x)	512	128	SA5
32(x)	512	64	SA6
8(2x)	1024	32	SA7
128(x)	512	256	SA8
32(x)	1024	64	SA9
8(2x)	1024	32	SA10
4(3x)	512	32	SA11
4(x)	512	8	SA12
32(x)	512	64	SA13
64(x)	1024	128	SA14
32(2x)	258	128	SA15
16(2x)	1024	64	SA16
16(x)	512	32	SA17
64(4x)	1024	1024	SA18

Molecular detection of norA gene: Sixteen of 18 *S. aureus* isolates were positive for *norA* gene. The results illustrated in fig(1) demonstrated that 16 MRSA isolates were (88%) harbored *norA* gene.

Detection of norA gene expression by qRT-PCR by one-step: The study of gene expression was conducted by select (6) *S. aureus* isolates from different sources. These isolates were tested after being treated with the Ciprofloxacin separately and treated by combination of Ciprofloxacin plus CCCP. In order to utilize qPCR for measuring changes in RNA transcript levels, there are several factors that must be taken into account. For one, it is important to ensure that RNA samples are of high quality and are not contaminated with significant amounts of genomic DNA that may yield false-positive amplification in the downstream qPCR reaction. Second parameter to consider is the choice of a "one-step" (cDNA synthesis and qPCR occur sequentially in the same master mix [17] . Third, a detection method must be chosen, using either fluorescently labeled primers/probes, or that fluoresce when bound to the double-stranded PCR product, since a new probe must be synthesized for each gene of interest [18]. In this study we explain the potentiating effect of (CCCP) against expression of efflux pump genes in *S. aureus*. We used *gmk* (guanylate kinase) housekeeping gene an endogenous control .The Reference gene was used in the gene expression to clarify its expression. It remained constant in the cells or tissues under investigation and different conditions [19]. The experiment of the quantitative RT-PCR reaction was completed by using six (6) from eighteen (18) of MRSA isolates accordingly to their source . The different sources of these isolates were distributed as (SA3 wound, SA7, urin, SA8, blood, SA18 ear, SA15 burn, SA10, nasal) .The quantitative changes in the mRNA expression levels were determined using comparative threshold cycle (CT) method ($2^{-\Delta\Delta C_t}$) for MRSA isolate present in table (4).

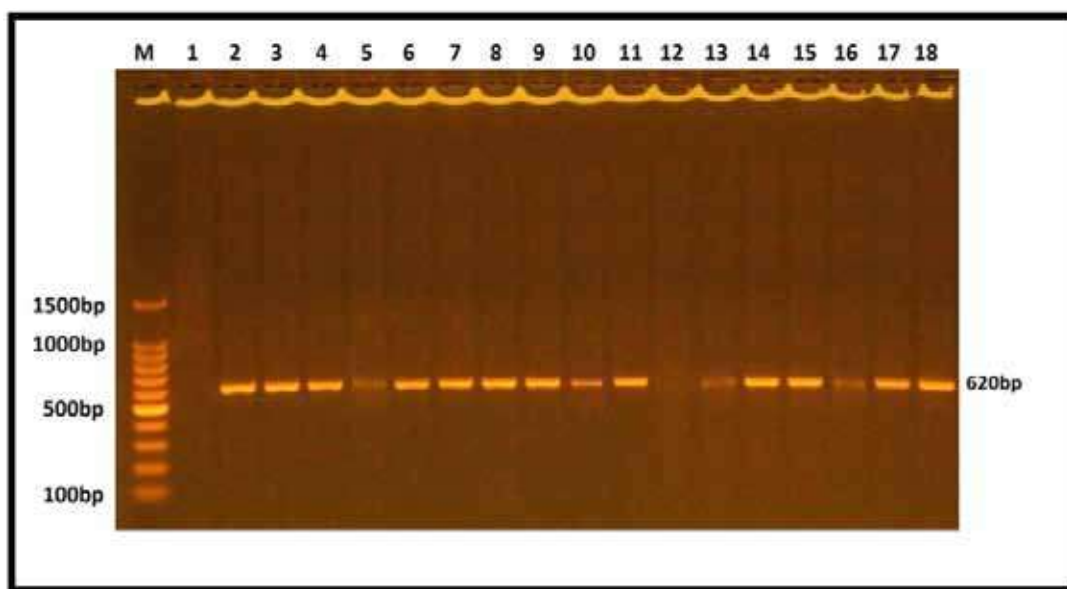


Figure (1): Agarose gel electrophoresis (2% agarose, 7V/cm, for 90 min) for norA gene (amplified size 620 bp) lanes 1-18 compared with (100 bp) DNA ladder lane 4M(SA1,12) negative amplification of norA gene, (SA2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 13, 14, 15, 16, 17, 8) positive amplification of norA gene.

Table (4): Gene expression of norA gene measured by qRT- PCR using FAM and BHQ1 Expression of norA gene compared with control (gmk reference gene)

Average	Folding	$\Delta\Delta Ct$	ΔCt	Mean norA	Mean HK	Samples	Group
1.0	1.0	0.0	2.7	13.1	10.4	3	Untreated
	1.0	0.0	3.7	13.9	10.2	7	
	1.0	0.0	0.3	16.8	16.5	8	
	1.0	0.0	2.5	15	12.5	18	
	1.0	0.0	-1.3	30.3	31.6	15	
	1.0	0.0	-1.5	17.3	18.8	10	
2.3	3.6	-1.8	0.9	15.7	14.8	3cip	Cip
	3.3	-1.7	2.0	20.1	18.1	7cip	
	0.7	0.4	0.8	19.8	19.0	8cip	
	3.9	-2.0	0.5	16.6	16.1	18cip	
	1.5	-0.6	-1.9	35.6	37.5	15cip	
	0.9	0.2	-1.3	21.1	22.4	10cip	
1.4	1.3	-0.4	2.4	17.9	15.5	3cccp	CCCP & Cip
	3.3	-1.7	2.0	18.5	16.5	7cccp	
	0.3	1.9	2.3	15.5	13.2	8cccp	
	1.5	-0.6	1.9	15.5	13.6	18cccp	
	1.7	-0.7	-2.1	31.1	33.2	15cccp	
	0.5	0.9	-0.6	19.8	20.4	10cccp	

The results demonstrated that four strains (SA3,7,15,18) revealed over expression of *norA* after treated by sub concentrations of Ciprofloxacin, no over expression of *norA* was observed in two isolates

(SA8,10) after treated with Ciprofloxacin. Also six isolates evaluated in the presence of CCCP & Cip by qRT-PCR analysis, gene expression of the *norA* was decreased in four isolates that treated with CCCP

& Cip as well as in more than half of strains only in (SA7) it remained the same as and (SA15) increase of gene expression them increase is very minor. Our result revealed that the isolates after treated with Ciprofloxacin have strong significant according to *p-value* at $P < 0.05$ in all isolates except SA7. Also our results show significant according to *p-value* at $P < 0.05$ after treated with CCCP & Cip in three isolates (SA7,15,10). These results indicate higher quantitative gene expression of *norA*. One isolates have been deposited in the National Center for Biotechnology Information (NCBI) with the accession number as Lc490694 for *norA* and the name of strain ISTM12 also same strain deposited in NCBI for 16sRNA and accession number MK775201.1

Discussion

Emergence and extension of antibiotic resistance among bacteria have led to the essential endeavor on the discovery of new antibacterial materials and modulators of antibiotic resistance. There are various mechanisms of antibiotic resistance in *S. aureus*. One of the most principal of them is the efflux pumps, which pull out antibiotics and reduction the intracellular concentration of the antibiotic^[20]. Our results confirm to the results of ^[21] which showed the gene expression was various among isolates and the gene expression increase with increasing MIC of ciprofloxacin of *S. aureus* isolates. Also ^[22] in Pakistan revealed that the efflux pump gene *norA* in *S. aureus* showed an increase in expression in the presence of Ciprofloxacin and over expression of *norA* was >3 . The study carried by ^[23] in China showed over expression of *norA* in 25 isolates from 51 isolates (49.01%) by qRT-PCR. Although different EPIs such as CCCP have been reported to block the ATP-binding site of the *norA* gene resulting in the inhibition of antimicrobial efflux and improved antimicrobial efficacy. Efflux pump activity alone is not responsible for fluoroquinolone resistance, mutations/deletions may occurs in the QRDR, *norA* coding ^[24]. Therefore, the addition of CCCP did not completely inhibit FQ resistance. This study was to investigate the inhibitory effects of CCCP on the expression of NorA efflux pump and decrease ciprofloxacin resistance in *S. aureus*. Synergistic potentiation of antibacterial effect of Ciprofloxacin with efflux pump inhibitor CCCP as well as serve as potent efflux pump inhibitors of *norA* expression. *S. aureus* and other pathogenic bacteria show altered expression patterns of their virulence genes at different infection sites depending on the growth conditions within each tissue. Therefore, analyses

of gene expression regulations under conditions that mimic host environments are important for determining bacterial pathogenesis.

Conclusions

In this study high proportion of efflux pump gene *norA* of MRSA isolates were recognized in patients of Baquba teaching hospital. Nonetheless, strong correlation was observed between phenotype and genotype of these isolates. The present study measured the synergistic effect in combination CCCP with Ciprofloxacin. This experiment also showed that the primer and probe for *S. aureus* targeting efflux pump gene was highly specific for expressing and RT-PCR has shown great probability for detecting viable pathogens.

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References

1. Furi L, Ciusa ML, Knight D, Di Lorenzo V, Tocci N, Cirasola D, Aragones L, Coelho JR, Freitas AT, Marchi E, Moce L. Evaluation of reduced susceptibility to quaternary ammonium compounds and bisbiguanides in clinical isolates and laboratory-generated mutants of *Staphylococcus aureus*. *Antimicrobial agents and chemotherapy*. (2013) Aug 1;57(8):3488-97.
2. Costa SS, Viveiros M, Rosato AE, Melo-Cristino J, Couto I. Impact of efflux in the development of multidrug resistance phenotypes in *Staphylococcus aureus*. *BMC microbiology*. (2015) Dec;15(1):232.
3. Poole K. Efflux pumps as antimicrobial resistance mechanisms. *Annals of medicine*. 2007 Jan 1;39(3):162-76.

4. Hassan KA, Liu Q, Henderson PJ, Paulsen IT. Homologs of the *Acinetobacter baumannii* AclE transporter represent a new family of bacterial multidrug efflux systems. *MBio*.(2015) Feb 27;6(1):e01982-14.
5. Du D, van Veen HW, Murakami S, Pos KM, Luisi BF. Structure, mechanism and cooperation of bacterial multidrug transporters. *Current opinion in structural biology*. (2015) Aug 1;33:76-91.
6. Schindler BD, Kaatz GW. Multidrug efflux pumps of Gram-positive bacteria. *Drug Resistance Updates*. (2016) Jul 1;27:1-3.
7. Mohammed-Ali MN, Jamalludeen NM. Isolation and characterization of bacteriophage against methicillin resistant *Staphylococcus aureus*. *J Med Microb Diagn*.(2015);5(213):2161-0703.
8. Jang S. Multidrug efflux pumps in *Staphylococcus aureus* and their clinical implications. *Journal of Microbiology*. (2016) Jan 1;54(1):1-8.
9. Mirzaie, a., noorbazargan, h., rahmati, h. and zandi, m., a study of gene expression and activity of nora efflux pump in clinical isolates of ciprofloxacin resistant *staphylococcus aureus*. *J Babol Univ Med Sci*; (2016). 18(10), PP. 63-70.
10. Truong-Bolduc QC, Dunman PM, Eidem T, Hooper DC. Transcriptional profiling analysis of the global regulator NorG, a GntR-like protein of *Staphylococcus aureus*. *Journal of bacteriology*. (2011) Nov 15;193(22):6207-14.
11. Brooks, G.F.; Carroll, K.C.; Butel, J.S. and Morse, S.A..*Jawetz Melnick and Adelbergs Medical Microbiology* . 24th.ed. The McGraw-Hill Companies, Inc., New York(2007).pp.224-232.
12. Forbes, BA., Sahm, DF., Weissfeld, AS., Bailey, & Scott's *Diagnostic Microbiology*. 12th ed. Philadelphia.,(2007). Mosby Inc.
13. CLSI. *Performance Standards for Antimicrobial Susceptibility Testing*. 27th ed. Wayne, PA: Clinical and Laboratory Standards Institute. (2017).
14. Couto I, Costa SS, Viveiros M, Martins M, Amaral L. Efflux-mediated response of *Staphylococcus aureus* exposed to ethidium bromide. *Journal of antimicrobial chemotherapy*. (2008) May 28;62(3):504-13.
15. Enright MC, Day NP, Davies CE, Peacock SJ, Spratt BG. Multilocus sequence typing for characterization of methicillin-resistant and methicillin-susceptible clones of *Staphylococcus aureus*. *Journal of clinical microbiology*. (2000) Mar 1;38(3):1008-15.
16. Schmittgen TD, Livak KJ. Analyzing real-time PCR data by the comparative C T method. *Nature protocols*. (2008) Jun;3(6):1101.
17. Valihrach L, Demnerova K. Impact of normalization method on experimental outcome using RT-qPCR in *Staphylococcus aureus*. *Journal of microbiological method*. (2012) Sep 1;90(3):214-6..
18. Bustin SA. Why the need for qPCR publication guidelines?—The case for MIQE. *Method*. (2010) Apr 1;50(4):217-26.
19. Rebouças ED, Costa JJ, Passos MJ, Passos JR, Hurk RV, Silva JR. Real time PCR and importance of housekeeping genes for normalization and quantification of mRNA expression in different tissues. *Brazilian Archives of Biology and Technology*. (2013)Feb;56(1):143-54.
20. Pourmand MR, Yousefi M, Salami SA, Amini M. Evaluation of expression of NorA efflux pump in ciprofloxacin resistant *Staphylococcus aureus* against hexahydroquinoline derivative by real-time PCR. *Acta Medica Iranica*. (2014):424-9.
21. Mohammed F, Marjani A, Ahlam KD. Identification of an efflux pump gene NorA in methicillin resistant *Staphylococcus aureus* in Baghdad. *World J Pharmaceutical Res*(2015).;4:346-56.
22. Khan SA. Molecular Characterization of Fluoroquinolone Resistance of Methicillin-Resistant Clinical *Staphylococcus aureus* Isolates from Rawalpindi, Pakistan. *Medical Research Archives*. (2015) Sep 4;2(2).
23. Liu Q, Zhao H, Han L, Shu W, Wu Q, Ni Y. Frequency of biocide-resistant genes and susceptibility to chlorhexidine in high-level mupirocin-resistant, methicillin-resistant *Staphylococcus aureus* (MuH MRSA). *Diagnostic microbiology and infectious disease*. 2015) Aug 1;82(4):278-83.)
24. Kwak YG, Truong-Bolduc QC, Bin Kim H, Song KH, Kim ES, Hooper DC. Association of norB over expression and fluoroquinolone resistance in clinical isolates of *Staphylococcus aureus* from Korea. *Journal of Antimicrobial Chemotherapy*. (2013) Aug 8;68(12):2766-72.

Serum Citrin and γ -Glutamyl Transferase as Biomarkers for Infantile Cholestasis Severity

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Abstract

One of the most important parameters to evaluate severity and type of cholestasis disease is gamma-glutamyl transferase and citrin protein measurements. The objective of this study was to assess the clinical value of serum citrin protein with gamma-glutamyl transferase in children with cholestasis. 60 subjects with diseases and 25 healthy subjects distributed into three groups, citrin and gamma-glutamyl transferase were measured for all case and control studies by enzyme linked immunosorbent Assay. The results showed serum citrin has a highly significantly decreased in an intra- and extrahepatic cholestasis groups when compared with control ($P < 0.001$), serum gamma-glutamyl transferase has a highly significantly elevated in an intrahepatic cholestasis group when compared with control ($P < 0.003$). From these findings it was concluded that serum gamma-glutamyl transferase level is a good marker in determining the severity of cholestasis disease, serum citrin may be useful in future to diagnose the cholestasis caused by citrin deficiency.

Keywords: γ -Glutamyl transferase (GGT), Biliary atresia (BA), Alagille syndrome (AGS), Progressive familial intrahepatic cholestasis (PFIC), Idiopathic neonatal hepatitis (INH), Citrin deficiency (CD).

Introduction

In neonate the jaundice is common, usually secondary to unconjugated or indirect hyperbilirubinemia, prolonged beyond 14 days of life, of new-onset, or at high levels, it must be evaluated for potentially life-threatening causes, such as evolving hepatobiliary dysfunction or infection. Cholestasis is the end effect of obstruction of the normal excretion of bile from the liver, giving rise to the abnormal accumulation of bile salts, bilirubin and lipids and abnormal level of GGT in the blood, the cholestasis in the infant may present as jaundice, pruritus, fat-soluble vitamin deficiency, or may evolve following or during acute liver failure, also anatomic or functional biliary obstruction is often

reported by the presence of acholic stools¹, dark urine or acholic stools or examination findings of hepatosplenomegaly and as cited².

Biliary Atresia (BA): Is defined as biliary obstruction caused by progressive fibrosis of intrahepatic and extrahepatic bile ducts with an unknown pathogenesis, if isn't treated immediately³.

Alagille syndrome (AGS): Is an autosomal dominant disorder affected by defects in the notch signalling pathway that affect multiple organ systems with phenotypic variability, AGS can be diagnosed clinically through the existence of as a minimum three of five major features: chronic cholestasis, ocular abnormalities, peculiar face phenotypes, skeletal abnormalities and cardiac disease⁴⁻⁵, also one of most important syndrome is related with a paucity of interlobular bile ducts histopathologically⁶.

Progressive familial intrahepatic cholestasis (PFIC): Define as mutations in several genes encoding proteins involved in bile acid homeostasis cause neonatal

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cholestasis. Progressive familial intrahepatic cholestasis (PFIC) types 1, 2 and 3 are a group of cholestatic situations caused by mutations in ATP8B1, ABCB11 and ABCB4 respectively, and defects in TJP2, encoding tight junction protein 2, can also cause severe cholestatic liver disease⁷⁻⁸. Several heterozygous variants in known PFIC genes may participate to disease in some cases⁹, but up to one third of cases stay idiopathic¹⁰. Infants usually have deep pruritus, but may also be presented with jaundice resulted from the cutaneous and intrahepatic accumulation of bile acids, respectively¹¹. A significant clinical finding in individuals with PFIC types 1 and 2 is the existence of a normal or low GGT out of proportion to the degree of cholestasis¹². Patients with PFIC type 3 have increased GGT².

Idiopathic neonatal hepatitis (INH)

Is a term employed to explain prolonged neonatal intrahepatic cholestasis in the first six months of life, whose histopathological lesion is characterized by the existence of “giant cells”, in the lack of other causes of type obstructive, infectious or genetic in whom a significant cause could not be recognized, the occurrence of INH is approximately 15% of neonatal cholestasis cases¹³.

Citrin Deficiency (CD): Is a mendelian disease existence because of biallelic mutations of SLC25A13 gene and in neonates of infants called neonatal intrahepatic cholestasis caused by citrin deficiency¹⁴. The protein product of this gene is designated as citrin, which, as the liver-type aspartate/glutamate carrier isoform 2 (AGC2), its role to export aspartate from the mitochondrial matrix in exchange for cytosolic glutamate and H⁺, playing significant roles in the urea cycle and malate-aspartate shuttle¹⁵⁻¹⁶. Failure to thrive and dyslipidemia are main in neonatal intrahepatic cholestasis caused by citrin deficiency¹⁷⁻²⁰. Specific metabolic and genetic diagnosis tests are time-consuming, costly and only available in a small number of academic centers, and they typically take weeks to months, these have restricted its use in the early diagnosis and treatment of infantile cholestasis, so to rapidly and correctly manage clinical patients, hard works are needed to develop the efficacy and accuracy of early diagnosis for infantile cholestatic patients²¹⁻²².

γ -Glutamyl Transferase (GGT): Also one of the most important parameter to evaluate the severity of cholestasis disease is (GGT) measurement, which it is a plasma membrane-bound enzyme, is an essential catalyst which facilitates glutathione hydrolysis, it

is established in many organs, but its presence in the liver has an important diagnostic use, the main role of cellular GGT is the metabolism of extracellular reduced glutathione, permitting precursor amino acids to be incorporated and reused for intracellular glutathione synthesis²³. In Allagile syndrome about 3 to 20 times of normal GGT¹, Low/normal levels of GGT in idiopathic neonatal hepatitis infants may be a predictor of more severe but recoverable disease²⁴.

Materials and Method

The study was executed during the term from January 2018 to June 2018 this study included 80 subjects with diseases and 25 healthy subjects and distributed into three groups : first group includes 40 patients with intrahepatic cholestasis diseases, second group: includes 20 patients with extrahepatic cholestasis diseases and third group: represents the apparently healthy control group which comprises of 25 subjects who do not suffer from liver disease or any chronic illness and matched with age and gender to patient groups. All samples were collected from Baghdad, Iraq, Al-Imameen Al-Kademen Medical City, Digestive Center at Medical City and Child’s Central Teaching Hospital. The exclusion criteria were representing by selected the patients who were do not suffered from dyslipidaemia and diabetes mellitus or any other disease that may interfere with the study and patients who were not underwent any type of therapy such as ursodeoxycholic acid and were stopped the treatment two weeks before investigations. The preparation of blood samples were done by collected about five millilitres of blood that obtained from veins of patients having cholestasis and healthy control subjects. Blood samples were left for 20 minutes at room temperature. After coagulation, sera were separated by centrifugation at 3000 rpm. for 10 min, aspirated and stored at -20 until assayed for GGT and citrin. They were measured using enzyme-linked immunosorbent assay (ELISA) kits. The human gamma-glutamyl transferase and human SLC25A13/citrin kits were obtained from kono Biotech Company. Ethical approval was obtained from institutional board review of school of medicine, Alnahrain University with reference number 14/75/666/01102017.

Data were analyzed using SPSS v.20 descriptive statistic were expressed as median and range. Inferential statistics were done by using Mann-Whitney test for dichotomous variables and Kruskal Wallis test for trichotomous variables.

Results

Table (1): Comparison between control vs three study groups by Mann Whitney test

Parameters		Control N=25	IHC N=40	EHC N=20
Citrin (pg/ml)	Median	175.0	49.5	40.5
	Range	49.0-802.0	17.0-700.0	11.0-69.0
	P value		<0.001	<0.001
GGT (ng/L)	Median	395.0	175.5	485.0
	Range	164.0-1573.0	80.0-1694.0	122.0-950.0
	P value		0.003	0.918

Table (2): Comparison between intra and extrahepatic cholestasis groups by Mann Whitney test

Parameters		IHC N=40	EHC N=20	P value
Citrin (pg/mL)	Median	49.5	40.5	0.121
	Range	17.0-700.0	11.0-69.0	
GGT (ng/L)	Median	175.5	485.0	0.183
	Range	80.0-1694.0	122.0-950.0	

Table (3): Comparison of citrin and GGT in IHC group according to cause by Kruskal Wallis test

Parameters		Allagile Syndrome N=12	PFIC N=15	Undiagnosed N=13
Citrin (pg/mL)	Median	53.0	45.5	45.5
	Range	17.0-700.0	32.0-88.0	31.0-157.0
	P value	0.601		
GGT (ng/L)	Median	1157.0	159.0	161.0
	Range	200.0-1694.0	105.0-242.0	80.0-659.0
	P value	0.002		

The median of serum citrin in the control, intra and extra-hepatic cholestasis groups were (175, 49.5 and 40.5) pg/ml respectively, has a highly significantly decreased in an intra- and extrahepatic cholestasis groups when compared with control ($P < 0.001$) but the median serum γ -glutamyl transferase in the control, intra and extra-hepatic cholestasis groups were (395, 175.5 and 485) ng/L respectively, has a highly significantly elevated in an intrahepatic cholestasis group when compared with control ($P < 0.003$) and has no significant difference when compared the extrahepatic cholestasis group with control group ($P = 0.918$) according to the Mann Whitney test as shown in table (1).

There was no statistical difference between the intrahepatic cholestatic patients and extrahepatic cholestatic group in serum citrin and serum γ -glutamyl transferase ($p = 0.121$ and 0.183) respectively according to the Mann Whitney test as shown in table (2). There was no statistical difference in serum citrin when compared the causes type of an intrahepatic cholestasis

group ($p = 0.601$). Also there was a significant elevated in serum γ -glutamyl transferase when compared Allagile syndrome group with PFIC and undiagnosed groups of an intrahepatic cholestasis group ($p = 0.002$) according to cause by Kruskal Wallis test as shown in table (3).

Discussion and Conclusion

γ -glutamyl transferase showed decreased in patients with intrahepatic cholestasis group but in extrahepatic cholestasis group showed no difference when compared with control group due to low level of γ -glutamyl transferase in the type progressive familial intrahepatic cholestasis and idiopathic neonatal cholestasis when compared with control as agreed with the result of previous study²⁴, a probable mechanism be presents to account for the low GGT levels and its association with worse liver disease. Perhaps defects in the hepatocellular canalicular adenosine triphosphate (ATP) dependent transport system drawn in bile formation and transport like to PFIC 1 or 2 may be also be occupied,

heterozygosity for the ATP8B1 gene or the ABCB11 gene has been postulated and, previously, heterozygosity for the bile salt export pump (BSEP) gene has been reported in association with transient neonatal cholestasis and normal GGT²⁵, as shown in table (1). But there is no difference when compared intrahepatic cholestasis group with extrahepatic cholestasis because each group had high level of γ -glutamyl transferase due to type of cholestasis: Allagile Syndrome and Biliary Atresia which agree with the result of previous study²⁶⁻²⁷, as shown in table (2).

According to the present data, the results of this study for the correlation analysis were showed a positive correlation between γ -glutamyl transferase, citrin and allagile syndrome and progressive familial intrahepatic cholestasis groups as shown in table (3).

In allagile syndrome and progressive familial intrahepatic cholestasis patients the citrin showed no difference when compared with undiagnosed group of intrahepatic cholestasis but γ -glutamyl transferase showed significant correlation with outcome of these groups in such it was elevated in allagile syndrome group when compared with progressive familial intrahepatic cholestasis and undiagnosed groups in which these results were in agreement with previous studies^{24,27}, so there was a significant decreased in an undiagnosed group in which this study suggest that undiagnosed group patients they were probably had either progressive familial intrahepatic cholestasis or idiopathic neonatal hepatitis after biopsy diagnosis making the chance of happening one of them that could suggested from the level of γ -glutamyl transferase in sera as agreed with the results of previous studies²⁴.

This study revealed that low levels of citrin was associated with thesis that may cholestatic patients have citrin deficiency origin of cholestasis disease, which agree with the finding of the significant association between the low levels of citrin and cholestasis disease may be attributed to mutation in SLC25A13 gene that responsible for citrin protein/carrier synthesis caused citrin deficiency^{18,22,28-29}.

Limitations: One of most difficult issues is the number of patient that suffer from cholestasis in Iraq and their knowledge how to get early to specialist centers for diagnosis when they suffer from jaundice in long term which may be having cholestasis in fact.

Conclusion

No studies have examined the relationship between citrin protein as biomarker and cholestatic diseases in humans, and this present study suggested the citrin protein as possible biomarker in laboratory biochemical findings to distinguish in future the intrahepatic cholestasis as citrin deficiency type from other metabolic or genetic types and to exclude specific metabolic and genetic diagnosis tests which are time-consuming, costly and only available in a small number of academic centers, and they typically take weeks to months. This new citrin biomarker test help in future for the early diagnosis and treatment of infantile cholestasis caused by citrin deficiency and to rapidly and correctly manage clinical patients and help the researchers in future to depend on this study results to develop the citrin method for evaluation the cholestatic patients by increase the number of patients.

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Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

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References

1. Lane, Erin and Karen F. Murray. "Neonatal Cholestasis". *Pediatric Clinics of North America*. 2017, 64(3), 621–39.
2. Fawaz, Rima et al. "Guideline for the Evaluation of Cholestatic Jaundice in Infants". *Journal of Pediatric Gastroenterology and Nutrition*. 2017, 64(1), 154–68.
3. Song, Zai, Rui Dong, Yuxia Fan, and Shan Zheng. "Identification of Serum Protein Biomarkers in Biliary Atresia by Mass Spectrometry and Enzyme-Linked Immunosorbent Assay". *Journal*

- of Pediatric Gastroenterology and Nutrition. 2012, 55(4), 370–75.
4. Subramaniam, P. et al. “Diagnosis of Alagille Syndrome-25 Years of Experience at King’s College Hospital”. *Journal of Pediatric Gastroenterology and Nutrition*. 2011, 52(1), 84–89.
 5. Liu, Yan, Hong Wang, Chen Dong, Jie-xiong Feng, and Zhi-hua Huang. “Clinical Features and Genetic Analysis of Pediatric Patients with Alagille Syndrome Presenting Initially with Liver Function Abnormalities”. 2018, 38(2), 304–305.
 6. Kaye, Adam J. et al. “Effect of Kasai Procedure on Hepatic Outcome in Alagille Syndrome”. *Journal of Pediatric Gastroenterology and Nutrition* 51. 2010, (3), 319–21.
 7. Kamath, Binita M., Kathleen B. Schwarz, and Nedim Hadžić. “Alagille Syndrome and Liver Transplantation”. *Journal of Pediatric Gastroenterology and Nutrition*. 2010, 50(1), 11–15.
 8. Sambrotta, Melissa et al. “Mutations in TJP2 Cause Progressive Cholestatic Liver Disease”. *Nature Genetics*. 2014, 46(4), 326–28.
 9. Goldschmidt, Monique L. et al. “Increased Frequency of Double and Triple Heterozygous Gene Variants in Children with Intrahepatic Cholestasis”. *Hepatology Research*. 2016, 46(4), 306–11.
 10. Fischler, Björn and Thierry Lamireau. “Cholestasis in the Newborn and Infant”. *Clinics and Research in Hepatology and Gastroenterology*. 2014, 38(3), 263–67.
 11. Lemoine, Caroline, Tanya Bhardwaj, Lee M. Bass, and Riccardo A. Superina. “Outcomes Following Partial External Biliary Diversion in Patients with Progressive Familial Intrahepatic Cholestasis”. *Journal of Pediatric Surgery*. 2017, 52(2), 268–72.
 12. Lu, Fang Ting et al. “ γ -Glutamyl Transpeptidase Level As a Screening Marker Among Diverse Etiologies of Infantile Intrahepatic Cholestasis”. *Journal of Pediatric Gastroenterology and Nutrition*. 2014, 59(6), 695–701.
 13. Ledesma-Ramírez, Sindy. “Hepatitis Neonatal Idiopática.” *Revista Mexicana de Pediatría*. 2016, 83(6), 208–14.
 14. Zhang, Zhan-Hui, Wei-Xia Lin, Qi-Qi Zheng, Li Guo, and 61 Song. “Molecular Diagnosis of Citrin Deficiency in an Infant with Intrahepatic Cholestasis: Identification of a 21.7kb Gross Deletion That Completely Silences the Transcriptional and Translational Expression of the Affected SLC25A13 Allele.” *Oncotarget*. 2017, 8(50), 87182–93.
 15. Palmieri, Ferdinando. “The Mitochondrial Transporter Family SLC25: Identification, Properties and Physiopathology”. *Molecular Aspects of Medicine*. 2013, 34(2–3), 465–84.
 16. Palmieri, Ferdinando. “Mitochondrial Transporters of the SLC25 Family and Associated Diseases: A Review”. *Journal of Inherited Metabolic Disease*. 2014, 37(4), 565–75.
 17. Song, Yuan Zong et al. “Genotypic and Phenotypic Features of Citrin Deficiency: Five-Year Experience in a Chinese Pediatric Center”. *International Journal of Molecular Medicine*. 2011, 28(1), 33–40.
 18. Song, Yuan Zong et al. “SLC25A13 Gene Analysis in Citrin Deficiency: Sixteen Novel Mutations in East Asian Patients, and the Mutation Distribution in a Large Pediatric Cohort in China”. *PLoS ONE*. 2013, 8(9), 15–18.
 19. Saheki, Takeyori et al. “Metabolomic Analysis Reveals Hepatic Metabolite Perturbations in Citrin/mitochondrial Glycerol-3-Phosphate Dehydrogenase Double-Knockout Mice, a Model of Human Citrin Deficiency”. *Molecular Genetics and Metabolism*. 2011, 104(4), 492–500.
 20. Seak Hee et al. “Biochemical and Molecular Characteristics of Citrin Deficiency in Korean Children”. *Journal of Human Genetics*. 2017, 62(2), 305–7.
 21. Chen, Huey Ling et al. “Diagnosis of BSEP/ ABCB11 Mutations in Asian Patients with Cholestasis Using Denaturing High Performance Liquid Chromatography”. *Journal of Pediatrics*. 2008, 153(6).
 22. Chen, Szu Ta et al. “Diagnosis of Neonatal Intrahepatic Cholestasis Caused by Citrin Deficiency Using High-Resolution Melting Analysis and a Clinical Scoring System”. *Journal of Pediatrics*. 2012, 161(4), 626–631.e2.
 23. Irie, M. et al. “Levels of the Oxidative Stress Marker γ -Glutamyltranspeptidase at Different Stages of Nonalcoholic Fatty Liver Disease”. *Journal of International Medical Research*. 2012, 40(3), 924–33.

24. Jian She Wang et al. "Significance of low or normal serum gamma glutamyl transferase level in infants with idiopathic neonatal hepatitis". *European Journal of Pediatrics* 2006, 165, 795–801.
25. Hermeziu et al. "Heterozygous bile salt export pump deficiency: a possible genetic predisposition to transient neonatal cholestasis". 2006, *JPGN* 42(1), 114–116.
26. Maria Angela et al. "Differential diagnosis of neonatal cholestasis: clinical and laboratory parameters". *J Pediatr (Rio J)*. 2010, 86(1), 40-44.
27. Han, S. et al. "Imaging Findings of Alagille Syndrome in Young Infants: Differentiation from Biliary Atresia". *British Journal of Radiology*. 2017, 90(1077), 20170406.
28. Szu-Ta Chen et al. "Diagnosis of Neonatal Intrahepatic Cholestasis Caused by Citrin Deficiency Using High-Resolution Melting Analysis and a Clinical Scoring System". *J Pediatr* 2012, 161, 626-31.
29. Yuan-Zong Song et al. "SLC25A13 Gene Analysis in Citrin Deficiency: Sixteen Novel Mutations in East Asian Patients, and the Mutation Distribution in a Large Pediatric Cohort in China" 2013, Volume 8, Issue 9, 1-13.

Some Metal Complexes of Mixed 1, 10 Phenanthroline and Schiff Base Ligand; Syntheses, Spectroscopic and DNA Cleavage Studies

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Abstract

Two series of metal complexes were prepared in this study, the first set from reaction of metal salts with Schiff base (HL¹) as a primary ligand (which prepared by condensation of Benzidine, 2-hydroxynaphthaldehyd and 9-anthracen carbaldehyd in a one pot step with 1:1:1 molar ratio. The second series was synthesized by reaction of two mixed ligands [HL¹] and 1,10-phenanthroline [L²] with the metal saltes in a 1:1:1 molar ratio. The Schiff base ligand and mixed ligand chelates characterization based on spectroscopic method; FT-IR, UV-Vis, ¹H-NMR along with elemental analysis, metal content, melting point, magnetic susceptibility and conductance measurements. The Schiff base ligand and mixed ligand complexes were found to have the general formulae [M(L¹)₂(H₂O)₂]. H₂O and [M(L¹)(1,10phen)] Cl. H₂O, where (M=Mn(II), Co(II), Cu(II), Ni(II), Zn(II) and Cd(II) respectively. Octahedral geometrical structures were proposed for (HL¹) complexes while a tetrahedral structure was proposed for the mixed ligand complexes. The interactions of prepared compounds with DNA were investigated by gel electrophoresis and Ultra-Violet spectroscopy. The results of DNA binding and cleavage experiments displayed that some metal complexes were able to interact with DNA in intercalative mode, these results suggested the possible utilization of metal complexes for pharmaceutical applications.

Keywords: Schiff-base ligand, Benzidine, DNA cleavage, DNA Interactions.

Introduction

Heterocyclic compounds classified as important class of compounds due to the high biological activities (anticancer, anti-inflammatory, antifungal and antibacterial) [1]. Some natural products, like nucleic acids, plants, chlorophyll and alkaloids contain heterocyclic system in their structure. Because of its ability to form stable complexes with many transition metals, heterocyclic compounds considered as important materials in coordination chemistry[2]. The components of the prepared (HL) ligand {L Khokra, 2016 #160;L

Khokra, 2016 #160;L Khokra, 2016 #160;L Khokra, 2016 #160}[Benzidine, 2-hydroxynaphthaldehyd and 9-Anthrylcarboxaldehyde], were commonly used in the field of medicinal chemistry because of their pharmacological, photographic and catalytic application[2,3]. Schiff bases derived from 2-hydroxy-1-naphthaldehyde have attracted a great interest for their photophysical and biological properties (non-linear optical behavior, thermo and phototropism). In the present study Schiff base ligand HL¹ derived from the condensation of Benzidine with 2-hydroxynaphthaldehyd and 9-anthrace carbaldehyd and its mixed ligand complexes in the presence of (1,10-phen) 1,10-phenanthroline as a secondary ligand have been prepared and characterized using different spectroscopic tools and thermal analyses. Furthermore, DNA cleavage properties of the metal complexes also have been evaluated[4].

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Materials and Method

Chemicals: All chemicals used were of the analytical grade of highest purity available. They included binzidine (Sigma/USA), 2-hydroxynaphthaldehyed (Aldrich/USA) and 9-anthracarbaldehyed (Sigma-Aldrich). The metal salts of $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$ (B.D.H), $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ (Merck), $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$, ZnCl_2 , $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (Fluka) and CdCl_2 (BDH) were used. Organic solvents were spectroscopic pure included absolute ethanol Sigma- Aldrich and Dimethyl sulfoxide (DMSO), acetic acid and Chloroform were providing from Sigma-Aldrich/USA.

DNA extraction and cleavage: DNA was extracted from donors blood samples following the protocol leaflet of gsyncTM DNA extraction kit from Geneaid/Taiwan.

Physical measurements: Melting points for prepared complexes were measured by electro thermal (Stuart melting point apparatus). Infrared spectra were recorded as potassium bromide by a Shimadzu 8400S FTIR spectrophotometer in the range 4000-400 cm^{-1} . The electronic spectra of the compounds were recorded by using double-beam (UV-Vis) spectrophotometer type UV 160A. ¹H- NMR spectra was acquired in DMSO-d⁶ solution using a Bruker-400 MHz at University of Tehran, Islamic Republic of Iran. The Chloride contents were determined using potentiometer titration method on a (686-Titro processor- 665. Dosimat Matron/Swiss). Mass spectra of ligand HL¹ were obtained by Electron Impact mass spectroscopy using Agilent Technologies Mod.5975C VL MSD. The spectra were recorded at University of Tehran, Islamic Republic of Iran. Electrical Conductivity measurements of the complexes were made with DMSO (10^{-3} mole.L⁻¹) solutions using model 4071 digital conductivity meter. Thermogravimetric analysis was carried out using Differential Scanning Calorimetry (DSC) on STA PT-600 Linseis Company/Germany. The measurement was conducted under argon atmosphere at a heating rate 10°C/min. Samples were recorded at College of Education for Pure Science (Ibn Al-Haitham) Baghdad University.

Synthesis:

Synthesis of ligand [HL¹]: The ligand was prepared from the reaction of (0.155g,1mmol) 2-Hydroxynaphthaldehyed and (0.185g,1mmol) 9-anthracencarbaldehyed with Benzidine (0.16g5,1mmol) in (30ml) ethanol with continuous stirring and (4-5) drops of (CH₃COOH) glacial acetic

acid. The reaction mixture was left under reflux at (70-80°C) in water bath for (5-6) hrs. Orange color product was obtained, separated by filtration after cooling, and finally washed with ethanol hot. This product yield was almost quantitative (63%) (C₃₈H₂₆N₂O) Molecular Weight: 526.64 g/mol. The reaction is shown in (scheme 1). Yield (0.9g,%63), M.P=215°C. IR data (cm^{-1}): 3437 ν (OH), 1622 (ν) ν (C=N), (1159, 1309) ν (C-N). The ¹H NMR spectrum of the ligand in DMSO-d₆ showed peaks at; δ H(300 MHz, DMSO-d₆: 9.9(OH), 8.9, 8.92(-N=C-H),6.58-8.2 (Ar-H),(3.29-3.45)(HDO).

Synthesis of ligand [HL¹] complexes.

Synthesis of [Mn(L¹)₂(H₂O)₂] (1): The metal complexes were prepared by adding (25ml) of ethanol solution of metal chloride (0.197g,1mmole) with ethanol solution of the prepared Schiff base (0.165g, 2mmole) followed by drop wise addition of KOH. The respective ligand, maintain the stoichiometric (1: 2) metal: ligand ratios. Reaction mixture was heated under reflux for (3-4) hours with constant stirring on a magnetic stirrer on a water bath and the solid metal complex compound that precipitated out were filtered and then washed several times with hot ethanol. Yield (73%) of the title complex [MnC₇₈H₅₆N₄O₂],m.p: (275) was obtained. See Scheme (2).M(II) = Mn, Co, Ni, Cu, Zn, Cd, n= 6(Co, Ni), 4(Mn), 2(Cu), 0(Zn, Cd), m=0; n=0

Synthesis of [Co(L¹)₂(H₂O)₂](2), [Ni(L¹)₂(H₂O)₂](3), [Cu(L¹)₂(H₂O)₂](4), [Zn(L¹)₂(H₂O)₂](5) and [Cd(L¹)₂(H₂O)₂](6)

A similar method to that mentioned in synthesis of Co (II) complex was used to synthesized the complexes of [HL¹] with MCl₂.nH₂O M(II) = [Cd (n=0),Zn (n=0), Cu (n=2), Mn (n=4), Co (n=6) and Ni (n=6)] ions. The physical properties of the complexes and their reactant quantity displayed in (Table 1).

Synthesis of the mixed ligand complexes: The present mixed ligand chelates were synthesized by adding solution of (20mL) (60-70°C) of the Schiff base ligand (1mmol, 0.5g) and (1,10-phenanthroline) (1mmol, 0.17g) with stirring and gradually to ethanolic KOH solution (1mmol, 0.19g) of metal chloride dissolved in absolute ethanol (20 mL). The mixture in each case was in stoichiometric amount (1:1:1) (Metal: ligand: (1,10-phen)) molar ratio. The resulting mixtures were refluxed for (4h) where upon the complexes were precipitated. They were separated by filtration, washed many times with ethanol and recrystallized from hot ethanol and

finally dried in air, the synthetic route presented in Scheme 3.

Results and Discussion

FT-IR spectrum of ligand [HL¹]: The FT-IR spectrum for (HL¹) showed a strong broad band at (3433) cm⁻¹ may indicate the presence of (N...H-O) and (NH...O-H) groups intramolecular hydrogen bonding due to phenolic OH groups of the phenol-imine forms, compared with the peak of the 2-hydroxy-1-naphthaldehyde at (3100) cm⁻¹[5]. The spectrum showed a band in the region (1622) cm⁻¹ stretching frequency of azomethine group (C=N). The appearance of this band and the disappearance of the two aldehydic carbonyl (C=O) bands of the 9-anthracarbaldehyde and 2-hydroxy-1-naphthaldehyde at (1650 and 1668) cm⁻¹ respectively, and disappearance of two bands of NH₂ groups, which indicated the involvement of the primary amine and aldehyde groups in the formation of the Schiff base. The medium intensity bands observed for ligand in the (1309) cm⁻¹ was assigned to ν (C-O) phenolic group vibration[6].

The Electronic Spectrum of ligand [HL¹]: The Electronic spectrum of [HL¹] shows peaks of shortest wave length presenting at (270 nm) (37037.04 cm⁻¹) (ϵ_{\max} =1.865 molar⁻¹ cm⁻¹) and (327 nm) (30581.04 cm⁻¹) (ϵ_{\max} =1.396 molar⁻¹ cm⁻¹) may be assigned to (π - π^* or n - π^*) transition of Schiff base aromatic rings [7].

Finally the peak at the range (433 nm) (23094.69 cm⁻¹) (ϵ_{\max} =2.179 molar⁻¹ cm⁻¹) in the Schiff base spectrum may be belonged to the (C=N) imine group and this peak may refer to the keto-amine quinoid tautomer shape of the Schiff base [8].

¹H-NMR Spectrum of ligand [HL¹]: The ¹H NMR spectra of naphthalimine derivative (HL¹) show that both phenol-imine form and keto-amine form are in equilibrium. Aromatic ring protons assigned by the multiplet chemical shifts at (δ =6.58-7.45 ppm) range [9]. The sharp signal at chemical shift (δ =8.9 and 8.92 ppm) can be assigned to the proton of the imine group proton (C=N)[10]. The singlet chemical shift at (δ =9.85 ppm) may be attributed to NH group, this confirmed the fact that there is ketotautomerism for the synthesized ligand[11]. The signal at (δ =9.9 ppm) may be considered to the OH proton in the carbonyl ring because of H.B. intramolecular type with the nitrogen (N) atom from the naphthalene ring (NH...O-H) and (N...H-O)[12]. The spectrum displayed chemical shifts at (δ _H = 2.51 ppm and 3.29 ppm) referred to DMSO, and the presence of water molecules in the solvent respectively[13].

Mass Spectrum of [HL¹]: The mass spectrum of (HL¹) is depicted in Figure (1). The parent ion peak adopted at $m/z^+ = 526.6$ [M+1]⁺ for C₃₈H₂₆N₂O; requires = 526.6[14]. The other peaks detected at $m/z^+ = 349.5$ -105.15 correspond to [C₂₄H₁₇N₂O]⁺-[C₇H₈N⁺]⁺.

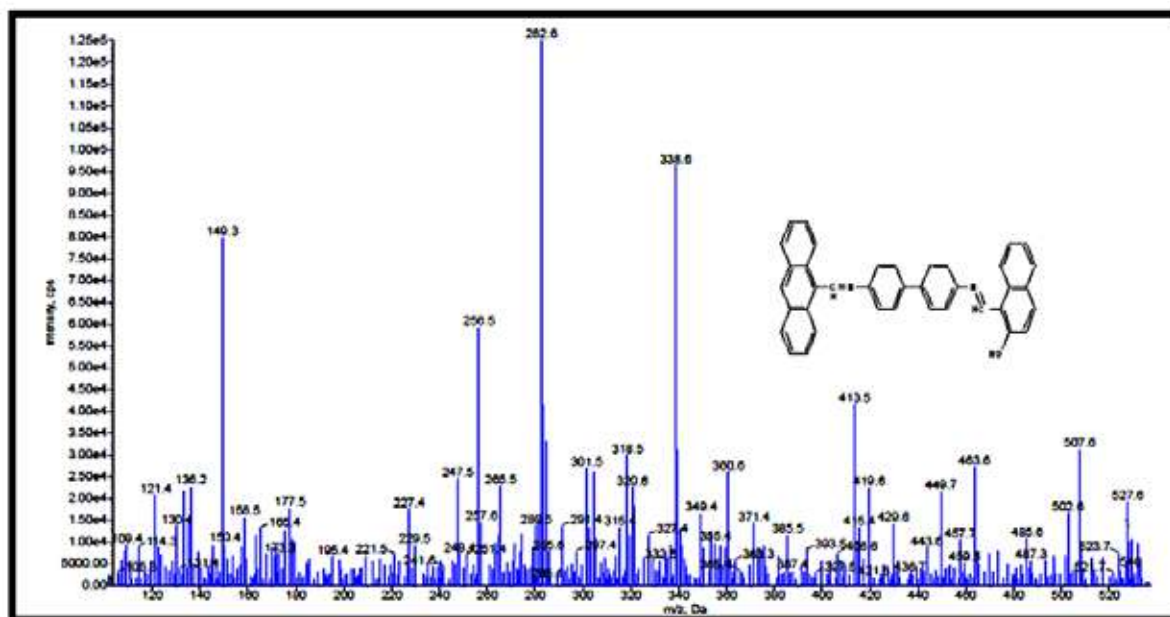


Fig. (1): GC-Mass spectrum of ligand [HL¹]

Thermal Decomposition of ligand [HL¹]: The thermo gram for ligand [HL¹] is placed in Figure (2). In the TGA curve, peak recognized at 346.34°C is related to the loss of (Oxygen) portions, (det. = 3.01534%, calc. = 3.0326%). The second step at 470.93°C that designated the loss of (C₂₁H₁₅N) fragment, (obs. = 53.35%, calc. = 53.38%). The third step at 595.34°C is related to the loss of (C₁₂H₁₀N) segments, (obs. = 12.46%, calc. = 12.92%).

The DSC analysis curve proved peaks at (248.4, 267.6, 595.34)°C refer to an endothermic decomposition process. Peaks Observed at 346.34 and 470.93°C were related to exothermic decomposition processes. The exothermic and endothermic peaks may demonstrate ignition of the natural ligand in an argon atmosphere. The last endothermic pinnacle may imply the ligand bond breaking [15].

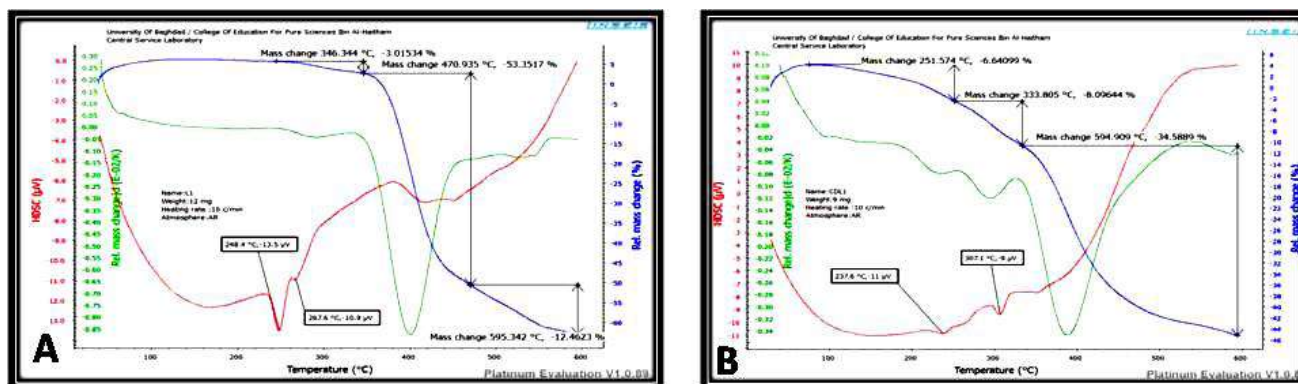


Fig. (2): (TGA and DSC) thermo gram of, A: [HL¹]Cl₂ and of, B: [Cd(L¹)₂(H₂O)₂] in an argon atmosphere

DNA Cleavage: Three types of DNA cleavage can be distinguished, namely 1-DNA hydrolysis, 2-oxidative cleavage and 3-photochemical cleavage, although the last two categories are quite closely related to each other. The interaction of metal complexes with DNA via intercalation has been explored by agarose (gel electrophoresis) and UV-Vis spectroscopy [16]. Many researchers attempt to study the interaction of DNA with small molecular models, because this is the target inside the living cells in order to try treating a wide range of diseases. The present study included the use of gel electrophoresis to ensure the occurrence of DNA cleavage

by incubation times 1 and 24 hours. The results showed that the longer the incubation period of the chemical compound in the presence of DNA more interaction achieved; that means the occurrence of DNA cleavage will be more. In addition to gel electrophoresis, the use of ultraviolet spectroscopy for chemical compounds in the presence of DNA for 1 and 24 hours was observed which results showed that the highest absorption peak of the compound before the addition of DNA and after the addition of DNA where a difference in the absorption peaks was observed and this indicates the occurrence of interaction between DNA and chemical compound [17].

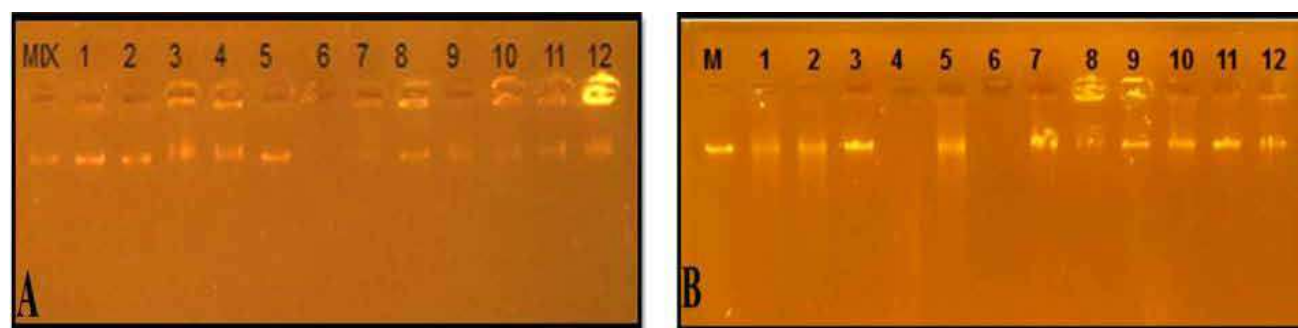


Fig. (3): Electrophoretograms of cleavage of DNA by metal (II) complexes (10µg/mL) in the absence of external agent at pH = 7.1, 1h incubation at 37°C. Lane (mix), DNA+DMSO) control;

Ligand one=1-((1E)-((4'-(anthracen-9-ylmethylene) amino)-[1,1'-biphenyl]-4-yl) imino) methyl) naphthalen-2-ol+ metal . Ligand two=HL¹+1, 10-phen+metal

While UV-Vis spectroscopy changes in light absorption when mixing complexes with DNA was observed, and calculated according to comparison with the control sample.

Table (1): UV-Visible spectra of ligand HL¹ and metal complexes in the presence and absence of DNA (1 hour)

No.	Compounds	λ max (nm) before mixing	Abs.	λ max (nm) after mixing	Abs.
	Control	-		270	0.120
	HL ¹	270	1.865	456	0.054
1	Mn	273	1.744	264	3.911
2	Zn	271	1.398	264	0.969
3	Ni	273	1.757	217	3.74
4	Co	266	1.03	263	1.107
5	Cu	274	1.897	217	3.965
6	Cd	271	1.347	264	0.598

Table (2): Infrared spectral data (cm⁻¹) of [HL¹] and its metal complexes.

Compounds	ν (OH) water	ν (OH) phenol	ν (C-H) arom.	ν (C-H) ald.	ν (C=N)	ν (C-O)	ν (M-N)	ν (M-O)
HL ¹		3437	3045(w)	2966-2875(w)	1622(s)	1309(m)	-	-
[Mn(L ¹) ₂ (H ₂ O) ₂]	3419	-	3049-3028(w)	2856(w)	1616(s)	1255(w)	515(m)	482(w)
[Co(L ¹) ₂ (H ₂ O) ₂]	3437	-	3033 (m)	2850(w)	1620(s)	1252(w)	513(m)	440(w)
[Ni(L ¹) ₂ (H ₂ O) ₂]	3419	-	3049-3028(m)	2850(w)	1614(m)	1255(w)	515(m)	405(w)
[Cu(L ¹) ₂ (H ₂ O) ₂]	3435	-	3047-3030(m)	2924-2870(w)	1616(s)	1254(w)	503(m)	461(w)
[Zn(L ¹) ₂ (H ₂ O) ₂]	3410	-	3043-3028(w)	2970-2922(w)	1618(m)	1211(m)	513(m)	467(w)
[Cd(L ¹) ₂ (H ₂ O) ₂]	3416	-	3047(m)	2925(w)	1618(s)	1213(m)	509(w)	420(w)

Br = Broad, M=Medium, S=Strong, W=Weak.

Table (3): Electronic spectral data for [HL¹] complexes.

Compounds	λ (nm)	ϵ (cm ⁻¹)	ϵ_{\max} (molar ⁻¹ cm ¹)	Assignment	Suggested structure
[Mn(L ¹) ₂ (H ₂ O) ₂]	814	12285	22	⁶ A _{1g} → ⁴ T _{1g}	Distorted Octahedral
	420	23809	1768	CT	
	326	30674	976	CT	
	273	36630	1744	Intra-ligand	
[Co(L ¹) ₂ (H ₂ O) ₂]	718	13917	10	⁴ T _{1g} → ⁴ A _{2g}	Distorted Octahedral
	680	14706	5	⁴ T _{1g} → ⁴ A _{2g}	
	423	23640	496	C.T	
	329	30395	292	C.T	
	266	37593	1.03	Intra-ligand	
[Ni(L ¹) ₂ (H ₂ O) ₂]	729	1371742	3	³ A _{2g} → ³ T _{1g}	Distorted Octahedral
	419	23866	1851	CT	
	326	30674	1058	CT	
	273	36630	1757	Intra-ligand	
[Cu(L ¹) ₂ (H ₂ O) ₂]	816	12254	10	² B _{1g} → ² A _{2g}	Distorted Octahedral
	422	23696	2133	CT	
	346	28401	1553	CT	
	324	30864	1435	CT	
	274	36496	1897	Intra-ligand	

Compounds	λ (nm)	ν (cm^{-1})	ϵ_{max} ($\text{molar}^{-1} \text{cm}^1$)	Assignment	Suggested structure
[Zn(L ¹) ₂ (H ₂ O) ₂]	416	24038	1078	CT	Distorted Octahedral
	326	30674	536	CT	
	271	36900	1398	Intra-ligand	
[Cd(L ¹) ₂ (H ₂ O) ₂]	416	24038	1078	CT	Distorted Octahedral
	327	30581	0581	CT	
	271	36900	1347	Intra-ligand	

Table (4): Electronic spectral data for [Mixed ligand] complexes.

Compounds	λ (nm)	ν (cm^{-1})	ϵ_{max} ($\text{molar}^{-1} \text{cm}^1$)	Assignment	Suggested structure
HL	433	23094	2179	$\pi \rightarrow \pi^*$	
	327	30581	1396	$\pi \rightarrow \pi^*$	
	270	37037	1865	$n \rightarrow \pi^*$	
1,10phenanthroline	257	38910	1352	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$	
[Mn(L) (phen)]Cl	475	21053	55	${}^6A_1 \rightarrow {}^4T_1$	Tetrahedral
	426	23446	1450	C.T	
	329	30395	802	C.T	
	264	37878	3706	Intra-ligand	
	208	47961	2673	Intra-ligand	
[Co(L) (phen)]Cl	693	14430	19	${}^4T_1 \rightarrow {}^4A_2$	Tetrahedral
	415	24096	3.216	C.T	
	276	36231	4000	Intra-ligand	
[Ni(L) (phen)]Cl	718.50	13917	10	${}^3A_2 \rightarrow {}^3T_1$	Tetrahedral
	420	23809	2259	C.T	
	320	31250	1409	C.T	
	263	38022	3964	Intra-ligand	
	228	43859	2344	Intra-ligand	
[Cu(L) (phen)]Cl	713.50	14015	8	${}^2B_1g \rightarrow {}^2A_1g$	Square planar
	425	23529	2356	C.T	
	324.50	30816	1746	C.T	
	268.50	37243	3968	Intra-ligand	
[Zn(L) (phen)]Cl	430.50	23228	2035	C.T	Tetrahedral
	327.50	30534	1063	C.T	
	263.50	37950	4000	Intra-ligand	
	226	44247	2542	Intra-ligand	
[Cd (L) (phen)]Cl	428	23364	840	C.T	Tetrahdral
	328	30487	504	C.T	
	262.50	38095	3393	Intra-ligand	
	206	48543	786	Intra-ligand	

Recommendations: Some chemical materials and compounds interacted with DNA and cleaved this nucleic acid and can be used as pharmaceutical agents.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

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References

- Asif, M., The pharmacological importance of some diazine containing drug molecules. *Sop Trans. Org. Chem*, 2014. 1: p. 1-16.

2. Fatiadi, A.J., New Chemical and Stereochemical Applications of Organoiron Complexes. *Journal of research of the National Institute of Standards and Technology*, 1991. 96(1): p. 1.
3. Hirohama, T., et al., Copper (II) complexes of 1, 10-phenanthroline-derived ligands: studies on DNA binding properties and nuclease activity. *Journal of Inorganic Biochemistry*, 2005. 99(5): p. 1205-1219.
4. Taha, Z.A., et al., Syntheses, characterization, biological activities and photophysical properties of lanthanides complexes with a tetradentate Schiff base ligand. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, 2011. 81(1): p. 570-577.
5. Wade, R.C., K.J. Clark, and P.J. Goodford, Further development of hydrogen bond functions for use in determining energetically favorable binding sites on molecules of known structure. 1. Ligand probe groups with the ability to form two hydrogen bonds. *Journal of medicinal chemistry*, 1993. 36(1): p. 140-147.
6. Alkazzaz, M.A.S.Y., Prof. Dr. Ibtissam Khalifa Jassim. 2014, University of Baghdad.
7. Erdem, E., et al., Synthesis and characterization of azo-linked Schiff bases and their nickel (II), copper (II), and zinc (II) complexes. *Transition metal chemistry*, 2009. 34(2): p. 167-174.
8. Bilge, S., et al., Intramolecular hydrogen bonding and tautomerism in Schiff bases: Part VI. Syntheses and structural investigation of salicylaldimine and naphthaldimine derivatives. *Journal of Chemical Sciences*, 2009. 121(6): p. 989.
9. Poonia, K., et al., In vitro anticancer activities of Schiff base and its lanthanum complex. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, 2016. 155: p. 146-154.
10. Sarikavakli, N. and G. Irez, Synthesis and complex formation of some novel vic-dioxime derivatives of hydrazones. *Turkish Journal of Chemistry*, 2005. 29(1): p. 107-116.
11. Tunçel, M. and S. Serin, Synthesis and characterization of new azo-linked Schiff bases and their cobalt (II), copper (II) and nickel (II) complexes. *Transition metal chemistry*, 2006. 31(6): p. 805-812.
12. Khaled, S., et al., Synthesis, characterization, and photophysical studies of some novel ruthenium (II) polypyridine complexes derived from benzothiazolyl hydrazones. *International Journal of Inorganic Chemistry*, 2013. 2013.
13. Braterman, P.S. and P. Braterman, *Metal carbonyl spectra*. Vol. 19. 1975: Academic Press London.
14. Světlík, J., et al., Three-component reaction and organocatalysis in one: Synthesis of densely substituted 4-aminochromanes. *Tetrahedron*, 2016. 72(47): p. 7620-7627.
15. Tobriya, S.K., Biological Applications of Schiff base and its Metal Complexes-A Review. *Int J Sci Res*, 2014. 3(9): p. 1254-1256.
16. Akram, S.M., et al., DNA binding and biological activity of mixed ligand complexes of Cu (II), Ni (II) and Co (II) with quinolones and N donor ligand. *Mediterranean Journal of Chemistry*, 2015. 4(5): p. 227-238.
17. Adhikary, A.K., N. Hanaoka, and T. Fujimoto, Simple and cost-effective restriction endonuclease analysis of human adenoviruses. *BioMed research international*, 2014.

The Relation between Adermatoglyphics and Dental Malocclusions of Iraqi Adults

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Abstract

Background: Dermatoglyphics is studying the surfaces of the hands and feet for epidermal ridges. Orodonatal patterns developed emberiologically at the same time. Various types of malocclusion have genetic predisposition affected environmentally. These malocclusions usually accompanied by various dermal patterns which are specific for each class.

Aims of the Study: To compare the dermatologyphics characteristic of patients with various classes of malocclusions.

Methodology: The patients were divided into four groups:

Group 1: class I, group 2: class II Div 1, group 3: class II Div 2, Group 4: class III malocclusion. The finger and palmar prints were recorded and analyzed for each type of pattern.

Results and Conclusion: The class II Div 2 pattern was correlated with higher frequency of whorls, while in class III, there was increased appearance of arches and radial loops with decreased incidence of ulnar loops.

Keywords: *Dermatoglyphics, Iraqi Adults; dental malocclusion.*

Introduction

Dermatoglyphics which includes the study of skin patterns and fingerprints, is one of the oldest sciences. Cummins and Midlo defined "Dermatoglyphics", as the study of complex configurations of the dermal ridges on palmar and planter surfaces of the hands and feet⁽¹⁾. The appearance of these dermal configurations starts in 12th week of intra uterine life and they are completed by the 24th week. Thereafter, the only change is in their size. It has been reported that Dermatoglyphics associate

with a number of conditions. One of these conditions is dental malocclusion. Palate and dentition developed at nearly the same time as the dermal patterns and this can explain the association between the dental malocclusion and Dermatoglyphics⁽²⁾. Many studies had been done to study the relationship of Dermatoglyphics with Dentistry. Most of these studies were done to investigate the relation between periodontal diseases and caries with Dermatoglyphics⁽³⁻⁶⁾. Only few studies have been conducted on the correlation of malocclusions with Dermatoglyphics⁽⁷⁻¹¹⁾. These studies were either inconclusive or they did not handle all the parameters. The present study was a comprehensive study which was done to study the correlation of the finger and palm patterns with various kinds of sagittal malocclusions.

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Material and Method

This study was conducted at the department of orthodontic, college of dentistry, university of Baghdad. The sample consisted of 96 (subjects) attending the

department of treatment of malocclusions, ranging in age from 18-25 years. They were divided into 4 groups of 24 each and each group was divided into Male and female groups of 12 each.

Exclusion Criteria:

- Patient who received orthodontic treatment in early age or those who are currently undergoing orthodontic treatment.
- Patient who had features of syndromes except malocclusions.
- Patient with big restorations or prostheses that can affect the geometry and volume of the crown.
- Patient with a trauma history or surgical procedures performed in the orofacial region.

Group 1: 24 subjects, with angle class I malocclusion.

Group 2: 24 subjects with angle class II Div I malocclusion.

Group 3: 24 subjects with angle class II Div 2 malocclusion.

Group 4: 24 subjects with angles class III malocclusion

For all groups, there was no evidence of skeletal malocclusion, so all subjects were considered as skeletal class I.

Procedure for Obtaining Palm and Finger Prints: Ink and roller method was the method of choice for the palm and finger prints recording as described by Cummins and Midlo (1). Before starting the prints recording, the hands of each subject were washed with soap and water in order to get rid of any dirt, sweat, or oily secretions and then the hands were dried using clean towel. Using an inking slab, little amount of ink was displaced over it and rolled over it until a thin film of ink covered the entire slap surface. The patient was instructed to stand in front of inking plate at a distance equal to the length of fore arm and to gently press the right hand palmar surface over the inking slab. The

palmar surface was then pressed gently over a white, clean paper and removed immediately. The same method was achieved for the left hand. For the individual finger print recording, the finger bulb was pressed in a right angle over the inking plate and then the finger was rolled and turned. Finally, the finger was placed on a white paper on the same rolling manner to get a clean rolled impression of each finger [Figure. 1].

The palm and finger prints of the individuals were considered under the following headings.

The Pattern on the Fingers of both Right and Left Hands: Arches, whorls, ulnar loops, radial loops, twined loops and central pocket loops were separately calculated for each digit. The occurrence frequency was recorded separately for right and left hands and then, combined scores for each of these were recorded (12). [Fig. 1]

Total Finger Ridge Count: Ridge count indicates the number of ridges between the triradius and the core or between two triradii. Ridge counts for patterns of finger tips were done by following the method of Cummins and Midlo^(1,12), The Total Finger Fridge Count (TFRC) demonstrate the ridge counts of all fingers .

Atd Angle of each Hand: The axial triradius‘t’ is an important landmark on all normally developed hands. This triradius is found near the proximal palmar margin, superficial to the wrist bones, near to the axis of the fourth metacarpal bone. The position of the triradius can be various in the proximal-distal direction.

The position of the axial triradius in the proximal region of the palm, near the wrist crease and it is denoted by the symbol ‘t’. The method which is most widely used to interpret the position of axial triradius in the palm is the ‘atd’ angle. This angle is formed by lines drawn from the digital triradius ‘a’ to axial triradius and to ‘d’. The more distal is the position of axial triradius, the larger is the ‘atd’ angle. Palms with patterns in hypothenar area may have more than one axial triradius. In such cases, the widest ‘atd’ angle i.e. the angle from the distal ‘t’ was recorded [figure-2].

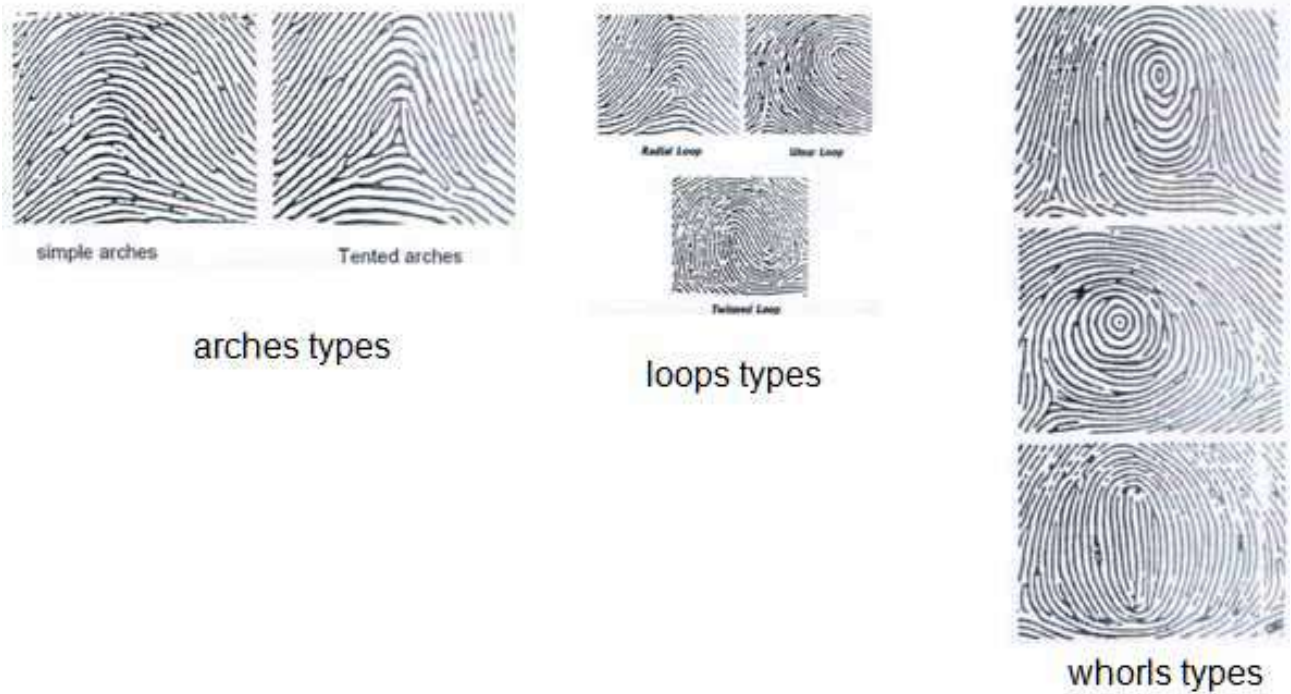


Figure 1: Finger Print Pattern Types

Results and Discussion

The frequency of digit patterns of class I (control), class II Div 1, class II Div 2 and class III on right and left hand combined showed increase arches in the experimental groups compared to control group and was found to be statistically significant ($p < 0.05$) due to x – linked inheritance. The frequency of digital patterns of the experimental groups showed decrease whorls compared to control group which was not found to be statistically significant which was also due to x – linked inheritance (Table 1).

The frequency of ulnar loops increased in class II malocclusion where as it decreased in class III

malocclusion compared to control group and was not statistically significant because of the presence of extra genetic material which increase or decrease the ulnar loops. Similar findings were observed by kharbanda et al⁽⁷⁾.

The frequency of radial loops is total increased in class II Div 2 and class III malocclusion groups and decreased in class II Div 1 which may be due to x. linked inheritance and the same finding were reported by forbes (15). (table-1).

The percentage frequency of digital patterns of males and females of each group were assessed. It was showed that the total finger ridge count was higher

in males than females in all groups. The percentage frequency of arches was higher in females than males while concerning whorls it was higher in males than females in all groups (table-2) . Holt⁽¹⁶⁾ showed that in males the presence of each ‘X’ chromosome diminishes the total number of ridges in patterns nearly 3 times as much as does the presence of each ‘Y’ chromosome and in females the reduction of ridges seen as ‘X’ chromosome complement increase and is less regular.

The percentage of finger ridge count decreased in all experimental groups when compared to control group (table-3) because this is entirely determined by one or more additive or co-dominant genes and also the finger ridge count follow a polygenic mode of inheritance. Similar finding were reported by penrose and loesch⁽¹⁷⁾.

The mean value of “atd” angle decreased in all experimental groups compared to the control group on both right and left hands (table-4). This is because the

plam grows more in length than breadth and the same was reported by penrose⁽¹⁸⁾.

From this study we can conclude the followings:
Class II Div 1 pattern accompanies the increase in frequency of arches on digit II and ulnar loops on digit IV except on digit I.

The class II Div 2 pattern accompanies the increase in frequency of arches on digit III and IV and decreased frequency of whorls except on digit I.

The craniofacial class III pattern accompanies the increase in frequency of arches on digit III and radial loops and the decrease in frequency of ulnar loops except on digit II and IV and whorl except on digit I.

No significant dermatoglyphic findings could be associated regarding digit V (small finger) with malocclusions.

Table 1: Percentage frequency of various types of digit patterns of class I, class II Div I, class II Div 2 and class III on right and left hand combined.

Pattern	Group	Digits					
		I	II	III	IV	V	Total
Arches	1	2.1	10.4	2.1	6.2	2.1	4.6
	2	0.0	27.1*	10.4	4.2	6.2	9.6*
	3	8.3	14.6	14.6*	8.3	4.2	10.0*
	4	10.4	18.7	14.6*	6.2	10.4	12.1*
Whorl	1	20.8	41.7	27.1	64.6	25.0	35.8
	2	35.5	39.6	18.7	45.8	16.7	31.2
	3	20.8	31.2	16.7	45.8	16.7	26.2
	4	37.5	18.7	14.6	43.7	20.8	27.1
Ulnar loops	1	70.8	33.3	70.8	25.0	72.9	54.6
	2	62.5	29.2	66.7	50.0**	77.1	57.1
	3	60.4	41.7	68.7	45.8*	77.1	58.7
	4	45.8	50.0	64.6	39.6	64.6	52.9
Radial loops	1	0.0	14.4	0.0	0.0	0.0	2.9
	2	0.0	4.2	2.1	0.0	0.0	1.2
	3	6.2	8.3	0.0	0.0	2.1	3.3
	4	2.1	12.5	6.2	8.3	2.1	6.2

*P< 0.05 **P < 0.01

Table 2: Percentage frequency of digital pattern of males and females in class I, class II Div 1, class II Div 2 and class III

Pattern	Class I		Class II Div 1		Class II Div 2		Class III	
	Male	Female	Male	Female	Male	Female	Male	Female
Arch	3.3	20.0	0.0	10.0	0.0	3.3	0.0	30.0
Whorl	50.0	20.0	55.0	40.0	46.7	16.7	80.0	20.0
Total finger ridge count	203.3	166.7	238.0	180.0	193.3	133.3	240.0	180.0

Table 3: Finger ridge count of right and left hands combined.

	Class I	Class II Div 1	Class II Div 2	Class III
Total finger ridge count	441	427	439	434
Percentage	183.75	177.92	182.92	180.8

Table 4: The average of atd angle in right and left hands.

Group	Right		Left	
	Mean	S. E	Mean	S.E
Class I	47.38	1.11	48.58	0.87
Class II Div 1	46.85	1.50	46.50	1.27
Class II Div 2	45.35	0.69	46.12	0.91
Class III	45.46	0.91	47.12	1.19

SE standard Error

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: The authors declare that they have no conflict of interest.

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References

- Cummins, Midlo. The topographic history of the volar pads (walking pads) in the human embryo". Embryo!. Carnig. Int. Wash.1929; 20: 103-09.
- Kanematsu N, Yoshida Y, Kishi N, Kawata K, Kaku M, Maeda K, et al. Study on abnormalities in the appearance of finger and palm prints in children with cleft lip, alveolus, and palate. J Maxillofac Surg. 1986;14:74-82.
- Sharma A, Somani R. Dermatoglyphic interpretation of dental caries and its correlation to salivary bacteria interactions: An in vivo study. J Indian Soc Pedod Prev Dent. 2009;27:17-21.
- Madan N, Rathnam A, Bajaj N. Palmistry: A tool for dental caries prediction! Indian Journal of Dental Research. 2011; 22(2): 213-18.
- Bhat PK, Badiyani BK, Aruna CN. Dermatoglyphics-A new diagnostic tool in detection of dental caries in children. Indian Journal of Forensic Medicine and Toxicology. 2012; 6(2): 24-28.
- Mathew L, Hegde AM, Rai K. Dermatoglyphic findings in oral clefts. J Indian Soc Pedod Prev Dent. 2005;23:179-82.
- Kharbanda O P, Sharma V P, Gupta D S. "Dermatoglyphic evaluation of mandibular prognathism". J. Ind. Dent. Assoc. 1982;54: 179-86.
- Mathew L, Hegde AM, Rai K. Dermatoglyphic findings in oral clefts. J Indian Soc Pedod Prev Dent. 2005;23:179-82.
- Reddy S. Prabhakar AR, Reddy WS. "A dermatoglyphic predictive and comparative study of Class I, Class II, Division 1, Division 2 and Class III malocclusions". J. Indian. Soc. Pedo. Prev. Dent. 1997;15(1): 13-19.
- Trehan M, Kapoor DN, Tandon P, Sharma VP. "Dermatoglyphic study of normal occlusion and malocclusion". J. Ind. Orthod. Soc. 2000; 33:11-16.
- Tikare S, Rajesh G, Prasad K W. Dermatoglyphics: A marker for malocclusion? Int DentJ. 2010; 60(4): 300-04.
- Cummins. Revised method of interpretation and formulation of palmar dermatoglyphics. Am J Phy Anthr. 1929; 12:415-502.
- Galton F. Finger Prints. 1892 Macmillan, London as cited in Henry, Sir Edward csi, Classification and Uses of Finger Prints, George Routledge and Sons Ltd.. London, 6thed, 1928 digitalised by University of California, sep 2007.
- Sharms V.P, Gupta D.S and Kharbanda Op.: Dermatoglyphic evaluation of retrognathism. J 1nd Dent Assoc. 1980;52:186.

15. Forbes Ap.; Finger prints and plam prints (dermatoglyphics) and palmer creases in gonadal dysgenesis pseudo hyper porathy roidism and kline–felter syndrome. *New Eng J Med* 1984; 270:12.
16. Holt S.B : Dermatoglyphics and sex chromosome in genital anomalies Ed, Rashad M.N Thomas spring field NY. 1964.
17. Penrose L.S and Loesch. D.; the effect of sex chromosomes on some characteristics of dermal ridges on plam and finger tipes genet. *Pol* 1969; 10:328.
18. Penrose LS.: finger print patterns and sex chromosomes. *Loncent* 1967;1:298.

Some Cardiac Indexes of Doping in Sport Comparative Analysis between Doping Users and Non-Doping Users

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Abstract

At present, the world is undergoing a major development in all life's aspects, which positively reflected on fundamental sciences and sport sciences. The principle of winning the match or losing depends on decent competition between sports teams. Steroids have been used in the past in the Olympic competitions since the 13th century when bicycles' racers in France used a medical mixture prepared from the substances of the (caffeine).

Belgium athletes used sugar pieces and others used alcohols. The first incident of drug-death-related, took place in 1882 when the British athlete Lenition died of using a large mixture of heroin and cocaine during a 200 kilometres bicycles' race between Bordeaux and Paris. In 1951 during the Winter Games in Oslo ice skitters used nitrogen and many capsules used as stimulants were found in homes as well.

Using steroids affects positively the athlete physical health fitness. However, this positive aspect contains side effects that have an impact on the athlete user's health. Experience has been proven that these side effects and damages sometimes reached to the extent of sudden death. For instance, if we assumed that one of the high-level athletes of any of the sports aspects of which the level is determined by muscular strength such as weight lifting, throwing, in the athletics ...etc., giving specific doses of the fourth set of these steroids leads to an increase in the physiological section of different muscular groups. Especially if taking these steroids is accompanied with private exercises of athlete muscular strength where the fibres' size increases. The number of the fibres remains constant, thus leads to an increase in the muscular strength, which is already linked with the distance increases in the case of throwing and weight increase in the case of weight lifting.

Using steroids leads to a positive impact on the athlete's physical fitness, however, this positive aspect contains negative effects of users and negatively affect the athlete individual's health. Hence the importance of research is reflected in the study of the comparison between who take steroids and dietary supplements and others of who do not, from the standpoint of the sports hall trainers.

Keywords: *Cardiacindexes, Doping and Sport.*

Introduction

There has recently been an increase in the conversation about athletes use of doping and has occupied an important space in both international newspapers and magazines. After their widespread in various types, this prompted the researchers and the concern people to actively study the pros and cons that occur to the doping users.

Iraq is one of the countries that has been broadly

influenced by doping, especially in the official institutions such as clubs and federations. In some case, informal ones such as bodybuilding halls and physical fitness centres. This is called to find out the positives about this subject and diagnose the negatives and stand on them.¹

Many sports institutions aspire to reach an advanced level in order to precede their competitors and to develop the physical and sports level. For other

purposes, through using unnatural elements and inject them in the body or take through the mouth before or after the races. Therefore, researchers have sought to highlight this important subject. It has become a source of concern to many athletes, trainers and others of those who take steroids without enough knowledge of the possible damages.²

Sports dopes vary of each other, there are some, which increase the physical fitness, some develop the kinetic abilities and others work on building the body huge. The international bodies have banned most of these dopes for their danger to the general health asserting that it leads to extraordinary efforts, and beyond the heart bearing capacity.

Besides its long-term effects, there are some dopes expand the blood vessels causing health problems such as a sharp drop in the blood. Also, some dopes are restricted to old people as they are beyond the heart ability to work. Hence, the research demand is reflected in knowing some of the cardiovascular indicators on the doping users and dietary supplements and others in the sports physical fitness halls(gyms). The continuous use of dopes causes health problem as they stimulate the body's functions to alert the nerves system. Many specialists in this area warn against taking dopes especially the masculine ones that are used for bodybuilding, this excessive use to dopes might sometimes lead to death.³

Also, many trainers in physical fitness' training or in sports centres know nothing about the dopes and their near-far level effects. Some players used dopes excessively, ignoring the negative effects. Therefore, the researchers wanted to highlights on dopes and their effects on the heart through comparative research between dopes users and non- dopes users. We assumed at the beginning of the research of having significant statistical differences and cardiovascular indexes amongst doping users in bodybuilding halls.

Based on the above, the objectives of this study, have been set as follows:

1. Recognizing some cardiovascular indexes to dopes users in bodybuilding training centres.
2. Recognizing some cardiovascular indexes of non-dopes users in the same centres.
3. Making a comparison of some cardiovascular indicators of dopes users and others in bodybuilding training centres.

And for achieving these objectives, the human aspect of this study has been set to be the bodybuilding players in the sports centre (gyms) in Babylon City for a period of 10 weeks.

Materials and Method

1. Research methodology: the researcher used the descriptive approach in comparison way to match the research objectives.
2. Sampling: the number of dopes users has reached (31) players and non- dopes users were (31) players. The average age of the two groups players is between 25- 30 years.
3. Devices and facilities:
 - a. The research facilities include the following:
 - Interview
 - Questionnaire
 - Tests and measurement
 - Observation
 - b. Devices and instruments used in the research are:
 - Pressure device
 - Device of (Polar) hears rate measure
 - Graphical analysis

Research Procedures:

1. **Prepare a questionnaire to the centres' supervisors:** The researchers have prepared a questionnaire containing two questions to identify steroids users of others, according to the supervisors' view. It is difficult to obtain information from the players might be for social or personal reasons.
2. **Determining the research's variables:** The researchers selected the heart's research variables (resting systolic pressure, resting diastolic pressure, resting pulse, voltage pulsation and voltage resistance) depending on several scientific sources in this area.⁴
3. **Select tests for variables:** The researcher used several the regulated devices to conduct the tests for hearts indicators:
 - a. Pressure device
 - b. Device of Polar

c. Ruffier Dickson testing for heart resistance to voltage⁵

Ruffier Dickson Test: The heartbeats were counted following Ruffier Dickson method which contains three different times:

1. In comfort we leave the athlete to rest for a while when he/she enters into the hall then to calculate his/her heartbeats.
2. Immediately at the end of the exercise he/she is about to do
3. One minute after the end of the exercise.

The examining method depends on the following protocol:

- *FC₀ (Determining the resting pulses):* The person stretching on the bed then we count pulses through hand wrist or neck within 10 seconds then multiply the total by 6 to get the number of the pulses per minute.
- *FC₁ (Determining the heartbeats immediately after the exercise):* the athlete performs 30 squatting or flexing times, within 45 seconds by the same rhythm, were the legs at a distance of 20 cm. immediately after the end of the exercise to count the pulses in the same way and record that.
- *FC₂ (Determining the heartbeats after one-minute):* after the end of the exercise, the athlete to rest for one minute then to count the pulses in the same way, time must be controlled carefully.

To work out Ruffier Dickson index, the following formula was used:

$$Ruffier\ Index = \frac{RC0 + FC1 + FC2 - 200}{10}$$

Where the coefficient of 200 is heartbeats average for high strength exercise for 10 seconds. Ruffier Dickson test result is compared to the table (1) to determine the level of adaptation.

Table (1): Interpreting the results of Ruffier Index (heart is adapted to exercise)

Index	Interpretation
< 0	Very good adaptation to exercise
0-5	Good adaptation to exercise
5-10	Average adaptation to exercise
10-15	Insufficient adaptation to exercise
15 <	Poor adaptation to exercise – further medical consultation is necessary

Identifying the obstacles and the problems that might encounter in the researching procedures (exploratory experiment) are taken into consideration, and summarised in the following:

- Perform tests to find out the time spent
- The sample individuals’ acceptance of the tests
- Response of the Assistant Workforce

For statistical analysis, (SPSS) software were used.

Results and Discussion

The results of the two groups under investigation (dopes users and no- dopes users) are illustrated in table (2). Table (2) shows that there are differences and variances in the arithmetical means’ values of tests of both groups (users and non-users) as well as there are differences and variances in the standards deviations. Whereas the sig-values of all are smaller than the (0.05) value, which indicates to a significant differences between the primary and secondary tests of the steroidsand nutritional supplements users’ group.

Table (2): Shows the standard deviations, arithmetical means of the two groups

Research Variable	Sample Numbers		Means		Standard Deviation		Sig-value	Significant Type
	User	Non-user	User	Non-user	User	Non-User		
Resting Diastolic Pressure	31	27	9.29	7.66	0.78	0.77	0.00	Significant
Resting Systolic Pressure			13.52	12.03	0.93	0.64	0.00	Significant
Resting Pulse			76.52	70.33	2.43	1.55	0.00	Significant
Heart Effort Resistance			7.80	3.74	1.16	0.85	0.00	Significant
Diastolic Pressure During the Physical Efforts			10.35	9.11	0.79	0.32	0.00	Significant
Systolic Pressure During the Physical Efforts			14.25	13.52	1.09	0.55	0.02	Significant
Pulses During the Physical Efforts			174	171	4.62	2.52	0.03	Significant

Throughout, what has been displayed in the above tables, it is shown that there are significant differences in all study variables. This means that there is a differentiation in health level of the two groups. For Diastolic and Systolic Pressure, it was shown that there were differences in favour of the dopes' users during resting time as well as during the physical stress.

High blood pressure is one of the most serious health problems that the steroids' user might be exposed to. This problem has been described as a deadly health problematic might be caused by doping.

Taking drugs and steroids pills results in rapid, immediate and sudden activation of the blood circulation. The high blood pressure of the dopes' user, who is likely to be infected, increase simply by starting with a certain stress and then causing another double infection. The sudden rise in the blood pressure may lead to death⁶.

Although dietary supplements are less harmful than dopes, but they have negatives that may accompany the athlete, such as, the creatinine, over-taking it may cause negative symptoms, taking overdoses may damage the kidney and it might also cause fluid retention in the body⁷.

As for other measured variables during pulse resting and physical stress too, there has found a significant difference between the two groups especially the rise in heartbeats rate of users. This may threaten the heart and infect it with arteries deceases. Scientists describe that as one of the most serious deceases that infect the heart, as the drugs substances have a direct effect on the blood cholesterol and rise it in a noticeable extent. It hinders blood pumping to the different organs and tissues of the body. Also, it leads to the stress of the heart's muscle and to a sudden feeling of tiredness. Thus, the non-users' heartbeats rates are suite the exerted efforts (i.e. the more physical effort increases, the more the heartbeat increases steadily.⁸

Conclusions

We can draw the following analysis' results:

- There are significant differences in the research variables between the dopes' users and no-dopes users in favour of the users.
- Rising of heartbeats rates of the two groups after the physical efforts comparing to the resting times.
- Decreasing in heartbeats rates of non-dopes' users

during resting time as a result of the athletes' adaption in comparing to dopes' users.

- Diastolic and systolic pressure was high during resting and efforts amongst steroids' users

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: The authors declare that they have no conflict of interest.

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References

1. Ashbaugh A, McGrew C. The role of nutritional supplements in sports concussion treatment. *Current sports medicine reports*. 2016 Jan 1;15(1):16-9.
2. Hashimoto T, Hussien R, Oommen S, Gohil K, Brooks GA. Lactate sensitive transcription factor network in L6 cells: activation of MCT1 and mitochondrial biogenesis. *The FASEB Journal*. 2007 Aug;21(10):2602-12.
3. Athab NA, Hussein WR, Ali AA. A Comparative Study for Movement of Sword Fencing Stabbed According to the Technical Programming in the Game of Fencing Wheelchairs Class B. *Indian Journal of Public Health Research & Development*. 2019;10(5):1344-7.
4. Athab NA. An Analytical Study of Cervical Spine Pain According to the Mechanical Indicators of the Administrative Work Staff. *Indian Journal of Public Health Research & Development*. 2019;10(5):1348-54.
5. Alsayigh HA, Athab NA. The Study of Rectus Femoris Activity after Knee Joint Rehabilitation. 2016;9(9):360-5.
6. Jumaah H, Ktaiman A, Abdul N, Athab K, Mohammed A. The Effect of Using Pain Management Techniques in the Rehabilitation of Chronic Lower Back Injury in Athletes and Non-Athletes. :108-12.
7. Alsayigh HA, Athab NA, Firas M. *Journal of Global Pharma Technology* The Study of Electrical Activity of the Triceps Brachia Muscle according to the Chemical Changes of Water Loss during Spike in Volleyball. 2017;57-62.
8. Piloto N, Teixeira HM, Teixeira-Lemos E, Parada

- B, Garrido P, Sereno J, Pinto R, Carvalho L, Costa E, Belo L, Santos-Silva A. Erythropoietin promotes deleterious cardiovascular effects and mortality risk in a rat model of chronic sports doping. *Cardiovascular toxicology*. 2009 Dec 1; 9(4):201-10.
9. Deligiannis AP, Mandroukas K. Noninvasive cardiac evaluation of weight-lifters using anabolic steroids. *Scandinavian journal of medicine & science in sports*. 1993 Mar;3(1):37-40.
10. Corsetti R, Lombardi G, Barassi A, Lanteri P, Colombini A, D'Eril GM, Banfi G. Cardiac indexes, cardiac damage biomarkers and energy expenditure in professional cyclists during the Giro d'Italia 3-weeks stage race. *Biochimica medica: Biochimica medica*. 2012 Jun 15;22(2):237-46.

Clinico-cytological Correlation of Cervical Pap Abnormality

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Abstract

Background: Few studies reported in Iraq about the clinicopathological correlation of Pap Smear results, and non was reported about this correlation among private clinic patient, as the knowledge of the authors. Therefore, this study was developed to study the clinic-pathological correlation of the Pap smear cytology results and the clinical presentation of the private clinic patients

Patient and Method: Cross sectional study of (144) patients presented to the privet clinic, during the period 1st January-1st September 2018. Information regarding age, job parity, marital status symptoms and patient complain and clinical examination of the patient was obtained via a structured questionnaire. The presenting signs & symptoms were compared with the Pap-smear findings and other factors. Cytological study done by cytopathology specialist. Conventional pap smear were used. Cytology was reported using Bethesda system. A single combined smear, was done for each patient by sampling the endocervix, first to obtain the cell sample. Scraping the ectocervix with the spatula and spreading the material rapidly onto the upper end of the slide. Spreading the endocervical material through the ectocervical material to the end of the slide. This procedure Performed quickly to prevent drying artifacts. Fixation of the slide done using spray fix by thoroughly soaking the cellular sample while holding the spray fixative container about 6-8 inches from the slide. Then allowing spray fixative to evaporate.

Results: NILM (negative for intraepithelial lesion or malignancy) found among 21(14.6%) of the patients 20 (13.9%) had cervicitis, and 1(0.7%) had atrophic changes in the cervix), Atypical Squamous Cell Undetermined Significant (ASCUS) 73(50.7%), followed by Low-grade squamous intra-epithelial lesion (LSIL) 39(27.1%), and High-grade squamous intra-epithelial lesions (HSIL) 9(6.3%). Squamous cell carcinoma was found among 2(1.4%) of the cases.

Conclusion: Iraqi women attending the priate clinic had high level of intraepithelial abnormality, even if it lower than other countries but it in need to be controlled by cervical cancer screening program, the common presenting symptom with increased rate of with various stages of intraepithelial lesion were post coital bleeding, and Irregular vaginal bleeding.

Keywords: *Conventional Pap smear, cervical cancer, clinical presentation.*

Introduction

Cervical cancer is the 2nd leading cause of cancer death among women 1, most of the cases occur in developing countries. 2 cervical cancer incidence in

Iraq, estimated to be 2.1 per 100.000 popula-tions 3. About (23.2%) of the Iraqi women had abnormal intraepithelial lesions. Most of the cervical abnormality is due to HPV infection, the prevalence of HPV infection among Iraqi women with intraepithelial lesion was (23.2%).4 the incidence of cervical cancer has decreased by more than 50% in the past 30 years, largely due to the increasing use of cervical cancer screening with cervical cytology 5. Invasive cancer of the cervix results from the progression of pre-invasive pre-cursor lesions called cervical intraepithelial neoplasia (CIN),

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or dysplasia. Not all pre-cursor lesions will progress to invasive can-cer many of the mild and moderate lesions may regress. The cytological changes which appear in pre-invasive lesions are nuclear enlargement, multinucleation, hyperchromasia with thin cytoplasm and perinuclear halo, in addition to the koilocytotic atypia.⁶

Cytological abnormalities were classified according to Bethesda classification reporting system as: atypical squamous cells of undetermined significance (ASCUS), low grade squamous intra-epithelial lesion (LSIL) and high grade squamous intra epithelial lesion (HSIL).⁷ Cervical cancer can be prevented through screening programs, designed to identify and treat the precancerous cytological abnormalities, it is able to identify about 90% of cytological abnormalities.⁸ Developed countries studies show that population based pap test screening among sexually active women decreased the mortality and morbidity from cervical cancer about 40%.⁹ In Iraq instead of increased rates of cancer and mostly diagnosed at advanced stage, there is no cancer screening programs only early detection clinics were present.^(10,11) Few studies reported in Iraq about the clinicopathological correlation of Pap Smear results, and none was reported about this correlation among private clinic patients, as the knowledge of the authors. Therefore, this study was developed to study the clinic-pathological correlation of the Pap smear cytology results and the clinical presentation of the private clinic patients

Patient and Method

Cross sectional study of 144 patients presented to the private clinic, during the period 1st Jan-1st Sept 2018. Inclusion criteria include married for at least 3 years, non pregnant, age ≥ 21 years, or married for at least 3 years, presented with signs and symptoms of .

Exclusion criteria: women with active vaginal bleeding, hysterectomy, and women with frank growth and/or who had never been sexually active or had undergone prior treatment for CIN or cancer cervix, or had unsatisfactory Pap smear were excluded from the study. Pap smear was done for all the patients.

Information regarding age, job parity, marital status symptoms and patient complaints and clinical examination of the patient was obtained via a structured questionnaire. The presenting signs & symptoms were compared with the Pap-smear findings and other factors.

Cytological study done by cytopathology specialist. Conventional pap smear were used. Cytology was reported using Bethesda system.

A single combined smear, was done for each patient by sampling the endocervix, first to obtain the cell sample. Scraping the ectocervix with the spatula and spreading the material rapidly onto the upper end of the slide. Spreading the endocervical material through the ectocervical material to the end of the slide. This procedure performed quickly to prevent drying artifacts. Fixation of the slide done using spray fix by thoroughly soaking the cellular sample while holding the spray fixative container about 6-8 inches from the slide. Then allowing spray fixative to evaporate.

Statistical analysis and data management: The Statistical Package for Social Sciences (SPSS, version 18) was used for data entry and analysis. Chi (χ^2) square test, and t- test was used to compare means and proportions of different factors among different groups of study sample. P value of ≤ 0.05 was regarded as statistically significant. Bar charts and tables used to present the data

Results

NILM (negative for intraepithelial lesion or malignancy) found among 21(14.6%) of the patients. 20(13.9%) had cervicitis, and 1(0.7%) had atrophic changes in the cervix), Atypical Squamous Cell Undetermined Significant (ASCUS) 73(50.7%), followed by Low-grade squamous intra-epithelial lesion (LSIL) 39(27.1%), and High-grade squamous intra-epithelial lesions (HSIL) 9(6.3%). Squamous cell carcinoma was found among 2(1.4%) of the cases, as shown in table 1.

Table 1: The patient distribution according to the pap smear cytology results

Pap Smear Results	Frequency	Percent
NILM (Negative for intraepithelial lesion or malignancy)	21	14.6
ASCUS	73	50.7
Low-grade squamous intra-epithelial lesion (LSIL)	39	27.1
High-grade squamous intra-epithelial lesions (HSIL)	9	6.3
Carcinoma	2	1.4
Total	144	100.0

*Inflammatory cervicitis, reactive changes and atrophic changes

The mean age of the patient was 39.8±11.9 years, rang(19-70 years), the mean age for carcinoma was 51±16.9 years it was higher than the HSIL (42.2±12.2), LSIL (38.6±12.4), ASCUS (39.3±11.6), NLIM (41.5±11.9), this relation statistically not significant P > 0.05, as shown in table 2. Regarding parity, there was no

difference among groups except for seq. cell ca. (4±1.4), rang (3-5), that is lower than the, HSIL (4.7±3), LSIL (4.4±2.3), ASCUS (4.5±3.1), NLIM (4.2±3.2), this relation statistically not significant P > 0.05, as shown in table 2.

Table 2: The correlation of the pap smear results, age, and parity.

Pap who classification	Parity				Age			
	N	Rang	Mean	Std. Deviation	N	Rang	Mean	Std. Deviation
NILM	21	(0-11)	4.2	3.2	21	(19-60)	41.5	11.9
ASCUS	73	0-11	4.5	3.1	73	(21-63)	39.3	11.6
Low-grade squamous intra-epithelial lesion (LSIL)	39	0-10	4.4	2.3	39	20-70	38.6	12.4
High-grade squamous intra-epithelial lesions (HSIL)	9	0-9	4.7	3	9	23-63	42.2	12.2
Carcinoma	2	3- 5	4	1.4	2	39-63	51	16.9
Total	144	0-11	4.6	3.1	144	19-70	39.8	11.9
P- value (F) ANOVA test			0.9 (0.06)NS				0.5(0.8) NS	

There is a significant relation between the Pap smear results and patient presenting symptoms: the only symptom that associated with seq. cell ca. is the Post menopausal bleeding (PMB) 1(33.3%) diagnosed as seq. cell ca. and 1(3.8%) of those had other symptoms (external genital warts) had seq.cell ca.

Most symptoms associated with increased rate of intra epithelial lesion was Post coital bleeding(PCB),

5(13.5%) NILM, and 32(86.5%) different stages of intraepithelial lesion.

Irregular vaginal bleeding also commonly presented with various stages of intraepithelial lesion 12(92.3%), while abdominal pain was dominantly diagnosed as LSIL 4(57.1%), these relations is statistically significant, as shown in table 3.

Table 3: The correlation of Pap smear cytology and the presenting symptom

Symptom	Pap smear cytology result					Total
	NILM	ASCUS	Low-grade squamous intra-epithelial lesion (LSIL)	High-grade squamous intra-epithelial lesions (HSIL)	Carcinoma	
Post coital bleeding (PCB)	5	21	6	5	0	37
	13.50%	56.80%	16.20%	13.50%	0.00%	100.00%
Vaginal discharge	8	29	21	0	0	58
	13.80%	50.00%	36.20%	0.00%	0.00%	100.00%
Irregularvag. bleeding	1	9	2	1	0	13
	7.70%	69.20%	15.40%	7.70%	0.00%	100.00%
abd. pain	0	3	4	0	0	7
	0.00%	42.90%	57.10%	0.00%	0.00%	100.00%
Post menopausal bleeding (PMB)	1	1	0	0	1	3
	33.30%	33.30%	0.00%	0.00%	33.30%	100.00%
others	6	10	6	3	1	26
	23.10%	38.50%	23.10%	11.50%	3.80%	100.00%

Likelihood Ratio =34.2, P-value=0.02 Significant

Physical examination was healthy cervix among 46(31.9%), Erosion 75(52.1%), suspicious features 18(12.5%), atrophic cervix 2(1.4%), cervicitis 3(2.1%).

there is no significant relation between the physical examination findings and the Pap smear results, as shown in table 4.

Table 4: The correlation of Pap smear cytology and the Physical examination

Physical examination	Pap smear cytology result					Total
	NILM	ASCUS	Low-grade squamous intra-epithelial lesion (LSIL)	High-grade squamous intra-epithelial lesions (HSIL)	Carcinoma	
Healthy	12	25	9	0	0	46
	26.10%	54.30%	19.60%	0.00%	0.00%	31.9%
Erosion	5	37	23	8	2	75
	6.70%	49.30%	30.70%	10.70%	2.70%	52.1%
Suspicious features	2	9	6	1	0	18
	11.10%	50.00%	33.30%	5.60%	0.00%	12.5%
Atrophic cervix	1	1	0	0	0	2
	50.00%	50.00%	0.00%	0.00%	0.00%	1.4%
Cervicitis	1	1	1	0	0	3
	33.30%	33.30%	33.30%	0.00%	0.00%	2.1%
Total	21	73	39	9	2	144
	14.60%	50.70%	27.10%	6.30%	1.40%	100.00%

Likelihood Ratio =0.9, P-value=0.9 not Significant

Discussion

NILM (negative for intraepithelial lesion or malignancy) found among 21(14.6%) of the patients 20(13.9%) had cervicitis, and 1(0.7%) had atrophic changes in the cervix, this was lower than found by Barzanjy B K et al¹²(88.4%), Atypical Squamous Cell Undetermined Significant (ASCUS) 73(50.7%), Low-grade squamous intra-epithelial lesion (LSIL) 39(27.1%), and High-grade squamous intra-epithelial lesions (HSIL) 9(6.3%). Squamous cell carcinoma was found among 2(1.4%) of the cases,

It goes with Mezaal MI,¹³ in Baghdad 2017, that Pap smears exhibiting lesions in the forms of NILM, ASCUS, LSIL, HSIL and Squamous Carcinoma were observed in (31.1%), (23.3%), (22%), (20%) and (3.3%) respectively, and goes with Abdurraheem A F, and Khudhairi J M¹⁴ 2014 in Baghdad HSIL (20%), squamous carcinoma (1%), and with Abdulla K N et al¹⁵ 2016 which found HSIL(29%), and LSIL(48%) among patient with unhealthy cervix attending gynecology clinic.

But these figures were higher than what found by Barzanjy B K et al¹²ASCUS (2.9%) to the presence

of LSIL (6.3%), HSIL (2.1%) and invasive carcinoma (0.1%). And Al-Rubaiee et al 2006¹⁶, which found (3.6%) of the sample was HSIL, and LSIL (33.7%). The difference is due to the fact that patients in our study were seriously ill and complain of chronic discharge, or irregular vaginal bleeding as it done among private clinic patients. In Saudi Arabia Magdy Hassan Balaha et al¹⁷ found that (53.3%) of screened patient had abnormal pap cytology, and only (40%) of these abnormal cytology was diagnosed as LSIL and HSIL. in Telangana (2017) the HSIL represent (25%), LSIL(62.9%) of the Tertiary Care Centre patients with Gynecological Complaints.¹⁸ There is a significant relation between the Pap smear results and patient presenting symptoms: the only symptom that associated with seq.cell ca. is the Post menopausal bleeding (PMB) 1(33.3%) diagnosed as seq. cell ca. and 1(3.8%) of those had other symptoms (external genital warts) had seq.cell ca. Most symptoms associated with increased rate of intra epithelial lesion was Post coital bleeding(PCB), 5(13.5%) NILM, and 32(86.5%) different stages of intraepithelial lesion. Irregular vaginal bleeding also commonly presented with various stages of intraepithelial lesion 12(92.3%), while abdominal pain was dominantly diagnosed as

LSIL 4(57.1%). Diagnosis of HSIL was (13.5%), of the post coital bleeding presentation, this lower than what found by Abdulla K N, et al¹⁵ 2016 in Baghdad(44%), and higher than Obeidat RA, and Saidi SA¹⁹ that studied cytological presentation of patient presented with post coital bleeding and found it (3.8%) had HSIL and cervical cancer (0.4%). LSIL was (16.2%) of post coital bleeding in this study this was lower than found previously in Iraq (49%)¹⁵. Obeidat RA, and Saidi SA¹⁹ (2012) found that (8.3%) of the post coital bleeding presentation was diagnosed as LSIL

Cervical cancer was (33.3%) of the post-menopausal bleeding presentation, and none of the post coital and irregular vaginal bleeding, while Obeidat RA, Saidi SA¹⁹ found that (0.4%) of post coital bleeding presented patient had cervical cancer.

Abnormal vaginal bleeding was diagnosed as HSIL in (7.7%), this was lower than Abdulla K N, et al¹⁵ 2016 in Baghdad (16%) .

Vaginal discharge diagnosed as LSIL among (36.2%) and non was diagnosed as HSIL, this was higher than found by Salih MM et al²⁰ 2017 LSIL (2%), and HSIL (1%).

The high percentage of squamous intraepithelial lesions that found among private clinic patient which was higher than reported in other countries indicate the need for screening program to be implemented in Iraq and to consider the private as well as the public health services, in implementation.

Conclusion

Iraqi women attending the private clinic had high level of intraepithelial abnormality, even if it lower than other countries but it in need to be controlled by cervical cancer screening program, the common presenting symptom with increased rate of with various stages of intraepithelial lesion were post coital bleeding, and Irregular vaginal bleeding.

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Al- Salhiya Health Center, Iraq and all experiments were carried out in accordance with approved guidelines.

References

1. Cervical cancer, human papillomavirus (HPV), HPV vaccines: Key points for policy-makers and health professionals. World Health Organization, 2007; WHO/RHR/08.14
2. Lawson HW, Henson R, Bobo JK, Kaeser MK. Implementing recommendations for the early detection of breast and cervical cancer among low-income women. *MMWR Recomm Rep* 2000; 49(RR-2): 37–55.).
3. World Health Organization [homepage on the Internet]. Catala d' Oncologia. Human Papiloma Virus Information Center Report-Iraq. [Updated 2010 Sept 15; cited 2011 Feb 15]. Available from: <http://apps.who.int/hpvcentre>.
4. Asan Ali Qasim AlNiyazee, SarabK. Abedalrahman, Zeena NAbdulrahman, Islam ARZadawy. Prevalence of Human papilloma virus positivity and cervical cytology. Is there a new HPV gene? *World Family Medicine*. 2019; 17(8): 9-13. DOI: 10.5742/MEWFM.2019.93667]
5. ACOG Practice Bulletin no. 109: Cervical cytology screening. *Obstet Gynecol*. 2009 Dec; 114(6):1409-20. [Medline].
6. Rosai J, Rosai A, Ackermani surgical pathology. 9th ed. St. Louis: CV Mosby; 2004.
7. Scott JR, Gibbs RS, Karlan BY, Haney AF, editors. Danforth's obstetrics and gynecology. 9th ed. Philadelphia, : Lippincott Williams and Wilkins; 2003
8. Sawaya GF, Grimes DA. New technologies in cervical cytology screening: a word of caution, *Obstetrics & Gynecology*, August 1999; 94(2):307–310.].
9. Patro BK, Nongkynrih B. Review of screening and preventive strategies for cervical cancer in India. *Indian J Public Health* 2007; 51:216-21
10. Abedalrahman SK, Al-Khalidy NA, Al-Hashimi AS, Al-Diwan JK. Accuracy of FNAB in diagnosis of breast lump. *Indian journal of public health research and development* 2019; 10(1):760-4.
11. Abedalrahman SK, Al-Khalidy N A, Al-Diwan J K. Advanced Stage at diagnosis among Iraqi breast cancer women. *Sudan Journal of Medical Sciences* 2019; 14(2):38-40, DOI 10.18502/sjms.v14i2.4690.

12. Barzanjy BK, Talat L A, Ismail SA * Cervical dysplasia: assessment and risk factors among women attending the Maternity Teaching Hospital in Erbil, Kurdistan-Iraq. Zanco J. Med. Sci., 2013; 17 (1): 286-93.
13. Mezaal MI, Alwan NA, Aziz IH, and Shalal M. Prevalence of HPV genotype in cervical cells among Iraqi patient with abnormal cervical pap smears. Iraqi journal of biotechnology 2017;16(2): 19-27.
14. Abdurraheem A F, KhudhairiJ M. Papanicolaou Smear Outcome of Referred Women to Health Facilities in Baghdad. Mustansiriyah Medical Journal 2014;13(1):33-37.
15. Abdulla K N, Alheshimi S J, Aljebory H S, Altaei TJ K - Evaluation of Pap smear data in Baghdad province . "International Journal of Scientific and Research Publications (IJSRP),2016;6(5):634-9.
16. Al-Rubaiee, N, Al-Alwan N. Application of the Bethesda System for Cervical Cytology Reporting. J Fac Med Baghdad, Baghdad Univ., 2006;48 (1): 41-47
17. Balaha MH, Al Moghannum MS, Al Ghowinem N, Al Omran S. Cytological pattern of cervical Papanicolaou smear in eastern region of Saudi Arabia. J Cytol. 2011;28(4):173–177. doi:10.4103/0970-9371.86343]
18. Dr MNP. Charan Paul1, Dr O Sirisha 2, Dr VSailaja 3, Dr Veldurthy Vijay Sreedhar 4, DrKodaliPavani 5, Dr T Vani 2 Study of Clinico-Cytological Profile of Female Patients from Rural Areas of Telangana Presenting to a Tertiary Care Centre with Gynecological Complaints International Journal of Health Sciences & Research (www.ijhsr.org)2017; 7(4):84-9.
19. Obeidat RA, SaidiSA . Prevalence of High-Grade Cervical Intraepithelial Neoplasia (CIN) and Cervical Cancer in Women with Post-Coital Bleeding (PCB) and Negative Smear: A Retrospective Study. GynecolObstet, 2012; 2:127. doi: 10.4172/2161-0932.1000127]
20. Salih MM, AlHag FTES, Khalifa MA, El Nabi AH. Cervical cytopathological changes among women with vaginal discharge attending teaching hospital. J Cytol. 2017;34(2):90–94. doi:10.4103/JOC. JOC_214_15

Effect of Vernald Way (VAKT) for Multiple Senses, Health Care and Clinical Learning in Dealing with Hardship and Written to the Reading First Stage Pupils

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Abstract

Current research aims at identifying the impact of vernald way (vakt) for multiple senses to address the hardship I have written and reading the first primary stage pupils with special needs in Babylon, and this study was conducted in primary schools under the special education classes – Centre, in order to achieve the goal Search follow Finder experimental method, then choose Finder school Safieddine ornaments the midair school trial sample jeweler school officer, reconnaissance search sample number/9 first grade students raise for the experimental group in the school of Safieddine number/10 students from the first grade. Breeding for control group at the midair school, and took the same test researcher with ten paragraphs check a handout and persistence, and achievement test Finder dish on my sample experimental and research officer at 30/4/2019, then use in squared Pearson correlation coefficient and (Ki 2) and t-test for equality Independent waltbiain statistical method for processing data, and results from the experimental group than the control group, indicating that the method vernald (vakt) for multiple senses may bluff and superior.

Keywords: *(Vernal Parana (vakt) Para as maramihang mega) (panda dam an pagbabasa) (nakasulat and harp).*

Introduction

I stop Finder on the magnitude of the problem and the difficulties experienced by pupils in special education in learning reading and writing in the previous discussion, so I felt that running reading and written hardship Wizard experience I have disabled the first primary stage using the method vernald (vakt) for the senses. That dyslexia is a specific learning difficulties, is nervous, and correct identification difficult features or freewheeling words and poor spelling and ability to interpret symbols, these difficulties are often the result of a deficit in the phonologic level of language, and are not proportional to the cognitive capacities Yen and proper education, notes of the secondary consequences of the problem of difficulties in comprehension and literacy and clerical experience weakness hindering the development of vocabulary and background knowledge¹³. And that reading and writing are a major problem for pupils who have learning difficulties, where 80% of the those students have difficulty reading and writing on

various skills, and that more than 25% of regular students they need to specialize in teaching reading and writing, and here lies the importance of teaching a Are built on proven scientific basis, specialized studies abound in recent years looking for effective teaching method and strategies for teaching pupils who have problems with reading and writing prevent attainment expected of them based on their environmental and health conditions to study. That the problems and difficulties in reading and writing to students with learning disabilities tend the vast majority of them who receive services with learning disabilities have problems and severe difficulties in reading and writing skills, and some are hard to cure, studies and research dealing with difficulties and problems Reading and writing have learning disabilities that their papers and their books or their books replete with numerous errors in spelling and grammar and structure, and complexity of the characters and styles of handwriting errors and dominated by the lack of control and regulation, often omit some words such as characters or characters The end or the Middle, and may

add some letters that are not associated with the word, and often the sentences they use short and disjointed and lacks meaning or content¹⁰. Researcher finds difficulty in reading and writing or reading and written hardship is one important cornerstone of academic learning difficulties, if not the key determinant and most importantly, where many researchers in the field of learning disabilities, dyslexia and writing represents the main reason Behind the school failure, dyslexia and writing case where the pupil is different from others in the processes of thinking and learning and skills take him auditory and Visual information storage and handling symbols, called in linguistic and non-linguistic communication processes and learning, where he finds Pupil difficulties in translating language to express ideas, thoughts, or understand the meaning of written words. Since in addition to learn reading and writing skills should continue to exercise it in the absence of practice reading and writing of pupils may have negative effects on children who are already defined categories and nominated for dyslexia and literacy, is a disorder that appears in pupil unable to learn Reading and writing despite having psychic powers despite receiving the appropriate education and training on how to read and write appropriate social and cultural background and dyslexia and writing in this case based on difficulties recognizing constitutive origin¹³. And pupils who suffer from problems with fluency literacy cannot distinguish words accurately reading the word punch slowly and without compiling the words complete sentence meaning, and many problems with reading, writing and reading decoding problems in reading the text orally by pupils who suffer from Learning disabilities and pupils who suffer from real problems in deciphering the words replacement to suffer from (disleksia/dyslexia) and often suffer from slow learning. And pupils who suffer from written hardship usually have poor written production, their intelligence and abilities do not appear when looking at something they write, and there are indications written hardship among pupils, and this is evident in that they usually write short sentences and taking an abnormally long time in writing and This is due to a problem written hardship, their usually unreadable and using the eraser too much as well as leave spaces between words, characterized by frequent mistakes and clerical due to adapt the sound with the appropriate literal format,

so that it does not represent the sounds heard in the word. Teaching method the method intended to provide skill to the pupil, there is no way or pattern tutorial or tools or means to suit all pupils with special needs in the classroom, and the severity and type of disability were factors affecting use of method and strategies and means, and shall Be modalities and styles and teaching strategies in special education variety based on oriented therapeutic diagnosis especially multi-sensory learning. There is no doubt that students who have difficulties in learning to read and write with impaired sensory perceptions as auditory or visual perception, pupil with dyslexia and writing down his ability compared to the average child in the process of receiving and analysis of information, and thus more in need To use more than one sensory channel in the process of learning these skills, meaning the urgent need to recruit more than cognitive tool in the learning process of association between written symbols and sounds it function defines a multiplayer mode senses¹³.

Methodology

This chapter includes select research methodology and sampling procedures and prepare his tool and applied and the statistical method used in analyzing data.

Sample Search: Into adopted experimental method, because it is suited to the nature of his research, for being not only describe the current status of the event or phenomenon but also a clear and intentional interference by the seeker in order to reshape reality appears to use certain changes procedures and then note the results accurately, analysis and interpretation¹⁸.

Action Research: Experimental Design: The experimental design is the plan Finder to get answers to questions and contains everything from currency researcher wishes to determine the problem and formulating hypotheses end data analysis and conclusions expected in access²⁵, depending type of experimental design On the nature of the problem and its variables and conditions sample, so the researcher adopted on experimental design with a partial seizure being compatible with the happenings of the current search, Figure 1.

Igbos (1):

Experimental na Disney Para samganaghahanap:

H	Combos	Independent variable	Dependent variable	Gadget
1.	Pilot	Parana ng Vernald (vakt) Para samaramihangmga panda dam	Koleksyon	Mental passbook
2.	Optical na	Tradisyunalnapamamaraan	Koleksyon	Pagsusuri ng mas magi.

Research community and appointed by:

Search Community: Saving all members of society or items or things that have properties one can observations (alagrsh, 2015 92), the researcher community primary school is opened in which rows of special education for boys and girls in the province of Babylon Centre for academic year (2018-2019), as a For the current search selection requires schools to be field of the search experience, the researcher visited the General Directorate of education Babylon book basic education faculty/14005 in 19/11/2018, approached school above-preparation and training departments of primary schools with special education classes with her book/2174 at 28/11/2018, and a copy to the Department of planning and statistics researcher visited the section got schools that opened the ranks of special education.

Search Sample: the sample is a subset in the original community, chosen in a certain way, and includes a number of elements of society and should be representative of the original community for uncles findings fully community (other meanings, 2012:86)

Sample School: in the midair school for boys picked because they contain special education first stage row elementary student population in/10 students, and then choose either school boys Safieddine being contains a row of first stage special education where pupils had/9 pupils, in a nest Weasel was a school for boys, experimental group Safieddine, the midair school for boys group officer.

Equal sets of search: Before the start of the experiment the researcher keen to conduct statistical research groups equal variables believed to affect the outcome of the experiment, including:(Chronological age calculated in months-school for parents-academic achievement for mothers), the researcher has obtained the data on those variables from direct pupils, school record, and after data collection and statistical treatment show

that the calculated values are smaller than scheduling freedom degree values (17) and when Level indication (0, 5) this shows that statistically equivalent research collection in chronological age in school for parents.

Requirements:

Experience Duration: In began his experience on Sunday 17/2/2019, equal period to search groups pupils, and ended on Monday, 29/4/2019.

Select material: select in scientific material that will study for two sets of experimental and research officer during a trial and a number of book reading decision taught to pupils in primary school year first phase (2018-2019) ⁸

Preparation of teaching plans: teaching plan is a package of regulatory measures established by the teacher to ensure the success of the process of teaching and learning goals, and described as a plan guide and teacher-oriented, then they are not rigid is applied literally, as well as their Flexibility to be adjustable and change ², as the educational process could not successfully go without prior planning, so the researcher prepared a syllabus for my reading topics for first grade that will be studied in the experiment, in the light of educational content and objectives Behavioral school article in accordance with the method vernald (vakt) for multiple senses of the experimental group, according to the traditional method for the control group, and the view finder anmozegitin plans of those plans to a group of experts in education and psychology and teaching method to solicit their views And their proposals, in the light of his researcher observant experts the necessary amendments until ready for application.

Search tool: the achievement test preparation: tests a sample of paragraphs or questions varied types of interpretation and translation for each paragraph of a certain predetermined, upon sentencing an individual

or group of individuals, a group of various stimuli to provoke certain responses to the individual And estimate that by giving him the proper degree reflect the desired behavior availability¹⁸, since the current search requires preparation test paragraphs pupils search groups to see the impact of the independent variable (vernal) in the dependent variable (address the hardship of reading books ABI) into test subjects taught in the course of decision taking into account test validity and reliability and objectivity.

Scoping Sample: Sample test Finder dish chosen reconnaissance ksdi-Zahawi school for boys consisting of number/9 special education students in the first grade and that was on Sunday, 14/4/2019.

Reliability Test: Reliability refers to the consistency of the results obtained from the application

calendar tool for several times, is the steady results and not steady the instrument itself¹⁴, since the first test was applied researcher on exploratory sample on Sunday two weeks after 14/4/2019 was prepared Article on Sunday 28/4/2019 test on the same sample, after correcting the results and apply the Pearson correlation coefficient turns out that stability is (0, 81) which is surely good, so I got the tool ready for application on a sample research pilot and officer.

Apply the Final Test: After you complete the search tool finalized researcher devoted Tuesday 30/4/2019 deadline for test pilot research and collection officer and assist teachers who studied art, and after completion of the test results have been corrected was given one degree For a correct answer and 0 for a wrong answer or abandoned.

Table 2. Ipinakikita ang t-haulage kinakalkula at experimental na group lames at optical

Group	Billing ng mga respondents	Ang pagtuturo	Kaibahan	Antes ng kakayahan	Kahalagahan ng T		Antes ng indecision
Pilot	9	8	0, 66	17	Kinakalkula	Crosstab	Estadiskita ng mga function samga antes naindecision (5, 0)
Optical na	10	5	1		7, 14	2, 110	

Interpretation of results: the results of the experimental group viewed than a statement of method-vernal (vakt) for multiple senses to control group that studied the regular way, and returns an into because.

- That special education students with learning difficulties including dyslexia and writing so modern vernald way motivate came to participate and learn as well as special hardship cringe.
- Vernald method (vakt) for multiple senses all senses so that enables pupils to benefit from the other senses is the sense of weakness, served and was promoter of learning.
- Vernald method (vakt) for multiple senses using intensive teaching of approximation concepts which encourage students and measurement in learning to read and write.
- The incentives recommended by the vernald method has positive effects on recurrence behavior of learning to read and write among special education students.

- Vernald method (vakt) for multiple senses found its way into the hearts of students interacting with the parameter was encouraged to discover their strengths and bright positive points to learn reading and writing.

Conclusions

- Vernald method (vakt) in teaching reading and writing to the disabled helped outweigh the experimental group control group.
- Vernald manner helped students from the receiver position to the position effective participant in the learning process and become their focus learning process.
- Students with dyslexia and writing found FOMC vernald way (vakt) for multiple senses to benefit from other senses is deactivated.

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the University of Babylon/College of Basic Education, Department Basic property and all experiments were carried out in accordance with approved guidelines.

References

1. Ado A. unang pag-aaral ang ilang Kalama alsiroat – pansin – katalusan – alaalamgaestudyantenanaranasan ang kahirapansaakademikong pag-aaral (dyslexia karamihan) Mentouri University-Faculty ng Humanities at Social Sciences – Kagawaran ng sikolohikal at afghan sa edukasyon, di-inilathala ng MPhil. 2011;201.
2. Hector, ang kaligtaan ay kaaya-aya. Pangkalahatang pamamaraan sa pagtuturo (mensch acting at kontemporaryong) belay ng culture napaglalathala, Oman Jordan. 2009;95.
3. Pedro P. Pagtuturo sa magabatang may mgakapansan sa pagkatuto. Pagmumuling-sigla ang belay, paglalathala at paglilimbag, Oman Jordan. 2009.
4. Si Pedro H. Aikman ang mga curricula Para sa mga estudyante ng may mga especial napangangailangan. Pagmumuling-sigla ang belay Para sa paglalathala, pamamahagi at paglilimbag, Oman Jordan. 2010.
5. Omar A. mga problem ng literacy sa minute na. angel kaligtaan Cairo Egypt. 2016.
6. Dhal, pag-aaral ng mgapalazzo . at pagsusuri ng oral na keying unwind ng mga stratehiya nan ang mga Bata sa pagkatuto Bashing ang mgapaghihirap. Algeria – Mentouri University-Faculty ng Humanities at Social Sciences department ng sikolohikal at afghan sa edukasyon, di-inilathala ng MPhil. 2005;6-8.
7. Alzaoikh N. napag-aaral ng mga still – FARC model vary) Internet site) n-thaw-n-thaw @ main it may hotels-in.com. 2016;11.
8. Narrator T. pagbabasa koi ng unang grade. I-11, Republican ng Iraq, ministry ng edukasyon, ang pangkalahatang pangangasiwaan ng curricula. 2017;76-110.
9. Rousing F. Pangangalaga ng mga tong may especial napangangailangan. Nagkakaisang sa Arabic namga company sa pagmamemerkado. Oman-Jordan. 2013;11-13.
10. Zagat F. Pag-aaral ng mgakapansanan – waltshkhsih ng teoretikal na Pundasyon at nakakagaling, University Publishing House, Cairo. 1998;492-516.
11. Baiting U. maharini school student achievement – mga sahib at collusion, ang Jadyera Para sa magapublikasyon at pamamahagi. 2010;85.
12. Baiting U. maharini school student achievement – mga sahib at collusion, ang Jadyera Para sa magapublikasyon at pamamahagi. 2010.
13. Sartawi, pay Aziz, et al . magpatinginsa doctor at gamut in ang mga problem sa pagbabasa . Weal publishing, Oman Jordan. 2009;52-178.
14. Shahabad, Norman. Pagkatuto at akademikong kalendaryo. Belay Chroma Para sa paglalathala at pamamahagi – Oman – Jordan. 2009;262.
15. Ababa A. pangkaisipang kapansanan at magbigay matukoy, Weal paglalathala, Oman Jordan. 2012.
16. Hussein S. at declawing still sa pag-aaral. at ang mga aplikasyon sa puritan ng guru at mag-aaral, tappet belay cultural nainstitusyon, Iraq ang Babylonia. 2018;21.
17. Alert H. Pundasyon ng Pananaliksik sa edukasyon at sikolohikal . Elder napamamaraan Para sa paglalathala at pamamahagi – Oman – Jordan. 2015.
18. Aziz A. unang tumbling sa pagsulat na pang-edukasyon Pananaliksik Dry House administration at economic na afghan, utanabi Street, Baghdad. 2019;67-121.
19. Omar S. Bud ng Pananaliksik sa edukasyon at afghan ng Tao. DAR Al-fir publishing – Oman – Jordan. 2010;103.
20. Grana M. ang akademikong pag-aaral ng mgasuliraninsa puritan ng pang-unaware at paghihirap. Alexandria Center Para sa mga anklet, mga Arab ng Hippo. 2003.
21. Martin H. Ang mga Katanga ng mga manor de dead nakapansanan, misalign Zane sartawi, mate, paaralang ng edukasyon, Universidad ng King Saud University anklet belay. 2006;194-195.

Evaluation of Antimicrobial Activity and Study of Raman Spectra for Malachite Green Dye in Aquaculture in Solid State and Liquid State

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Abstract

This papers include the study of Raman spectra for different forms (solid and liquid) of the malachite green dye. Three concentrations (10^{-3} , 10^{-4} , 10^{-5}) Ml of dye solution are prepared in the water solvent and Raman spectra were measured using a wavelength laser beam (532 nm) A total of (11) major vibration patterns were obtained for the dye in concentration (10^{-3}) and (6) vibration patterns in concentration (10^{-4}) while the number of vibration patterns (5) in concentration (10^{-5}) Using a (pld) technique, a solid form(film) of dye was prepared on its own, When Raman spectra was measured, (8) vibratory patterns appeared, while the vibration patterns of dye were decreased when the dye film was prepared with the polymer. Vibration patterns were observed in all models prepared The most prominent (C-N str, C-H ben, C=C str).

Keywords: Antimicrobial activity, Raman spectra, malachite green.

Introduction

Visible radiation, which is emitted from most organic dyes, helps to be used as an effective medium in dye lasers. This has been considered the first tunable laser in the visible spectrum because it possesses a broad fluorescence spectrum, This allowed the laser output to be toned at any value selected within this broad range .Because of the abundance of fluorescent dyes, it is possible to select compounds that can produce laser emission, in any part of the ultraviolet, Visible, Near-infrared. The dye lasers produce a laser output, which can be toned to the wavelength range of 340 nm to 1.2 μ m, depending on the type of dye used¹. That distinguishes dye laser from solid and gas state lasers can be used as an effective medium in the liquid state. This results in high optical quality, which facilitates cooling operations and high pulse repetition rates. This leads to be a gain for a dye solution that is much larger than a gain in the gaseous state, plus it has to be approximated to the gain of solid state materials. Hard plastic rods - made from dyes embedded in plastic materials - can be used as effective media. The active medium in the organic dye laser is a fluoride organic material. Typical materials used as an effective medium are (Rhodamine), belonging to the

(Xanthenes) family. These material are formed from their strong absorption ranges located in the visual ray region, and these substances are stimulated by optical pumping². The dye used in this research is malachite green antimicrobial in aquaculture³. The signal that stand out from the dye lasers is a short pulse with wide spectral contents. These lasers are excite by the use of flashlights that are specially designed to produce high output power and It has a short period of pulse output. In addition, the dye laser has a high conversion efficiency, so it can produce short pulses, as:

$$\gamma_{\text{gain}} \propto 1/\tau$$

τ : Pulse time - γ : gain

These pulses can reach nanoseconds (10-9 n.sec) and pichoseconds (10-12p sec).Therefore, dye lasers will eliminate many of the constraints that stand in front of spectral studies that require high analytical ability, especially in the field of element enrichment, the separation of isotopes, as well as in the field of industrial and medical applications ⁴.Polymers are large molecules made up of small, interconnected units called the monomer. Polymers are sometimes crystalline and sometimes noncrystalline or a mixture of the two

⁵Most polymers lacking high electrical conductivity, so their uses are limited to their chemical and mechanical properties. As for the electrical uses of polymers, they are limited to electrical insulators because they have good electrical insulation properties ⁶. One of the organic polymer isolates poly acetylene (PA) was discovered in 1977 which is characterized by the possibility of converting it into a polymer conductor by treating it with appropriate defects through oxidation and reduction ⁷. Also, different types of ring and aromatic polymers have been discovered which behave in the same manner as these polymers have led to the formation of a new type of polymers called Conducting Polymers⁸. As this type of polymers very quickly got great attention and wide by researchers because the main reason behind the interest of researchers with these polymers is the possibility of using these materials in electronic applications, in addition to the acquisition of electronic circuits integrated dimensions under microwaves can be using these Polymers are easier to use than inorganic semiconductors⁹. As the use of this type of polymers in electronic applications led to the opening of a new branch called Molecular Electronics¹⁰. Some problems arose in the early stages of the discovery of this type of polymers. These problems hindered the development of these polymers. One of these problems is that they cannot be damaged in any of the solvents (Insoluble) or their fusion (Infusible). But in recent years, conductive polymers have been found to be able to melt and melt by adding some chemicals to the monomer unit¹¹. The conductivity of some conductive polymers can be increased by increasing the rate of impurities. Among the polymers that are connected is the polymer (polyniline), which is considered one of the important polymers, and one of the characteristics of this polymer is the possibility of dissolution. This led to its presence in a conductive manner which is thermally and environmentally stable ¹². Polyniline polymer is characterized by high electrical properties (in the process of pitting) with proton acids, and can be found polyethylene either in the form of insulation (base) or salt (conductive) ¹³.

Raman Spectroscopy: The Raman Effect occurs when electromagnetic radiation impinges on a molecule and interacts with the polarizable electron density and the bonds of the molecule in the phase (solid, liquid or gaseous) and environment in which the molecule finds itself. For the spontaneous Raman effect, which is a form of inelastic light scattering, a photon (electromagnetic

radiation of a specific wavelength) excites (interacts with) the molecule in either the ground rovibronic state or an excited rovibronic state. This results in the molecule being in a so-called virtual energy state for a short period of time before an inelastically scattered photon results. The resulting inelastically scattered photon which is “emitted”/“scattered” can be either of higher (anti-Stokes) or lower (Stokes) energy than the incoming photon as shown in Figure 1. In Raman scattering the resulting rovibronic state of the molecule is a different rotational or vibrational state than the one in which the molecule was originally, before interacting with the incoming photon (electromagnetic radiation). The difference in energy between the original rovibronic state and this resulting rovibronic state leads to a shift in the emitted photon’s frequency away from the excitation wavelength, the so-called Rayleigh line. The Raman effect is due to inelastic scattering and should not be confused with emission (fluorescence or phosphorescence) where a molecule in an excited electronic state emits a photon of energy and returns to the ground electronic state, in many cases to a vibrationally excited state on the ground electronic state potential energy surface.

If the final vibrational state of the molecule is more energetic than the initial state, the inelastically scattered photon will be shifted to a lower frequency for the total energy of the system to remain balanced. This shift in frequency is designated as a Stokes shift. If the final vibrational state is less energetic than the initial state, then the inelastically scattered photon will be shifted to a higher frequency, and this is designated as an anti-Stokes shift. Raman scattering is an example of inelastic scattering because of the energy and momentum transfer between the photons and the molecules during the interaction. Rayleigh scattering is an example of elastic scattering, the energy of the scattered Rayleigh scattering is of the same frequency (wavelength) as the incoming electromagnetic radiation.

A change in the molecular electric dipole-electric polarizability with respect to the vibrational coordinate corresponding to the rovibronic state is required for a molecule to exhibit a Raman effect. The intensity of the Raman scattering is proportional to the electric dipole-electric dipole polarizability change. The Raman spectra (Raman scattering intensity as a function of the Stokes and anti-Stokes frequency shifts) is dependent on the rovibronic (rotational and vibrational energy levels of the ground electronic state) states of the sample. This dependence on the electric dipole-electric

dipole polarizability derivative differs from infrared spectroscopy where the interaction between the molecule and light is determined by the electric dipole moment derivative, the so-called atomic polar tensor (APT); this contrasting feature allows one to analyze transitions that might not be IR active via Raman spectroscopy, as

exemplified by the rule of mutual exclusion in Centrosymmetric molecules. Bands which have large Raman intensities in many cases have weak infrared intensities and vice versa. For very symmetric molecules, certain vibrations may be both infrared and Raman inactive (within the harmonic approximation)[14].

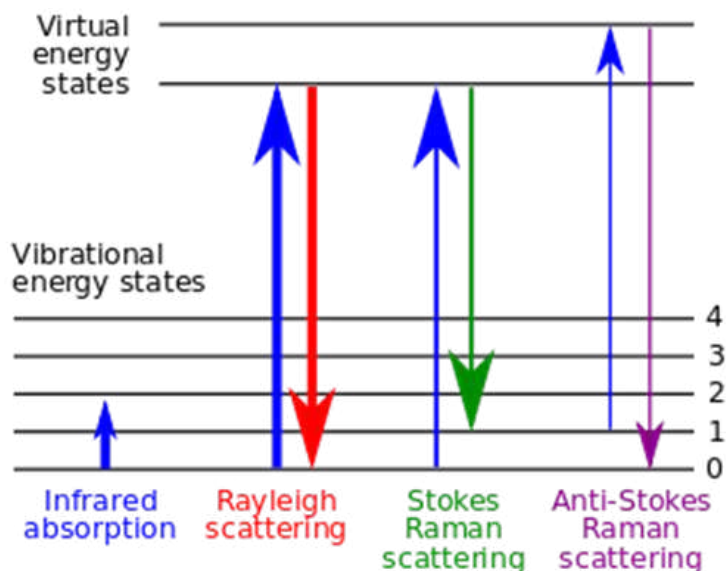


Figure 1: Energy-level diagram showing the states involved in Raman signal. The line thickness is roughly proportional to the signal strength from the different transitions[15].

Pulse laser deposition mechanism (PLD): The process of scraping of the material occurs when the laser pulse is subjected to the hard target and is under gaseous conditions. And that the materials can be deposited on a slice or assembled or shaped in a powder. Although some applications such as applications fuel cells [carbon nanotubes] need to produce powder with nanoparticles[16,17]. However, most applications require nanoparticles in thin films.

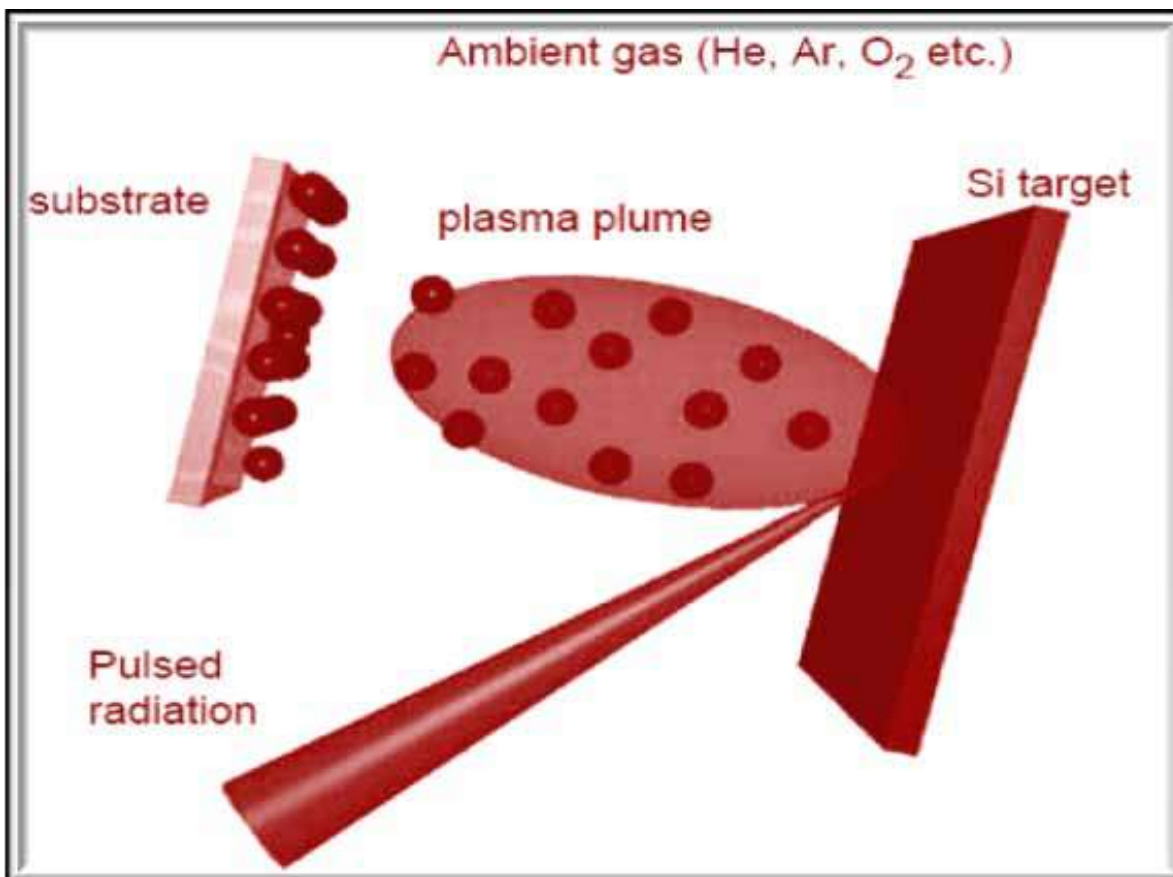
Figure (2) shows the mechanism of pulse laser deposition. Lasers are usually used at UV wavelengths (192-248 nm) or through the second and third compatibility of the Nd-yag laser with wavelength (355,532 nm) and plasma is weakly absorbed for these wavelengths, reducing the effect of plasma on the skimming process. This technique is performed by focusing the laser beam on the target surface, which rotates at a 45° incidence angle. The energy density is usually between 108-109 W/cm². The incidence laser induce the plasma cloud to expand perpendicularly

to the surface of the slide, which is placed on a rotary surface only a few centimeters from the target. The slide holder is kept at room temperature or heated to improve the adhesion of the film to the chip. These slides are usually carried out with inert gas (He, Ar) and the gas is maintained at a low pressure (0.01-20 Torr). They are discharged from the air before being filled with gas.

The target material shall be placed in a high vacuum chamber and shall be at an angle of 45° with the incidence pulse laser. The atoms and flying ions are deposited from the target on the base, where the surface of the target and the surface of the base are parallel but have a certain distance[18].

1. The laser beam is placed directly on the surface of the target, and the focal lens is used. It is suitable for the laser beam to pass through an optical window that allows the laser beam to pass into the sediment chamber or use a glass door to allow the laser beam to pass.

2. The target material is rotated at levels x, y for the laser beam, so that the focus of the laser beam is ensured to remain regular with each pulse.
3. Before sedimentation, the sedimentation bases are heated primarily to make the film highly adhesive.
4. When gas and film material interaction are needed during the membrane growth process, the vacuum chamber of the laser deposition system is equipped with different gases such as (He, Ar, O₂) and others.



Figure(2). Pulse laser deposition mechanism¹⁷

Preparation of the Samples: A concentration of 1x10⁻⁴ M l malachite green dye solution in chloroform solvent was prepared. The powder was weighting using an electronic balance type (BL 210 S) Germany having a sensitivity four digits.

$$W = \frac{M_w \times V \times C}{1000} \quad \dots(1)$$

where

W: weight of the dissolved dye (gm)

M_w :molecular weight of the dye (gm/mol)

V: the volume of the solvent (ml)

C : the dye concentration (mol/l)

Different concentrations were provided according to the following equation:

$$C_1 V_1 = C_2 V_2 \quad \dots(2)$$

where

C₁: primary concentration

C₂: new concentration

V₁: the volume before dilution

V₂ :the volume after dilution

Deposition of samples by laser pulse deposition:

The pulsed laser deposition method was used to prepare nanoparticles of nanoparticles. This system consists

of the main parts shown in Fig. 5-3) consisting of the discharge chamber, the Nd-YAG pulse laser with a wavelength of 1064nm, a convex lens made of quartz with a focal length 30cm, window made of quartz glass, pressure control screen, rotary pump, spread pump, there are a set of steps we follow to prepare membranes which are as follows:

1. Clean the vacuum chamber using acetone alcohol and a soft cloth with attention to leaving the room for 24 hours exposed to air .
2. Put the floors of glass number 4 on the slide holder so that it is against the target on the rotor target holder so that the distance between the target and ground 4cm .
3. The Nd-YAG laser beam focuses on 140mj and pulse 150 of the PANI polymer using a convex lens with a focal distance of 30cm on the rotor target at a 45° angle.
4. Close the discharge chamber with all the valves closed and start the discharge by opening the rotary pump valve and when the pressure reaches 10⁻³ mbar The rotary pump valve is closed and the pump valve is opened until the chamber vacuum is reached 10⁻⁵ mbar.



Fig(3): Pulse laser deposition system.

5. Heat the floor using a halogen lamp until the temperature reaches 250C to increase the adhesion of the material to the ground.
6. After reaching the discharge required with the survival of the vacuum chamber valve is open, the laser pulses are given and the result is the case of the plasma that contains the particles that will be deposited on the ground.
7. Get the membranes are injected with a material poly aniline on the glass floors and undergoes visual and structural tests and electrical.

Results and Discussion

Raman Spectra:

Raman Spectra of Solution:

Table (1): Vibration modes for malachite green dye solution at concentrations 10⁻³ and intensity and wave number

Mode	Wave No.(cm ⁻¹)	Intensity(mol/cm ⁻²)
C-H ₂ str	2878	348
C-H _{str}	2742	402
C=N _{str}	2241	2090
C=C _{str}	1624	4772
N-H _{ben}	1499	1823
C-H _{ben}	1377	2736
C-H _{i-o-p} def.	1302	1369
C-N _{str}	1226	1255
C-H _{o-o-p} def	1183	1497
C-H _{2 o-o-p} def.	919	563
C-C _{str.}	810	654

Table (2). Vibration modes for malachite green dye solution at concentrations 10⁻⁴

Mode	Wave number(cm ⁻¹)	Intensity(mol/cm ²)
C=C _{str}	1629	801.02
N-H _{ben}	1499	250.5
C-H _{ben}	1377	358.8
C-H _{i-o-p} def	1307	143.9
C-N _{str}	1231	147.3
C-H _{o-o-p} def	1188	154.7

Table (3). Vibration modes for malachite green dye solution at concentrations 10^{-5} .

Mode	Wave No. (cm^{-1})	Intensity (mol/cm^2)
C=N _{str.}	2212	162
C=C _{str.}	1629	392
C-H _{str.}	1377	118
C-N _{str.}	987	224
C-C _{str.}	891	266

Conclusions

By studying the Raman spectra of prepared liquid samples it was observed that vibration patterns decreased with less concentration. When studying the Raman spectra of the solid form of dye (dye film), 8 vibration patterns were obtained. When studying the Raman spectra of the polymer film (poly Aniline), two types of vibration emerged. When adding polymers to the dye and studying Raman spectra, we note that the vibration patterns were reduced to (5).

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Science Collage for Women, Babylon University, Iraq and all experiments were carried out in accordance with approved guidelines.

References

1. B Snavely. Organic Molecular Photo physics, ed. by (J.B.Birks), John Wiley & Sons. 1973; 1: 23.
2. B Snavely. Proc. IEEE.1969; 57: 1374.
3. Adina R,Alexandra O. influence of surfactants on the fading of malachite green ‘‘ central European journalof chemistry, vol 6,pp. 1895- 1066, 2008.
4. SG Rautian, I Sobelmann Opt . Spectry. 1961; 10: 65 .
5. L Stockman, WR Mallory, KF. Tittle Proc.IEEE. 1964; 52: 318 .
6. BI Stepanov, AN Rubinov, J Appl. Spectry, 1966; 4: 159 .
7. AN Rubinov, BI Stepanov, Opt . Spectry, 1966; 22: 330.
8. PP Sorokin, JR Lankard, IBMJ . Res. Develop.1966; 11: 162.
9. W Schmidt, FP Schafer, Z Natuforsch.1967; 22: 1563 .
10. OG Peterson, SA Tuccio, BB Snavely, Appl . Phys. Letters,1970; 17: 245.
11. M Fukuda, K Mito. Solid – State Dye Laser with Photo –Induced Distributed Feed Back”. J. Appl. Phys.2000; 39.
12. A Costela, F. Florido, I. Garcia – Moreno and J.M. Figuera, J. Appl.Phys.1995; 7.
13. A Douglas, F James, R Stanley. Principles of Instrumental Analysis”, (6th ed.). Belmont, CA: Thomson Brooks/Cole. 2007; 169–173.
14. A Milekhin, N Yeryukov, A. Toropov, D. Dmitriev, E. Sheremetand D. RT Zahn, “Raman scattering of InAs/AlAs quantum dotsuperlattices grown on (001) and (311)B GaAssurfaces”Nanoscale Research Letters, 7:476, pp. 2-5, 2012.
15. Vogel A, Noack J, Nahen K, Theisen D, Busch S, Parlitz U, Hammer DX, Noojin, GD, Rockwell BA, Birngruber, R., Appl. Phys. B. 1999.
16. Heba S. Preparation of Copper Oxide Nanoparticles (CuO) and Cu₂O by Laser and Studying its Synthetic and Optical Properties”, Department of Applied Science, University of Technology, Master Thesis. 2009.

Improvement in Vitro Fertilization and Embryo Cleavage Rate of Mice Oocytes by Using Repaglinide with Supplementation of IVF Medium

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Abstract

Considering to progresses in the scientific reproductive research in both clinical medicine and basic science, in vitro fertilization (IVF) is one of the assisted reproductive technologies (ART) that is widely used for treatment infertility and increasing of pregnancy rate at infertile couples. In this study it was examined the effect of repaglinide on in vitro fertilization and embryo cleavage in mice oocytes. It was used female NMRI mice at 8 weeks old that after superovulation with injecting 5 IU of PMSG, followed by injection 5 IU of hCG at 48 h later. After preparation of sperm for in vitro insemination, MII oocytes randomly divided in two groups; control without repaglinide in IVF medium and treatment with 1 μ M concentration of repaglinide in IVF medium. Fertilized 4–6 h post IVF were oocytes washed and put in 50 μ l droplets of culture medium. IVF and embryo development was assessed for 24, 48, 72, 96 and 120 h. The results showed that, in vitro fertilization, embryonic cleavage rate and the parameters of blastocysts quality such as the total cell number, trophoctoderm (TE), ratio of TE/ICM and size of blastocyst in the repaglinide group were significantly higher than the control.

Keywords: Repaglinide, Oocytes, In vitro fertilization, Embryo cleavage, Mice.

Introduction

Human reproduction research has been focused on both scientific aspects and development of method for infertility treatments. One of the method of assisted reproduction technology that widely used to treat of infertility, is in vitro fertilization of oocyte¹. During natural conditions, oocytes from mammalian species are fertilized in the fallopian tube, and the female reproductive tract provides the safe environment that the zygotes progress into cleaved embryos². During the IVF process,

gametes and the pre-implantation embryos are exposed to in vitro conditions, which are not completely similar, the oviducts and uterus as a natural environment³. In the current decade, in the IVF field significant advances have been made with an emphasis on improvement of clinical pregnancy outcome, for example in the many aspects such as induction of ovulation, drugs and diets, designing different cultivating systems and specially IVF culture media that play a major role in this success^{4,5}. There are numerous commercially available culture media that contain various components including nutrients, vitamins and growth factors⁶. However, the evidence for a role of the composition of IVF culture media in these outcomes is often insufficient and controversial. The current media are mostly designed based on data from many years of laborious animal studies which are not always transferable in human embryology⁷. The greatest success and considerable information concerning *in vitro* culture requirements for

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different stages of preimplantation embryos have been reported for mouse embryos due to similarity of the basic metabolic pathways between human and mice⁸. In the all animal species, calcium signals have critical roles in the fertilization and the progresses of developmental events⁹. A rise in intracellular Ca^{2+} is require for resumption of meiosis in the oocyte and causes to triggering the embryonic developmental program that called egg activation¹⁰. ATP-sensitive potassium (KATP) channels have been identified in the cell membranes of cardiac, skeletal, smooth muscle and oocyte, which connect the cell metabolism and membrane electrical activity.

Materials and Method

All chemicals were purchased from Sigma Chemical Corporation (St. Louis, MO) and Life Global USA) unless repaglinidethat purchased from Farabi Corporation, Iran. Adult female and male National Medical Research Institute (NMRI) mice were kept under standard conditions (20-25°C temperature, 50% humidity and 12 hours dark–light period) and fed with food and water. This experiment were performed according to the ethical guidelines for the Care and Use of Laboratory Animals in Razi University.

Collection of MII oocyte: Female mice aged 6–8 weeks (n= 30) were superovulated with intraperitonealy injection of 5 IU of pregnant mare serum gonadotropin (PMSG) and fallowed by injection of 5 IU human chronic gonadotropin (HCG) after 48 h of injection of PMSG. 16–18 h after HCG injection, the superovulated female mice were dissected by cervical dislocation and MII oocytes were collected from the oviduct and cleaned from cumulus cells by pipetting.

Preparation of sperm: Caudal epididymis of 12 weeks old male mice were removed and cut in several zones. They placed in 1 ml of Hams-F10 medium containing 16 mg/ml of BSA and incubated at 37°C in 5% CO₂/air for at least 30 min to allow sperm dispersion and capacitation. Then, by employing the swim-up technique, the supernatant containing motile spermatozoa was removed carefully. This solution was used to make 100-150 ml droplets of sperm suspension.

In vitro fertilization: IVF was performed as previously described with some modifications (Giritharan *et al.*, 2007). MII oocytes were randomly divided in two groups and placed in the droplets of in vitro fertilization medium (IVF medium). In the control group IVF medium containing of Life global medium

containing 16 mg/ml of BSA. In the repaglinide group IVF medium supplemented with 1μM concentration of repaglinide. 10 μl of sperm suspensions (final concentration of 1×10^6 sperm/ml) were added to 100 μl droplets of IVF medium that consist of a group of about 10 MII oocytes overlies by mineral oil and, incubated for 4-6 h. Then the oocytes were pipetted to remove the attached sperm and examined under a microscope for the presence of a second polar body or two pronuclei (2 PN) to confirm fertilization.

Embryo Culture: At 4–6 h post-IVF, the zygotes from control and repaglinide groups were cultured in groups of 10 zygotes per 30-μl drop of culture medium (life global medium consisting 4 mg/ml of BSA) that overlies by mineral oil and incubated at 37°C and 5% CO₂.

Embryo Monitoring: The embryos were monitored daily under an inverted microscope (Olympus, IX71: Japan), and the embryo developmental rate was recorded at 24, 48, 72, 96 and 120 h post-IVF. At the end of culture period, the expanded blastocysts with a clear inner cell mass (ICM) were randomly selected by another observer and made ready for size measurement and differential staining.

Blastocyst Measurements: Blastocyst quantitative measurements of morphological features were performed according to the method described previously for human embryos (Richter *et al.*, 2001). They were taken with the use of the measurement program for the Digital camera (Olympus; DP 72). Blastocyst diameter (from outer zona to outer zona) was recorded, along with the longest length and widest perpendicular width (in micrometers). A single size measurement for each blastocyst was calculated by using Factor Analysis. Blastocyst shape was quantified by calculating a roundness index (RI; RI = length divided by width). Blastocyst size was quantified by calculating length + width/2

Differential staining of blastocyst: According to the expanding, expanded and partially hatched stages, the blastocysts selected for calculating the number of total blastomeres by differential staining assay. Differential staining to separate the inner cell mass and trophoctoderm cellswere done according to the method described by Park *et al.*, (2002). Briefly, the zona-intact blastocysts were first incubated in 500μl of 100 μg/ml of propidium iodide (PI, Sigma) and 1% Triton X-100 at 37°C for up to 10 s or until trophoctoderm

visibly changed color to red and shrank slightly under a dissecting microscope.

Statistical analysis: All of the data were analyzed with SPSS software program (version 19: SPSS. Link., Chicago, IL) and the percentage IVF rate and embryo development rate was analyzed by chi-square test. The blastocyst measurement and cell number was evaluated by T-test and indicated as means±standard error of the mean (SEM). For differences between control and treatment groups, p<0.05 was considered statistically significant.

Results

In vitro fertilization rate: The effect of supplementation of IVF media with repaglinide on in vitro fertilization of MII oocyte seen from the percentage of pronucleus formed at 4-6 h post- IVF. In vitro fertilization rate for control and repaglinide groups were respectively; 84.64±0.18 and 94.36±0.05 that significantly difference was observed between two groups (Table1).

Evaluation of embryo development: The effect of supplementation of IVF medium with repaglinide

on preimplantation embryo development examined from the percentage of the forming of 2 cells, 4-8 cells, morula and blastocyst at 24, 48, 72, 96 and 120 h of in vitro culture (Tab1, Fig1). Results showed that at 24 h of culture the percentage of 2-4 cells in the control and repaglinide groups were 78.30±4.23, 5.21±2.80 and 81.74±2.88, 9.31±3.40, respectively; there was significant differences in 4 cells embryos. At 48 h of culture the percentage of 4-8 cells embryos were 59.16±1.52, 17.97±0.77 and 57.98±0.69, 28.72±1.04, respectively; there were significant differences in 4-8 cells embryos. At 72 h of culture the percentage of 8 cells- morula-blastocyst were 29.53±4.99, 45.33±7.97, 1.77±1.44 and 19.8±4.07, 63.23±3.35, 6.20±1.86, respectively; significant differences was observed in 8 cells embryos, morula and blastocyst. At 96 h of culture the percentage of morula and blastocyst were 9.72±1.53, 61.88±5.16 and 9.19±2.60, 73.93±3.46, respectively; there was significant differences in blastocysts stage. At 120 h of culture the percentage of blastocyst and degenerated embryos were 71.22±4.67, 5.33±2.20 and 84.52±2.27, 2.03±1.00, respectively; significant differences were observed between control and repaglinide groups.

Table 1: Embryo development in the control and repaglinide groups at different time of in vitro culture

Groups	0h N. MII	4-6h Fertilized oocyte%	24h 2-cell% 4-cell%	48h 4-cell% 8-cell%	72h 8-cell% Mor% Blast%	96h Mor% Blast%	120h Blast% Deg%
Control	235	84.64±0.18 ^a	78.30±4.23 ^a 5.21±2.80 ^a	59.16±1.52 ^a 17.97±0.77 ^a	29.53±4.99 ^a 45.33±7.97 ^a 1.77±1.44 ^a	9.72±1.53 ^a 61.88±5.16 ^a	71.22±4.67 ^a 5.33±2.20 ^a
Repaglinide	225	94.36±0.05 ^b	81.74±2.88 ^a 9.31±3.40 ^b	57.98±0.69 ^b 28.72±1.04 ^b	19.8±4.07 ^b 63.23±3.35 ^b 6.20±1.86 ^b	9.19±2.60 ^a 73.93±3.46 ^b	84.52±2.27 ^b 2.03±1.00 ^b

Data are presented as means±SEM. N: Total number. a/b Values within columns with different superscripts are significantly differences (chi-square test, p < 0.05)., Mor: morula; Blast: blastocyst; Deg: degenerated.

Measurement of blastocyst diameter and cell number: At 96h post-IVF, the parameters relate to the blastocysts quality such as the total cell number, trophectoderm (TE), inner cell mass (ICM), ratio of TE/ICM, shape and size of blastocysts were assessed (Tab2, Fig2). Results indicated that the mean of total cell number in the control and repaglinide groups were 52.27±1.38 and 63.44±0.90, respectively; the mean of TE cell number were 37.62±1.08 and 46.17±0.61, respectively; the mean of ICM cell number were

14.65±0.49 and 17.24±0.34, respectively; ratio of TE/ICM were 2.62±0.08 and 2.69±0.03, respectively; shape of blastocysts were 0.97±0.02 and 0.99±0.02, respectively and size of blastocysts were 68.17±0.69 µm and 80.22±0.53µm. Significant differences were observed in the total cell number, TE cell number, ratio of TE/ICM and size of blastocysts in the repaglinide group in comparison to the control group, but there were not a significant difference in the ICM and shape of blastocysts between control and repaglinide groups.

Table 2: Comparison of blastocysts cell number and size in the control and repaglinide groups after 96h of in vitro fertilization of mice MII oocytes

Group	N. Blastocysts	N. Total cells	N. TE	N. ICM	TE/ICM	Size of blast (µm)	Shape of blast (RI)
Control	30	52.27±1.38 a	37.62±1.08a	14.65±0.49 a	2.62±0.08 a	68.17±0.69 a	0.97±0.02 a
Repaglinide	30	63.44±0.90b	46.17±0.61b	17.24±0.34 a	2.69±0.03 b	80.22±0.53 b	0.99±0.02 a

Data are presented as means±SEM. N: number. a/b Values within columns with different superscripts are significantly differences (t-Test, p < 0.05). TE: trophoctoderm; ICM: inner cell mass.

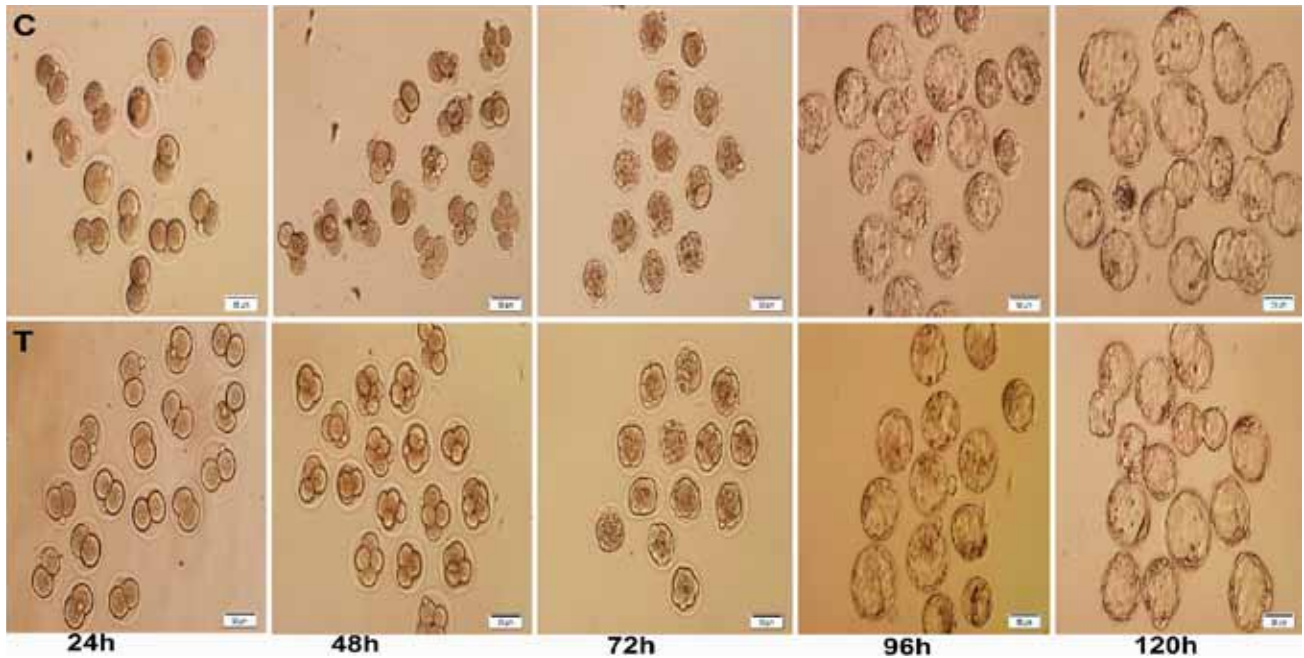
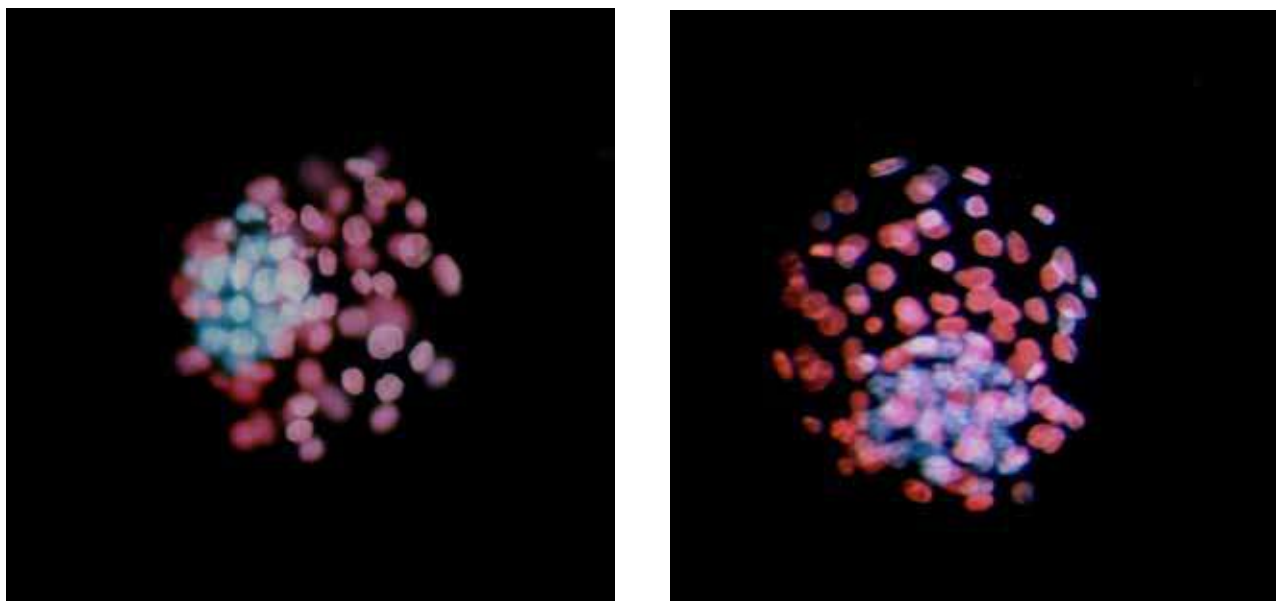


Figure 1: Embryo development in the control and repaglinide groups at different time of in vitro culture (Scale bar: 50 µm)



a.

b.

Figure (2) Differential staining of mouse blastocyst by propidium iodide (PI) and Hoechst 33258 A: Control group, B: Repaglenide group, ICM: Blue color, TE: Pink color (Scale bar: 20 µm)

Discussion

Repaglinide with hypoglycemic activity is widely used for the treatment of non-insulin-dependent diabetes mellitus, which by inhibition of K-ATP channels on the pancreatic β cells membrane, via opening the voltage gated calcium channels and subsequently increasing of intracellular calcium lead to depolarization of the cell membrane and finally insulin secretion from these cells¹¹. In this study, we examined their in vitro fertilization and embryonic cleavage rates of mice MII oocytes, after supplementation of IVF medium with repaglinide. Our results showed that supplementation of IVF medium with 1 μ M concentration of repaglinide, cause to significantly improvement, in the IVF rate and subsequently embryo development rate during in vitro culture. Ultimate goal of in vitro fertilization studies such as examine of basic molecular physiological, morphological process during IVF of gametes are used for human infertility treatment and produce of embryos in the domestic animal industry. The preimplantation mammalian embryos at the in vivo condition, for more development influenced by autocrine, paracrine and endocrine factors. The results from study of Blancato and Seyler (1990) showed that incubation of sperm and eggs with a Ca^{2+} channel blockers such diltiazem and 8-(N,N-diethylamino)octyl-3,4,5-trimethoxybenzoate (TMB-8) at 30 and 3 μ M concentrations caused to depression of fertilization and depressed progression of mouse embryos from 2-cell to blastocyst stage at compared with controls.

Conclusion

Despite the importance of gametes quality on embryonic development, often suboptimal embryo culture conditions are largely responsible for poor in vitro embryo development. Many efforts have been made to improve the formulations of IVF culture media for more improvement of pregnancy and implantation rates. Considering this subject, our results suggest that supplementation of IVF medium with repaglinide can be improve the in vitro fertilization and developmental competency of preimplantation mouse embryo.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the University of Babylon/college of science, Iraq and all experiments were carried out in accordance with approved guidelines.

References

1. Eskew A, Jungheim E. A History of Developments to improve in vitro Fertilization. Missouri medicine.2017; 114(3): 156.
2. Desai N, AbdelHafez F, Bedaiwy M, Goldfarb J. Live births in poor prognosis IVF patients using a novel non-contact human endometrial co-culture system. Reproductive biomedicine online.2008; 16(6): 869-874.
3. Feuer S, Rinaudo P. Preimplantation stress and development. Birth Defects Research Part C: Embryo Today: Reviews.2012; 96(4): 299-314.
4. Andersen A, Goossens V, Gianaroli L. Assisted reproductive technology in Europe. Results generated from European registers by ESHRE. Human Reproduction.2007; 22(6): 1513-1525.
5. Vajta G, Rienzi L, Cobo A, Yovich, J. Embryo culture: can we perform better than nature?. Reproductive biomedicine online.2010; 20(4): 453-469.
6. Chronopoulou E, Harper J. IVF culture media: past, present and future. Human reproduction update.2014; 21(1): 39-55.
7. Harper J, Cristina M, Lundin K. When and how should new technology be introduced into the IVF laboratory?. Human reproduction.2011; 27(2): 303-313.
8. Ménéz Y, Hérubel F. Mouse and bovine models for human IVF. Reproductive biomedicine online.2002; 4(2): 170-175.
9. Miao Y, Williams C. Calcium signaling in mammalian egg activation and embryo development: the influence of subcellular localization. Molecular reproduction and development.2012; 79(11): 742-756.
10. Ridgway EB, Gilkey J, Jaffe L. Free calcium increases explosively in activating medaka eggs. Proceedings of the National Academy of Sciences.1977; 74(2): 623-627.
11. Guardado R, Prioletta A, Jiménez L. The role of nateglinide and repaglinide, derivatives of meglitinide, in the treatment of type 2 diabetes mellitus. Archives of medical science: AMS.2013; 9(5): 936.
12. Wheeler, M. B., Clark, S. G., & Beebe, D. J. (2003). Developments in in vitro technologies for swine embryo production. Reproduction, Fertility and Development, 16(2), 15-25.

13. Acevedo JJ, Mendoza-Lujambio I, de la Vega-Beltran JL, Trevino CL, Felix R, Darszon A. KATP channels in mouse spermatogenic cells and sperm, and their role in capacitation. *Dev Biol.*2006; 289:395–405.
14. Brayden J. Functional roles of KATP channels in vascular smooth muscle. *Clinical and Experimental Pharmacology and Physiology.*2002; 29(4): 312-316.
15. Du Q, Jovanović S, Sukhodub A, Barratt E, Drew E. Human oocytes express ATP-sensitive K⁺ channels. *Human reproduction.*2010; 25(11): 2774-2782.
16. Duque P, Hidalgo C, Gómez E, Pintado B. Macromolecular source as dependent on osmotic pressure and water source: effects on bovine in vitro embryo development and quality. *Reproduction Nutrition Development.* 2003; 43(6): 487-496.
17. Fernandes G, Dasai N, Kozlova N, Mojadadi A, Gall M, Drew E, Barratt E, Madamidola OA, Brown SG, Milne AM, Martins da Silva SJ, Whalley KM, Barratt CL, Jovanović A. A spontaneous increase in intracellular Ca²⁺ in metaphase II human oocytes in vitro can be prevented by drugs targeting ATP-sensitive K¹ channels. *Hum Reprod.*2016; 31: 287-297.
18. FitzHarris G, Larman M, Richards C. An increase in [Ca²⁺] i is sufficient but not necessary for driving mitosis in early mouse embryos. *Journal of cell science.*2005; 118(19): 4563-4575.
19. Flagg T, Enkvetchakul D, Koster J. Muscle KATP channels: recent insights to energy sensing and myoprotection. *Physiological reviews.*2010; 90(3): 799-829.

Kurdish Traditional Herbal Medicine to Treat Mouth Thrush

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Abstract

Natural plant products are one of the important fields of research for the prevention of immunological complications. Recently, herbal medicine and plant extracts have been utilized as a substitute for commercially accessible chemical drugs for control of infection diseases. Because of chemical drugs have unpleasant side effects and caused rug-resistant microorganisms. This study aimed to evaluate the effect herbal mixture of *Rhuscoriaria* L. and peppermint water extract on five common oral bacteria. The well-plate system in BHIA (Brain Heart Infusion Agar) medium was used for primary assessment of the antibacterial properties of water extract plants. The minimum inhibitory concentration (MIC) of the extract was determined against each microorganism using macrodilution method. Diameter of the zone of growth inhibition was proportional to the concentration of the extract tested. This study found that the largest MIC was observed to be against *Staph.aureus*. Despite the usage of herbal combination of *Rhuscoriaria* L. and peppermint water extract has been recorded in prevention of mouth thrush for 10 donor patients. Therefore, both materials have a great potential to be developed as a safe and strong antibacterial activity against pathogens concerned with oral infections.

Keywords: *Rhuscoriaria* L., *Menthapiperita* L., Water extracts, Antibacterial activity.

Introduction

Medicinal plants have been used to treat various diseases since ancient times¹. Many species of plants reported to have pharmacological properties through different secondary metabolites²⁻⁴. Recent studies indicated that bioactive compounds have increased interest in plants as potential therapeutic agents with antimicrobial activities^{5,6} these agents have fewer side effects, better patient tolerance, and relatively less expensive compared to conventional antibiotics⁷. According to World Health Organization (WHO), more than three quarters of the world population depend on plants and their extracts for health needs⁸. In this connection, Sumac is the common name for genus (*Rhus*) containing more than 250 individual flowering plant

species in the Anacardiaceae family⁹. *Rhuscoriaria* can grow in non-agricultural areas and it is commonly used as a spice by grinding the dried fruit with salt and also widely used in the Middle East Asiatic medicinal herb, especially for wound healing^{10,11}. The extracts of *R. coriaria* fruit have been shown to contain high levels of polyphenols for example, anthocyanins, Gallic acid, and hydrolysable tannins¹². A variety of biologically active phytochemicals of *R. coriaria* utilized within natural medicinal products as antibacterial, antiseptic, antiviral, anti-dysenteric, anti-diarrheic, antispasmodic, astringent, hepatoprotective, protistocidal, analgesic, antiulcer, ant gastric, antioxidant and anti-inflammatory¹³. Peppermint or mint (*Menthapiperita* L.) is also an important medicinal plant belonging to the Labiate family¹⁴. The leaves are stalked opposite, toothed and the flower is irregular in shape¹⁵. Peppermint leaves contain around 0.5-4% volatile oil consisting of 50-78% free menthol, menthofurane, monoterpene, and traces of jasmine 0.15% to significantly improve the quality of the oils¹⁶. Herbalists consider Peppermint as an astringent, antiemetic, antiseptic, carminative, analgesic, diaphoretic, antimicrobial, mild bitter, rubefacient, and

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stimulant¹⁷⁻¹⁹. In addition, menthol and peppermint oil have moderate antibacterial effects on both gram-positive and gram negative bacteria²⁰. Watery extracts of peppermint leaves were antiviral^{21,22}. Oral health greatly affects the overall quality of life, and poor oral health has a greatly affects chronic conditions and systemic diseases²³. In the oral cavity, more than 700 bacterial species were detected. Some of these bacteria were implicated in oral diseases like caries and periodontitis²⁴. Many oral infections are corrected by herbal medicines²⁵. To the best of our knowledge, there are no available reports on the optimizing the extraction of polyphenols as alternative natural Kurdish treatment on bacterial and viral infection of the mouth. Therefore, in this study has been attempted the use and identification of medicinal plants that are used in safely traditional medicine to treat mouth infection.

Materials and Method

Sample Preparation: *Rhuscoriaria* and Peppermint locally agriculture in Kurdistan region were collected from the Erbil bazaar.

- Extract preparation. In order to prepare the extract, 100mL of water was added to 10 g of *Rhuscoriaria* and the mixture was boiled for 5 minutes.
- Extract preparation of peppermint by adding 100mL of water to 10 g of peppermint leaves and then boiled on burner for five minutes.
- The *Rhuscoriaria* and peppermint were combined together in water and again the mixture was boiled for about 5 minutes.

In all cases the mixture stored at room temperature for 2 hours to allow the infusion process. Lastly, the obtained mixture was filtered through Whatman No.1 filter paper. After that, the extract could be used directly in treatment or were dry at 40°C and stored in a sterile bottle at 4°C.

Pathogenic Microorganisms: *The bacterial strains including *Streptococcus mutants*, *Staph.aureus*, *E.coli* and *Pseudomonusaeruginosa* of patients after lab diagnosis [26] were received from medical laboratory in ministry.

*Microbial suspension with a bacterial count of 1.5×10^8 CFU/mL was prepared with normal saline solution²⁷. The prepared microbial suspension for each bacterial strain was cultured on plates containing Brain Heart Infusion Agar and then wells with 6 mm diameter were created²⁸.

100 µl of the extract solution prepared with sterile distilled water at ratio 1:1, 1:2, 1:3, 1:4, 2:1, 3:1, 4:1 gm of *Rhuscoriaria*: Peppermint gradually per 100 mg/ml of sterile water.

The tests were done in three replicates and all plates were stored at 37° C overnight. To determine the MIC afterwards, the diameter of growth inhibition zone was measured compared to the negative control group.

Treatment of patients with Thrush:

Ten donors of diagnosed oral thrush infection had being treated with prepared herbal mixtures by swabbing over the thrush three times daily.

Result and Discussion

In this research, primary evaluation of the antibacterial effect the herbal mixture of *Rhuscoriaria*L. and peppermint water extracts were done utilizing the well-plate technique²⁹. For each bacterial strain subjected to distinct extract levels, the mean diameter (mm) of the growth inhibition area is concluded in Table(1) *Rhuscoriaria*L. And peppermint water extracts demonstrated antibacterial impact on the contemplated microscopic organisms since the growth of all five bacterial strains were repressed by different concentrations of the extract. The growth inhibition area diameter was proportional to the extract concentration of *Rhuscoriaria*L. and peppermint within the third ratio. However, diameter of the growth inhibition zone began to decrease at (1:4) ratio for *Rhuscoriaria*L. and peppermint, respectively. The size (diameter) of growth inhibition area ranged from 6 to 20 mm.

Staph.aureus was noted with the biggest growth inhibition zone as a consequence of extract exposure was at (4:1) ratio. Similarly, these observations were recently reported by other researcher³⁰.

Table (1): Presented effect of different Rhus:Pepp.ratio on microbial growth(MIC diameter)

Ratio Rhus: Pepp.	MICdiameter of microbial growth inhibition zone measured in mm				
	Str. mutants	Staph.aureus	E.coli	Ps.aeruginosa	Candida.
1:1	6	7.5	6.5	7	7
1:2	6.5	6.5	7	7.5	7
1:3	8	9	8	8.5	8
1:4	6	6	6	6	6
2:1	11.5	13	12	11.5	13
3:1	17	17	17	17	16.5
4:1	19.5	20	19	18.5	19.5

Treatment of patient with Thrush: Ten donors of diagnosed oral thrush infection had being treated with prepared herbal mixtures by swabbing over the thrush three times daily. After that, the patients fill painless within few hours, while they healing of infection. In addition, the healing of donor patients with thrush is a practical guide to the use of this herbal mixture as a popular positive healing treatment among people.

Conclusion

The herbal medicines have shown to have a wide array of biological properties like antioxidant, antimicrobial, and anti-inflammatory effects. As concluded that both products have activity against pathogenic bacteria whatever the sumac extract killed the bacteria while the other one (mint)acts as a mild anesthetic. Therefore, the findings of this research are very encouraging and indicate that this herb should be explored further to investigate its potential in the treatment of infectious diseases. For the future study, as the combinations of several spices could be proven to possess higher inhibitory effects on specific bacteria than those of individual spices.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Erbil Medical Technical Institute, Erbil Polytechnic University-Erbil-Iraq and all experiments were carried out in accordance with approved guidelines.

References

1. Ul Hassan H, Murad W, Tariq A, Ahmad A. Ethnoveterinary study of medicinal plants in Malakand Valley, District Dir (Lower), Khyber Pakhtunkhwa, Pakistan. *Ir Vet J* 2014;67 (1):6.
2. El-Kamali H, MY El-Amir. Antibacterial activity and phytochemical screening of ethanolic extracts obtained from selected Sudanese medicinal plants. *Curr. Res. J. Biol. Sci.*2010; 2: 143-146.
3. Lalitha P, KA Arathi, KS Shubashini, J Hemalatha. Antimicrobial activity and phytochemical screening of an Ornamental Foliage plant, Pothosaurea(Linden ex Andre). *Int. J. Chem.*2010;1: 63-71.
4. Hussain H, A Badawy, A Elshazly. Chemical constituents and antimicrobial activity of Salix bserrata. *Rec. Nat. Prod.*2011; 5:133-137.
5. Pavithra PS, VS Janani, KH Charumathi, R Indumathy, S Potala. Antibacterial activity of plants used in Indian herbal medicine. *Int. J. Green Pharm.*2010; 4: 22-28.
6. Alagesaboopathi C. Antimicrobial potential and phytochemical screening of Androgra phis affinis Nees-An endemic medicinal plant from India. *Int. J. Pharm. Pharm. Sci.*2011; 3:157-159.
7. Vermani K, S Garg. Herbal medicines for sexually transmitted diseases and AIDS. *J. Ethnopharmacol.*2002; 80: 49-66.
8. N Sadale, BA Karadge. Survey on ethno-medicinal plants of Ajara Tahsil, District Kolhapur, Maharashtra-(India),” *Trends in Life Sciences.* 2013; 2.

9. USDA A. Germplasm Resources Information Network. USDA. Beltsville, USA. 2007.
10. Sezik E, M Tabata E. Traditional medicine in Turkey I. Folk medicine in northeast Anatolia. *J Ethnopharmacol.* 1991; 35: 191-196.
11. Wyk B, M Wirik. *Medicinal Plants of the World*. Briza Publications, Pretoria. Yu, J., M. Ahmedna and I. Goktepe, 2005. Effects of processing method and extraction solvents on concentration and antioxidant activity of peanut skin Phenolics. *Food Chem.* 2004; 90: 199-206.
12. Kosar, M., B. Bozan, F. Temelli and K.H.C. Baser, 2007. Antioxidant activity and phenolic composition of sumac (*Rhus coriaria* L.) extracts. *Food Chem.*, 103: 952-959.
13. Nasar SM, AK Halkman, I Al-Haq. Inhibition of some foodborne bacteria by alcohol extract of sumac (*Rhus coriaria* L.). *J. Food Safety.* 2004; 24: 257-267.
14. Kirethekar I. *Indian Medicinal Plants*. 1985; 714-716.
15. Clark, R.K., Menory, R.C. 1980. Environmental effects of peppermint (*Mentha piperita*). *Aust J. Plant Physiology*, 7: 685-692.
16. Dew M, Evans J. Peppermint oil for the irritable bowel syndrome; a multi-center trial. *Br. J. Clin Pract.* 1984; 38: 394-395.
17. Hoffman D. *The complete illustrated holistic herbal*. Rockport, MA: Element Books Inc., 1996.
18. Forster S. 1996. Peppermint: *Mentha piperita*, American Botanical Council – Botanical Series. 306:3-8.
19. Mimica Dukic N, Bozin B. Antimicrobial and antioxidant activities of three *Mentha* species essential oils. *Planta Medica.* 2003; 69: 413-419.
20. Diaz R, Quevedo J, Ramos A, Cabo P, Cabo J. Phytochemical and antibacterial screening of some species of Spanish Lamiaceae. *Fitoterapia.* 1988; 59: 330-333.
21. Hirobe C, Palevitch D, Tayeka K, Itokawa H. Screening for antitumor activity of crude drugs (IV): Studies on cytotoxic activity of Israeli medicinal plants. *Natural Medicine.* 1994; 48: 168-170.
22. Alkofahi A, Abdelaziz A, Mahmoud I. Cytotoxicity, mutagenicity and antimicrobial activity of forty Jordanian medicinal plants. *International Journal of Crude Drug Research.* 1990; 28: 139-144.
23. Palombo EA. Traditional medicinal plant extracts and natural products with activity against oral bacteria: Potential application in the prevention and treatment of oral diseases. *Evid Based Complement Alternat Med.* 2011; 680354.
24. Aas JA, Paster BJ, Stokes LN, Olsen I, Dewhirst FE. Defining the normal bacterial flora of the oral cavity. *J Clin. Microbiol.* 2005; 43 (11): 5721-32.
25. Hoseinishad M, Nosratipour A, Moghaddam SM, Khajavi A. Homeopathy in dentistry: A review. *Int J Contemp Dent Med Rev* 2015; 2015:1-5.
26. Kamel F, Jarjes S. *Essentials of Bacteriology and Immunology*. Hawler Polytechnic University/ Hawler Technical Health College, Erbil-Iraq. 2015.
27. Kamel FH, Ismael HM, Mohamammad AS, Amin S. Approaches for development of new Nano-silver printing ink. *Research Journal of Pharmaceutical, Biological and Chemical Sciences.* May–June RJPBCS. 2017; 8(4): 103.
28. Kamel F, Saeed C, Amin AM, Qader SS. Magnetic Field Effect on Growth and Antibiotic Susceptibility of *Staphylococcus aureus*. *Al-Nahrain University Journal For Science.* 2014; 3: 138-143.
29. Kamel F, Saeed C, Amin A. Development of in-vitro susceptibility testing for pathogenic bacteria. *Journal of Life Sciences, USA.* 2013; (7): 2.
30. Vahid E, Sarmast Z, Abdolazimi Z, Mahboubi A, Amdjadi P, Kamalinejad M. Effect of *Rhus coriaria* L. water extract on five common oral bacteria and bacterial biofilm formation on orthodontic wire. *Iranian journal of microbiology.* 2014; 6(4): 269.

Evaluation of Students' Self-management and Academic Achievement in the University of Baghdad

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Abstract

Objective(s): To evaluate university students' self-management and academic achievement; to compare between these students relative to their self-management and academic achievement; and to determine the relationships between these students' self-management, academic achievement and their socio-demographic characteristics in the University of Baghdad. For the period of November 2nd 2018 to May 30th 2019.

Method: A descriptive design, using the evaluation and comparison approaches, is employed throughout the study. Two self-evaluation questionnaires are constructed for the purpose of the presents study. Content validity and internal consistency reliability are determined for the study instruments through a pilot study. A non-probability, purposive sample, of (80) university students is selected from the Medical Colleges, College of Engineering, College of Sciences and College of Education in the University of Baghdad. Data are collected through the use of the study instruments and the structured interview technique as means for data collection for the period of February 21st 2019 to March 20th 2019. Data are analyzed through the application of the descriptive statistical data analysis approach which includes frequency, percentage, mean, total score and range and inferential statistical data analysis approach of Analysis of Variance and Multiple Linear Regression.

Results: The study depicts that most of the college students experience fair to good level of self-management and good level of academic achievement.

Conclusion: The study concludes that students do not present differences in their self-management and academic achievement. Self-management is affected by students' gender and education and academic achievement is influenced by students' socioeconomic status

Keywords: *Evaluation, Comparison, Self-management, Academic Achievement, University of Baghdad.*

Introduction

Self-management is a key assistant for all learning (for children and adults!) for both materials and academic courses, and other content areas, or skills. Self-management allows students to follow through plans to complete the tasks, and study of the tests, and continue to focus in the classroom. In adults, it is important that the objectives of access in the field of learning, such as the development of new professional skills ⁽¹⁾. Self-management helps students become successful learner. It refers to the strategies, techniques and method that we use to guide the activities and behaviors effectively when it comes to the study, including self-management,

setting goals, planning and time management. Self-management is an essential skill that will help them throughout their lives ⁽²⁾. Students should be invited to the learning management process in the classroom. Here are some of the tools used by many teachers to enable students to self-management ⁽³⁾. It found self-management techniques to be more effective in student behavior management interventions mediated by the teacher. When self-management strategies are related to behavioral interventions and equal Functionally, the students increased the amount of time in the job, and showed social behaviors more convenient, and completed more tasks. Self-management interventions

for student self-monitoring include: notes both the students and records the target behaviors and self-assessment: It compares the performance/her with the specified criteria and self-education student is directed oriented student behavior through the use of personal data and setting goals: Students set a target and create a personal commitment and guidance for progress towards this goal⁽⁴⁾. Academic achievement for students is the current level of student learning. More specifically, for the purposes of each student succeed in the accountability act (ESSA), academic achievement refers to the percentage of students in the school that meets their learning standards currently classroom level or beyond. This achievement is measured using tests at the state level in math and reading. Achievement is measured also by using assessments in the case of science, but will not be used scientific assessments of accountability under ESSA. Often measure the academic achievement of the students in terms of the semester or cumulative average point for graduates (GPA) or the number of courses or credit hours that have been completed⁽⁵⁾. Research concerned with the phenomenon of academic performance of students during the learning process based on the average score points (GPA). In this regard, students' ability to control the factors that affect the learning process, which is called academic self-management affected. A successful student is regarded as the one who is able to control the factors which influence their learning process. A study is conducted to verify the role of academic self-management in improving students' academic achievement. The quantitative methodology with a simple random sampling technique is employed. The total samples are (105) students of Padjadjaran University. The results show that (78%) of the subjects possessed high academic self-management, meaning that the majority of subjects used academic self-management to control factors which influence the learning process. The final model of academic self-management can be used in order to empower students to improve their academic achievement, so that they have capital to move forward and build their future⁽⁶⁾. Based on the early stated evidence, the present study ought to evaluate students' self-management and academic achievement at Colleges in the University of Baghdad.

Methodology

A descriptive design, using the evaluation and comparison approaches, is carried throughout the present study to evaluate colleges students' self-management and academic achievement; to compare

between these students relative to their self-management and academic achievement; and to determine the relationships between these students' self-management, academic achievement and their socio-demographic characteristics in the University of Baghdad for the period of November 2nd 2018 to May 30th 2019. The study is conducted on students at Medical Colleges (Medicine, Dentistry, Pharmacy and Nursing), College of Engineering, College of Sciences, and Ibn Al-Rushud College of Education in the University of Baghdad. A "non-probability" purposive, sample of (80) university students, is selected. The sample is comprised of (20) students from Medical Colleges (Medicine, Dentistry, Pharmacy and Nursing), (20) students from College of Engineering, (20) students from College of Sciences, (20) students from Ibn Al-Rushud College of Education. It is consisted of (40) males and (40) females and (18-27) years old. Each student, who has participated in the present study, has signed a consent form for the agreement to be involved in the study and as prerequisite for the ethical consideration. Two questionnaires, Students' Self-management (21) items and Students' Academic Achievement (20) items, are constructed for the purpose of the study throughout review of relevant literature and consultation with a panel of experts. A pilot study is carried out from January 7th 2019 to February 20th 2019 to determine the internal consistency reliability and content validity of the study instruments. The internal consistency reliability of the questionnaires is determined through the use of split-half technique and the computation of Cronbach alpha correlation coefficient. A purposive sample of (20) student is gathered for the purpose of the reliability of the study instruments. The results indicate that the correlation coefficient is ($r = 0.87$) for the self-management questionnaire and ($r = 0.88$) questionnaire to the academic achievement questionnaire. Such scores reveal that the study instruments are adequately reliable measures for the concepts underlying the present study. Content validity of the study instruments is determined by panel of (12) experts. These experts are faculty members at the early mentioned colleges in the University of Baghdad. They are provided with copies of the questionnaires and asked to review and evaluate the study instruments for content clarity and adequacy. Their responses depict that the study instruments are valid measures for the phenomena underlying the study. Data are collected through the use of the study instruments and the structured interview technique as means for data collection for the period of February 21st 2019 to March 20th 2019. Data is analyzed

by applying descriptive statistical data analysis approach which includes the frequency, percentage, mean, total score and range and inferential statistical data analysis approach which includes analysis of variance and multiple linear regression.

Results

Table (1): Overall Evaluation of the Colleges Students’ Self-management

Frequency and Percentage	Levels	List
4 (5%)	Poor (21–34.33)	1
30 (37.5%)	Fair (34.34–43.67)	2
46 (57.5%)	Good (43.68–63)	3

This table depicts that most of the college students have experienced good level of self-management (57.5%) but more than one third of them have experienced fair level of self-management (37.5%).

Table (2): Overall Evaluation of the Colleges Students’ Academic Achievement

Frequency and Percentage	Levels	List
0 (0.0%)	Poor (20–22.33)	1
0 (0.0%)	Fair (22.34–34.67)	2
80 (100%)	Good (34.68–60)	3

This table depicts that all of the colleges’ students have experienced good level of academic achievement (100%).

Table (3): Analysis of Variance for the Comparison between Students Relative to Their Self-management

Source of Variance		Sum of Squares	Df	Mean Square	F	Sig.
SMM	Between Groups	1149.633	11	104.512	1.752	0.218
	Within Groups	477.167	8	59.646		
	Total	1626.800	19			
SME	Between Groups	591.383	11	53.762	0.353	0.944
	Within Groups	1219.167	8	152.396		
	Total	1810.550	19			
SMS	Between Groups	846.833	11	76.985	0.657	0.746
	Within Groups	937.167	8	117.146		
	Total	1784.000	19			
SMEDUC	Between Groups	495.667	11	45.061	0.506	0.854
	Within Groups	712.333	8	89.042		
	Total	1208.000	19			

SMM= Self-management of Medical Students, SME= Self-management of Engineering Students, SMS= Self-management of Sciences Students, SMEDUC= Self-management of Education Students, df= Degree of Freedom, F= F- statistics, Sig.= Level of significance at $p \leq 0.05$

The results, from this table, reveal that there are no significant differences between self-management for students with regard to the type of total differences.

Table (4): Analysis of Variance for the Comparison between Students Relative to their Academic Achievement

Source of Variance		Sum of Squares	Df	Mean Square	F	Sig.
AAM	Between Groups	1150.050	18	63.892	0.354	0.890
	Within Groups	180.500	1	180.500		
	Total	1330.550	19			
AAE	Between Groups	1072.050	18	59.558	0.191	0.966
	Within Groups	312.500	1	312.500		
	Total	1384.550	19			

Source of Variance		Sum of Squares	Df	Mean Square	F	Sig.
AAS	Between Groups	957.300	18	53.183	0.879	0.700
	Within Groups	60.500	1	60.500		
	Total	1017.800	19			
AAEDUC	Between Groups	1465.500	18	81.417	0.563	0.801
	Within Groups	144.500	1	144.500		
	Total	1610.000	19			

AAM= Academic Achievement of Medical Students, AAE= Academic Achievement of Engineering Students, AAS= Academic achievement of Sciences Students, AAEDUC= Academic achievement of Education Students, df= Degree of Freedom, F= F- statistics, Sig.= Level of significance at $p \leq 0.05$

Results are presented from this table that there were no statistically significant differences between the academic achievements of students with regard to the type of college.

Table (5): The Relationship between Students’ Self-management and their Socio-demographic Characteristics

Model	Unstandardized Coefficients		Standardized Coefficients	T	Sig.
	B	Std. Error	Beta		
(Constant)	52.395	6.342		8.262	0.000
Gender	-8.624	2.441	-0.455	-3.533	0.001
Education	3.661	1.147	0.432	3.192	0.002
Socioeconomic Status	0.005	0.126	0.003	0.039	0.969

Dependent Variable: Self-management B= Regression Coefficient, Std. Error= standard error, t= T-test, Sig.= Level of Significance

This table depicts that there is highly significant relationship between students’ self-management and their gender and education only and age is excluded out of the regression model.

Table (6): The Relationship between Students’ Academic Achievement and their Socio-demographic Characteristics

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
(Constant)	32.861	9.824		3.345	0.001
Gender	5.667	3.781	0.357	1.499	0.138
Education	-0.407	1.777	-0.057	-0.229	0.819
Socioeconomic Status	0.556	0.195	0.381	2.856	0.006

Dependent Variable: Self-management B= Regression Coefficient, Std. Error= standard error, t= T-test, Sig.= Level of Significance

This table indicates that there is highly significant relationship between students’ academic achievement and their socioeconomic status only and age is excluded out of the regression model.

Discussion

Findings out of the data analysis indicate that most of the colleges’ students have practiced fair to good level of self-management. Such findings are very obvious in the overall evaluation of colleges’ students’

self-management (Table 1). This can be interpreted in a fashion that the colleges’ students have experienced this varied level of self-management as result of their inadequate background relative to such management. It has been reported that successful learner can achieve own learning goals through self-management. It denotes to approaches, procedures and method that can be castoff to straight students’ actions and performances efficiently. When it originates to study, self-management contains goal setting, planning and managing the time.

Self-management is a main ability that will benefit students during their life ⁽²⁾. Self-management helps students control impulses, set goals, and get organized so they can be strong self-motivators. Students who can regulate their emotions, control impulses and manage stress are more likely to identify goals and consistently meet them. The students have to be provided with goal-setting, the breadth and depth of research on the topic of self-management and how growing this skill can temper the current problem. Students will assess strategies that schools and other educators use to empower students with self-management mindsets and skills and tweak them so they are relevant to the classroom and students. While there are relatively simple self-management interventions, it is important to note that this course will not provide a cure-all methodology, but strategies and foundational knowledge to grow the students' self-management skills in the long term ⁽⁷⁾. Findings out of the data analysis reveal that all of the colleges' students have experienced good level of academic achievement. Such findings are very noticeable in overall evaluation of colleges' students' academic achievement (Table 2). This can be justified in a manner that the colleges' students are well-oriented toward this achievement regardless to their educational background or colleges. Academic achievement is the current level of student learning. More specifically, academic achievement refers to the percentage of students in the school who meet the education standards currently classroom level or beyond. This achievement is measured using tests at the state level in math and reading. Achievement is measured also by using assessments in the case of science, but will not be used scientific assessments of accountability under which ESSA. Why Does Academic Achievement Matter? A standards-based education system promotes equity by establishing a baseline of knowledge and skills that all students, regardless of their background, should master as part of their education. Measuring academic achievement provides key information about students' mastery of standards. Identifying schools where many students are struggling to achieve proficiency on state tests provides a reasonable starting point when searching for schools that would most benefit from support. Looking at academic achievement data in combination with other information helps to prioritize schools for support. More broadly, academic achievement for all students is one of the key goals of the public school system, and mastery of state standards provides students with useful skills for a fulfilling and productive life. While not all aspects of achievement can be efficiently measured and

compared statewide, it is important to include some measurement of academic achievement when evaluating and prioritizing support for schools. The tests used to measure academic achievement are meant to provide system-level data about how schools, districts, and the state are functioning. An individual student's scores should not be used to determine, for example, which courses they can or cannot take during their K-12 years. Schools should look at multiple sources of student-level data when planning instruction and support for individual students ⁽⁸⁾. Such comparison shows that there are no differences between colleges' students' self-management (Table 3) and academic achievement (Table 4). In general, such findings present evidence that these students almost share the same level of self-management and academic achievement regardless of differences in their area of study or specialty. Analysis of such relationship indicates that there is highly significant relationship between students' self-management and their gender and education (Table 5). Such findings can be explained in a mode that the better the students' education the well they perform self-management, as well as male and female students present different application of self-management through their study. There is also a very important relationship between the academic achievement of the students and their socioeconomic status (Table 6). This can be clarified in a way that the better the students' socioeconomic status the advanced their academic achievement. A study is looking at the relationship between socio-economic status (SES) peer academic achievement and individual. Results of the study indicate that the social status of the family, peers, in particular, has a large independent and objective academic achievement on the impact of the individual, which is only slightly less than the social status of the family of the individual ⁽¹¹⁾.

Conclusion

Most of the colleges' students experience fair to good level of self-management and good level of academic achievement probably due to their education and orientation. Colleges' students do not present differences in their self-management and academic achievement due to the level of their consciousness of such issues. Self-management, for students, is affected by their gender and education. Academic achievement is influenced by the students' socioeconomic status.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the -Kindy College of Medicine, University of Baghdad, Iraq and all experiments were carried out in accordance with approved guidelines.

References

1. Transforming Education (TE). What is Self-management? 2019.
2. Student Learning Development (SLD). Self-management.2019; 1: 112-116.
3. Miller B. Tools for Student Self-management. Available at:
<https://www.edutopia.org/blog/tools-for-student-self-management-andrew-miller>. 2019.
4. Rogers L. Tips for Student Self-management in Classroom. Available at: <https://aspergers101.com/self-management/>.2019.
5. Minnesota Department of Education (MDE). Academic Achievement. 2017.
6. Kadiyono L, Hafiar H. The Role of Academic Self-management in Improving Students' Academic Achievement. 2017; 1: 5-10.
7. McEvoy K. Building Students' Self-Management Skills. 2019.
8. Department of Education (DOE). Academic Achievement. Available at:[file:///C:/Users/x c 9 b 7 n b p p 2 8 j 2 h r h m b y / D o w n l o a d s / A c a d e m i c % 2 0 A c h i e v e m e n t % 2 0 S u m m a r y . 2 0 1 7](file:///C:/Users/x%20c%209%20b%207%20n%20b%20p%202%208%20j%202%20h%20r%20h%20m%20b%20y%20/D%20o%20w%20n%20l%20o%20a%20d%20s%20/A%20c%20a%20d%20e%20m%20i%20c%20A%20c%20h%20i%20e%20v%20e%20m%20e%20n%20t%20S%20u%20m%20m%20a%20r%20y%202017).
9. Zhang X. A Study on Influential Factors of College Students' Self-management Based on Grounded Theory. Advances in Computer Science Research (ACSR).2017; 76: 512-518.
10. Virtanen P, Nevgi A. Disciplinary and Gender Differences among Higher Education Students in Self-regulated Learning Strategies. Educational Psychology.2010; 30(30): 1-8.
11. Caldas S, Bankston C. Effect of School Population Socioeconomic Status on Individual Academic Achievement. The Journal of educational Research.2012; 112(11): 269-277.

Health Promotion Program about Sun Protection among Outdoor Workers in Helwan University

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Abstract

The current study aimed to assess the effect of health promotion program about sun protection among outdoor workers in Helwan University. Design: A quasi-experimental design was used. Setting: This study was conducted at the Landscape and Campus outside Cleaning in Helwan University.

Sample: A purposive sample of 90 workers was recruited.

Tools: An interview questionnaire was used to assess workers' knowledge regarding effects of the sun and sun care issues, their attitudes and practices regarding sun protection before and after program.

Results: Revealed that more than half of workers were exposed to sun burn and sun stroke in the last twelve months. Also, they had poor level of knowledge, inadequate practices and negative attitudes regarding sun protection at pre-intervention. However, after intervention, the outdoor workers had good level of knowledge with adequate practices for sun protection and positive attitudes, with highly statistically significant differences between pre–post interventions. Conclusion: the study revealed that the intervention seemed to change the knowledge, practices and attitudes of subjects toward sun protection. This, in turn implies that awareness to sun protection could be important to reduce risk of skin cancer in Egypt.

Keywords: Health Promotion Program, Sun Protection, Outdoor Workers.

Introduction

Sunlight is the main source of ultraviolet radiation (UVR). All people need some sunlight, but too much sun exposure can be dangerous and cause so much damage. The amount of damage caused by the UV rays depends on the intensity and the duration of the exposure. The greatest burden of disease from most exposure to UVR, are cutaneous malignant melanomas and non-melanoma skin cancers developing. In addition, UVR

causes sunburn, skin photo-ageing, cortical cataracts, and reactivation of herpes of the lip.¹ There has been a significant increase in the incidence of skin cancer throughout the world in the last few decades, although increasing public awareness of the dangers of skin cancer and advancement of diagnostic, about 2–3 million cases of non-melanoma skin cancer and 132,000 cases of malignant melanoma skin cancer are diagnosed every year over all worldwide. Studies have found that 65–90% of the cases of melanoma skin cancer are caused by UV rays.² Recently, Abeck³ found that, more than three million non-melanoma skin cancers and 150. 000 melanomas are diagnosed around the world annually, and found that high levels of ultraviolet exposure led to a larger number of new cases.

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Significance of the study:

Subjects and Method

Research Design: A quasi-experimental design was used in the current study.

Setting: The present study was conducted in Helwan University Landscape and Campus outside cleaning sites.

Subjects and Sampling: A Purposive sample which included all available outdoor workers was recruited for they study, their total numbers was 105 workers and the actually included in the study were 90 workers working at Landscape and Campus outside cleaning in Helwan University

Tools of Data Collection: Based on the literature review and pervious studies, the researchers developed data collection instruments. It was written in Arabic language, and included the following interviewing questionnaire:

Part I: A structured questionnaire to assess demographic data of population such as, age, gender, educational level, marital status, residence, type of work, time of sun exposure, history of sun burn, history of sun stroke, and family history of skin cancer.

Part II: Workers' knowledge regarding sun risk factors and effects on health: Questions assessed the workers' knowledge about effects of the sun and sun care issues as time of sun exposure, and measures to protect self from sun exposure.

Scoring System: For knowledge items, a correct complete answer was scored (three points) and a correct incomplete answer was scored (2), while the wrong answer or don't know was given (1). According to workers answers, their knowledge was categorized into "Good knowledge" (43-63) "Average knowledge" (22-42) and "Poor knowledge" (< 21).

Part III: Workers' attitude regarding sun protection: it contains questions about workers attitudes and beliefs regarding sun protection such as: place of work requires us to protect from the sun, working in the sun is in itself something that deeply disturbs me; working under the sun is part of worker daily life.

Scoring System: For attitude items, agree answer was scored (3) and not sure answer was scored (2), while the not agree was given (1). According to workers answers, their attitudes were categorized into positive

attitude (27-39) and negative attitude < 26 points.

Part IV: workers' "done and not done" practices regarding sun protection: It includes questions about behaviors of workers regarding sun protection

Scoring System: For practice items, always answer was scored (3) and sometimes answer was scored (2), while never was given (1). According to workers' answers, their practices were categorized into adequate practices $\geq 60\%$ and inadequate practices $< 60\%$.

Validation of the Tool: Three experts in Community Health Nursing revised it and some modifications were done according their opinions. The content and face validity of the study tools were measured to evaluate the individual items as well as the entire tools used for the study as being relevant and appropriate to test what they wanted to measure.

Reliability of the tool: Reliability was applied by the researchers for testing the internal consistency of the tool, by administration of the same tool to the same subjects under similar conditions two times 15 days apart. Answers from the repeated testing were compared (Test-retest reliability was (0.82) and Cronbach's Alpha reliability was 0.890.

Operational Design: The study to be completed passed through different phases which included: preparatory phase, pilot study, and field work phase.

Preparatory phase: A review of the past and current available related literature covering all aspects of the research subject using available books, journals, articles and nursing magazines in order to get a clear picture on the research problem, as well as to develop the study tool for data collection, and preparing sessions and designing booklet for program.

Pilot study: It was conducted on 11 workers; they represented about 10% of the total study sample. The aim of the pilot study was to evaluate clarity, feasibility, applicability as well as the time estimated to fill the developed tool. According to the obtained results modifications such as omission, addition and re-wording were done. The pilot study was excluded from the main study sample.

Fieldwork: After having been granted the permission to collect data, the researchers met with the workers to explain the aim of the work, methodology and estimated duration of its fulfillment. By this time,

the tool was developed after extensive review of the related literature, validation by experts, and finalized through pilot-testing.

Assessment Phase: Before distribution of the questionnaire, the researchers met with the workers, introduced themselves, and explained the aim and benefits of the study as well as its procedures to obtain their consent and to establish trust relationship and gain their cooperation and confidence.

Procedure: A review of the previous and recent Arabic and English related literature covering various aspects of the problem was done, using available books, articles, periodicals, journals and internet search to get acquainted with the research problem and develop the study tool. Potential subjects were approached by the researchers, at that time the nature and purpose of the study were explained.

Administrative Design: Permission for carrying out the study was obtained by submission of an official letter from the Director of the Faculty of Nursing, Helwan University to the Director of workers at Helwan University. The letter indicated the purpose of the study and its procedures.

Statistical Design: Data entry and statistical analysis were performed using personal computer software, the Statistical Package for Social Sciences (SPSS), version 20.0. Suitable descriptive statistics were used such as; frequency, percentage, mean and standard deviation. In addition, correlation coefficient (r) test was used to estimate the closeness association between variables. Paired t test was used to compare mean score between both studied variables. The p-value is the degree of significance and using the correlation (r) test.

Results

Table (1): Frequency Distribution of the Workers’ Knowledge Pre/Post Health Promotion Program about Effects of the Sun (no=90).

Knowledge	Pre-program			Post-program			Paired t test	P value
	Wrong answer	Incomplete	Complete	Wrong answer	Incomplete	Complete		
	%	%	%	%	%	%		
• Sun bathing is damaging to health	77.8	10.0	12.2	43.3	11.1	45.6	5.369	0.001**
• Tanned skin does not protect from sunlight.	73.3	11.1	15.6	40.0	15.6	44.4	4.863	0.001**
• Vitamin D is absorbed from the sun through the skin	74.4	4.4	21.1	37.8	44.4	47.8	4.677	0.001**
• It is dangerous to stay in the sun for a long time with sunscreen	76.7	6.7	16.7	35.6	12.2	52.2	6.481	0.001**
• Staying out of the sun for regular intervals do not to prevent sun burn	75.6	5.6	18.9	35.6	12.2	52.1	6.158	0.001**
• Sun burn can occur even when the sun on the skin does not feel warm	77.8	5.6	16.7	36.7	12.2	51.1	6.741	0.001**
• Exposure to the sun increases aging, wrinkling and discoloration of the skin	82.2	3.3	14.4	35.6	11.1	53.3	7.770	0.001**
• A tan is evidence of damage to the skin	85.6	1.1	13.3	40.0	10.0	50.0	7.466	0.001**
• It is possible to become sunburnt on a cloudy day	77.8	12.2	10.0	44.4	11.1	44.4	5.846	0.001**
• Sunlight is not beneficial behind the window glass	75.6	7.8	16.7	41.1	10.0	48.9	5.540	0.001**

**Significant (P<0.05)

Table (1) shows highly statistical significant improvements in workers’ knowledge level at the post health promotion program– test, than that of pre-test in all knowledge items regarding effect of the sun (P < 0.001).

Table (2): Frequency Distribution of the Workers’ Knowledge Regarding Sun Care Issues Pre/Post Health Promotion Program (No = 90).

Knowledge	Pre-program			Post-program			Paired t test	P value
	Wrong answer	Incomplete	Complete	Wrong answer	Incomplete	Complete		
	%	%	%	%	%	%		
• In the sun people need to drink fluids to avoid dehydration	85.6	1.1	13.3	36.7	17.8	45.6	7.661	0.001**
• It is not OK to fall asleep in the sun	81.1	3.3	15.6	35.6	13.3	51.1	7.417	0.001**
• Sitting under a tree/umbrella can provide some protection	81.1	18.9	0.0	41.1	4.4	54.4	6.611	0.001**
• Burn may occur on a cloudy day	84.4	2.2	13.3	42.2	4.4	53.3	7.317	0.001**
• The sea is not protecting from sunburn	78.9	6.7	14.4	46.7	4.4	48.9	5.689	0.001**
• Wearing a hat/T-shirt can help in protecting the body from sun burn	84.4	2.2	13.3	41.1	6.7	52.2	7.245	0.001**

**Significant (P<0.001)

Table (2) shows highly statistically significant improvements in workers’ knowledge levels at the post health promotion program–test, than that of pre-test in all knowledge items regarding sun care issues (P<0.001).

Table (3): Mean and Standard Deviation of Total Scores of Knowledge of the Sun Protection pre/post of Health Promotion Program (No=90).

	Mean±SD	Paired t-test	P-value
Pre knowledge	28.033±11.85820	9.088	0.000**
Post knowledge	44.322±15.0719		

**Highly significant (P<0.001)

Table (4) shows highly statistically significant improvement in the workers’ total mean scores of knowledge level in the post–test than that of the pre-test (P < 0.001).

Table (4): Frequency Distribution of Workers’ Sun Protection Practices Pre/Post Health Promotion Program (no=90).

Practice	Pre-program			Post-program			Paired t-test	P-value
	Never	Sometimes	Always	Never	Sometimes	Always		
	%	%	%	%	%	%		
• Wear something on your head	48.9	40.0	11.1	4.4	28.9	66.7	10.404	0.000**
• Wear hat with a surrounding brim	41.1	54.4	4.4	4.4	28.9	66.7	11.523	0.000**
• Wear a long-sleeved shirt	20.0	72.2	7.8	2.2	32.2	65.6	9.504	0.000**
• Wear shirt with a collar	51.1	43.3	5.6	8.9	37.8	53.3	9.907	0.000**
• Limit the time for exposing sun at midday	62.2	36.7	1.1	16.7	41.1	42.2	9.379	0.000**
• Wear sunscreen	71.1	26.7	2.2	14.4	42.2	43.3	11.302	0.000**
• Wear sunglasses	63.3	21.1	15.6	14.4	47.8	37.8	7.007	0.000**
• Wear gloves	56.7	28.9	14.4	16.7	52.2	31.1	4.407	0.000**
• Wear gear	57.8	40.0	2.2	18.9	53.3	27.8	7.408	0.000**

**Highly significant (P<0.001)

Table (4) shows that there are highly statistically significant difference between pre and post workers' practices at all items of the health promotion program. So, this table reflects the positive improvement of health educational promotion program ($p < 0.000$).

Table (5): Mean and standard deviation of total scores of practice pre & post of health promotion program (No= 90).

Total practice score Mean±SD		Paired t-test	P-value
Pre-practice	13.8778±3.56584	11.892	0.000**
Post-practice	21.3333±4.79466		

**Highly significant ($P < 0.001$)

Table (5) shows highly statistically significant improvement in the workers' total mean scores of practice level in the post-test than that of the pre-test ($P < 0.000$).

Table (6): Mean and Standard Deviation of Total Scores of Attitude Pre/Post of Health Promotion Program (no= 90).

Total of attitude scores Mean±SD		Paired t-test	P- value
Pre attitude	24.4667±2.41345	10.483	0.000**
Post attitude	31.0222±5.73179		

**Highly significant ($P < 0.001$)

Table (6) reveals highly statistically significant improvement in the workers' total mean scores of attitude levels in the post-test than that of the pre-test ($P < 0.000$).

Consistent with the prior research findings, the results of the current study revealed that the intervention program for outdoor workers regarding sun protection practices indicated better improvement in their practices with statistically significant differences from pre to post program. As well, a study done by Duffy et al.¹⁵ reported that the implementation of the sun safety intervention was an effective method to change behaviors of operating engineers in USA related to sun protection during work time especially during summer period. Similarly, Houdmont et al.¹⁷ found that after intervention the participants demonstrated significant positive change on their behavior measures; the most change was in using of a shade/cover when working in the sun. Inconsistent with the previous results a research done by Malik¹⁶ which indicated that the behavior changes of respondents did not show statistically significant results from before to after the intervention. As well, Bahakim et al.¹³ found that most of participants in their study were aware about the effect of sun and had positive attitude about sun safety. However, proper sun exposure practices and sun protection practices was low.

Conclusions

The results of this study have specified a low level of awareness among the outdoor workers as regards sun exposure dangers and sun protection measures. Majority of them had negative attitude toward sun protection. Additionally, this study indicated that sun protection practice was generally inadequate among outdoor workers, as well as more than half of them had sunburn and sunstroke in the past year. The health promotion program led to statistically significant improvement in knowledge, changing attitudes, and behaviors among outdoor workers about sun protection and safety. Continued efforts in this forum can potentially lead to develop policy at work area for the protection the workers from sun harmful effect.

Conflicts of Interest: There are no conflicts of interest.

Financial support and sponsorship: Nil

Ethical Clearance: A written consent was taken from the workers' Director. An oral consent was obtained from each worker, who agreed to participate in the study. They were assured that anonymity and confidentiality of information given will be guaranteed

and they have the right to withdraw from the study at any time without given any reason.

References

1. Maverakis E, Sukhov A. UV radiation: The risks and benefits of a healthy glow. 2016.
2. Parker CG, Williams M, Driggers P. Sun exposure knowledge and practices survey of maintenance squadrons at Travis AFB. *Military Medicine*.2015; 180(1):26-31.
3. Abeck, D. *Skin Cancer-Index*. 2018
4. Boyas JF, Nahar VK, Robert T, Brodell RT. Skin protection behaviors among young male Latino Day laborers: An exploratory study using a social cognitive approach. *Dermatology Research and Practice*. 2016; 1-10.
5. Ali YH, Taha A, Khallaf A. Incidence, recurrence and complications after facial skin cancer excision: Retrospective analysis of multi-Institutional experiences. *J Head Neck Spine Surg*. 2018; 2(4):555-594.
6. Ramezanzpour A, Niksirat A, Rad SG. Knowledge, attitude and behavior practice toward sunscreen use among hospital personnel in comparison with laypeople in Zanjan, Iran. *World Applied Sciences Journal*. 2013; 22(5): 683-689.
7. Alawad A, Alyassin H, Alrefai A, Jairoun AA, Shahwan M. Assessment of sun health awareness levels among medical sciences female students at Ajman University. *Ejpmr*. 2017; 4(4): 623-628.
8. AlGhamdi KM, AlAklabi AS, AlQahtani AZ. Knowledge, attitudes and practices of the general public toward sun exposure and protection: A national survey in Saudi Arabia. *Saudi Pharmaceutical Journal*. 2016; 24: 652–657.
9. Lai YC, Yew YW. Sunburns and Sun-Protective Behaviors after a Diagnosis of Melanoma. *Skinmed*.2018; 16(6):379-383.
10. Ragan KR, Buchanan Lunsford N, Thomas CC, Tai EW, Sussell A, Holman DM. Skin cancer prevention behaviors among agricultural and construction workers in the United States, 2015. *Prev Chronic Dis*. 2019; 16:180446.
11. Saridi M, Lionis DS, Toska A, et al. Evaluation of students' knowledge and attitudes on sun radiation protection. *International journal of caring sciences*. 2016; 9(2):400-408.
12. Gao Q, Liu G, Liu Y. Knowledge, attitude and practice regarding solar ultraviolet exposure among medical university students in Northeast China. *J Photochem Photobiol B*. 2014; 140:14-9.
13. Bahakim NO, Alanazi BG, Alead MY, et al. Sun exposure behaviours, attitudes and protection practices among Prince Sultan Bin Abdulaziz University Student-A survey study. *JPMA*. 2016; 66:1528-1534.
14. Al-Mutairi N, Issa BI, Nair V. Photoprotection and vitamin D status: A study on awareness, knowledge and attitude towards sunprotection in general population from Kuwait, and its relation with vitamin D levels. *Indian J Dermatol Venereol Leprol* 2012;78:342-349.
15. Duffy SA, Hall SV, Tan A, et al. The sun Solutions intervention for operating engineers: A randomized controlled trial. *Cancer Epidemiol Biomarkers Prev*.2018; 27 (8): 864-873.
16. Malik S. Assessing the impact of the SunWise Program on youth sun safety knowledge, attitudes, and behaviors in Clark County, Nevada. UNLV Theses, Dissertations, Professional Papers, and Capstones. 2016.

Cyclic Fatigue Resistance of One Curve, Hyflex EDM and Neolix NiTi Files in Simulated Curved Canals

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Abstract

Objectives: The aim was to evaluate the cyclic fatigue resistance of One curve (OC), Hyflex EDM (HEDM) and Neolix (NE) files in simulated curved canals.

Study Design: Forty-five NiTi files in three groups (n=15 files/group) of OC, HEDM and NE files, respectively tested in a custom-made cyclic fatigue testing device designed to have 60° curvature in a stainless-steel simulated canal with 5 mm radius of curvature. All files rotated until fracture occur to determine the time to fracture, number of cycles to fractures (NCF) and length of the fractured fragment. Scanning electron microscope (SEM) was used to examine the fracture surface topography of the broken instruments (n=2/group). ANOVA and Tukey test was used to statistically analyses the results at significance level at 95% confidence level.

Results: OC files needed more time to fracture compared to HEDM and NE files ($p < 0.05$), respectively, However, there was no significant difference of NCF between HEDM and OC file ($p > 0.05$). NE file has significantly lower NCF than that of HEDM and OC file ($p < 0.05$), respectively. There was no significant difference between all files in the mean length of the fractured fragment ($p > 0.05$). SEM images of NE showed more pores compared to OC and HEDM, however, OC revealed rougher fractured surface than that of HEDM and NE.

Conclusions: OC and HEDM showed comparable resistance to cyclic fatigue in simulated curved canals, despite metallurgical differences among those NiTi file systems. NE files showed the lowest resistance to cyclic fatigue compared to HEDM and OC file.

Keywords: One curve, cyclic fatigue, Hyflex, Neolix, C-Wire.

Introduction

Advantages of the introduction of the rotary NiTi files into endodontics compared to conventional stainless-steel hand files were numerous such as

efficiency in cutting, faster preparation time and better preservation of the canal geometry^(1, 2). Nevertheless, there is always the risk of breakage of these files because of cyclic fatigue and torsional stress, despite their super-elastic properties^(3, 4). The cyclic fatigue cause breakage in files after repeated cycles of tension and compression occurs, which causes mechanical failure and fracture of the instrument, usually, this occurs often in curved canals clinically^(5, 6). Because of this and to decrease the chance of fracture and improve the flexibility of these instruments, different approached have been proposed including metallurgical modifications of NiTi alloys and modifications in cross-sectional designs of these instruments^(7, 8). Recently, many file systems introduced

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to the field that possess different material properties and designs including One curve (OC) (Micro-Mega, Besancon, France), Hyflex EDM (HEDM) (Coltene/Whaledent, Altstätten, Switzerland) and Neolix (NE) (Neolix, châtres-la-Forêt, France). The newly introduced OC, which made with C-wire technology, has a variable cross-section combined with continuous rotation to ensures excellent cutting efficiency and a perfectly centered trajectory. On the other hand, HEDM is manufactured by the process of electro discharge machining (EDM), which involve using electric current to machine the alloy in a well-controlled and repeatable way difficult to be achieved with conventional techniques⁹. Similarly, wire-cut electrical discharge machining process was used to produce NE to improve cutting efficiency and result in faster root canals preparations. Previous studies showed the superior cyclic fatigue resistance of HEDM^(9, 10) and OC¹¹, against other NiTi files, however, there is no study comparing the cyclic fatigue resistance of these metallurgically different files to the knowledge of the authors

Materials and Method

Cyclic Fatigue Resistance: Forty-five NiTi files in Three groups (OC, HEDM, and NE) (n=15 NiTi rotary files/system) were used for this study. All instruments have comparable size (OC (size 25, taper 0.06), HEDM (size 25, various taper) and Neolix (size 25, taper 0.12). all instruments were tested for single step cyclic fatigue resistance using custom-made device, designed to have single 60° curvature simulated canals, the center of curvature of the simulated canals was approximately 5 mm from the tip of the instrument and the simulated canals have 5mm diameter. The device consists of the main-frame to which mobile wood support is connected to the electric handpiece and a stainless-steel block containing the simulated canals. The electric handpiece is mounted on a mobile device to allow precise and reproducible placement of each instrument inside the simulated canal. All instruments were used with a Wave one endodontic motor (Dentsply Maillefer, Ballaigues, Switzerland). The device is shown in figure (1).

The simulated canal was filled with distilled water and a glass cover was fixed by a clipper above the stainless-steel block before insertion of the file inside the canal. All instruments were rotated according to manufacturer' recommended speed and torque. HEDM operated with 500 RPM and torque 2.5 N.cm., OC operated with 300 RPM and torque 2.5 N.cm., NE operated with 300 RPM

and torque 1.5 N.cm. The instance of fracture was based on visual observation of the fracture occurring in the instrument. Time of the fracture recorded in seconds with a stop-watch. The time (T) to fracture in seconds converted to minutes and multiplied by the speed (RPM) to obtain the number of cycles to fracture (NCF) for each instrument according to the equation, $NCF = RPM \times T$. The length of the fractured instruments was measured to determine the length of the fractured piece of each file. All specimens were tested by an endodontist with a minimum of five years' experience. SEM topographical analysis of the fractured instruments was performed using SEM microscope (FEI Co., Ltd., Cambridge) for two specimens from each group.

Statistical Analysis: The data of time to fracture, NCF and length of the fractured fragment were analyzed by (SPSS 24.0; SPSS Inc, Chicago, IL) one-way ANOVA and Tukey test were used to determine any statistical difference amongst groups at a significance level of 95% confidence interval.

Results

The data of time to fracture, NCF and length of the fractured fragment are presented in Table (1). There was a significant difference between all files regarding time to fracture ($p < 0.05$). The mean time to fracture of OC, HEDM and NE files were (3.545, 2.418 and 1.852 minutes), respectively. OC time to fracture was significantly higher than that of HEDM and NE ($p < 0.05$ and $p < 0.05$), respectively. There was a significant difference in NCF between all three files ($p < 0.05$). The mean NCF of OC, HEDM, and NE were (1053.5, 1118 and 505.5), respectively. There was no significant difference between HEDM and OC in NCF ($P > 0.05$). However, NE has a significant lower NCF compared to that of HEDM and OC $p < 0.05$, respectively. There was no significant difference in the length of the fractured fragment among different types of files ($p > 0.05$). The mean length of the fractured fragment was (4.497, 3.506 and 3.992 mm) for OC, HEDM, and NE, respectively.

SEM images of the surface topography of the fractured instruments are presented in figure (2). HEDM and NE instruments showed the crater-like surface texture on the unfractured surface of the instruments (Figure 2 A and B). On the other hand, OC showed smooth surface topography on the unfractured surface (figure 2 C). All instruments showed a resilient fracture of cyclic fatigue failure. NE fractured surface showed

more pores (arrows Figure 2 K) compared to OC and HEDM. At higher magnifications (1000x, 2000x and 5000x), the topography of the fractured surface of OC showed higher roughness than that of HEDM and NE respectively (Figure 2 D-L).

Discussion

One of the most common complications during root canal preparation is the fracture of the NiTi rotary file during the procedure¹². It was reported that the fracture of the file during clinical use, mainly related to cyclic fatigue^(13, 14). The present study evaluated and compare the cyclic fatigue resistance of the different NiTi file systems manufactured from different alloys and after different heat treatment in simulated single curvature canals. An artificial canal block was used to standardize the conditions and minimizes the influence of other mechanisms of failure (including torsional stress) aside from cyclic fatigue¹⁵. For testing the cyclic fatigue, the extracted tooth was not an ideal model because the objective of this study was to determine the physical properties of the files, and there are no two root canals perfectly identical. Heat generation during the testing procedure because of friction between the walls of the simulated canals and the instrument can occur. Also, local temperature elevation may affect the cyclic fatigue resistance of the NiTi rotary files^(16,17). To control the local temperature, a lubricant or coolant during the testing procedure was recommended¹⁶. In the present study, distilled water was used to prevent the elevation of the temperature. Cyclic fatigue resistance is measured by the number of cycles to fracture (NCF) when NCF increased the fracture resistance increased. Some studies depend on the number of cycles to fracture^(18,19), others depend on the time to fracture¹⁵. In the present study, the number of cycles and the time to fracture were calculated. Cross section design, type of the alloy and the manufacturing process influence the cyclic fatigue of NiTi instruments²⁰. The improved cyclic fatigue of OC can be attributed in part to the use of C-Wire technology by using proprietary heat treatment with a controlled memory property. The austenitic transformation temperature is elevated by thermal processing of NiTi alloys²¹, to improve the performance of the instrument by enhancing arrangement of crystal structure²². It has been reported that OC was more resistant than other heat treated and conventional NiTi alloy files in resisting cyclic fatigue¹¹. In other studies, The HEDM file showed the highest resistance to cyclic fatigue compared to other NiTi files, where Spark-machined peculiar surface is the

main feature of HEDM, the cyclic fatigue resistance of HEDM files was higher than Hyflex CM file (HCM, Coltene/Whaledent)^(9,10). Also, HEDM resists cyclic fatigue significantly better than ProTaper Universal and Pro-Taper Gold files²³. HEDM was the first instrument manufactured with EDM technology, which is a non-contact thermal erosion process. EDM cause local melting and partial evaporation of minor portions of the materials by generated electrical sparks, leaving surface finish with a typical crater-like²⁴. Metallurgical differences between HEDM and OC did not cause a difference in cyclic fatigue lives of both files in the present study. Even there was a difference in rotations speed between both files, which may influence the cyclic fatigue of rotary endodontic instruments²⁵, the cyclic fatigue resistance of HEDM and OC was comparable.

Also, it has been reported that small core diameter improve instruments' cyclic fatigue^(23, 26). OC has the lowest taper (0.06) compared to HEDM (various taper) and NE (0.12), therefore, OC had the lowest core diameter compared to other tested NiTi files. Beside the metallurgy of the alloy, this finding could be considered as another factor that might enhance the cyclic fatigue resistance of OC instrument. Apart from a metallurgical difference of these rotary systems, the cross-sectional design of the files is different which may contribute to their cyclic fatigue resistance. OC has a variable asymmetrical cross-section in single file. HEDM files has three different cross-section designs; The rectangular cross-section at the tip provides more 'core material', which provide a higher resistance to fracture of this file; Then the trapezoidal cross-section in the middle and finally near the handle, the cross section become triangle which increases the flexibility of file there²⁷. NE has a non-homothetic rectangular section along the blade. Several studies have reported that the dimension of the cross-sectional area is a more important factor in cyclic fatigue resistance than the type of alloy^(9, 23). Comparison of the cross-sectional areas of the OC, HEDM, and NE requires further investigation. In the current study, the presence of various factors that can influence the cyclic fatigue resistance of a file, such as the properties of the materials, design, and dimensions of the instrument. These factors cannot be eliminated in total as they are specific for each file system. This hardens the quantification of the effect of each variable on the cyclic fatigue life of the tested NiTi files¹³. However, clinicians need to choose the suitable instruments to shape curved canals and avoid fracture of

the instrument, it can be concluded that OC and HEDM files were comparable to each other and more resistant to cyclic fatigue than NE file in simulated curved canals.

However, *in vivo* studies need to confirm the findings of this study.

Table 1: Mean±Standard deviation of Time to fracture, NCF and length of the fractured fragments after cyclic fatigue test.

Variables	Groups	Descriptive statistics					p-value
		N	Mean	S.D.	Min.	Max.	
Time to fracture (min.)	One curve	15	3.545 ^{a,b}	0.415	2.9	4.2	P<0.05
	Hyflex EDM	15	2.418 ^a	0.438	2	3.283	
	Neolix	15	1.852 ^b	0.409	1.317	2.5	
Number of cycles (NCF)	One curve	15	1053.5 ^c	89.040	925	1160	P<0.05
	Hyflex EDM	15	1118 ^d	100.687	1000	1266	
	Neolix	15	505.5 ^{c,d}	82.511	395	605	
Length of fracture fragment (mm)	One curve	15	4.497	0.389	3.74	4.87	p>0.05
	Hyflex EDM	15	3.506	0.446	2.91	4.03	
	Neolix	15	3.992	1.522	2.61	6.76	

a, b, c and d, identical superscript letters refer to a statistically significant difference between relevant groups (p<0.05).

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Conflict of Interest: None to declare.

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References

- Peters OA. Current challenges and concepts in the preparation of root canal systems: a review. *J Endod.* 2004;30(8):559-67.
- Gao Y, Gutmann JL, Wilkinson K, Maxwell R, Ammon D. Evaluation of the impact of raw materials on the fatigue and mechanical properties of ProFile Vortex rotary instruments. *J Endod.* 2012;38(3):398-401.
- Sattapan B, Nervo GJ, Palamara JE, Messer HH. Defects in rotary nickel-titanium files after clinical use. *J Endod.* 2000;26(3):161-5.
- Simon S, Machtou P, Tomson P, Adams N, Lumley P. Influence of fractured instruments on the success rate of endodontic treatment. *Dent Update.* 2008;35(3):172-9.
- Wycoff RC, Berzins DW. An in vitro comparison of torsional stress properties of three different rotary nickel-titanium files with a similar cross-sectional design. *J Endod.* 2012;38(8):1118-20.
- Luebke NH, Brantley WA. Torsional and metallurgical properties of rotary endodontic instruments. II. Stainless steel Gates Glidden drills. *J Endod.* 1991;17(7):319-23.
- Pérez-Higueras JJ, Arias A, José C. Cyclic fatigue resistance of K3, K3XF, and twisted file nickel-titanium files under continuous rotation or reciprocating motion. *J Endod.* 2013;39(12):1585-8.
- Lopes HP, Gambarra-Soares T, Elias CN, Siqueira Jr JF, Inojosa IF, Lopes WS, et al. Comparison of the mechanical properties of rotary instruments made of conventional nickel-titanium wire, M-wire, or nickel-titanium alloy in R-phase. *J Endod.* 2013;39(4):516-20.
- Pirani C, Iacono F, Generali L, Sassatelli P, Nucci C, Lusvarghi L, et al. HyFlex EDM: superficial features, metallurgical analysis and fatigue resistance of innovative electro discharge machined NiTi rotary instruments. *Int Endod J.* 2016;49(5):483-93.

10. Shen Y, Tra C, Hieawy A, Wang Z, Haapasalo M. Effect of Torsional and Fatigue Preloading on HyFlex EDM Files. *J Endod.* 2018;44(4):643-7.
11. Elnaghy AM, Elsaka SE. Cyclic Fatigue Resistance of One Curve, 2Shape, ProFile Vortex, Vortex Blue, and RaCe Nickel-Titanium Rotary Instruments in Single and Double Curvature Canals. *J Endod.* 2018;44(11):1725-30.
12. Shahabinejad H, Ghassemi A, Pishbin L, Shahravan A. Success of ultrasonic technique in removing fractured rotary nickel-titanium endodontic instruments from root canals and its effect on the required force for root fracture. *J Endod.* 2013;39(6):824-8.
13. Cheung G, Peng B, Bian Z, Shen Y, Darvell B. Defects in ProTaper S1 instruments after clinical use: fractographic examination. *Int Endod J.* 2005;38(11):802-9.
14. Inan U, Gonulol N. Deformation and fracture of Mtwo rotary nickel-titanium instruments after clinical use. *J Endod.* 2009;35(10):1396-9.
15. Plotino G, Grande N, Testarelli L, Gambarini G. Cyclic fatigue of Reciproc and WaveOne reciprocating instruments. *Int Endod J.* 2012;45(7):614-8.
16. Shen Y, Cheung GS-p, Bian Z, Peng B. Comparison of defects in ProFile and ProTaper systems after clinical use. *J Endod.* 2006;32(1):61-5.
17. de Vasconcelos RA, Murphy S, Carvalho CAT, Govindjee RG, Govindjee S, Peters OA. Evidence for reduced fatigue resistance of contemporary rotary instruments exposed to body temperature. *J Endod.* 2016;42(5):782-7.
18. Ye J, Gao Y. Metallurgical characterization of M-Wire nickel-titanium shape memory alloy used for endodontic rotary instruments during low-cycle fatigue. *J Endod.* 2012;38(1):105-7.
19. Pedullà E, Franciosi G, Ounsi HF, Tricarico M, Rapisarda E, Grandini S. Cyclic fatigue resistance of nickel-titanium instruments after immersion in irrigant solutions with or without surfactants. *J Endod.* 2014;40(8):1245-9.
20. Tripi TR, Bonaccorso A, Condorelli GG. Cyclic fatigue of different nickel-titanium endodontic rotary instruments. *O Surg, O Med, O Path, O Radiol, and Endodont.* 2006;102(4):e106-e14.
21. Shen Y, Zhou H-m, Zheng Y-f, Campbell L, Peng B, Haapasalo M. Metallurgical Characterization of Controlled Memory Wire Nickel-Titanium Rotary Instruments. *J Endod.* 2011;37(11):1566-71.
22. Plotino G, Grande NM, Cotti E, Testarelli L, Gambarini G. Blue Treatment Enhances Cyclic Fatigue Resistance of Vortex Nickel-Titanium Rotary Files. *J Endod.* 2014;40(9):1451-3.
23. Kaval ME, Capar ID, Ertas H. Evaluation of the cyclic fatigue and torsional resistance of novel nickel-titanium rotary files with various alloy properties. *J Endod.* 2016;42(12):1840-3.
24. Theisen W, Schuermann A. Electro discharge machining of nickel-titanium shape memory alloys. *Materials Science and Engineering: A.* 2004;378(1):200-4.
25. Mahtabi M, Shamsaei N, Mitchell M. Fatigue of Nitinol: the state-of-the-art and ongoing challenges. *J mech behav biomed mater.* 2015;50:228-54.

Pediatric Hodgkin Lymphoma in Sulaimaniya Province of Iraqi Kurdistan

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Abstract

Background: Hodgkin lymphoma (HL) is a highly curable malignancy. It is a unique neoplasm, in which the malignant cell, the Reed-Stenberg cell (RSC), it constitutes approximately 40% of all lymphomas that present during childhood.

Objective: Obtain local data on the pattern of childhood and adolescent Hodgkin lymphoma in our community at presentation and then compare it with the international figure.

Patients and Method: Eighty five patients with newly diagnosed pediatric Hodgkin lymphoma were admitted to Hiwa Hematology/Oncology hospital in the Sulaimaniya province of Iraqi Kurdistan were included in this study.

They were studied prospectively from March 2006 to March 2014.

Result: Data analyzed using SPSS software; version 13 and P-value obtained by Chi-square test, a median age at diagnosis was about 13.7 years with peak age of incidence was between 15-18 year, with male predominance. Most common site of the primary tumor was cervical lymph nodes; Nodular sclerosis was the most common histopathology and the majority was stage IIA.

Conclusion: The stage in our study was age dependent but neither there was relation between the site of the primary tumor and the risk categories nor relation between risk categories and sex.

Keywords: *Hodgkin lymphoma, Stage, Sex distribution, Risk Category.*

Introduction

Formally known as Hodgkin's disease, Hodgkin lymphoma (HL) is a highly curable malignancy. It is a unique neoplasm in which the malignant cell, the Reed-

Stenberg cell (RSC), represents only a small proportion of cells constituting the bulk of the tumor. It also has very particular clinical characteristics and distinct biological behavior.

Hodgkin lymphoma is a rather rare malignancy in the pediatric population; however, it constitutes approximately 40% of all lymphomas that present during childhood and is the most common malignancy in adolescents and young adults. In all age groups, Hodgkin lymphoma is highly sensitive to chemotherapy and irradiation. In fact, Hodgkin lymphoma was the first cancer to be cured with radiation therapy alone or with a combination of several chemotherapeutic agents. The

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cure rate for children and adolescents with Hodgkin lymphoma has steadily improved over the years, particularly with the introduction of combined radiation and multiagent chemotherapy.¹ This therapeutic success has come at the price of serious long-term toxicities, such that a 30-year survivor of Hodgkin lymphoma is more likely to die of therapy-related complications than from Hodgkin lymphoma. Therefore, the therapeutic paradigm has shifted toward reducing treatment-associated toxicity while maintaining high cure rates. This new paradigm has led to the current risk-adapted, response-based approach to the treatment of Hodgkin lymphoma. (2, 3, 4)

Patients and Method:

Eighty five patients with newly diagnosed pediatric Hodgkin lymphoma were admitted to Hiwa Hematology/Oncology hospital in the Sulaimaniya province of Iraqi Kurdistan were included in this study.

They were studied prospectively from March 2006 to March 2014.

Inclusion Criteria:

1. All children and adolescents aged 18 years or younger.
2. Both male and female.
3. Histopathologically proved Hodgkin lymphoma.
4. Newly diagnosed patients who were not treated previously by chemotherapy.

Exclusion Criteria:

1. Age more than 18 years.
2. Relapsed Hodgkin lymphoma or previously treated with chemotherapy.

Study requirements included: All the targeted patients had their Sulaimaniya facilities of histopathological diagnosis, CBC, blood film, ESR, liver function test, serum alkaline phosphates, hepatitis B serology, hepatitis C serology, human immunodeficiency virus serology, renal function test, serum electrolyte, serum LDH, serum ferritin level, abdominal U/S, CXR, Echocardiography.

CT-scan and/or MRI of the primary site, chest and abdomen.

Bone marrow aspirate and trephine biopsy was done for those with one or more of the following criteria:

1. Patients with clinical stage III or stage IX.
2. Patients with B symptoms.
3. Patients with cytopenia on CBC.
4. Patients with elevated serum alkaline phosphates.

PET scan and EB virus Study were not done for the majority of the case because it was not available.

The patients were staged according to the Modified Ann Arbor Staging system.^(1, 5, 6)

Results

Among 85 patients with HL studied, 59 patients (69.41%) were male and 26 patients (30.58%) were female. The male: female ratio was 2.27:1.

Figure 1 shows sex distribution of HL in our study.

A median age at diagnosis was about 13.7 years with peak age of incidence was between 15-18 years. Table 1 and figure 2 show the age distribution.

Table 1: Age Distribution of HL at Diagnosis.

Age in years	No. of patients	Percent (%)
0-4	4	4.7
5-9	17	20
10-14	25	29.4

The most common site of the primary tumor was the cervical lymph nodes which were the primary site of the tumor in 48 out of 85 patients (56.47%), followed by isolated mediastinal primary which occurred in 13 patients (15.29%), axillary lymph nodes primary in 8 patients (9.41%), primary inguinal lymph nodes involvement occurred in 7 patients (8.23%), retroperitoneal lymph nodes primary in 5 patients (5.88%) and isolated splenic involvement occurred in 4 patients (4.7%). Figure 3 shows the percent of the patients in relation to the site of the primary tumor.

Among the 85 patients with HL studied 44 patients (51.76%) were NSHL, 23 patients (27.05%) were MCHL, 12 patients (14.11%) was LRCHL, 1 patient (1.17%) were LDHL and 5 patients (5.88%) were NLPHL.

Regarding Staging of the studied patients, 9 patients (10.59%) were Stage I, three of them (3.53%) with B symptoms, 37 patients (43.53%) were Stage II, 12 of them (14.12%) with B symptoms, 31 patients (36.47%) were Stage III, 9 of them (10.59%) with Stage III B and

8 of patients (9.41%) were Stage IV, three of them with Stage IV B.

According to their Hodgkin Lymphoma Risk Categories depending on the Stage and Number of Nodal Sites and the presence of Bulky Disease, favorable-risk pediatric Hodgkin lymphoma (stage IA or IIA with < 3 nodal sites, and some IIIA without bulky disease) were occurred in 31 (36.47%) patients, intermediate-risk disease (stage IIA bulky disease with extension or =3 nodal sites, stage IB, IIB, stage IIIA, stage IVA) in 42 (49.41%) and advanced or unfavorable pediatric Hodgkin lymphoma (all other patients that were not included in the favorable or the intermediate risk groups) in 12 (14.12%) patients.

Figure 6 shows the percentage of the Risk categories.

Our study showed that there is significant correlation between age and risk categories with favorable risk category occurred more in younger age and high risk category found in older children and adolescent.

Table 2 shows the relation between age and the risk categories.

Chi square test showed that the difference among the Risk Category and the Age was statistically significant (P- value = 0.02997).

Table 2: Relation between Age and the Risk Categories (P-value = 0.02997).

Risk Categories Number/(Percentage)			
Age in Years	Favorable Risk Group	Intermediate Risk Group	High Risk Group
0-4	2 (50%)	1 (25%)	1 (25%)
5-9	12 (70.59%)	4 (23.53%)	1 (5.88%)
10-14	9 (36%)	13 (52%)	3 (12%)
15-18	8 (20.51%)	24 (61.54%)	7 (17.95%)

This study found that there was statistic significant correlation between age and sex as there was more male predominance in young patients less than 10 years, while male to female ratio tend to be decrease with increasing age.

Table 3 shows Age in Relation to the Sex (P-value =0.03408).

Table 3: Age in Relation to the Sex (P-value =0.03408).

Age In Years	Male No./total (%)	Female No./total (%)
0-4	3/4 (75%)	1/4 (25%)
5-9	15/17 (88.24%)	2/17 (23.53%)
10-14	20/25 (80%)	5/25 (20%)
15-18	21/39 (53.85%)	18/39 (46.15%)

Also there was significant correlation between Age and Histopathology of HL in our study with MCHL found to be more common among children less than 10 years old (P-Value = 0.05).

Table 4 Shows the Relation between Age and Histopathology.

Table 4: Relation between Age and Histopathology (P-Value = 0.05).

Age In Years	NSHL No./Total (%)	MCHL No./Total (%)	LRCHL No./Total (%)	LDHL No./Total (%)	NLPHL No./Total (%)
0-4	1/4(25%)	1/4(25%)	1/4(25%)	0/4(0%)	1/4(25%)
5-9	2/17 (11.8%)	8/17(47.1%)	5/17(29.4%)	0/17(0%)	2/17(11.8%)
10-14	16/25(64%)	5/25(20%)	3/25(12%)	0/25(0%)	1/25(4%)
15-18	25/39(64,1%)	9/39(23.1%)	3/39(7.7%)	1/39(2.6%)	1/39(2.6%)

This study showed that there was significant statistic relation between histopathology and risk categories, with more advance risk categories were found in LDHL and NSHL, and favorable risk group was found in

LRCHL and NLPHL (P-value = 0.00827). The relation between risk categories and histopathology was showed in table 5.

Table 5: Risk Categories to Histopathology Correlation (P-value = 0.00827).

Risk Categories	NSHL No./Total (%)	MCHL No./Total (%)	LRCHL No./Total (%)	LDHL No./Total (%)	NLPHL No./Total (%)
Favorable Risk Group	17/31(54.84%)	2/31(6.45%)	9/31(29%)	0/27(0%)	2/31(6.45%)
Intermediate Risk Group	21/42(50%)	15/42(35.71%)	3/42(7.14%)	0/42(0%)	3/42(7.14%)
High Risk Group	6/12(50%)	5/12(41.7%)	0/12(0%)	1/12(8.3%)	0/12(0%)

There was no significant statistic relation between the site of the primary tumor and the risk categories in our study. Table 6 shows this relation (P-Value = 0.78195).

Table 6: Primary Site in Relation to Risk Categories (P-Value = 0.78195).

Site of the primary tumor	Risk Categories		
	Favorable Risk Group (No.)	Intermediate Risk Group (No.)	High Risk Group (No.)
Cervical lymph nodes	21	23	4
Mediastinal primary	2	8	3
Axillary lymph nodes	3	3	2
Inguinal lymph nodes	2	4	1
Retroperitoneal lymph nodes	2	2	1
Spleen	1	2	1

Also there was no significant statistic relation between risk categories and sex as shows in table 7 (P-Value = 0.66731).

Discussion

Pediatric Hodgkin’s Lymphoma Cancer continues to be the leading cause of death in children younger than 15 years old, and lymphomas are among the most common cancers seen in children. Fortunately, survival rates for childhood cancers have increased significantly over the years. Children respond to and deal with chemotherapy better than adults. Today, 96% of children diagnosed with Hodgkin’s disease will survive 5 or more years. However, those with high-risk disease continue to have poor outcomes.

The total number of cases studied was eighty five, over a period of eight years. We found that males were affected more than females with The male: female ratio was 2.27:1; also our study found that there was significant correlation between age and sex as there was

more male predominance in young patients less than 10 years, while male to female ratio tend to be decrease with increasing age, this figure is similar to male: female ratio in most large studies which showed that children younger than 5 years show a strong male predominance (M:F = 5:3) and children aged 15 to 19 years show a slight female predominance (M:F = 0.8).^(7,8)

Peak age incidence at presentation in our study was (15-18) years which was represent (45.9%), In the United States, the incidence of Hodgkin lymphoma is age-related and is highest among adolescents aged 15 to 19 years (29 cases per million per year), with children ages 10 to 14 years, 5 to 9 years, and 0 to 4 years having approximately threefold, eightfold, and 30-fold lower rates, respectively. In non-European Union countries, there is a similar rate in young adults but a much higher incidence in childhood.⁹

A median age at diagnosis was about 13.7 years in our study which was younger than that showed by study done in USA (median age: 15.6).^(10, 11)

This younger median age at diagnosis in our study might result from possibly relation to EB virus infection in earlier age in our region, but this needs to be confirmed by studying the EB virus genomes in the HL cells.

Conclusion

Pediatric Hodgkin's Lymphoma was higher in male than female in our community. A median age at diagnosis was about 13.7 years with peak age of incidence between 15-18 years and the majority of the patients presented with cervical lymph nodes primary at the time of diagnosis. Nodular sclerosis histopathology is the most common. Most of the patients had stage II with Intermediate risk category. There was strong correlation between age and advanced stage which meant that stage is age dependent and significant correlation between age and sex as there was more male predominance in young patients less than 10 years. Also there was significant correlation between age and histopathology of HL in our study with mixed cellularity found to be more common among children less than 10 years old. Neither there was relation between the site of the primary tumor and the risk categories nor relation between risk categories and sex. Despite absence of PET scan for the majority of patients for proposed risk stratification system for purpose of risk categories, significant number of our patients got intermediate and high risk category.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the College of Nursing, University of Sulaimani, Kurdistan Region, Republic of Iraq and all experiments were carried out in accordance with approved guidelines.

References

- Arya LS, Dinand V. Current strategies in the treatment of childhood Hodgkins disease. *Indian Pediatr.* Nov 2005;42(11):1115-28.
- Wikipedia - Hodgkin's lymphoma accessed 6-21-2008.
- Percy CL, Smith MA, Linet M. Cancer Incidence and Survival among Children and Adolescents: United States SEER Program 1975-1995: Lymphomas and Reticuloendothelial Neoplasms [Surveillance, Epidemiology, and End Results Web site]. National Cancer Institute: Surveillance Epidemiology and End Results. 1999.
- Staal SP, Ambinder R, Beschoner WE, Hayward GS, Mann R. A survey of Epstein-Barr virus DNA in lymphoid tissue. Frequent detection in Hodgkin's disease. *Am J ClinPathol.* Jan 1989;91(1):1-5. [Medline].
- Hjalgrim H, Askling J, Rostgaard K, Hamilton-Dutoit S, Frisch M, Zhang JS, et al. Characteristics of Hodgkin's lymphoma after infectious mononucleosis. *N Engl J Med.* Oct 2 2003;349(14):1324-32.
- Weiss LM, Chen YY, Liu XF, Shibata D. Epstein-Barr virus and Hodgkin's disease. A correlative in situ hybridization and polymerase chain reaction study. *Am J Pathol.* Dec 1991;139(6):1259-65.
- Ries LA, Kosary CL, Hankey BF, et al., eds.: SEER Cancer Statistics Review 1973-1995. Bethesda, Md: National Cancer Institute, 1998. Also available online. Last accessed April 04, 2014.
- Percy CL, Smith MA, Linet M. Lymphomas and reticuloendothelial neoplasms. In: Ries LA, Smith MA, Gurney JG., eds.: Cancer incidence and survival among children and adolescents: United States SEER Program 1975-1995. Bethesda, Md: National Cancer Institute, SEER Program. NIH Pub. 1999; 99-4649:35-50.
- Ries LAG, Harkins D, Krapcho M. SEER Cancer Statistics Review, 1975-2003. Bethesda, Md: National Cancer Institute, 2006.
- Macfarlane GJ, Evstifeeva T, Boyle P. International patterns in the occurrence of Hodgkin's disease in children and young adult males. *Int J Cancer.* 1995;61 (2): 165-9.
- Friedman DL. Variants at 6q21 implicate PRDM1 in the etiology of therapy-induced second malignancies after Hodgkin's lymphoma Timothy Best. *J. Natl. Cancer Inst.* 2010;102, 1083-1095.

Association between Social Media Addiction and Life Satisfaction among University Student

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Abstract

Objectives: The present study aims to assess the level of social media addiction and the level of life satisfaction among university students; and to determine the association between social media addiction and life satisfaction.

Methodology: A descriptive, cross-sectional design that is initiated for the period of January 1st to May 1st, 2018 on a sample consisted of (200) students which was selected by convenient sampling method from five colleges at University of Baghdad that are: College of Nursing, College of Arts, College of Sciences, College of Physical Educations, and Ibn Rushed College of Education. The questionnaire is designed and adopted which consists of three parts; the first part is contained the covering letter and the demographic variable of the students, the second part is concerned with Social Media Addiction Scale, and the third part concerned with Satisfaction with Life Scale. The data have been collected through the utilization of the self-administrative report as a mean of data collection and analyzed by application of statistical package for social science IBM SPSS (v. 24)

Results: The result referred that student are showing moderate level of social media addiction (60%) and moderate level of life satisfaction (66.5%). there is strong positive correlation between life satisfaction and social media addiction among students evidenced by high significance at p-value= 0.005.

Conclusions: The study concluded that social media addiction is positively influence the life satisfaction evidenced by positive association.

Keywords: *Social Media Addiction, Life Satisfaction, University Students.*

Introduction

Interpersonal relationship is the key for satisfying human's needs to belong and relate with others ¹. Recently, in the last decades, coincidentally with the development of information technology, particularly the quick deployment of internet-related social media applications such as Facebook WeChat, Instagram, or other applications; the patterns of interpersonal communication are dramatically changed ^(2,3). It has been shown that dependence on social media networks is associated with various health problems and psychological problems ^(4,5). Social media addiction can be seen as one form of internet addiction, in which the individuals show a forcing behavior to access social

media usage ⁶. The individuals who have been addicted on social media use are frequently worried about their social media accounts and are driven by uncontrollable motive to use the social media applications ⁷. The researches about social media addiction refer that individual with such addiction have many symptoms that can be manifested in mood, cognition, physical and emotional reactions, in addition to psychological and interpersonal relationship problems; the incidence of social media addiction was approximately 12% among users over social network sites ⁸. "According to the Internet World Stats (2017), the number of Internet users worldwide has reached to four billion. The proportion of Internet and social media usage (e.g. Facebook) to population is 27.7 and 11.7% in Africa; 45.2 and 13.4% in Asia; 77.4

and 39.9% in Europe; 59.6 and 55.8% in Latin America; 56.7 and 30.3% in the Middle East; 88.1 and 62.1% in North America; 68.1 and 51.7% in Australia. In Turkey is 59.6% and that of social media (Facebook) is 53.2%.”⁹ It has found that life satisfaction as well as self-esteem to be the predictor of internet addiction¹⁰. There are some conflicting outcomes with respect to the effect of social media on life satisfaction; from one view point, an extraordinary group of research demonstrates that there is a positive connection between life satisfaction and social media use. On the other side, there is a connection between the intensity of social media use and life satisfaction¹¹. There are growing number of researches about the connection between social media usage and human psychology. Some of them demonstrate that people who are using social media network are tending to be happy. Others look into life satisfaction as personal contentment. An argument demonstrates that people with low level of life satisfaction are improving their psychological well-being by joining in social media. The important argument about the connection between life satisfaction and social media usage and how it lead to problematic usage is that individuals are trying to spend more time on using of social media applications to avoid the feeling of dissatisfaction and then seeking psychological satisfaction⁹. For these reason, the current study is focusing on determining the association between social media addiction and life satisfaction among university students after determining the intensity of social media addiction and level of life satisfaction.

Objectives of the Study: The present study aims to assess the level of social media addiction and the level of life satisfaction among university students; and to determine the association between social media addiction and life satisfaction.

Methodology

The design of the study is descriptive, cross-sectional design that is initiated for the period of January 1st to May 1st, 2018; an assessment approach is applied in order to achieve the earlier stated objectives. The ethical consideration of research is achieved by obtaining the agreement from the Committee of Research Ethics at College of Nursing, University of Baghdad. In addition, the agreements of the students were asked for participation in research by filling the participation consent in covering letter of the questionnaire. For the purpose of administrative and arrangements issues for conducting the research, the permission was asked from University of Baghdad, Department of Students

Affairs, in addition, the secondary permission were obtained from the colleges that involved in this study. The permission facilitates the entrance of researcher to the colleges and meeting the students. The setting of the study includes five colleges at university of Baghdad that are: College of Nursing, College of Arts, College of Sciences, College of Physical Educations, and Ibn Rushed College of Education. These colleges were selected by researcher through simple random method (pool sample). The sample of the study includes (200) undergraduate students who are studying at the colleges that mentioned above, the researcher used the convenient sampling method (non-probability sample) in which the students were selected purposively. According to Soper¹², the sample size that must achieve the parameters of anticipated effect size of 0.15, the desired statistical power level of 0.80, one predictor, and a probability level of 0.05; the minimum required sample size would be 54. The questionnaire of the study is designed by researcher which consists of three parts; the first part is contained the covering letter and the demographic variable of the students as well as the variable related to social media usage; the second part is concerned with Social Media Addiction Scale; and the third part include the Life-Satisfaction Scale. Social Media Addiction Scale was adopted¹³ and consisted of 30 items which were rated into three levels of Likert scale and scored the follows: yes (3), to some extent (2), no (1). The level of addiction was estimated by calculating the cut off points for the total mean of scores for the scale as mild=30 - 50, moderate= 51 - 70, and severe= 71 - 90. Life Satisfaction with Life Scale was adopted¹⁴ and consisted of 5 items which were rated into five levels of Likert scale and scored the follows: strongly agree (5), agree (4), neutral (3), disagree (2), and strongly disagree (1). The level of satisfaction was estimated by calculating the cut off points for the total mean of scores for the scale as low=5 - 11, moderate= 12 - 18, and high= 19 - 25. The reliability and validity of the two scales were depended on the reliability and validity of the original scales that refer they were valid and reliable^(13,14). The data have been collected through the utilization of the self-administrative report as a mean of data collection. The questionnaire was distributed after being willing to answer the questionnaire and participate in the study. Statistical analyses were conducted by using statistical package for social science (IBM SPSS Statistics) version 24.0. Data analysis was employed through the application of descriptive and inferential statistical approaches to achieve the objectives of the study.

Results

Table 1: Distribution of the Students according to Variables related to Use of Social Media Account

No.	Variables		f	%
1	Having Laptop	No	103	51.5
		Yes	97	48.5
		Total	200	100
2	Having smartphone	No	0	0
		Yes	200	100
		Total	200	100
3	Having Account	No	0	0
		Yes	200	100
		Total	200	100
4	Hours of using account	3 hours	89	44.5
		4 – 6 hours	74	37
		7 – 9 hours	37	18.5
		Total	200	100

f: Frequency,%: Percentage

This table reveals that (48.5%) are having laptop, and all of the students having smartphones (100%). All of the students also are having accounts on different applications (100%). (44.5%) of the students are spending three hours on using these applications.

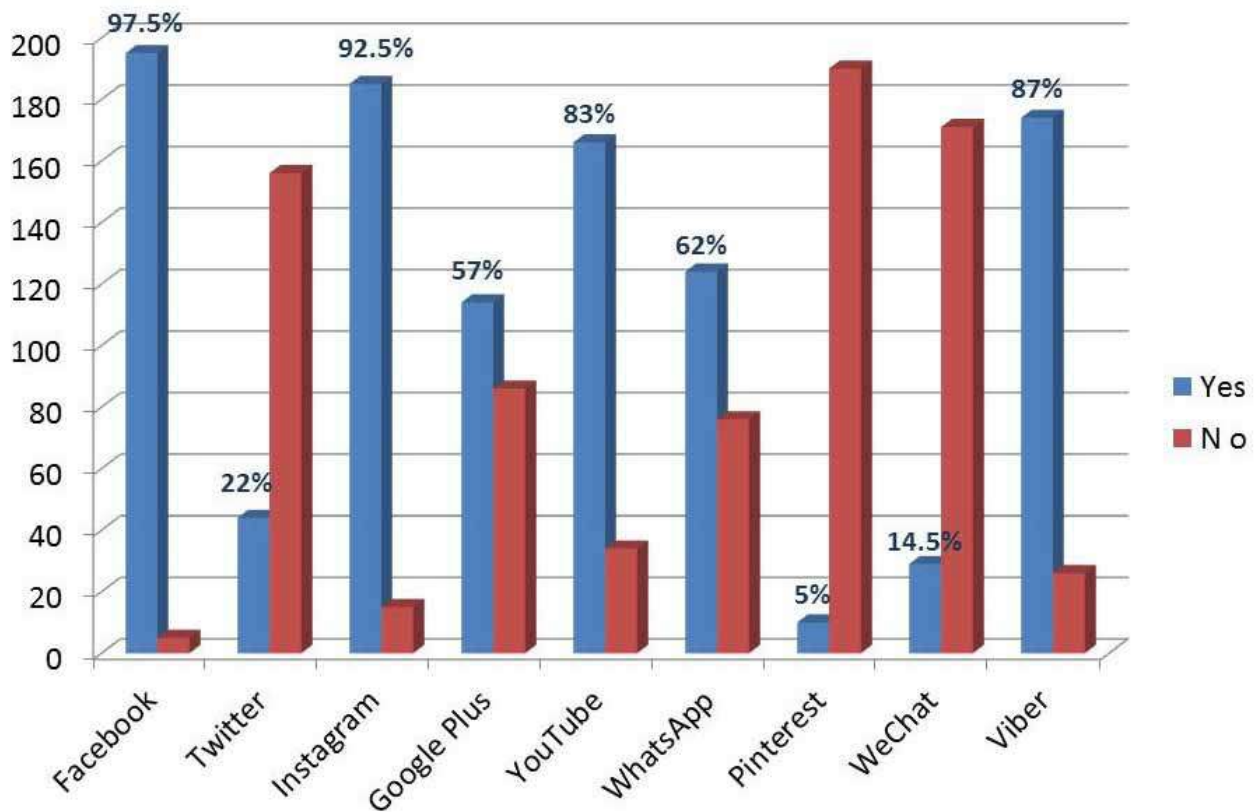


Figure 1: Distribution of the Students according to Use of Social Media Account (N=200)

This figure indicates that most of the students are having Facebook, Instagram, YouTube, and Viber accounts (97.5%, 92.5%, 83%, and 87%), only (22%) of them are having Twitter accounts, and (57%) are having Google Plus accounts, (62%) are having WhatsApp accounts, only (5%) are having Pinterest accounts, and only (14.5%) are having WeChat accounts.

Table 2: Level of Social Media Addiction among Students

Levels of Addiction	f	%	M.S	SD
Mild	48	24	1.92	0.629
Moderate	120	60		
Severe	32	16		
Total	200	100		

f: Frequency, %: Percentage, M.S: Mean of score, SD: Standard Deviation, Mild= 30-50, Moderate= 51-70, Severe= 71-90

This table indicates that students are showing moderate level of social media addiction (60%).

Table 3: Level of Life Satisfaction among Students

Levels of Addiction	f	%	M.S	SD
Low	19	9.5	2.15	0.562
Moderate	133	66.5		
High	48	24		
Total	200	100		

f: Frequency, %: Percentage, M.S: Mean of score, SD: Standard Deviation, Low= 5-11, Moderate= 12-18, High= 19-25

This table shows that (66.5%) of the students are moderately satisfied with their life while only (24%) of them are highly satisfied.

Table 4: Correlation between Social Media Addiction and Life Satisfaction of Students (N=200)

Correlation		Addiction	Self-Esteem
Addiction	Pearson Correlation	1	0.220**
	Sig. (2-tailed)	--	0.002
Self-Esteem	Pearson Correlation	0.220**	1
	Sig. (2-tailed)	0.002	--

This table indicates that there is strong positive correlation between life satisfaction and social media addiction among students evidenced by high significance at p-value= 0.005 respectively.

Discussion

The descriptive analysis of the students' demographic variables refer that are males, from third and fourth academic stage, from morning studies, and are students at scientific colleges. The highest percentage among the students is having laptop, and all of them having smartphones, and having accounts on different applications. Less than half of the students are spending three hours on using these applications. Such findings may reflect the needs for using the technology in education especially for scientific colleges. But from the other side, this may presents that they using smartphones and laptops for entertainment. The last statistics about using smartphone in Iraq refers that the number of mobile phone subscription is increasing from 2002 to 2017, in which the number of users in 2017 is refer to (33.34) million ¹⁵. Regarding use of social media accounts, the students are having Facebook, Instagram, YouTube, and Viber accounts as popular social media sites. The researcher sees that the students are using these social media for communication and entertainment purposes. Most of the social media statistics refer that Facebook is the popular among users; the last statistics about social media in Iraq refers that the users of Facebook are present (53.38%), YouTube users are (41.21%), Twitter (3.45%), Instagram (1.05%), and Pinterest (0.83%) ¹⁶. such statistics provide a supportive evidence for current study results. The findings regarding social media addiction among students refer to moderate level of addiction. This finding may be not a confirmative diagnosis of social media addiction, but at the same time is considered as indicator that should be taken in consideration of mental health among students and other individuals. Consideration of such findings may explain some of the reason behind social media addiction; the most of these reasons is the mood status represented by depression, anxiety, weakness in communication skills, and social fear as well as fear of the future. All these symptoms may lead the students to use social media networking to get rid of this mood status. Young individuals who use social media networking sites are unaware of the time spent in the use of those sites, which leads them to ignore their responsibilities in real life over time. Individuals who find it difficult to form relationships in real life will use social media networking. On the other hand, some young individuals cannot maintain the level of communication with friends and family in the real life, so, leading them to make communication over social media networking. A study provides supportive evidence for this study that found

significant social media addiction among his sample¹⁷. Regarding the finding of life satisfaction, the students were showing moderate life satisfaction. Satisfaction with life is one of the indicators that indicate the mental health of the individual, so the level of satisfaction with life among students in the current study indicates that students perceive their lives as being full of various pressures, including those related to the educational environment, including those related to daily life. The finding is slightly different from others studies results such as the study of Behlau who found a high level of life satisfaction among the students⁽¹⁸⁾. The main objective of current study is to determine the association between social media addiction and life satisfaction; the bivariate correlation analysis of finding indicates that there is strong positive correlation between life satisfaction and social media addiction among students. A study has supportive evidence for this study that found a significant relationship between Facebook addiction and life satisfaction¹¹. The interpretation of the current study finding is depicted with the contents of related literature that the students who perceive life dissatisfaction will emerge in the use of social media accounts. So, they will avoid the perception of dissatisfaction. Sahin stated “the main argument about how life satisfaction leads to problematic internet or social media use is that people prefer to spend more time on the internet so as to avoid the feeling of dissatisfaction and to seek psychological satisfaction”⁹. Therefore, the positive relationship in current study may be interpreted based on this hypothesis that stated by Sahin.

Conclusions

Based on the results, the study concluded that university students showing moderate level of social media addiction and life satisfaction scores, and social media addiction is positively influence the life satisfaction evidenced by positive association.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the College of Nursing, University of Baghdad, Iraq and all experiments were carried out in accordance with approved guidelines.

References

1. Wang Q. The Autobiographical Self in Time and Culture. New York, NY: Oxford University Press. 2013.
2. Smith A, Anderson M. Social media use in 2018.
3. StoneC, Wang Q. From conversations to digital communication: The mnemonic consequences of consuming and sharing information via social media. *Topics in Cognitive Science*,1-20. 2018.
4. Marino C, Finos L, Vieno A, Lenzi M, Spada M M. Objective Facebook behavior: Differences between problematic and non-problematic users. *Computers in Human Behavior*; 2017;73:541–546.
5. MarinoC, Gini G, Vieno A, Spada MM. A comprehensive meta-analysis on problematic Facebook use. *Computers in Human Behavior*, 2018; 83: 262–277.
6. Starcevic V. Is Internet addiction a useful concept? *Australian and New Zealand Journal of Psychiatry*,2013; 47: 16–19.
7. AndreassenCS, Pallesen S. Social network site addiction-an overview. *Current Pharmaceutical Design*; 2014;20: 4053–4061.
8. Hou Y, Xiong D, Jiang T, Song L, Wang Q. Social media addiction: Its impact, medication, and intervention. *Cyberpsychology: Journal of Psychological Research on Cyberspace*; 2019;13(1).
9. Sahin G. The Predictive Level of Social Media Addiction for Life Satisfaction: A study on University Students. *The Turkish Online Journal of Educational Teaching*; 2017;16(4).
10. BozoglanB, Demirer V, Sahin I. Loneliness, self-esteem, and life satisfaction as predictors of Internet addiction: a cross-sectional study among Turkish university students. *Scandinavian Journal of Psychology*; 2013;54(4): 313e319.
11. Blachnio A, Przepiorka A, Pantic I. Association between Facebook addiction, self-esteem and life satisfaction. A cross sectional study. *Computers in Human Behaviors*; 2016;55: 701-705.
12. Soper DS . A-priori Sample Size Calculator [Software]; 2019.
13. Younis B. Addiction to Social Network and its Relationship to Mental Disorders among University Students in Gaza Governorate. A thesis submitted

- to Al-Azhar University. College of Education. Department of Psychology. 2016.
14. Diener E, Emmons RA, Larsen R J, Griffin S. The Satisfaction with Life Scale. *Journal of Personality Assessment*; 1985;49: 71-75.
 15. Holst A. Number of mobile cellular subscriptions in Iraq from 2002 to 2017 (in millions) 2018.
 16. Kirik A, Rslan A, Cetinkaya A, Gul M. A Quantitative Research on the Level of Social Media Addiction among Young People in Turkey. *International Journal of Science Culture and Sport*; 2015;3(3).
 17. Behlau S. Life Satisfaction: A study of Undergraduate and Graduate Students. A thesis submitted to Rowan University, The Graduate School, 2010.

Assessment of Psychosocial and Physical Factors Associated with a Substance Re-abuse after Treatment among Patients with Addiction at Psychiatric Teaching Hospitals in Baghdad City-Iraq

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Abstract

Background: The high rate of relapse is an especially frustrating problem and one of the most problems that face the substance abusers after a period of treatment remains old news. Little studies are documented about the addiction relapse in Iraq.

Objective: The current study aims to assess the causative factors affecting the substance abuse-related relapse. And find out the relationship between the clinical and demographic characteristics with relapse.

Methodology: A descriptive study was conducted from November 20th 2016 to May 1th 2017 on addict patients in Baghdad City. Purposive (non-probability) samples of 30 relapsed addicts who are inpatient in Ibn-Rushd Psychiatric Teaching Hospital and the Psychiatric unit of Baghdad Teaching Hospital who had undergone treatment for substance dependency and they had at least one episode of relapse during the period of addiction. The study uses the self-administrated questionnaire. The data has been analyzed by using the descriptive statistics (Frequencies, Percentages, Means and Standard Deviations (SD) and the inferential statistics (Chi-square to find out the relationships between the socio-demographic and clinical characteristics of addicts with relapse).

Results: The findings of the current study revealed that all relapsed patients are males with age ranged from 20 years to more than 50 years. The highest percentages of the addict patients were addicted to alcohol and two third of them have one previous admission. The results indicated that the factors of psychosocial and physical are associated with relapse to problematic alcohol or illicit drug use. There is no significant relationship between socio-demographic and clinical characteristics with relapse.

Recommendations: The researchers recommended may be there treatment programs focusing on teaching the clients how to cope with the relapse and control the feeling of craving for alcohol drink and substance abuse.

Keywords: Substance Abuse, Relapse, Addiction.

Introduction

Substance abuse is a global and an important challenging and costly health problem which leading to physical, mental and psychiatric outcomes in persons, families and communities⁽¹⁾. It has a profound effect on all areas of society; this includes high costs in terms of healthcare provision, the effect on individuals in

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terms of physical and psychological problems and their families, and has harmful effects on society through criminal and violence issues⁽²⁾. There are 76.3 million people with alcohol use disorders worldwide and 15.3 million with drug use disorders⁽³⁾. Al-Hemiaryetal, 2015 reported in their survey that there is a high rate of alcohol and drug abuse in Iraqi population ⁽⁴⁾. Relapse means the return to uncontrolled substance use, it occurs when a client resumes an abusive pattern of use after a period of treatment, the problem of relapse remains to be challenge to many substance abusers post treatment for substance dependency ⁽⁵⁾. Many factors are being associated with relapse such as peer group influence, poor family support and personality characteristics ⁽⁶⁾. Insufficient rehabilitation phase, lack of programming for the occupation of addicts after discontinuing, low self-esteem, presence of family problems, negative mood states, presence of addicted friends and contaminated environment, are cited as a cause of relapse ⁽⁷⁾. Motivation to stop substance abuse and insight into the addiction problems are good prognostic factors to avoid relapse ⁽⁸⁾. The abstinent individuals who are contributed in rehabilitation program should be integrated back into society unless the treatment may fail; craving and relapse depend on successful treatment ⁽⁹⁾.

Objectives of the Study:

The study aims to:

1. To assess the factors of substance abuse related relapse among addicts person.
2. To find out the relationship between the cause of relapse and demographic characteristics for those populations.

Methodology

A descriptive analytic study was conducted from November 20th 2016 to May 1st 2017 on addict patients in Baghdad City. Purposive (non-probability) samples of 30 relapsed addicts who are inpatient in Ibn-Rushd Psychiatric Teaching Hospital and the Psychiatric unit of Baghdad Teaching Hospital who had undergone treatment for substance dependency and they had at least one episode of relapse during the period of addiction. The study uses the self-administrated questionnaire. To assess the causes of relapse the study adapted from the reasons for drinking and drug use questionnaire by Zywiak et al. (1996)⁽¹⁰⁾. The questionnaire comprised three parts:

- a. The socio-demographic characteristics of the addict patients such as: age, marital status, educational level, residence, occupation and monthly income.
- b. The data related to substance abuse such as: type of substance abuse, previous admission, the main reason for you taking the first drink.
- c. Assessment of the causes of substance abuse related relapse (20 items), and it is consist form (20 items) gives a total score. The score ranged from 1-3 (3= agree, 2=neither agree nor disagree, 1= disagree) the score was interpreted as disagree (1-1.33), neither agree nor disagree (1.34-2.67), and agree (3.68-4.00).

The data has been analyzed by using the descriptive statistics (Frequencies, Percentages, Means and Standard Deviations (SD) and the inferential statistics (Chi-square to find out the relationships between the causes of the relapse and the socio-demographic characteristics of addicts).

Results

Table 1: Distribution of the sample according to the data related to substance abuse

No.	Characteristics	f	%	
1	Types of substance abused:	Alcohol	11	36.7
		Narcotics	9	30.0
		Both	10	33.3
		Total	30	100
2	No. of Previous relapses:	One	18	60.0
		2 – 3	11	36.7
		4 – 5	1	3.3
		Total	30	100.0
3	The main reason for you taking the first drink:	social factors	16	53.3
		psychological factors	6	20.0
		physical factors	3	10.0
		other factors	5	16.7
		Total	30	100.0

This table indicated that more than half of sample are alcohol abused (36.7%) and 33.3% of them are abusing alcohol and narcotics, while only 30.0% are abusing narcotic only. The previous admission shows that more than half of them are admitted to the hospitals once (60.0%). Regarding the main reason for you taking the first drink, the analysis of data shows that more frequent reasons are social factors (53.3%).

Table 2: Descending distribution of the sample according to the causes of substance abuse relapse (N=30)

No.	Reasons for drinking again	M	SD	Sig.
1	I felt angry with myself because things were not going my way	2.53	0.681	H.S
2	I felt frustrated with myself because things were not going my way	2.90	0.403	H.S
3	I felt bored	2.30	0.837	S
4	I felt anxious	2.47	0.730	H.S
5	when I saw alcohol I just had to give in	2.90	0.403	H.S
6	I felt sad	2.23	0.679	S
7	I was in a good mood and felt like getting high	2.20	0.847	S
8	I wanted to see what would happen if I tried drink	2.20	0.887	S
9	I just felt tempted to drink out of the blue and went off to get a drink	2.40	0.814	H.S
10	Someone offered me a drink	2.67	0.711	H.S
11	I felt frustrated because of my relationship with someone else	2.50	0.630	H.S
12	I was with others having a good time and we felt like getting drunk together	2.13	0.937	S
13	I felt others were being critical of me	2.63	0.615	H.S
14	I saw others drinking	2.43	0.817	H.S
15	I felt could not cope with my stressful work environment	2.23	0.774	S
16	I was transferred to another more stressful department at work	1.47	0.776	S
17	I felt physically ill.	1.93	1.129	S
18	I felt pain.	2.00	1.220	S
19	I felt ill or in pain but this was not due to withdrawal from alcohol.	1.88	1.039	S
20	I discovered I have a terminal illness/my health began to deteriorate due to my health status.	1.65	0.783	S
	Total	2.34	0.747	H.S

No: Number, M: Mean, SD: Standard Deviation, Sig: Significant

This table reflects the mean distribution of the questions related to reasons for drinking and takes drugs again after treatment. All items are showing significant to high significant its mean the respondents are agree with questions relating to reasons for drinking again after treatment.

Table 3: Association between demographic variables and relapse among Substance Abusers (N=30)

Characteristics	Relapse	Chi-square	d.f	P-Value ≤ 0.05	Significance
Age		65.420	57	0.208	N.S
Level of education		96.091	95	0.449	N.S
Marital status		61.286	57	0.325	N.S
Residence		45.119	38	0.199	N.S
Occupation		77.987	76	0.415	N.S
Monthly income		43.275	38	0.256	N.S

d.f: degree of freedom, P: Probability, N.S: Not significant, S: Significant

This table shows that socio-demographic characteristics of substance abusers are not associated with causes of relapse at p-value ≤ 0.05.

Table 4: Association between Clinical Characteristics and relapse among Substance Abusers (N=30)

Characteristics	Relapse	Chi-square	d.f	P-Value ≤ 0.05	Significance
Types of substance abused		96.091	38	0.592	N.S
No. of Previous relapses		47.540	57	0.810	N.S
Causes of treatment seeking		49.958	57	0.734	N.S

d.f: degree of freedom, P: Probability, N.S: Not significant, S: Significant

This table indicates that there is no significant association between clinical characteristic of substance abusers and cause relapse at $p\text{-value} \leq 0.05$.

Discussion

The findings in table (1) show that all addict patients were males with age ranged from 20 to more than 50 years with mean 24.65 years and $SD = 6.883$, this may be due to men tend to drink more than women, and they are more likely to be substance abusers and they have a financial independence in this age which allowing them to easily acquire an addictive substance, this result was consistent with Sharma et al, 2012 who reported that all subjects in their study were males⁽⁶⁾, and close to Matoo et al., (2009) who found the mean age was $30 \pm (9.3)$ years old who live in urban area⁽¹¹⁾. Hammerbacher and Lyvers, 2005 who found that the clients were over 18 years of old with mean 31.8 years⁽¹²⁾. Table (1) also indicated that the highest percentage of subjects in the sample are married and were at primary level of education, and they reported a barely sufficient monthly income, these results were similar to findings of Kassani et al, 2015 who found that married subjects were more than other groups⁽¹⁾, and close to Sharma et al, 2012 who reported that the highest percentage of the sample were at primary educational level and had lower middle class of socio economic status⁽⁶⁾.

The current study results show in table (2) indicated that the highest percentage (36.7%) of the addict patients were addicted to alcohol; In Iraq, easy availability of alcohol more than other types of substances, Al-Hemiary et al, 2015 reported in their survey that the prevalence of alcohol abuse in Iraq was higher than drug abuse⁽⁴⁾. The findings also revealed the number of previous relapse was one relapse (63.3%). This result is similar with study of Kaundal et al., (2016) who reported the 56% patients had one relapse and 44% patients had two relapses in the past⁽¹³⁾. So, the result show the main reason for taking

the first drink was social factors. This result is consistent with study of Chetty,(2011) who found that their first drink was due to peer pressure⁽⁵⁾.

The findings in table (3) revealed that the psychosocial and physical reasons are main causes for drink and take drugs again. This result was consistent with Zhuang et al., 2012 a number of studies have shown that alcohol and drug relapse in patients was related to the three aspects of physical, psychological and social factors⁽¹⁴⁾. The researcher suggested the widespread and easy availability of drugs and alcohol linked to increase tendency to substance abuse thus will increase the chance of relapse too. Also may be explained by that in the anticipation stage of the addiction cycle which is commonly called "craving" a person begin to seek substance again after a period of abstinence.

In table (4) the findings revealed that there is no significant relationship between socio-demographic variables and relapse. This result is contradict with study of Kaundal et al., (2016) there is a significant association of relapse among patients with alcohol and drug dependence syndrome with demographic and psychosocial variables⁽¹³⁾. Also this result is consistent with study by Anton et al., 2006 who said "although widely researched for an extensive period of time; little is actually known and documented about the exact causes of relapse. Even less is known about the effect of personal and demographic contributors to relapse"⁽¹⁵⁾. The current study results show in table (5) that there is no significant relationship between clinical variables related addiction and relapse. This result is inconsistent with Kaundal et al., (2016) who found the clinical parameters such as the number of previous relapses emerged as significant determinants of relapse⁽¹³⁾. The researchers explain this result that the patients who had relapsed in this study had experienced a higher number of undesirable life events, low self-efficacy and negative coping behavior.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the College of Nursing, University of Baghdad, Baghdad City, Iraq and all experiments were carried out in accordance with approved guidelines.

References

1. Kassani A, Niazi M, Hassanzade J, Menati R. Survival Analysis of Drug Abuse Relapse in Addiction Treatment Centers, International Journal of high Risk Behavior. 2015; 4(3).
2. National Collaborating Centre for Mental Health- NCCMH, Drug Misuse, Psychosocial Intervention (NICE clinical guideline no 51), The British Society and the Royal College of Psychiatrist, 2008.
3. Smedslund G, Berg RC, Hammerstorm KT, Sterio A, Leiknes KA, Dahl, HM, Karlsen K. Motivation interviewing for substance abuse, Cochrane Collaboration, John Wiley & Sons. Inc, 2011.
4. Al-Hemiary NJ, Hashim MT, Al-Diwan JK, Razzaq EA. Alcohol and drug abuse in post-conflict Iraq, Fac Med Baghdad. 2015; (57): 290-294.
5. ChettyM, Taut F. Causes of relapse post treatment for substance abuse dependency within the South African police services, a thesis submitted for fulfillment of Master Degree in social work, Faculty of Humanities, University of Pretoria, 2011.
6. Sharma AK, Upadhaya, SK, Bansal P, Nijhawan, M, Sharma DK. A study of factors affecting relapse in substance abuse, Indian J.L.Sci. 2012; 2(1): 31-35.
7. Narimani M, Sedeghieh SA. A study of the rate and causes of addiction relapse among volunteer addicts seeking help at the center for the prevention of addiction affiliated to the welfare organization, Ardabil province, Iran, Research Journal of Biological Sciences. 2008; 3(2): 258-264.
8. Goldstein A. Addiction, from biology to drug policy, second edition' Oxford University Press, 2001.
9. Mayet S, Winstock A, Strangm J. Opioids: heroin, methadone, and buprenorphine, The New Oxford Textbook of Psychiatry, Oxford University Press, 2009.
10. Zywiak, W, Connors GJ, Maisto SA, Westerberg VS. Relapse research and the reasons for drinking questionnaire: a factor analysis of Marlatt's relapse taxonomy. Addiction. 1996; 91:121-130.
11. Mattoo SK, Chakrabarti S, Anjaiah M. Psychosocial factors associated with relapse in men with alcohol or opioid dependence, Indian J Med Res 2009; 130: 702-708.
12. Hamerbacher M, Lyvers M. Factors associated with relapse among clients in Australian substance disorder treatment facilities, Journal of Substance Use. 2005; 11(6): 387-394.
13. Kaundal P, Indrajeet S, Tulika J. Assessment of psychosocial factors associated with relapse in patients with alcohol dependence: a retrospective observational study, International Journal of Basic & Clinical Pharmacology 2016.
14. Zhuang X, Wang Y, Chow EP, Liang Y. Risk factors associated with HIV/HCV infection among entrants in methadone maintenance treatment clinics in China: A systematic review and meta-analysis. Drug Alcohol Depend. 2012; 126: 286-295.
15. Anton RF, O'Malley SS, Ciraulo DA, Cisler RA, Couper D, Donovan DM. Combined pharmacotherapies and behavioral interventions for alcohol dependence: the Combine study: a randomized controlled trial. J Am Med Asso. 2006; 295(17): 2003-17.

Slow Learners: Across-Sectional Study among Primary School Children in Kirkuk City

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Abstract

Background and Aims: Slower learners are pupils who have lower IQ scores than the average score of 100 but do not fall into mental disabilities. This study aimed to describe the sociodemographic characteristics of primary school children as well as to explore certain factors related to slow learning among these children in Kirkuk city

Methodology: A constructed questionnaire was completed by 102 randomly selected children, who were diagnosed with a slow learner, in Kirkuk city, during 2017. The questionnaire consisted of two parts, the first related to sociodemographic variables and the second related to clinical findings. Frequency, percentage, and Chi-Square Goodness of Fit were used for statistical analysis using SPSS version 19.

Results: The study revealed that more than half of the pupils were male which constitute (63.7%), more than half of their parents had low educational level, and most of them had moderate economic status (60.8%), majority of them live with both parents (87.3%).

Conclusion: In spite of the limitations of this study, it could be fairly concluded that low birth weight, type of delivery and genetic factors were considered as predictive factors for slow learning. So, more antenatal care had recommended for all mothers, especially who had risks of pregnancy.

Keywords: *Slow Learner, School Children, Males, Females.*

Introduction

Slow learner, that is a child with limited scope for attainment, is distinct from the mentally handicapped child. The slow learners are not interested in studying under traditionally accepted systems of education their handicap is related to their scholastic performance.¹ Normally, learners have an average IQ between

(85_115). Whereas, slow learners have intelligence test scores below the average score but above the range of mental impairment. The number of children with this problem is about 14% as this percentage increases the remaining students who have problems in special education.²

The slow learner does not learn successfully due to general socio-cultural problems, related to residence, poverty, parents relationships, personal factors are related to long illness, long absence from the school, poor cognitive characteristics, frustrating past language classroom experience, while the environment variables include, poor home facilities for learning skills, adverse parenteral attitudes toward education, inappropriate opportunities in school (large classes), poor quality of teaching, repeated changes of school and consequent

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changes in teaching styles and content. The emotional factors are related to the feeling of inadequacy and lack of confidence in self, extreme timidity and anxiety giving rise to a poor level of attainment, negative attitude to school and teachers.³

In general slow learners may exhibit some or all of these characteristics depending on their age and degree of problems of acquiring knowledge at school, they are recurrently immature in their relation with others, they cannot do multifaceted activities, and do very slowly and poorly in school, they lose track of time and cannot convey what they have learned from one task to another well, with inability to have long term goals and dealing with symbolic materials i.e language, numbers, and concepts is very limited and inferior to that of average students, slow learners prefer concrete learning to abstract learning, they gain from direct teaching and do not acquire skills incidentally.⁴

Special education in Iraq for slow learners starts at the age of six years from the first grade and continues until the fourth grade. Students who pass in the fourth grade continue with their classmates. Each class consists of 6 to 12 students. The curricula of these classes are the same as those of their colleagues in the academic curriculum. But there is a difference in the teaching

method of that group.⁵ The current study, therefore, is an attempt to describe sociodemographic attributes of the primary school children, besides exploring some related factors of slow learning among primary school children in Kirkuk city.

Methodology

This was a cross-sectional study carried out at primary schools in Kirkuk city for the period of first January, to the end of March 2017. Non-probability sampling a purposive sample of 102 pupils who were diagnosed with the slow learner by a group of specialists in Kirkuk Education Directorate. A special questionnaire was constructed for proper data collection based on an extensive review of related kinds of literature and studies. It consisted of two parts, the first related to sociodemographic variables and the second related to the health information related to the study sample. The validity of the instrument was done by (6) experts and test-retest technique was used to determine reliability. A descriptive (frequency and percentage) and inferential statistics (Chi-Square Goodness of Fit) were used for data analysis using SPSS version 19. An ethical issue of the participant was considered through taking their parent consent to participate their children as a sample in the study

Results

Table 1. Distribution of the study sample (N=102) according to some health history information

Health History Information	Frequency	Percent	p- value
	F	%	
Type of delivery			
Normal	86	84.3	0.001
Cesarean	16	15.7	
Total	102	100	
Birth weight			
<2.5 kg	65	63.7	0.006
≥2.5 kg	37	37.3	
Total	102	100	
Problems of			
Speaking	48	47.7	<0.001
Hearing	16	15.7	
Visual	23	22.5	
Total	102	100	

Discussion

According to the findings of table (1) show that the majority of slow learners (84.3%) had history of normal delivery and the remaining (15.7%) of them had delivered by caesarian section. There are some problems during childbirth that affect the baby. For example, the umbilical cord wrapped up prevents oxygen from reaching the fetus, which in turn causes brain problems and then problems in learning in the future.⁶ Regarding to birth weight of children, more than halve (63%) of them were under (2.5 kg). there are several factors for low birth weight (<2.5 kg), and most of these factors have existed during pregnancy like Injury or ailments, cigarette smoking, alcohol drinking, which might lead to other negative consequences.⁶ Osman (2012) elicited that problem in speaking, hearing and visual abilities considered as genetic causes of slow learners.⁷ In the present study most of the members of the sample had problem in speaking and hearing abilities so that, they are vulnerable for learning problems including slow learning.

Conclusion

Most of the slow learners were young children, male pupils outnumber female pupils, their parents had low educational level, they have moderate economic status, majority of them live with their parents (father and mother), and most of them had no other family members with slow learner. Low birth weight, type of delivery and genetic factors were considered as predisposing factors for slow learning. So that, more antenatal care should be provided for all mothers especially those with high risk of contributing factors during pregnancy.

Conflict of Interest: None of the authors have any conflicts of interest to declare.

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Ethical Clearance: The project was approved by the local ethical committee in University of Kirkuk. Informed consent was taken from each students parent.

References

1. The 2nd International conference on education for slow learners. Department of Education Annamalai University Annamalinagar - 608 002. Tamilnadu-India; 2018. Available from: http://www.auteachereducation.org/images/conf_book_2018.pdf. Accessed January 21, 2020.
2. Steven R. Rescuing Students from the Slow Learner Trap, National Association of Secondary School Principals, the preeminent organization for middle level and high school leadership; 2010.
3. Tuija A, Timo A. Assessment of Learning Disabilities: Cooperation between Teachers, Psychologists and Parents, 1st edition, Suomen Yliopistopaino Oy; 2011. p: 18
4. Learning Disability. Special Needs Trust| Learning Disability. Available from: <http://www.dimobitrust.org.uk/autism/learning-disability>. Accessed September 8, 2019.
5. World Rehabilitation Fund, Inc. "Situation Analysis of Different Social Welfare Issues in Iraq", Beirut-Lebanon, summer 2003 REPORT October 13, 2003, p: 32. Available from: <http://www.worldrehabfund.org/publications/WRF-IRAQ-Report-October-2003.pdf>. Accessed September 8, 2019.
6. Clark MJD. Community health nursing: advocacy for population health. Upper Saddle River, NJ: Pearson Prentice Hall; 2008.
7. Osman MA. Slow learning: its causes and how to deal with him, Manhal Educational; 2012. Available from: <http://www.manhal.net/>. Accessed September 9, 2018.

lncRNAs as New Biomarkers in Systemic Lupus Erythematosus: A Prospective Study

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Abstract

Aim: To investigate serum levels of two Immune-related functional lncRNAs, growth arrest-specific transcript 5 (GAS5) and metastasis-associated lung adenocarcinoma transcript 1 (MALAT1), in Egyptian patients with SLE and to evaluate their relationship with disease activity.

Method: The present study was a case-control study that was carried out on 39 patients with SLE and 46 age and sex-matched healthy controls. The expression levels of GAS5 and MALAT1 were measured using by real-time polymerase chain reaction (PCR).

Results: There were statistically significant differences between cases and controls in GAS5 ($p < 0.001$) and MALAT1 expression ($p < 0.01$). The mean GAS5 was significantly higher in the control; while the mean MALAT1 expression was significantly higher in SLE patients. The ROC curve revealed that GAS5 was a good discriminant with AUC 0.849 with sensitivity 93.5% and specificity 74.3%. Moreover, MALAT1 was a good discriminant to differentiate cases from controls with AUC 0.3 with 95% CI (0.162 - 0.438), the most suitable cut-off point was ≥ 2.1 with Sensitivity 93.5% and Specificity 72.5%.

Conclusion: GAS5 and MALAT1 may serve as potential biomarkers for the diagnosis and monitoring of the SLE, both lncRNAs exhibited a good diagnostic accuracy to discriminate between SLE patients and healthy controls.

Keywords: lncRNAs; Systemic Lupus; Biomarker; Diagnostic Accuracy.

Introduction

Systemic lupus erythematosus (SLE) is a progressive, chronic, disorder that affects multiple systems with recurrent episodes of exacerbations and remissions¹. According to recent epidemiological figures, the estimated global incidences of SLE ranges

from 0.3-23.2 per 100 000 person-years². Although the exact pathogenesis of SLE is still unclear, it is widely believed that the disease arise as a result of abnormal autoimmune process; patients with SLE were found to have defective clearance of apoptotic cells with subsequent development of auto-antigens and dysregulated immune responses (affecting both innate and adaptive immunity)^{3,4}. Various environmental and hormonal factors were linked to increased risk of SLE in genetically susceptible individuals⁵. SLE is characterized by wide range of clinical manifestations that mainly affects women in their reproductive age, patients with SLE often present with fatigue, weight loss, myalgias and muscle weakness, recurrent infection, and migratory polyarthropathy⁶. Moreover, a considerable proportion of the patients present with multiple systems affection

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such as lupus nephritis, pericardial disorders, valvular abnormalities, and cognitive dysfunction⁷.

Therefore, it is critical to diagnose SLE early and identify patients with increased risk of high disease activity in order to optimize SLE outcomes. Over the past few decades, a wide spectrum of biomarkers have emerged for early detection of SLE including antibodies, complement and complement split products, cytokines, chemokine biomarkers, and epigenetics-related biomarkers such as noncoding RNAs⁸. The noncoding RNAs are regulatory RNAs that control many biological process such cell cycles, apoptosis, and remodeling⁹. Long noncoding RNAs (lncRNAs) are the largest proportion of mammalian non-coding transcriptome (larger than 200 nucleotides) that are key components of many structural, activating, and/or functional roles within the body¹⁰. Previous study has shown that lncRNAs play significant role in the pathogenesis of different diseases such as cancer and neurological disorders^{11,12}. Recently, a growing body of evidence reported increased expression of a number of lncRNAs in SLE patients. Owing to their immune-related functions and regulatory role in apoptosis, lncRNAs are proposed to contribute significantly in the molecular pathogenesis of SLE¹³. Thus, they may serve as accurate biomarkers of SLE development and activities.

We performed this study to investigate serum levels of two Immune-related functional lncRNAs, growth arrest-specific transcript 5 (GAS5) and metastasis-associated lung adenocarcinoma transcript 1 (MALAT1), in Egyptian patients with SLE and to evaluate their relationship with disease activity.

Materials and Method

Study Design and Patients: The present study was a case-control study that was carried out from November 2017 to August 2018 in the Medical Biochemistry Department, Cairo University. The study included 39 patients who were diagnosed with systemic lupus erythematosus (SLE) and 46 age and sex-matched healthy controls. Adults patients (aged >18 years old) with diagnosis of SLE according to the 2012 Systemic Lupus International Collaborating Clinics (SLICC) criteria were included¹⁴. We excluded patients who had any other illnesses that might affect the results of the study such as chronic liver, familial hypercholesterolemia, thyroid and parathyroid diseases, and malignancy as well as any other rheumatic disease.

Data Collection: All patients were subjected to full history taking and clinical examination including SLE Disease Activity Index (SLEDAI). In addition, we recorded the results of complete blood count (CBC), bleeding profile, and kidney function tests. The expression levels of GAS5 and MALAT1 were measured using by real-time polymerase chain reaction (PCR).

Expression levels of the studied lncRNAs: Whole blood samples (5ml) were taken from SLE patients and controls. Serum was separated from the whole blood for quantitative expression of long non-coding RNAs by real-time PCR. RNA was extracted from serum by miRNeasy extraction kit (Qiagen, Valenica, CA) using QIAzol lysis reagent according to the manufacturer's instructions. Sixty ng of total RNA were used in the reverse transcription (RT) step in final volume 20µl RT reactions using RT2 first strand Kit (Qiagen, Valenica, CA) according to the manufacturer's instructions. Serum expression levels of the studied lncRNAs were evaluated using GAPDH as internal control and ready made primers (MALAT-1 and GAS-5) and Maxima SYBR Green PCR kit (Thermo, USA) according to the manufacturer's protocol. The primer sequences for GAPDH were as follows: F 5'-CCCTTCATTGACCTCAACTA-3', R 5'-TGGAAGATGGTGTGATGGGATT-3'.

Twenty µl reaction mixtures was used in RT-PCR by mixing 10µl master mix, 1µl readymade assay primer, cDNA, and RNAase-free water using Rotor gene Q System (Qiagen).

PCR conditions were as follow: 95°C for 10min, followed by 45 cycles at 95°C for 15s and 60°C for 60s. The cycle threshold (Ct) is the number of cycles required for the fluorescent signal to cross the threshold in real-time PCR. Gene expression relative to internal control ($2^{-\Delta Ct}$) was calculated. A melt curve analysis was done to ensure specificity of the corresponding RT-PCR reactions. Fold change was calculated using $2^{-\Delta\Delta Ct}$ for relative quantification. Using the data analysis of web portal, we calculated fold change/regulation with $\Delta\Delta Ct$ method, in which ΔCt was calculated between gene of interest and an average of reference genes, followed by $\Delta\Delta Ct$ calculations [ΔCt (patient) – ΔCt (control)]. Fold change is then calculated using $2^{-\Delta\Delta Ct}$ formula.

Study's Outcomes: The primary outcome in the present study was the association between the expression levels of GAS5 and MALAT1 with SLE. The secondary outcome was the relation between the expression of the two lncRNAs and the activity of the disease.

Statistical Analysis: Data entry, processing, and statistical analysis were carried out using SPSS version 22.0. Frequency tables with percentages were used for categorical variables and descriptive statistics (mean and standard deviation) were used for numerical variables. The normality of the data was assessed using the Shapiro-Wilk Test. Tests of significance (Chi-square, student's t-test, or Mann Whitney's test) were used according to the normality of the data. The recessive operative characteristics (ROC) curve was performed to assess the diagnostic performed of studied gene expressions in discrimination between SLE patients and control group. A p-value<0.05 is considered statistically significant.

Results

The present study included 39 patients with SLE and 46 normal controls were included. The mean age of the patients was 29.68 ±6.96 years; while the majority

of patients were female (89.7%). The mean duration of disease of the included patients was 5.72 ±5.53 years. The mean ESR and CRP was 51.69 ±36.14 mm/hr and 1.81 ±3.86mg/L. In addition, the mean total leucocyte count was 6.70 ±2.96 x1000 cell/mm³. Regarding kidney function, all mean renal function parameters were within the normal range at the baseline. Only 33.3% of the patients had vasculitis, and only one patient (2.6%) had myositis. On the other hand, 33.3% and 46.2% of the patients had arthritis and pericarditis, respectively. In addition, 15 (39.1%) of patients were ANA positive and only 5 (10.9%) patients were DNA positive. The mean of C3 of the included cases was 54.13 ±35.13 mg/dl and C4 level was 10.12 ±10.02 mg/dl. The mean of SLE disease activity index (SLEDAI) in included cases was 5.75 ±5.32. Table 1 shows the baseline characteristics of the included patients.

Table 1: Baseline characteristics of the included subjects

Variables	Patients (N =39)	Control (N =46)	P-value
Age (Years)	29.68 ±6.96	33.5 ±9.5	0.1
Age at Onset (Years)	24.42 ±5.08	----	----
Disease Duration (Years)	5.72 ±5.53	-----	-----
Gender, No (%)			
1. Female	35 (89.7%)	39 (84.7%)	0.46
2. Male	4 (11.3%)	7 (15.3%)	
ESR	51.69 ±36.14	----	----
CRP	1.81 ±3.86	-----	-----
TLC	6.70 ±2.96	----	----
PTC	248.78 ±91.92	-----	-----
Vacuties	13 (33.3%)	----	----
Arthritis	13 (33.3%)	-----	-----
Myositis	1 (2.6%)	----	----
Pericarditis	21 (53.8%)	-----	-----
SLEDAI score	5.75 ±5.32	-----	-----

*Data are presented as mean (SD), median (IQR), or No. (%)

In term of the primary outcome of the present study, there were statistically significant differences between cases and controls in GAS5 (p <0.001) and MALAT1 expression (p <0.01). The mean GAS5 was significantly higher in the control; while the mean MALAT1 expression was significantly higher in SLE patients (Figure 1). The ROC curve analysis revealed

that GAS5 was a good discriminant to differentiate cases from controls with AUC 0.849 with sensitivity 93.5% and specificity 74.3%. Moreover, MALAT1 was a good discriminant to differentiate cases from controls with AUC 0.3 with 95% CI (0.162 - 0.438), the most suitable cut-off point was ≥ 2.1 with Sensitivity 93.5% and Specificity 72.5% (Figure 2 & 3).

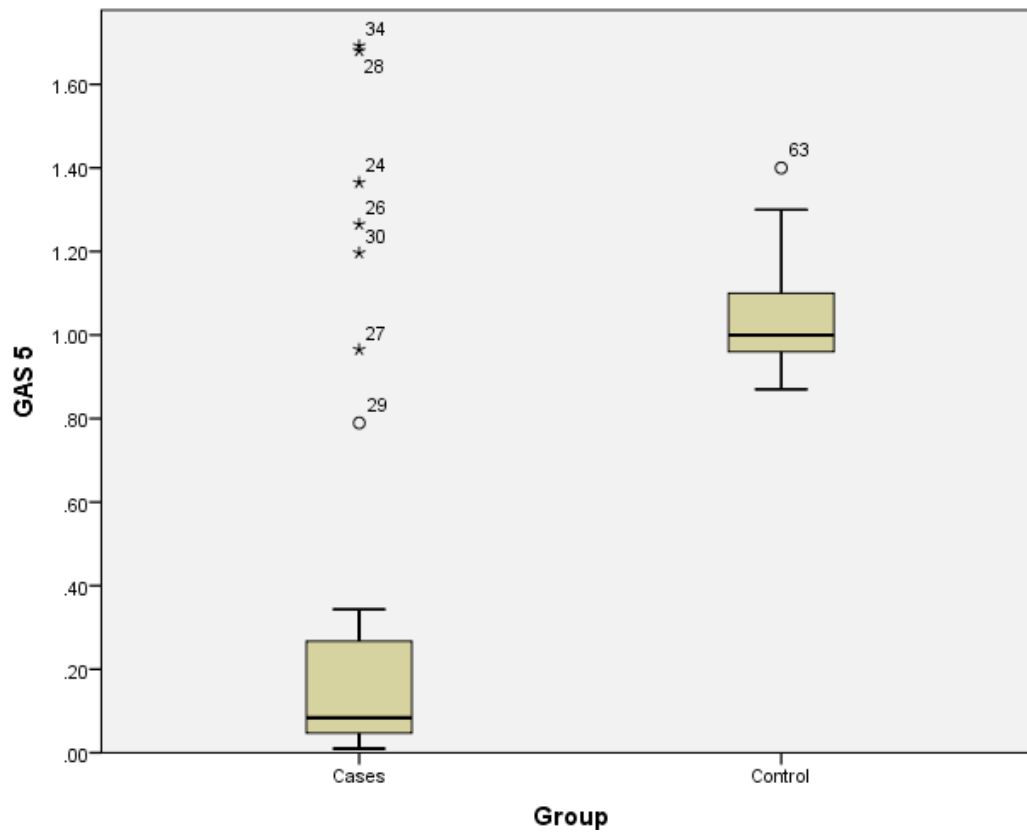


Figure 1: The difference in GAS5 expression

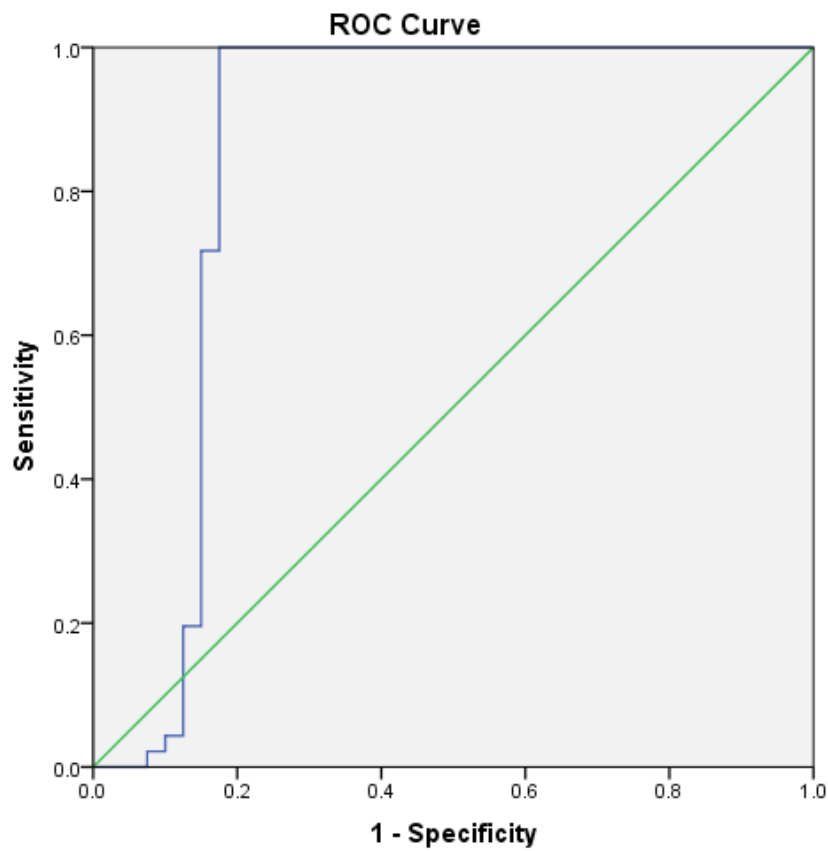


Figure 2: ROC curve analysis to explore the discriminant ability of GAS5 to differentiate between cases & controls

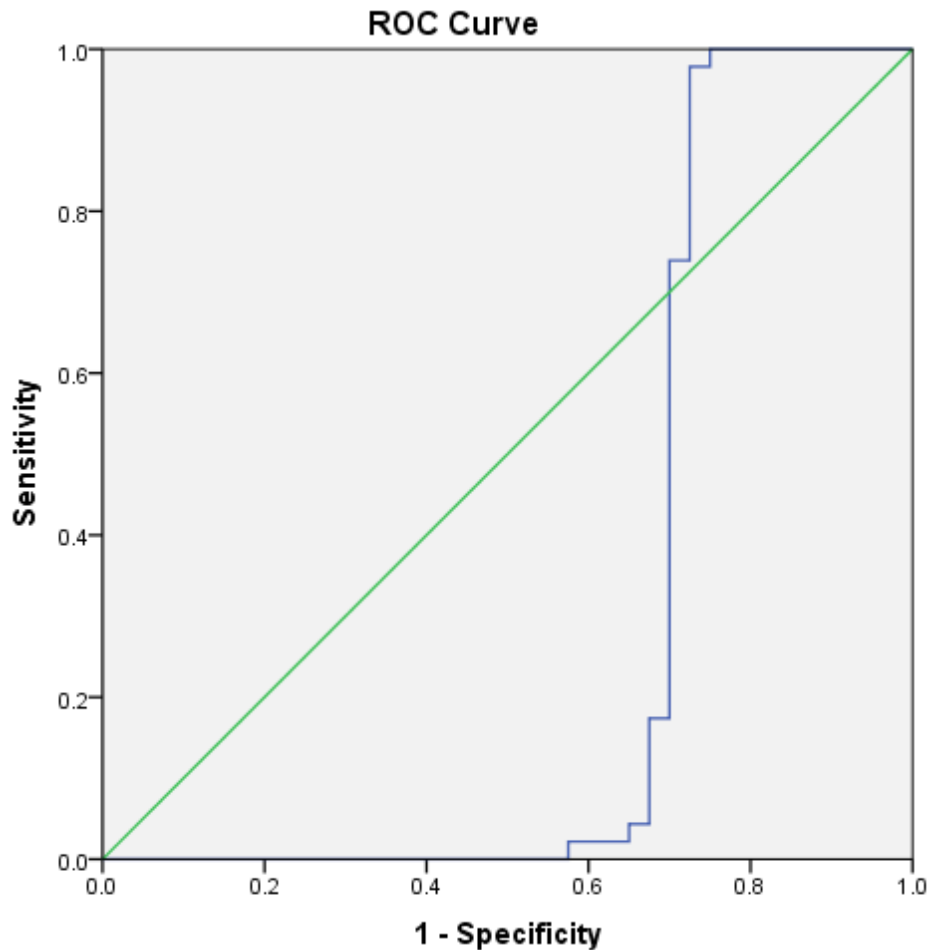


Figure 3: ROC curve analysis to explore the discriminant ability of MALAT1 to differentiate between cases & controls

Notably, patients with rash and mucosal ulcer had statistically significant higher GAS5 ($p=0.037$ and 0.002 , respectively). Similarly, Patients with vasculitis had statistically significant lower MALAT1 ($p=0.023$). The correlation analysis showed that there were statistically significant negative correlation between MALAT1 and GAS5 ($r=-0.314$; $p=0.003$). In contrary, there were no statistically significant correlations between clinical variables and GAS5 or MALAT1.

Discussion

In the present study, both GAS5 and MALAT1 yielded good diagnostic performances for the detection of SLE. At cutoff values of <0.3 , the GAS5 had a sensitivity of 93.5% and specificity of 74.3% for the detection of SLE. Similarly, an expression of MALAT1 of ≥ 2.1 had similar performance. On the other hand, the expression of both lncRNAs correlated significantly with some of the disease activities.

Over the recent few years, lncRNAs were implicated in the development and progression of many diseases including cardiovascular diseases, cancers, and autoimmune disorders¹⁵⁻¹⁷. Owing to their role in the development of immune system, lncRNAs are promising biomarkers for many autoimmune diseases including SLE. In the present study, we demonstrated that both GAS5 and MALAT1 yielded good diagnostic performances for the detection of SLE. At cutoff values of <0.3 , the GAS5 had a sensitivity of 93.5% and specificity of 74.3% for the detection of SLE. Similarly, an expression of MALAT1 of ≥ 2.1 had similar performance. In concordance with our findings, Wu and colleagues¹⁸ performed a two-stage study to explore the plasma levels of five lncRNAs (GAS5, linc0949, linc0597, HOTAIRM1 and linc-DC) and their potential as SLE biomarkers. Compared with healthy controls, the expression level of GAS5 was significantly down-regulated. When SLE patients were divided according

to the presence of LN, the results showed that the levels of GAS5 was also significantly down-regulated in both subgroups relative to healthy controls. Furthermore, the plasma level of GAS5 could distinguish SLE from healthy controls with 65.03% sensitivity and 93.75% specificity. Similarly, Suo and colleagues¹⁹ assessed the expression of GAS5 and microRNA (miR)-21 in SLE, and attempted to explore their association with clinical features. The results revealed that GAS5 was significantly lower in CD4+ T cells of patients with SLE compared with those in control subjects; however, there were no significant differences in GAS5 expression regarding the presence of nephritis. Another prospective study by Li and colleagues²⁰ included 85 SLE patients and 71 healthy controls to investigate the lncRNAs expression levels. It was found that GAS5 expression level was significantly lower in SLE patients than healthy controls.

Regarding MALAT1, Yang and colleagues²¹ analyzed the expression of MALAT1 in 39 SLE patients and 45 matched normal controls. They found that MALAT1 was abnormally increased in the patients with SLE and predominantly expressed in monocytes. In monocytes of patients with SLE, silencing MALAT1 significantly reduced the expression of IL-21. Furthermore, their study demonstrated that MALAT-1 exerts its detrimental effects by regulating silent information regulator 1 (SIRT1) signaling.

The present study also investigated the association between clinical characteristics of SLE patients and the expression of both GAS5 and MALAT1. Patients with rash and mucosal ulcer had significantly higher GAS5. In addition, patients with vasculitis had significantly lower MALAT1. Similarly, Suo and colleagues¹⁹ reported that the levels of GAS5 were higher in patients with ulceration than in those without.

There was no significant association of the SLEDAI with the GAS5 or MALAT1. However, Wu and colleagues¹⁸ reported that GAS5 level was significantly lower in more active SLE patients than in less active cases. In addition, GAS5 level was negatively associated with SLEDAI-2K score in patients with SLE. Moreover, plasma level of GAS5 was also negatively correlated with the ESR.

We acknowledge that the present study has number of limitations. The sample size of the included patients was relatively small which may affect the generalizability

of our findings. Moreover, the study was single-center experience. In addition, we could not control for potential confounding factors such as different clinical characteristics and different treatment strategies among patients.

Conclusion

In conclusion, GAS5 and MALAT1 may serve as potential biomarkers for the diagnosis and monitoring of the SLE, both lncRNAs exhibited a good diagnostic accuracy to discriminate between SLE patients and healthy controls. Moreover, GAS5 and MALAT1 were significantly higher in patients with rash and mucosal ulcer; while there was no statistically significant correlation between disease activity and lncRNAs expression. However, due to the descriptive nature of the present study, further studies on the exact role of lncRNAs in SLE pathogenesis are still needed.

Conflict of Interest: All authors confirm no financial or personal relationship with a third party whose interests could be positively or negatively influenced by the article's content.

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Ethical Clearance: The protocol of the present study was registered by the local ethics committee of Cairo University Teaching hospital.

References

1. Gurevitz SL, Snyder JA, Wessel EK, Frey J, Williamson BA. Systemic Lupus Erythematosus: A Review of the Disease and Treatment Options. *Consult Pharm.* 2013;28(2):110-121. doi:10.4140/TCP.n.2013.110
2. Rees F, Doherty M, Grainge MJ, Lanyon P, Zhang W. The worldwide incidence and prevalence of systemic lupus erythematosus: a systematic review of epidemiological studies. *Rheumatology.* 2017;56(11):1945-1961. doi:10.1093/rheumatology/kex260
3. Bijl M, Reefman E, Horst G, Limburg PC, Kallenberg CGM. Reduced uptake of apoptotic cells by macrophages in systemic lupus erythematosus: Correlates with decreased serum levels of complement. *Ann Rheum Dis.* 2006. doi:10.1136/ard.2005.035733
4. Lisnevskaja L, Murphy G, Isenberg D. Systemic

- lupus erythematosus. *Lancet* (London, England). 2014;384(9957):1878-1888. doi:10.1016/S0140-6736(14)60128-8
5. La Paglia GMC, Leone MC, Lepri G, et al. One year in review 2017: systemic lupus erythematosus. *Clin Exp Rheumatol*. 35(4):551-561. <http://www.ncbi.nlm.nih.gov/pubmed/28721860>. Accessed May 17, 2019.
 6. Romain PL. Overview of the clinical manifestations of systemic lupus erythematosus in adults. UP to date. 2012.
 7. Maidhof W, Hilas O. Lupus: an overview of the disease and management options. *P T*. 2012;37(4):240-249. <http://www.ncbi.nlm.nih.gov/pubmed/22593636>. Accessed May 17, 2019.
 8. Liu C-C, Kao AH, Manzi S, Ahearn JM. Biomarkers in systemic lupus erythematosus: challenges and prospects for the future. *Ther Adv Musculoskelet Dis*. 2013;5(4):210-233. doi:10.1177/1759720X13485503
 9. Yang JX, Rastetter RH, Wilhelm D. Non-coding RNAs: An Introduction. In: Springer, Dordrecht; 2016:13-32. doi:10.1007/978-94-017-7417-8_2
 10. Mercer TR, Dinger ME, Mattick JS. Long non-coding RNAs: Insights into functions. *Nat Rev Genet*. 2009. doi:10.1038/nrg2521
 11. Brito GC, Fachel AA, Vettore AL, et al. Identification of protein-coding and intronic noncoding RNAs down-regulated in clear cell renal carcinoma. *Mol Carcinog*. 2008. doi:10.1002/mc.20433
 12. Modarresi F, Faghihi MA, Patel NS, Sahagan BG, Wahlestedt C, Lopez-Toledano MA. Knockdown of BACE1-AS Nonprotein-Coding Transcript Modulates Beta-Amyloid-Related Hippocampal Neurogenesis. *Int J Alzheimers Dis*. 2011. doi:10.4061/2011/929042
 13. Zhao C-N, Mao Y-M, Liu L-N, Li X-M, Wang D-G, Pan H-F. Emerging role of lncRNAs in systemic lupus erythematosus. *Biomed Pharmacother*. 2018;106:584-592. doi:10.1016/j.biopha.2018.06.175
 14. Petri M, Orbai AM, Alarcón GS, et al. Derivation and validation of the systemic lupus international collaborating clinics classification criteria for systemic lupus erythematosus. *Arthritis Rheum*. 2012. doi:10.1002/art.34473
 15. Wang J, Wei F, Zhou H. Advances of lncRNA in autoimmune diseases. *Front Lab Med*. 2018;2(2):79-82. doi:10.1016/J.FLM.2018.07.004
 16. McPherson R, Pertsemlidis A, Kavaslar N, et al. A common allele on chromosome 9 associated with coronary heart disease. *Science* (80-). 2007. doi:10.1126/science.1142447
 17. Gibb EA, Vucic EA, Enfield KSS, et al. Human cancer long non-coding RNA transcriptomes. *PLoS One*. 2011. doi:10.1371/journal.pone.0025915
 18. Wu G-C, Li J, Leng R-X, et al. Identification of long non-coding RNAs GAS5, linc0597 and lnc-DC in plasma as novel biomarkers for systemic lupus erythematosus. *Oncotarget*. 2017. doi:10.18632/oncotarget.15569
 19. Suo QF, Sheng J, Qiang FY, Tang ZS, Yang YY. Association of long non-coding RNA GAS5 and miR-21 levels in CD4+T cells with clinical features of systemic lupus erythematosus. *Exp Ther Med*. 2018. doi:10.3892/etm.2017.5429
 20. Li LJ, Zhao W, Tao SS, et al. Comprehensive long non-coding RNA expression profiling reveals their potential roles in systemic lupus erythematosus. *Cell Immunol*. 2017. doi:10.1016/j.cellimm.2017.06.004
 21. Yang H, Liang N, Wang M, et al. Long noncoding RNA MALAT-1 is a novel inflammatory regulator in human systemic lupus erythematosus. *Oncotarget*. 2017. doi:10.18632/oncotarget.20490

Dandruff Disease; Reason and its Right Solution

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Abstract

More than half of the world's population has dandruff, and people spend more than ten billion annually to defeat them. This study found by known experimental tests that dandruff is a mix of different molecules; saturated fatty acid, dead cells and dust. A fifteen teenagers (22-25 years old) were randomly choiced for investigating some important information about dandruff. These teenagers indicate that they used many treatments last years without getting good results also they mentioned that dandruff appear in winter and it disappears at summer. In addition, they feel embarrass when see that their hairs have dandruff and sometimes itchy or hard one causing pain leading to unlikely behavior. This research contain the right treatment for this unlikely disease.

Keywords: Dandruff, Malassezia, Combing, Fungi and white crusts.

Introduction

Malassezia species inhabit the skin of all warm blooded animals and cause a myriad of problems, from allergies and infections in humans and horses to ear infections in cats. Admittedly, nonlethal skin conditions aren't serious infectious diseases like AIDS or bird flu, but several features make our research both interesting and broadly applicable⁽¹⁾.

Dandruff is a common scalp condition in which small pieces of dry skin flake off of the scalp. If you have dark hair or you're wearing dark colors, you may notice the flakes in your hair or on your shoulders. Dandruff may also make your scalp itch.

Many people believe that dandruff is caused by poor hygiene, but this is not true. Although infrequent shampooing can make dandruff more obvious, researchers are still studying the causes, which appear to be complex. The most effective way to treat and control dandruff is to use dandruff shampoo and scalp treatments⁽²⁻⁴⁾.

Experimental Part:

This section was included three parts:

A. For identifying the dandruff nature is it oils or not! a copper acetate test was used for dandruff samples as follow:

Put dandruff samples in 5 ml of ether for each then add five drops from copper acetate 10% to dandruff samples and noticing the product's color⁽⁵⁾.

B. Salkowski test was done for characterizing is dandruff is fatty acid like or cholesterol like molecules. Put dandruff samples in 5 ml of ether then for each sample add 5 ml from concentrated sulfuric acid. Shake until two layers has appear, upper layer should have red color while lower one has green, this colors for compounds like cholesterol molecule⁽⁵⁾.

C. Samples of dandruff were sent to biology department to recognize which species exist in dandruff samples⁽⁶⁾.

D. Randomly 50 teenagers (22-25 years old) were asked about dandruff disease during them lives are they got it or not? In addition to another questions.

Results

Oil kind in Dandruff samples is saturated fatty acid with dust and dead cells remnants [6]. Biology staff indicate that the dandruff samples contain a kind of Malassezia fungi either Malassezia globosa or Malassezia restricta. They indicate that it is difficult to recognize between which Malassezia kind is because they do not have necessary database. However, they show that above fungi have about 8 species. They

have given following picture about what they found in dandruff sample:



Figure (1): Malassezia fungi that appear in dandruff sample⁽⁶⁾

The 50 teenager about 49 from them have a dandruff recently or before that. They insure that this disease increase at winter than other seasons, in addition, they used many treatments but there is no sufficient one treated this disease 100% it keeps return each winter. Moreover, these teenager feel embarrassing when see white species of dandruff on their clothes.

Discussion:

Anatomy of each hair of human's bodies that their follicles contain special glands release specific oil called sebum that consisting from triglycerides and fatty acids (57%), wax esters (26%), squalene (12%), and cholesterol (4.5%)⁽⁶⁾. Experimental part show that dandruff samples do not contain cholesterol or other like molecules. However, cholesterol has less percent difficult to cause dandruff or maybe they have small activity but it is not like triglycerides or wax ester.

Malassezia fungi should have lipase enzyme able to break the ester bond of triglycerides or wax ester resulting; free fatty acids, glycerol and wax molecules. These lipids have special properties make them look like magnetic mass attracting other molecules such as dust or remaining of died cells producing white species called dandruff. In fact, free fatty acids have low melting points so they appear at cold weather while do not at hot weather because they condense at cold weather.

Dandruff reason is so clear but getting rid of this unlikely white species is hopeless because fighting of fungi creatures is useless. This fact is well known because all fungi when facing bad circumstances they form fungal spore can stand with strong conditions easy to spread out over air molecules to another person causing dandruff again and so on therefore removing of Malassezia fungi is hopeless with its spore in addition they are normal flora existing in most creatures⁽⁶⁾.

Either it result from special fungi or another reason dandruff disease is unlikely disease so this research find that doing right combs in one time for at least two days should lead to remove dandruff, right combs means not strong but normal and well. This behavior should do for all hair over the scalp for removing different fungi, cells remnant...etc. In addition, fungi species need dark, net, quiet medium⁽⁴⁾ so repeating comb each two days will removing above conditions leading to remove this annoying fungi. Therefore, well combing for all scalp each two days is good treatment for dandruff, it is amazing treatment.

Most teenager of this research indicated that they do not combing all them hair they comb only upper hair adding special lipids to do nice style. These aspects absolutely lead to dandruff. Most behaviors of teenager lead to dandruff therefore well combing for all scalp one time for each two days should successfully removing dandruff.

Conclusion:

Human's scalp normally excrete lipids such as triglyceride or cholesterol for wetting hair of the scalp, each hair have its gland that have above lipids. There are fungi species have lipase enzyme able to hydrolyze these lipids called Malassezia. It is a fact that there is no successful treatment for fungi species because if anyone remove them their spores should come back again or another person must transfer them again so this way there is no successful treatment for dandruff. Teenagers indicated that dandruff crusts come after the shower due to water molecules forced hydrophobic lipids for aggregating each other. Therefore, best treatment for dandruff is well combing each two days for removing all above things.

Ethical Clearance: There is no ethical clearance in this research.

Source of Funding: This research has been done by self-funding of the author.

Conflict of Interest: There may be a conflict of interest about this research.

References

1. Dawson T. L. New Research Yields First-of-its-Kind Dandruff Treatment. pgscience.com, The Magic Behind The Brand, U.S; 2019.
2. American Academy of Dermatology. Dandruff: How to treat; 2018.
3. Baran R. and Maibach H. Textbook of Cosmetic Dermatology. CRC press, Taylor and Francis Group, Boca Raton, 2017.
4. Arndt K. and Hsu J. Manual of Dermatologic Therapeutics. Lippincott William and Wilkins, Wolters Kluwer Health, India; 2007.
5. Sulyman R. R. and Fathel Allah Y. J. Practical Biochemistry. Baghdad University; 1989
6. Personal communications with special staff in biology department-college of science- Misan University; 2019.

Processes Correction of Hybrid Problem-Based Learning Tutorial Sessions

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Abstract

Background: Globally, many variants of problem-based learning are operational in medical colleges. The hybrid variant of problem-based learning (PBL) is a difficult venture and needs special consideration. As a part of self-assessment process, medical schools need to have mechanisms in place to enable “Independent learning and self-directed promise” of PBL philosophy. This study gathered students’ perceptions on PBL tutorials sessions to course correct any deviations in hybrid PBL implementation.

Method: Using a pre-validated questionnaire, this cross-sectional study conducted from February 2019 to March 2019, collected students’ feedback on their experience with the processes of the PBL in College of Medicine at Jouf University. Students’ responded to the questionnaire on a five-point Likert scale. For simplicity, the responses were grouped “agree”, “neutral”, and “disagree.” Chi-square test assessed variation between groups.

Results: Forty-three students’ returned the fully completed questionnaire: 23 (53.48%) were females and 20 (46.5%) were males. Interactive learning component of PBL received higher rating (65.1%): a significantly ($p < 0.01$) higher degree of agreement by the female students. Opinion on content similarity between PBL and lectures was shared equally (50%) by female and male students. The students were skeptical about the fairness in tutors’ evaluation of students in PBL sessions, however, more male students were satisfied ($p < 0.01$) compared to female students.

Conclusions: The study concludes existence of similarity of contents between lectures and PBL sessions. Tutors’ attitudes and tutor’s fairness in evaluation of students’ PBL sessions is a concern. Limiting the number of supporting lectures, training students and tutors in PBL processes are studys’ suggestions for successful implementation of hybrid PBL strategy.

Keywords: *Cognitive skills, Hybrid-PBL philosophy, Tutor dynamics, Tutor feedback, Preclinical skills.*

Introduction

The original form of problem-based learning (PBL) is currently non-existent⁽¹⁾. More and more medical schools around the globe have opted for this instructional

strategy. The characteristics of these medical schools and local constraints shaped its implementation, giving birth to a number of variants of problem-based learning⁽¹⁻⁶⁾. PBL has undergone evolution, the implementation of genus PBL has resulted in the development of many species all striving for the basic promise of PBL philosophy^(7,8).

One review on hybrid PBL implementation came up with the core condition of having PBL tutorials of small groups and the independent study, however, other emphasize on instructional method of traditional lectures, clinical skills and labs to support the PBL theme and to keep them at the minimum and not excluded^(9,10).

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With the near absence of the pure PBL strategy, the flourishing hybrid strategy is commonly seen in practice; hence some researchers have coined the term of standard PBL to describe the hybrid PBL strategy^(1,11,12).

Hybrid PBL instructional strategy implementation is a challenging task, the supporting lectures, subject-related labs and the skill labs are delivered by the subject experts, thereby the system runs the risk of transmitting knowledge directly which is in conflict with the independent learning and self-directed promise of PBL philosophy. Furthermore, chances of adding more topics to the side by side lecture-based strategy is a common practice, rendering the second PBL session ineffective⁽¹³⁻¹⁶⁾. Faculty involved with the implementation of hybrid PBL curricula lacks an overall orientation on the philosophy of PBL and rather receive a focused initial training on running the PBL session, which they conceive as routine small group discussion as in traditional curricula⁽¹⁾.

Over the years, many medical colleges in Saudi Arabia has moved away from the traditional instructional teaching to new PBL instructional strategy and have mostly implemented the hybrid PBL instruction strategy⁽¹⁷⁻¹⁹⁾. Many reports from Saudi Arabia on the hybrid PBL strategy are satisfactory⁽²⁰⁻²⁴⁾. However, many of these findings are based on the information collected from the preclinical phase students highlighting the probable element of bias of positive responses.

The College of Medicine at Jouf University implements hybrid PBL System that forms an integral part of preclinical phase of undergraduate medical study. The teaching staff mostly come from conventional lecture-based curriculum, however, they receive an orientation on the processes of PBL tutorial sessions. There is every possibility of a conflict between the concept and reality in implementation. In this backdrop, the current study gathered opinions from the clinical phase students regarding the processes of PBL tutorial sessions.

Method

This cross-sectional study involved the fourth year students of College of Medicine at Jouf University. The study conducted between February 2019 and March 2019 included both female and male students who have passed the preclinical phase. The first three years of

basic sciences (preclinical phase) in an integrated system in which students learn in PBL sessions augmented by lectures, skill labs and laboratory classes. Since the inception of College of Medicine at Jouf University, there has been no change in teaching strategy.

A pre-validated questionnaire collected information on the perception regarding the PBL sessions⁽²⁵⁾. The participation was voluntary and required a proper consent. The sample size was calculated by epi-info 7 software. A conservative guesstimate of 12% of the participants' having good perception regarding the PBL session, 42 students were required at 95% confidence level and 5% margin of error. The questionnaire was distributed to the fourth year students during the midday break. Eight statements evaluated the students' feedback on the processes involved in the PBL session. Three questions evaluated the perceptions of tutor preparedness for the PBL session and about the evaluation processes of the students' contribution in the session. The local committee on bioethics (LCBE) at Jouf University approved the study protocol vide no: 5-16-4/1440.

Statistical Analysis: Statistical Package for Social Sciences version-20 (IBM Corporation, Armonk, NY USA) was used for data analysis. The data was coded before entry. The five-point Likert scale responses were merged as "agree" "neutral" and "disagree". Chi-Square test was used as a test of significance to measure variation between the males and females. The results were considered significant at a p-value of <0.05.

Results

A total of 47 questionnaires were received from the fourth year students, four questionnaires were incomplete. The 43 remaining questionnaires were analyzed, 23 (53.48%) from the females and 20 (46.5%) from male students. The overall mean score of agreement to the eight questions was 6.11 ± 3.27 . The results show, 40% of males and 30% of females agreed to replace the PBL for lectures respectively. The females (52.2%) were more in agreement with the statement on receiving adequate training on PBL sessions. A higher proportion (65.1%) of the students felt that the PBL is an interactive method of learning, females reporting a significantly ($p < 0.01$) higher level of agreement. Repetition of the contents between PBL and lectures was a common concern shared equally (50%) by females and males (Table 1).

Table 1: Students perception on the processes of the PBL session

Questions	Categories	Total Participants n (%)	Male n (%)	Female n (%)	P-value
PBL can substitute lectures	Agree	15 (34.9)	8(40.0)	7(30.4)	0.80
	Neutral	9(20.9)	4(20.0)	5(21.7)	
	Disagree	19(44.2)	8(40.0)	11(47.9)	
There is proper students' training before starting the PBL session	Agree	20(46.5)	8(40.0)	12(52.2)	0.60
	Neutral	9(20.9)	4(20.0)	5(21.7)	
	Disagree	14(32.6)	8(40.0)	6(26.1)	
PBL is an interactive method of learning	Agree	28(65.1)	8(40.0)	20(87.0)	0.002
	Neutral	4(9.3)	2(10.0)	2(8.7)	
	Disagree	11(25.6)	10(50.0)	1(4.3)	
There is a repetition between PBL and lectures	Agree	22(51.2)	10(50.0)	12(52.2)	0.31
	Neutral	12(27.9)	4(20.0)	8(34.8)	
	Disagree	9(20.9)	6(30.0)	3(13.0)	
Students contribute equally in PBL session	Agree	13(30.2)	6(30.0)	7(30.4)	0.69
	Neutral	11(25.6)	4(20.0)	7(30.4)	
	Disagree	19(44.2)	10(50.0)	9(39.2)	
I give feedback to the others	Agree	25(58.1)	16(80.0)	9(39.2)	-
	Neutral	8(18.6)	0(0.0)	8(34.8)	
	Disagree	10(23.3)	4(20.0)	6(26.0)	
I contribute in group discussions Students contribute equally in PBL session	Agree	36(83.7)	18(90.0)	18(78.3)	-
	Neutral	4(9.3)	2(10.0)	2(8.7)	
	Disagree	3(7.0)	0(0.0)	3(13.0)	
I attend PBL session on time	Agree	39(90.7)	18(90.0)	21(91.3)	-
	Neutral	4(9.3)	2(10.0)	2(8.7)	
	Disagree	0(0.0)	0(0.0)	0(0.0)	

Overall mean of agreement: 6.11±3.27

Approximately half (51.2%) of the students' agreed tutors' preparedness for the PBL session. The majority of the students were either neutral (32.6%) or disagreed (20.9%) with the fairness of tutors' student evaluation

of sessions. The male students showed a significantly ($p < 0.01$) higher agreement with fairness in the evaluation process compared to females (60.0% vs 34.8%) (Table 2).

Table 2: Students perception about tutors' facilitation of sessions.

Questions	Categories	Total Participants n (%)	Male n (%)	Female n (%)	P-value
Tutors are prepared to run the session	Agree	22(51.2)	10(50.0)	12(52.2)	-
	Neutral	6(14.0)	0(0.0)	6(26.1)	
	Disagree	15(34.8)	10(50.0)	5(21.7)	
Tutors evaluate students in fair way	Agree	20(46.5)	12(60.0)	8(34.8)	0.01
	Neutral	14(32.6)	2(10.0)	12(52.2)	
	Disagree	9(20.9)	6(30.0)	3(13.0)	
Tutors feedbacks were helpful to improve students' performance	Agree	23(53.5)	10(50.0)	13(56.6)	0.33
	Neutral	7(16.3)	2(10.0)	5(21.7)	
	Disagree	13(30.2)	8(40.0)	5(21.7)	

Overall mean of agreement: 1.51 ±1.26

Discussion

Many medical schools across the globe have adopted problem-based learning as an innovative student centered learning strategy. This new educational strategy helps develop collaborative and cognitive learning, and interpersonal communication skills consistent with the desired attributes of a competent physician⁽²⁵⁻²⁹⁾.

Medical schools in this part of the world have adopted PBL instructional strategy, assuring a high quality medical practice consistent with international standards. Education ministry in Saudi Arabia has endorsed this new instructional system resulting in the increased adoption of the hybrid PBL system in medical schools across the nation. In the current study, interactive learning component of the PBL received a high (65.1%) perception rating consistent with earlier reports describing the PBL an innovative instructional strategy improving the learning outcomes compared to traditional strategies⁽³⁰⁻³²⁾. This finding is also in agreement with reports from medical schools across Saudi Arabia^(22,33-35). This finding supports interactive learning component of the hybrid PBL system in the College of Medicine at Jouf University. The PBL derived interactive learning skills not only helps students' knowledge to bloom but also has a positive effect on the harmony of small group discussions^(15,36). Azer (2005) reported that group dynamics are proportional to interpersonal interactions, ability to arrive at the hypothesis to resolve the problem in the tutorial session and students' training in critical thinking⁽³⁷⁾ It is essential to maintain proper group dynamics for better outcomes of a PBL sessions. However, reports have also blamed PBL educational strategy as time consuming with no impact on the gain in knowledge⁽³⁸⁾. These conflicting finding about the PBL strategy across medical schools necessitates evaluation of the processes of PBL tutorials that can help in course correction and prevent a dysfunctional hybrid PBL system.

In the current study, 83% of the students' showed a positive perception in the group discussions. It has been noted that students' preparation holds key of a purposeful participation in the group discussions⁽²¹⁾. In our study fewer students' showed dissatisfaction in the group discussions that might indicate sufficient time slots for self-directed learning between the first and last PBL session and may also point to an effective academic advising by the faculty to achieve the learning objectives of the PBL scenario. This skill of group

discussion learned in the preclinical phase may help students' understanding of the clinical subjects and needs reinforcement during bedside teaching sessions. The faculty involved in clinical teaching should be encouraged to devote sufficient time for group discussions in clinical phase to keep this skill persistent for long-term learning. Cognitive skills and persistent motivation affect the outcome of the tutorial group. Student interactions and knowledge sharing during PBL sessions are features of a successful implementation of PBL tutorial sessions^(6,39).

The number of supporting lectures in the hybrid PBL should be minimum and should not directly transfer the knowledge that extinguishes the problem trigger⁽⁴⁾, hence the supporting lectures on the weeks' theme should be unbiased for the success of the PBL philosophy. In general, more than one third of participants agreed PBL can substitute the lectures and another one half of participants perceived the content repetition. This finding highlights the need for medical education specialists and a need to rectify these issues to avoid a dysfunctional hybrid PBL implementation.

The other components that affect a successful PBL implementation include the tutors' facilitation process and the students' training on the PBL, both of which are critical to avoid the dysfunctional hybrid PBL implementation. Students' training on PBL is important for purposeful group discussions and overall tutorial group productivity⁽⁴⁰⁾. Nearly half of the participants agreed to receive a training about PBL tutorials that is essential for the success of PBL session. The positive impact on students' training has been reported in literature⁽⁴¹⁾. Reports from KSA have shown lack of orientation and training of students' end up with a poor performance of PBL sessions⁽²⁵⁾. For the successful implementation of hybrid PBL, several limiting factors are considered that include, educational environment, tutor learner attitude, PBL scenarios and the optimal assessment method⁽³²⁾. In the current, only half of the participants opined satisfaction with tutors' preparedness for the PBL tutorial session.

Tutors positive attitude has been reported as an important factor in the implementation of a successful PBL program⁽³²⁾. However, other reports have highlighted the tutor dynamics in enhancing or suppressing the development of PBL skills of critical thinking and collaborative learning skills among the students^(17,40). These less positive perceptions about

tutors' attitude ask questions. Faculty development program in College of Medicine at Jouf University need to focus on tutor skills for success of the hybrid PBL strategy⁽⁴²⁻⁴⁵⁾. Tutors constructive feedback is crucial for the improvement of student learning outcomes^(21, 46). Tutors feedback towards the end of session helps the students to identify their weakness and strengths. In the current study, half of the students were satisfied with the tutors' feedback in the improvement of their performance.

Our study participants presented with conservative estimates on the tutors' evaluation of students' in the PBL sessions. The majority of the students were either neutral or disagreed with the fairness of their evaluation by the tutor. Similar finding has been earlier reported from Saudi Arabia⁽²⁵⁾. The perception on tutors' attitude and fairness in the assessment process highlight the need for tutor trainings.

The results of this study should be interpreted in the lights of some limitations. These limitations in the current study need to be addressed in future researches. The first real limitation lies in the single centre study that may not reflect the perceptions of medical students across the country. Second limitation is questionnaire-based data collection. Thirdly it involves students of the clinical phase only that might have affected the lack of seriousness of responses. The choice of the study participants is the strength of the study. The study involves students from the clinical phase having no compulsion of being positive in their responses. Furthermore, proving insights about the PBL processes retrospectively after furthering their experience with clinical phase teaching could be presumed more rational than preclinical experiences only. The future research should include in depth discussions with preclinical and clinical phase students and tutors to identify the barriers in successful implementation of hybrid PBL strategy

Conclusions

PBL tutorial sessions are effective interactive sessions, however, repetition of the contents between the PBL and lectures exist. Fairness in students' evaluation by tutors remains a concern. The study advocates revising PBL strategy in College of Medicine at Jouf University to improve the outcomes of PBL sessions with special emphasis on reducing the number of lectures and an effective evaluation by the tutors.

This study offers suggestions of potential benefit

to the implementation issues of hybrid PBL strategy. Sufficient number of time slots for self-directed learning (SDL) can help students' complete the learning issues for the 2nd PBL session and enhance group discussions. Improving problem trigger of scenario, minimizing the frequency of supporting lectures and by avoiding direct transfer of knowledge will foster self-directing learning. Students' pre-PBL training and training of tutors' on the facilitation process is of importance to bypass a dysfunctional hybrid PBL. Effective assessment method of students' during PBL sessions as well as a well-constructed PBL scenario can help successful outcome. Tutors training on the evaluation of PBL sessions through faculty development program can bring positive attitudinal change and fairness in the assessment.

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References

1. Malik AS, Malik RH. What really is Hybrid Problem-Based Learning Curriculum? A review. 2018.
2. Fox CR. A Liberal Education for the 21 st Century: Some Reflections on General Education. *Currents in Teaching & Learning*. 2016;8(2):5-17.
3. Johnson M, Hayes MJ. A comparison of problem-based and didactic learning pedagogies on an electronics engineering course. *International Journal of Electrical Engineering Education*. 2016;53(1):3-22.
4. Lim WK. Dysfunctional problem-based learning curricula: resolving the problem. *BMC medical education*. 2012;12(1):89.
5. Paulins VA, Moeller GJ. Implementing and evaluating a student success initiative (SSI) to support enhanced and active learning in a merchandising mathematics course. *International Journal of Fashion Design, Technology and Education*. 2017;10(1):8-15.
6. Saporova D, Nolan NS. Evaluating the appropriateness of electronic information resources

- for learning. *Journal of the Medical Library Association: JMLA*. 2016;104(1):24.
7. McLean M, Arrigoni C. How we capitalised on casual PBL facilitators' expertise and experience to add value to our medical programme. *Medical teacher*. 2016;38(3):246-9.
 8. Moro C, McLean M. Supporting students' transition to university and problem-based learning. *Medical Science Educator*. 2017;27(2):353-61.
 9. Clyne AM, Billiar KL. Problem-Based Learning in Biomechanics: Advantages, Challenges, and Implementation Strategies. *Journal of biomechanical engineering*. 2016;138(7):070804.
 10. McGrath D, Crowley L, Rao S, Toomey M, Hannigan A, Murphy L, et al. Outcomes of Irish graduate entry medical student engagement with self-directed learning of clinical skills. *BMC medical education*. 2015;15(1):21.
 11. Ahmad M, Khan HS, Hasan S, Asim M. HYBRID PROBLEM BASED TEACHING AS AN ATTEMPT TO IMPROVE LEARNING OUTCOMES. *Pakistan Journal of Physiology*. 2015;11(3):40-2.
 12. Bridges S, Yiu CK, Botelho MG. Design considerations for an integrated, problem-based curriculum. *Medical Science Educator*. 2016;26(3):365-73.
 13. Amoako-Sakyi D, Amonoo-Kuofi H. Problem-based learning in resource-poor settings: lessons from a medical school in Ghana. *BMC medical education*. 2015;15(1):221.
 14. Ismail NAS, Alias E, Arifin KT, Damanhuri MHA, Karim NA, Aan GJ. Perception of content and non-content expert facilitators of PBL according to students' performance levels. *Pakistan journal of medical sciences*. 2015;31(6):1537.
 15. Ju H, Choi I, Rhee BD, Tae-Lee J. Challenges experienced by Korean medical students and tutors during problem-based learning: a cultural perspective. *Interdisciplinary Journal of Problem-Based Learning*. 2016;10(1):8.
 16. Pluta WJ, Richards BF, Mutnick A. PBL and beyond: Trends in collaborative learning. *Teaching and learning in medicine*. 2013;25(sup1):S9-S16.
 17. Alkhuwaiter SS, Aljuailan RI, Banabilh SM. Problem-based learning: Dental student's perception of their education environments at Qassim University. *Journal of International Society of Preventive & Community Dentistry*. 2016;6(6):575.
 18. Bin Abdulrahman KA. The current status of medical education in the Gulf Cooperation Council countries. *Annals of Saudi medicine*. 2008;28(2):83-8.
 19. Mumtaz S, Latif R. Learning through debate during problem-based learning: an active learning strategy. *Advances in physiology education*. 2017;41(3):390-4.
 20. Al-Damegh SA, Baig LA. Comparison of an integrated problem-based learning curriculum with the traditional discipline-based curriculum in KSA. *JOURNAL-COLLEGE OF PHYSICIANS AND SURGEONS OF PAKISTAN*. 2005;15(10):605.
 21. Aldayel AA, Alali AO, Altuwaim AA, Alhussain HA, Aljasser KA, Abdulrahman KAB, et al. Problem-based learning: medical students' perception toward their educational environment at Al-imam Mohammad ibn saud islamic University. *Advances in medical education and practice*. 2019;10:95.
 22. Alduraywish AA, Mohager MO, Alenezi MJ, Nail AM, Aljafari AS. Evaluation of students' experience with Problem-based Learning (PBL) applied at the College of Medicine, Al-Jouf University, Saudi Arabia. *JPMA The Journal of the Pakistan Medical Association*. 2017;67(12):1870-3.
 23. AlHaqwi AI, Mohamed TA, Al Kabba AF, Alotaibi SS, Al Shehri AM, Abdulghani HM, et al. Problem-based learning in undergraduate medical education in Saudi Arabia: Time has come to reflect on the experience. *Medical teacher*. 2015;37(sup1):S61-S6.
 24. Shamsan B, Syed A. Evaluation of problem based learning course at college of medicine, qassim university, saudi arabia. *International journal of health sciences*. 2009;3(2):249-58.
 25. Al-Drees AA, Khalil MS, Irshad M, Abdulghani HM. Students' perception towards the problem based learning tutorial session in a system-based hybrid curriculum. *Saudi medical journal*. 2015;36(3):341.
 26. Dearnley N, Scott-Smith W, editors. Accelerated learning at masters' level: problem based learning of diagnostic reasoning skills by physician associate students. *Research Matters: Articles from the Pedagogic Research Conference 2017; 2018:*

- Centre for Learning and Teaching, University of Brighton Press.
27. Dunsmuir S, Frederickson N, Lang J. Meeting current challenges in school psychology training: the role of problem-based learning. *School Psychology Review*. 2017;46(4):395-407.
 28. Liu L, Du X, Zhang Z, Zhou J. Effect of problem-based learning in pharmacology education: A meta-analysis. *Studies in Educational Evaluation*. 2019;60:43-58.
 29. Okubo Y, Matsushita S, Takakuwa Y, Yoshioka T, Nitta K. Longitudinal PBL in undergraduate medical education develops lifelong-learning habits and clinical competencies in social aspects. *The Tohoku journal of experimental medicine*. 2016;238(1):65-74.
 30. Babiker MEI. Student's Perception About Problem Based Learning for Teaching Basic Medical Science and Preclinical Phases at the College of Medicine, University of Bisha, Kingdom Saudi Arabia: University of Gezira; 2018.
 31. Sule R. Medical Students and Faculty Perceptions Towards a Case Based Learning Intervention at an Indian Medical College 2016.
 32. Treesirichod A, Chansakulporn S, Phivthong-ngam L, Kusumaphanyo C, Sangpanich A. The Attitudes of Medical Students towards Problem-Based Learning during the Clinical Years. *South-East Asian Journal of Medical Education*. 2018;12(1).
 33. Berkel H, Schmidt H. On the Additional Value of Lectures in a Problem-Based Curriculum. *Education for Health*. 2005;18(1):45-61.
 34. Ibrahim ME, Al-Shahrani AM, Abdalla ME, Abubaker IM, Mohamed ME. The effectiveness of problem-based learning in Acquisition of Knowledge, soft skills during basic and preclinical sciences: medical Students' points of view. *Acta Informatica Medica*. 2018;26(2):119.
 35. Ibrahim NK, Al-Sharabi BM, Al-Asiri RA, Alotaibi NA, Al-Husaini WI, Al-Khajjah HA, et al. Perceptions of clinical years' medical students and interns towards assessment method used in King Abdulaziz University, Jeddah. *Pakistan journal of medical sciences*. 2015;31(4):757.
 36. Yadav RL, Piryani RM, Deo GP, Shah DK, Yadav LK, Islam MN. Attitude and perception of undergraduate medical students toward the problem-based learning in Chitwan Medical College, Nepal. *Advances in medical education and practice*. 2018;9:317.
 37. Azer SA. Challenges facing PBL tutors: 12 tips for successful group facilitation. *Medical teacher*. 2005;27(8):676-81.
 38. Emerald NM, Aung PP, Han TZ, Yee KT, Myint MH, Soe T, et al. Students' perception of problem based learning conducted in phase I medical program, UCSI University, Malaysia. *South East Asian Journal of Medical Education*. 2013;7(2):45-8.
 39. Stankunas M, Czabanowska K, Avery M, Kalediene R, Babich SM. The implementation of problem-based learning in health service management training programs: Experience from Lithuanian University of Health Sciences. *Leadership in Health Services*. 2016;29(4):392-401.
 40. Nanda B, Manjunatha S. Indian medical students' perspectives on problem-based learning experiences in the undergraduate curriculum: One size does not fit all. *Journal of educational evaluation for health professions*. 2013;10.
 41. Dent J, Harden RM, Hunt D. *A practical guide for medical teachers: Elsevier health sciences*; 2017.
 42. Aarnio M, Lindblom-Ylänne S, Nieminen J, Pyörälä E. How do tutors intervene when conflicts on knowledge arise in tutorial groups? *Advances in Health Sciences Education*. 2014;19(3):329-45.
 43. AL-SHAWWA LA. Preparing Faculty Members as PBL Tutors in King Abdul Aziz University, Jeddah Saudi Arabia, L. *The Medical Journal of Cairo University*. 2011;79(2).
 44. Azer SA. Facilitation of students' discussion in problem-based learning tutorials to create mechanisms: the use of five key questions. *ANNALS-ACADEMY OF MEDICINE SINGAPORE*. 2005;34(8):492.
 45. Chung E-K, Hitchcock MA, Oh S-A, Han E-R, Woo Y-J. The relationship between student perceptions of tutor performance and tutors' background in problem-based learning in South Korea. *International Journal of Medical Education*. 2011;2:7.
 46. AlHaqwi AI, Al-Wahbi AM, Abdulghani HM, Van der Molen HT. Barriers to feedback in undergraduate medical education. *Saudi Med J*. 2012;33(5):557-61.

Mumps Cases Reported in Tertiary Hospital During 2017-2018 in Baghdad, Iraq

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Abstract

Background: Mumps is a disease caused by the mumps virus. It spread from human-to-human via direct contact or by airborne droplets. Initial signs and symptoms often include fever, muscle pain, headache, poor appetite, and feeling generally unwell. This is then usually followed by painful swelling of one or both parotid salivary glands

Method: A cross sectional study conducted in Al-Yarmouk teaching hospital during the period from January 2017 through December 2018. All patients of different ages and from both sexes diagnosed with mumps were included in this study.

Results: Most infections 72.1% occur in age groups ≥ 15 years. The high percentage of cases occur in males (62.5%). Cases reported among the vaccinated patients in all age groups, 16 patients (55.2%) of children were ≤ 14 years of age. Those who don't know about their vaccination state constitute (77.3%) of patient aged ≥ 15 . There was a significant association between immunization state and age. High percent of infection in 2017 were in March (14.4%), April (10.6%) and January (7.7%) while lowest rates of infection were showed in year 2018 for the same period.

Conclusion: The role of vaccination was limited in protection of patients against mumps disease; third booster dose of mumps vaccine is recommended to prevent future epidemics.

Keywords: Mumps, Baghdad, vaccination.

Introduction

Mumps is a disease caused by the mumps virus⁽¹⁾. It spread from human-to-human via direct contact or by airborne droplets. Initial signs and symptoms often include fever, muscle pain, headache, poor appetite,

and feeling generally unwell⁽²⁾⁽³⁾. This is then usually followed by painful swelling of one or both parotid salivary glands⁽³⁾⁽⁴⁾. Symptoms typically occur 16 to 18 days after exposure and resolve after 7 to 10 days⁽¹⁾⁽²⁾. About one third of people have mild or no symptoms, these are often more severe in adults than in children⁽²⁾. Immunity is generally life long and develop after either inapparent or clinical infections⁽⁵⁾. Live mumps vaccines are available as monovalent mumps vaccine, bivalent measles-mumps (MM) vaccine, and trivalent measles-mumps-rubella (MMR) vaccine. Following the use of mumps vaccine in the USA in the late 1960s, disease incidence declined dramatically, and by the 1980s very few cases were reported⁽⁶⁾. However, large,

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sporadic mumps outbreaks began to appear globally, involving a high percentage of persons with a history of vaccination⁽⁷⁾. In Iraq, the total number of mumps' cases reported in 2003 was 7051 case. The number of cases increased to 11821 during January to April 2004. There was a dramatic reduction in the number of cases (less than 1500) reported in the following 8 months (May to December 2004)⁽⁸⁾.

Studying mumps antibodies, Quasim (2010) in Mousal city found seropositivity against mumps virus among different age groups was 68%⁽⁹⁾. Study done by Baiee and Hatif (2018) they found that about half of the patients (56%) were vaccinated against the mumps disease in two districts located in the southern region of Babylon governorate⁽¹⁰⁾. Park et al. (2007) examine the discriminate between primary and secondary vaccine failure in a highly vaccinated population for mumps after an outbreak of mumps occurred in Gyeonggi, Korea in 2006⁽¹¹⁾. Vaccination coverage during the years 2008 and 2009 was 92.4% and 93.6% respectively indicating a highly vaccinated population in the village in Orange County in New York State where the mumps outbreak occurred⁽¹²⁾. WHO recommends immunization coverage of 90% to prevent outbreaks of mumps⁽¹³⁾.

Aim of Study: The current study designed to determine the rate of occurrence of mumps in 2017-2018(minor outbreak) in Baghdad.

Patients and Method

A cross sectional study conducted in Al-Yarmouk teaching hospital during the period from January 2017 till December 2018.

All patients of different ages and from both sexes diagnosed with mumps were included in this study. Data were obtained from the hard and soft records in the “Communicable Disease Control Program”/public healthunit.

Data were grouped tabulated and presented as frequencies ant percentages Chi-square test was performed using statistical package for Social Sciences (SPSS) Version 24.0. P-value of 0.05 and less was considered as significant.

Results

The total number of cases were 104, the range was 2-68 years, and the mean and standard deviation of age was (27.08±15.287).

Table-1 showed the older age group represented the largest one 75(72.1%), they were at the age group of 15 years and older. The smallest age group 29(27.9%) were of the less and equal 14 years. Male were affected more than female in this study (62.5% and 37.5% respectively). Higher percentage of occupation were the employed 51(49%) while the lowest rate was in those without working 7(6.7%).

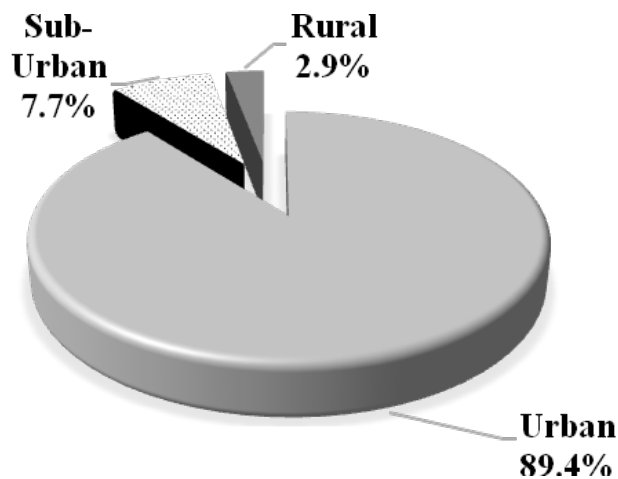


Figure 1: Distribution of patients according to residency

Figure-1 represented the residency of the patients where 89.4% came from urban area, 7.7% came from suburban, and the remaining 2.9% were from rural areas.

Table 1: Main characteristics of the study sample

Variables (N=104)	N	%
Age Groups		
≤14	29	27.9
≥15	75	72.1
Gender		
Male	65	62.5
Female	39	37.5
Occupation		
Employee	51	49.0
Worker	9	8.7
Not working	7	6.7
Student	26	25.0
Child	11	10.6

Bar chart in figure-2 shows that the highest frequency of cases in year 2017 occurred in March (14.4%) and the lowest in December was not cases registered and most cases in the year 2018 in October, November and December were the same percent (4.8%) and lowest in June was (0%).

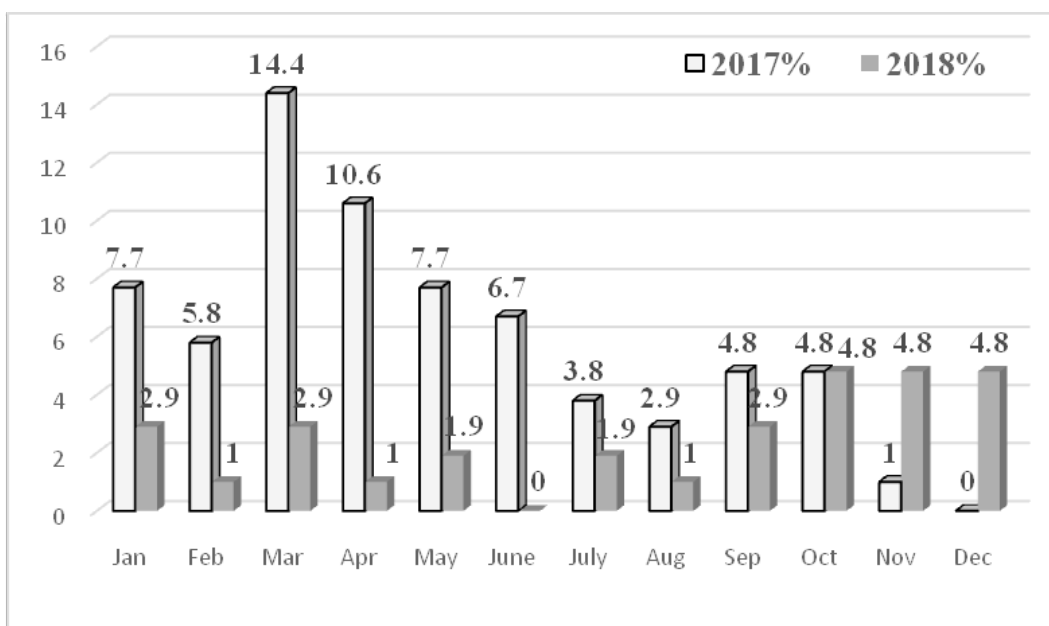


Figure 2: Distribution of cases according to months in years 2017 & 2018

Cases of mumps reported among the immunized patients in all the age groups, 16 patients (55.2%) of children were ≤14 years of age. For those aged ≥15 the rate of occurrence of mumps was higher among the Don't know about their vaccination constitute (77.3%). Significant association between immunization state

and age was (P = 0.002). Patients of both sexes had the infection in spite of being vaccinated male (33.8%) and female (25.6%). Although the relationship between immunization state and infection was not significant (P = 0.653) (table-2).

Table 2: Distribution of immunization status according to age and gender

Variables	Immunization								P-value
	Yes		No		Don't Know		Total		
	N	%	N	%	N	%	N	%	
Age Groups									
≤ 14	16	55.2	1	3.4	12	41.4	29	100	0.002*
≥ 15	16	21.3	1	1.3	58	77.3	75	100	
Total	32	30.8	2	1.9	70	67.3	104	100	
Gender									
Male	22	33.8	1	1.5	42	64.6	65	100	0.653
Female	10	25.6	1	2.6	28	71.8	39	100	
Total	32	30.8	2	1.9	70	67.3	104	100	

*Statistically significant

Table 3 showed the highest rate of recorded mumps cases was during Springs (39.4%) followed by Autumn at a rate of (23.1%) which is very close to that during Winter (22.1%) the lowest rate was during Summer (15.2%). Children and adult encounter the infection mainly in Spring (41.4%) and (38.7%) respectively.

The highest infection rate among male was in Spring 44.6%) and among female was during Autumn (35.9%). There was no significant relationship between season of recorded cases in one hand and the age and gender in the other hand P=0.173 and P=0.081 respectively.

Table 3: Occurrence of cases in relation to seasons

Variables	Season										P-value
	Springe		Summer		Autumn		Winter		Total	%	
	N	%	N	%	N	%	N	%			
Age Groups											
≤ 14	12	41.4	3	10.3	4	13.8	10	34.5	29	100	0.173
≥ 15	29	38.7	13	17.3	20	26.7	13	17.3	75	100	
Total	41	39.4	16	15.4	24	23.1	23	22.1	104	100	
Gender											
Male	29	44.6	12	18.5	10	15.4	14	21.5	65	100	0.081
Female	12	30.8	4	10.3	14	35.9	9	23.1	39	100	
Total	41	39.4	16	15.4	24	23.1	23	22.1	104	100	

Discussion

Age, gender and occupation: Three quarter of patients in this study were adult, age ≥ 15 years old. This agree with Jasminka et al. study in 2015 in Vojvidina, Serbia who found most of their study samples occurs in age groups of 15 29 years of old (14). But disagree with Areej study in 2018 in Baghdad who found most of the patients were in the age group below 15 years of age (15).

Regarding the gender, the results of our study demonstrated that males affected more than females, this could be explained by that male more moving outside doors and they usually engaged in different types of work leading to high person to person contact. This findings went with the findings of Areej, in 2018 (15) and with Jasminka et al. in 2015 in Vojvidina (14).

Regarding the occupation, About half of the sample were employee, Yu G et al. in 2018 found in his study in Guangxi, China that slightly higher than half of the patients were students (16).

Residence: Regarding the residence, the results demonstrated that the higher percentage of exposure in urban areas (89.4%), Baiee HA, Weli H, 2017 in Babylon province, Iraq which agree with this study who found most of study samples in urban more than rural areas (10).

Time (Month`s exposure): The results of this study revealed that the higher percentage of exposure was in March 2017 followed by the percentage in October, November and December 2018, Baiee and Hatifin 2017 in Babylon province, Iraq showed results that disagree with this study, they found most of most of cases were

in January (10) Again disagree with Areej in 2018, who depict most cases occurred in January (15).

Immunization Status: Regarding immunization status the results illustrated that the higher percent of cases occurred among immunized patients in age groups ≤14 years, this disagree with Jasminka et al. in 2015, Serbia which depict high cases occurred in age groups 20 - 29 and 15 - 19 years of old respectively (14). Also disagree with Whelan et al. in 2010 in Netherlands who found most cases recorded in cases aged 22 years of old vaccinated with two doses (17).

We found that infection affect vaccinated patients of both sex with male affected slightly more than female. This in agreement with Orlikova et al. 2016 in Czech Republic which demonstrate higher males affected than females (18).

Season occurrence with age and gender: during spring season highest number of cases reported in age group of ≤ 14 years this in contrast to Yi-Chien et al. 2015 in Taiwan which illustrated that most cases in summer season (19).

Regarding to the gender the results illustrates that the higher percent of males cases occurred in spring but the higher percent of female cases occurred in autumn which agree with Sawsan and Al-Hasnawi, 2018 in Karbala, Iraq which showed that most males infected in March (spring) season while most females in the last of November (autumn) and first December (winter) (20).

Ethical Issue: A formal clearance was taken from the Ethical Committee of Al-Yarmouk teaching hospital. All used data were confidentially kept for the purpose of the study.

Source of Funding: Self-funding

Conflict of Interest: We declare that there was no any conflict of interest.

References

- Atkinson, William. Mumps Epidemiology and Prevention of Vaccine-Preventable Diseases. Public Health Foundation. May 2012; 12th ed. pp. Chapter 14. ISBN 978-0-9832631-3-5. Archived from the original on 6 July 2016.
- “Mumps virus vaccines”(PDF). Weekly Epidemiological Record. 82 (7): 49–60. 16 February 2007. PMID 17304707. Archived(PDF) from the original on 16 March 2015.
- Johnson, Jonas T, Rosen, Clark A, Bailey, Byron J, Bailey’s head and neck surgery—otolaryngology. 1934; 5th ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins. 2013. ISBN 9781609136024. OCLC 863599053.
- Hviid A, Rubin S, Mühlemann K. Mumps. *The Lancet*. March 2008; 371 (9616):932–44. doi:10.1016/S0140-6736(08)60419-5. PMID 18342688.
- Heath K, Noel B, Sally M. *The blue book, Guidelines for the control of infectious diseases*. 1st ed.; 1996. p.139.
- McNabb SJ, Jajosky RA, Hall-Baker PA, Adams DA, Sharp P, Anderson WJ, et al. Summary of notifiable diseases - United States, 2005. *Morb Mortal Wkly Rep*. 2007; 54:1-92.
- Rota JS, Turner JC, Yost-Daljev MK, Freeman M, Toney DM, Meisel E, et al. Investigation of a mumps outbreak among university students with two measles-mumps-rubella (MMR) vaccinations, Virginia, September–December 2006. *J Med Virol*. 2009; 81:1819-1825.
- Alwan A. *Health in Iraq: The Current Situation, Our Vision for the Future and Areas of Work*. 2nd ed.; December 2004. P. 27. Available from: www.who.int/hac/crises/irq/background/Iraq_Health_in_Iraq_Second_edition.pdf.
- Quasim TM. Seroepidemiological study of mumps in Mosul. *Iraq J Pharm*. 2010; 9(1):1.
- Baiee HA, Hatif W. Epidemiological characteristics of Mumps outbreak in the south districts of Babylon province during the years 2016-2017. *Medical Journal of Babylon*. 2017; 14:3.
- Park DW, Nam MH, Kim JY, Kim HJ, Sohn JW, Cho Y, Song KJ, Kim MJ. Mumps outbreak in a highly vaccinated school population: assessment of secondary vaccine failure using IgG avidity measurements. *Vaccine*. 2007; 25 (24): 4665-70.
- Kutty PK, McLean HQ, Lawler J, Schulte C, Hudson JM, Blog D, Wallace G. Risk factors for transmission of mumps in a highly vaccinated population in Orange County, NY, 2009-2010. *Pediatr Infect Dis J*. 2014; 33:121-5.
- Gupta RK, Best J, MacMahon E. Mumps and the UK epidemic 2005. *Br Med J* .2005; 330:1132-1135.
- Jasminka N, Vesna KJ, Vesna M, Zorica S, Vladimir P, Caude PM, et al. A Mumps Outbreak in Vojvodina, Serbia, in 2012 Underlines the Need for Additional Vaccination Opportunities for Young Adults; October 23, 2015.
- Areej AH. Infection Rate of Mumps in Iraq during 2016. *Journal of Pharmacy and Biological Sciences (IOSR-JPBS)*. Vol. 13, Issue 2ver. VI (Mar.-Apr. 2018), PP. 50-53. Available from: www.iosrjournal.org.
- Yu G, Yang R, Wei Y, Yu D, Zhai W, Cai J, et al. Spatial, temporal, and Spatiotemporal analysis of mumps in Guangxi Province, China, 2005 – 2016. *BMC Infectious Disease*; 2018. 18:360.
- Whelan J, van Binnendijk R, Greenland K, Fanoy E, Khargi M, Yap K, et al. Ongoing mumps outbreak in a student population with high vaccination coverage, Netherlands, 2010. *Euro Surveill* 15: pii 19554.
- Orlikova H, Maly M, Lexova P, Sebestova H, Limberkova R, Jurzykowska L, et al. Protective effect of vaccination against mumps complication, Czech Republic, 2007 – 2012. *BMC Public Health*; 2016. 16: 293.
- Yi-Chien Ho, Bo-Hua Su, Huey-Jen Su, Hsiao-Ling C, Chuan-Yao L, Huifen C, et al. The association between the incidence of mumps and meteorological parameters in Taiwan; *Human Vaccines & Immunother* 2015;11(6):1406-1412. doi: 10.1080/21645515.2015.1029687
- Sawsan M, Al-Hasnawi J. Incidence of chickenpox and mumps in Karbala Governorate with their seasonal variation. *Iraq Med. J*. Vol.2, No.1; winter 2018. 24-27.

Treatment Options of Peyronie's Disease

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Abstract

Objective: Peyronie's disease (PD) is a localized fibrous scar in the tunica albuginea of the penis resulting in a palpable penile plaque, penile pain on erection, penile curvature and erectile dysfunction. This study evaluated our own experience with clinical outcomes after different method of treatment for PD.

Patients and Method: The study included 62 patients with PD aged from 33-72 years. Two groups of patients were evaluated, the first one (Non-surgical) included 44 patients, 30 of them treated with oral therapy and 14 patients had intralesional Verapamil injection. The second group (Surgical) included 18 patients, 10 had plication of the tunica albuginea in the contralateral side of the fibrous plaque, and 8 patients had penile prosthesis implantation.

Results: Oral therapy associated with improvement of penile bending in 50% and improvement of painful erection in 40%. Intralesional Verapamil injection results in improvement of penile bending was 56% and improvement of painful erection 70%. The plication of the tunica albuginea results in improvement of penile bending 80%, improvement of painful erection 70% and improvement of erectile function 60%. With penile prosthesis implantation, all patients had improvement of penile bending and 83% of them had improvement of painful erection. Post-operative patient's satisfaction increased gradually by time from 3 to 9 months.

Conclusion: The proper choice of treatment for PD affects its outcome. For surgery, the preferred option is plication in mild to moderate deformities with considerable penile length while penile prosthesis is reserved for patients with erectile dysfunction.

Keywords: Urology, Surgery, Peyronie's disease, erectile dysfunction, penile prosthesis.

Introduction

Peyronie's disease (PD) is a connective tissue disorder of the penis which affects the tunica albuginea with excessive fibrosis and plaque formation, but the exact etiology and pathophysiology remain unclear^[1].

Non-surgical treatment of PD includes oral, intralesional and shockwave therapies. For the acute

phase, there are numerous available oral drugs, but with weak scientific evidence. For intralesional injections, collagenase clostridium histolyticum is currently the only approved drug for the management of PD and a palpable plaque with dorsal or dorsolateral curvature $>30^\circ$, whereas calcium channel blockers and interferons (IFN) remain as off-label options^[2].

Surgical treatment of PD is indicated in cases with significant, stable deformity and associated with high success rates ^[3]. The surgical management should aim to correct the curvature, preserve erectile function and penile length, and minimize morbidity. The available evidence-based data could not determine the best surgical treatment of PD^[4].

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The aim of this study was to evaluate outcome of the treatment modalities of PD either non-surgical or surgical treatment to overcome this public clinical problem.

Patients and Method

This observational prospective study included 62 patients with PD, characterized by mild to moderate degree of penile angulation and painful erection, who attended the outpatient, Urology and Andrology clinic at Minia University Hospital, from December 2013 to September 2018, after approval from the department of ethical committee.

The patients were divided according to the method of treatment into 2 distinct groups: non-surgical or surgical. The inclusion criteria for non-surgical group were: acute phase of the disease with short duration from its onset (3-6 months), and preference from the patients who refused the surgical intervention. The inclusion criteria were for surgical group were severe penile angulation during erection to the degree that it affected patient's sexual life with his partner, failure of medical treatment for at least 6 months therapy, and erectile dysfunction not responding to oral therapy. The exclusion criteria for non-surgical group were: severe penile angulation, and severe degree of erectile dysfunction. The exclusion criteria for surgical group were: major renal or hepatic impairments, history of myocardial infarction or cerebrovascular strokes, and uncontrolled diabetes mellitus.

The patients were evaluated by medical and sexual history, Questionnaire for PD [5], and physical examination during the first visit according to initial evaluation and treatment provided to them. The patients were divided into two main groups. The first group (non-surgical), included 44 patients who received oral therapy with L-Carnitine, Vitamin E and Colchicine for 6 months (n= 30), or intralesional injection with verapamil injection (n= 14). The second group (surgical), included 18 patients, 10 of them were operated upon for Tunica Albuginea plication (Figure 1- A, B, and C), and the other 8 patients were operated upon for penile prosthesis implantation surgery (Figure 1- D, E, and F) when there were severe degree of erectile dysfunction. All of patients in the surgical group were followed in outpatient clinic every 1 week for 1 month, then every 2 weeks for 2 months and every 2 months for 1 year. Postoperative patient satisfaction was estimated at 3, 6, and 9 months

using the Modified Erectile Dysfunctions Inventory of Treatment Satisfaction (MEDITS) questionnaire.

The statistical analysis was performed using the IBM-SPSS statistics software version 20. Continuous variables of data were represented as mean and standard deviation and qualitative data were represented as number and percentage. Differences in the mean of continuous variables were analyzed using t student test. Differences in the percentage of qualitative variables were analyzed using Chi-square test. The values $P < 0.05$ were regarded statistically significant.

Results

The included patients aged from 33 years to 72 years with mean age of 50.9 ± 7.2 years, and the highest incidence (38.7%) was from 51 to 60 years old. The results of penile Doppler Ultrasound included arterial insufficiency in 40 patients (65.3%), and venous leak in 22 patients (34.7%). In 18 patients who underwent surgical intervention, the preoperative risk factors were smoking (83%), diabetes mellitus (66%), hypertension (50%). and previous penile trauma (50%).

Regarding the effects of oral therapy and intralesional therapy on penile bending and erectile function (Table 1), 15 out of 30 patients (50%) who received oral therapy had significant improvement in curvature from 30 degrees to 18 degrees, and only 12 cases (40%) had improvement of painful erection. In a group of 14 patients who received intralesional therapy, 8 patients (56%) had improvement in penile curvature from 40 degrees to 22 degrees with a decrease in plaque size from 3 cm to 2.2 cm, and 10 patients (70%) showed improvement of painful erection. As regards results of surgical intervention (Table 1), 8 cases out of 10 (80%) developed improvement of penile bending from 40° to 10° after Tunica Albuginea plication, whereas all patients of penile prosthesis implantation (100%) developed improvement of penile bending from 45° to 0° .

Regarding the postoperative outcome in the group of 18 patients with surgical intervention (Table 2), early postoperative pain was addressed as discomfort in 11 patients (61%), tolerable in 4 patients (22%), and distressing in 3 patients (17%). Postoperative edema detected in 6 patients (33%), 3 of them had DM and the other 3 were hypertensive. Persistent pain during intercourse was detected in 6 patients (33%), 2 of them (11%) after plication of tunica albuginea and the other 4 patients (22%) after penile prostheses surgery

and resolved within few weeks. Superficial wound infection was detected in 5 patients (28%) and managed successfully, three of them were diabetic.

The MEDITS questionnaire was used to determine postoperative patient satisfaction (Figure 2). There

was gradual increase in means of (MEDITS) from 3, 6 and 9 month respectively. The score was 72.3 ± 18.8 at 3 months, 80.3 ± 17.2 at 6 months and 84.2 ± 16.7 at 9 months after surgery, which had a statistically significant difference ($P < 0.01$).

Table 1: Effects of different method of treatment of 62 patients with PD on penile bending and erectile function.

Variables	Non-surgical treatment			Surgical treatment		
	Oral therapy (n=30)	Intralesional injection (n=14)	P-value	Tunica Albuginea plication (n=10)	Penile prosthesis implantation (n=8)	P-value
Improvement of bending	15 (50%)	8 (56%)	0.71	8 (80%)	8 (100%)	0.19
Improvement of painful erection	12 (40%)	10 (70%)	0.06	7 (70%)	7 (87%)	0.40

Table (2): Postoperative outcome in the group of 18 patients with surgical intervention.

Variables	Surgical treatment (n=18)
Early postoperative pain:	
- Discomfort	11(61%)
- Tolerable	4 (22%)
- Distressing	3 (17%)
Postoperative edema	6 (33%)
Persistent pain during intercourse	6 (33%)
Superficial wound infection	5 (28%)

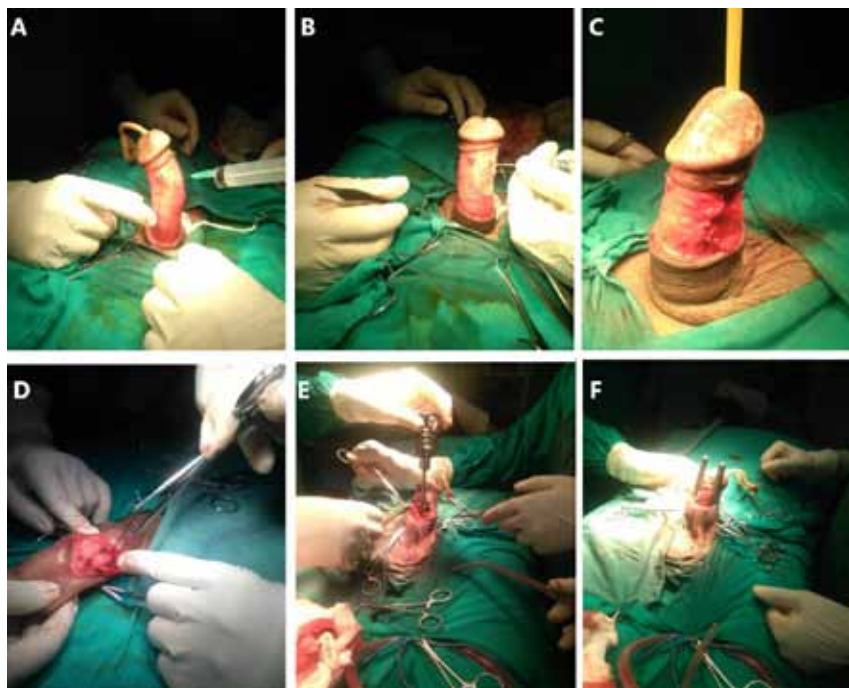


Figure 1: Tunica Albuginea plication: A) degloving of penile skin and intra cavernously injection with saline. B) Plication of other side of the deviation. C) Correction of the deviation. Penile prosthesis implantation: D) Penoscrotal incision and placement of stay sutures. E) Dilatation of cavernous tissue using urethrotome. F) Implantation of the penile prosthesis.

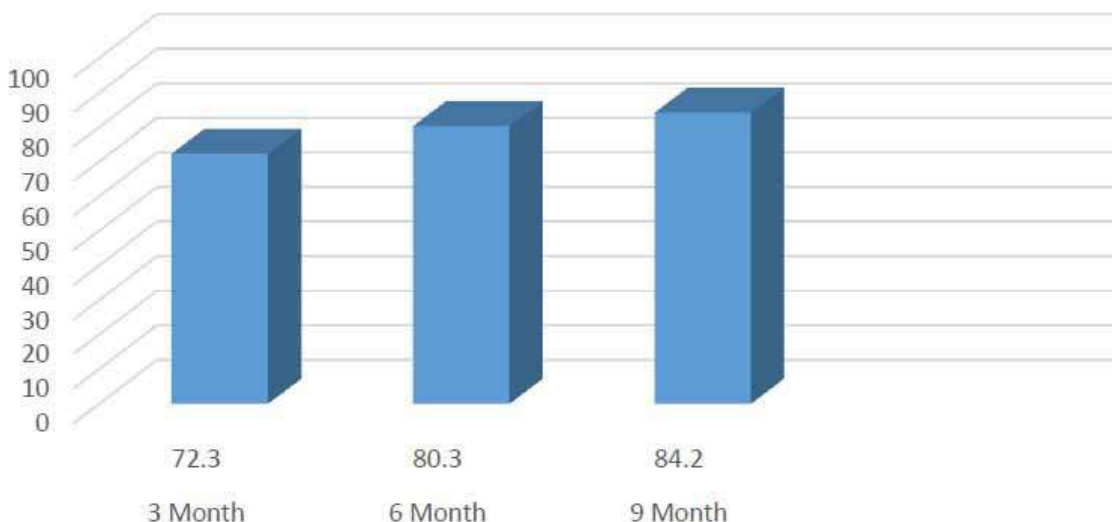


Figure 2: Mean scores of Modified Erectile Dysfunctions Inventory of Treatment Satisfaction (MEDITS) Questionnaire at 3, 6 and 9 months after surgery.

Discussion

There are many options for treatment of PD with a variation in their indications and outcomes. In our cases of oral therapy with a combination of Vitamin E, Colchicine, and L-Carnitine for 6 months, penile bending improved in 50% and only 40% showed improvement of painful erection. Use of Colchicine alone or combined with vitamin E has conflicting results in literature. Prieto Castro et al [6] reported decrease in the plaque size and improvement of the curvature in the vitamin E – Colchicine group with significant difference in comparison to ibuprofen group. Safarinejad MR [7] stated that the combination of vitamin E and colchicine might be a useful therapeutic option during the early stages of PD in patients with specific criteria of inflammatory activity. Moreover, we added L-carnitine in the treatment of PD as it has antioxidant properties and its antiproliferative effects on endothelial cells.

In our study, intralesional injection of verapamil in 14 patients resulted in 56% improvement in penile bending and 70% improvement in painful erection. The intralesional verapamil injections could be advocated for the treatment of nonqualified acute phase or chronic plaques to stabilize disease progression or reduce penile curvature [8]. Longer treatment periods of concentrated Intralesional verapamil in younger men with small plaques but large curvature have been shown to receive the optimal benefit [9].

Surgical management allows for rapid and reliable correction of penile deformities that can be sustained for patient life. As no one procedure could be considered as a universal surgical standard of care or the optimal procedure, many procedures exist as penile plication, plaque incision/excision with grafting, and penile prosthesis implantation. But, penile reconstructive procedures do not fall into the domain of all urologic surgeons [10]. In our study, we performed plication surgery in 10 patients and penile prosthesis implantation in 8 patients. The plication procedures, the most common surgical treatment for PD, are attractive due to their good results as high degree of curvature correction and their relatively low risk of adverse effects. With the presence of many techniques for plication, the success and satisfaction may vary with the technique, but these differences do not reflect superiority of one technique over another and direct comparisons across the observational studies cannot be made [11].

In our study, 80% in the plication group and 87% in the prosthesis group had improvement in penile pending (curvature) with curvature correction rates range from 40% (with plication)-100% (with prosthesis). In literature the overall patient satisfaction ranges from 68–100%. The literature shows plenty of studies in which the curvature correction rates range from 42–100% [10]. Patient satisfaction after surgery may be related to straightening and improved sexual performance; while

dissatisfaction may correlate with many factors as postoperative penile shortening, erectile dysfunction, pain, change of penile shape, and worsening of curvature and sensation. Therefore, it is useful to inform the patient preoperatively about the suspected penile length loss by illustration on the long side of the penis, as measured during erection by measuring the difference in length between the long and short side of the penis [12].

In our study, the patients with penile prosthesis got 100% curvature correction and 100% satisfaction. Prosthesis implantation remains the gold standard treatment for PD requiring surgery especially that occurring concurrently with refractory erectile dysfunction. It's appropriate for severe deformity refractory to non-surgical management or failed plication/grafting, and with profound penile instability [11]. PD deformity correction rates with penile prosthesis implantation range from 84–100% [13]. Review of observational studies in literature reported curvature improvement of greater than 80% [14].

In conclusion, the choice of treatment for PD depends on the phase of the disease, stabilization of the plaque, and the presence of erectile dysfunction, which affect the outcome of treatment and patient satisfaction. The surgical procedure can allow rapid and reliable outcomes for correction of PD when the plaque is stabilized. The plication techniques are preferred for mild to moderate deformity with considerable penile length, and the penile prosthesis implantation is reserved for patients with erectile dysfunction.

Ethical Clearance: Taken from Faculty of Medicine, Minia University committee

Source of Funding: Self

Conflict of Interest: None to declare

References

- Hussein AA, Alwaal A, Lue TF. All about Peyronie's disease. *Asian J Urol.* 2015;2(2):70-78.
- Yafi FA, Pinsky MR, Sangkum P, Hellstrom WJ. Therapeutic advances in the treatment of Peyronie's disease. *Andrology.* 2015;3(4):650-60.
- Bilgutay AN, Pastuszak AW. Peyronie's disease: What's around the bend? *Indian J Urol.* 2016;32(1):6-14.
- Gaspar S, Santos Dias J, Martins F, Lopes T. Recent surgical advances in Peyronie's Disease. *Acta Med Port.* 2016;29(2):131-8.
- Coyne KS, Currie BM, Thompson CL, Smith TM. The test-retest reliability of the Peyronie's disease questionnaire. *J Sex Med.* 2015;12(2):543-8.
- Prieto Castro RM, Leva Vallejo ME, Regueiro Lopez JC, Anglada Curado FJ, Alvarez Kindelan J, Requena Tapia MJ. Combined treatment with vitamin E and coichicine in the early stages of Peyronie's disease. *BJU Int.* 2003;91(6):522-4.
- Safarinejad MR. Therapeutic effects of colchicine in the management of Peyronie's disease: a randomized double-blind, placebo-controlled study. *Int J Impot Res.* 2004 Jun;16(3):238-43.
- Cavalini G, Modenini F, Vitali G. Open preliminary randomized prospective clinical trial of efficacy and safety of three different verapamil dilutions for intraplaque therapy of Peyronie's disease. *Urology* 2007; 69: 950–954.
- Moskovic DJ, Alex B, Choi JM, et al. Defining predictors of response to intralesional verapamil injection therapy for Peyronie's disease. *BJU Int* 2011; 108: 1485–1489.
- Chung E, Ralph D, Kagioglu A, Garaffa G, Shamsodini A, Bivalacqua T, et al. Evidence-Based Management Guidelines on Peyronie's Disease. *J Sex Med.* 2016 Jun; 13(6):905-23.
- Bella AJ, Lee JC, Grober ED, Carrier S, Benard F, Brock GB. 2018 Canadian Urological Association guideline for Peyronie's disease and congenital penile curvature. *Can Urol Assoc J.* 2018;12(5):E197-E209.
- Deveci S, Martin D, Parker M, Mulhall JP. enile length alterations following penile prosthesis surgery. *Eur Urol.* 2007;51(4):1128-31.
- Nehra A, Alterowitz R, Culkun DJ, et al. Peyronie's disease: AUA guideline. *J Urol.* 2015;194:745–53.
- Levine LA, Mulhall JP, Wang R. In: Peyronie's Disease Surgical Management. Chile KA, editor. AUA Core Curriculum, American Urological Association Education and Research Inc.; 2016. [Accessed Sep 30, 2019]. https://university.auanet.org/core_topic.cfm?coreid=103.

Port Terminal Analysis Operation Towards Health, Safety, Security and Environment (HSSE) Approach

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Abstract

Health Safety Security and Environmental (HSSE) are common concept used to assess company's operating performance and their supply chain majority in prominent company with high risk exposure. However, this concept has largely been underutilized within the ferry port terminal's operation. This study asks whether the HSSE principles can applied in the ferry port terminal in Indonesia in regard sustainable aspect. In particular, it examines whether Ferry port terminal of Merak can be considered as Ecoseaport. It focuses on major ferry port terminals at inter-island hub because of the increasing volume and movement of people and vehicles in the last five years. This research is aligned with the Indonesia government policy on 'Maritime Axis' and is relevant with the cancellation of the Sunda Strait bridge development. Through at system dynamics simulation, this research ultimately aims to contribute to the improvement of knowledge of stakeholders that will influence a concept formulation and implementation of policy and stands appropriately of HSSE aspect. A System Dynamics approach of this research is intended to analysis and formulated all those elements involved in ferry port terminal operation against wharf capacity, port carrying and supportive capacity, passenger, vehicle and motorcycle inflow and vessel availability to transporting and movement. It was concluded that during Muslim's feast period with number of passenger, motorcycle and vehicle stock were drastically increased than normal operation. This will affect to HSSE performance, especially health aspect which corresponding with escalate on number patient to be visited to health posts against safety, security and environmental dimension. Whilst vessel frequency for passenger and vehicle loading purpose are stagnant mode since in 2018 as per simulation being constructed. Meanwhile, health cases reported by port medical officer is becomes major concerned which need takes into attention by port management operation and governmental related parties.

Keywords: *Ecoseaport, HSSE, System Dynamics, Sustainability.*

Introduction

Merak port was situated in Banten Province Indonesia, is a public port inter island that serving between western tip of Java and southern Sumatra island with approximelay 30.6 km away. Port harbour

Merak is the gateway of cross paths land connecting between Java and Sumatra island¹. Merak port has land area coverage of approximately 15 hectares, with physical boundaries territorial at north and east side to the hills, west and south side to Sunda strait. Inter island ferry port at Bakauheni is a public port that serving the crossing between the south end of Sumatra to tip of western Java island. To realize an effectiveness and efficient of transportation system, it should be directed to improve services by bringing together to their interests or expectation amongst relevant services parties. Whereas number of vehicle and motorcycle are continue increased every year, especially during holiday and

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annual muslim's feast period in regard home coming and back flowing traditions to their home town. In the view, area for services improvement related to infrastructure and supporting facilities are essential implemented and shall taken into immediate effectively and efficiently to be able its transportation system has realible, quality services, pricing affordability, safety and bring HSSE concept into their operations³.

One of strategy to improve ferry port terminal is by implemented Ecosoport concept, instead of Ecoport terms that normally use in Europe. A port by implement Ecosoport or green concept may lead to healthy and environmental sounds to develop port is being useful in terms of social, economic and ecological, and become a prerequisite in respect port which would like to compete in the global transportation arena (Despina et al., 2011). Through Ecosoport concept, various of environmental issues in the port such a deteriorated of sea water quality, air pollution and noise, reduce biodiversity, reduction of health condition and safety are systemically designed, implemented, monitored, reviewed, re-implemented and organize by port management, including stakeholder². This cycle will continues endlessly or never ending process for environment quality improvements (Rickard and Egels, 2012). Ecosoport is concept for environmentally sound port, which directs the development of port to be useful, and environmentally (Pavlic et al., 2014). The management priority shall take for environmental sustainability, energy efficiency and reduce the impact to marine ecosystems and coastal areas⁴.

Material and Method

This study employed both qualitative and quantitative method and exploratory design with sequential procedure. The initial is applied for qualitative then proceed with quantitative. SPSS (Statistical Package for Service Solutions) was used for processing the questionnaires. The system dynamics thru powersim studio 8 Enterprise application are intended to formulate HSSE (Health Safety Security and Environment) performance as ecosoport pillar being constructed at ferry ports terminals, against users and available facilities, including wharf space during annual going back home town during peaks period. HSSE data performance reference are consisted of health, safety, security and environmental cases against passengers, motorists and anyone who utilize ferry port terminal facilities. Secondary and primary data's that was obtained

quantitative and qualitatively have also carried out to aim and getting an accurate picture of the systematic and relationship between determined variables through data collection and analysis⁷. The qualitative method acquired through focused interviews, and quantitative are then used to synthesize the dynamic of ferry ports management principle for Ecosoport, particularly with regard to HSSE aspect.

Findings and Discussion

The causal loop diagram to construct the model consists of 10 (ten) loops with details of 3 (three) positive (reinforcing) and 7 (seven) negative loops (balancing). There were 26 (twenty six) identified variables used to develop a dynamic model of sustainable ecosoport on inter-island ferry port terminal. The main variables used as stock are passengers, vessel trips, health posts, and number of health. The dynamic sustainability model for ferry port terminal based to ecosoport through HSSE concept approach in Merak, Banten Province, was compiled by simplifying several variables that were thought to influence real conditions. Simplification is done by setting the limits and assumptions of the model. The limits set forth in the model are focused on the dynamics of health cases that are influenced by endogenous variables and do not include exogenous variables, i.e. cases of passengers which visiting health posts that must appropriately handle at the ferry port terminal as the most predominant driven factor, rather than other aspects i.e. safety, security and environmental. The assumptions used to construct dynamic models in research methodology during the peak flow of homecoming period are as follows:

- a. The dynamics number of passengers, motorists, small vehicles, and large vehicles entering the port are considered constant.
- b. Peak passengers occur at night time, in the range H-7 and H+7 from peak of homecoming flow period is within fixed conditions.
- d. The variability of user behavior of ferry port terminal against HSSE perception and insight, is considered as the driven factor for ecosoport dimension is constant⁸.
- e. The case number of safety, security and environmental aspect in the element of ecosoport is not so dominant compared to health cases and assumed to follow trend based on yearly reference data.

- h. The type and pattern of illness need to be treated are similar with yearly reference data¹. terminal, vessel trip, health case and health post provided by ferry port terminal operator starting from reference data in 2012 until 2029 are mentioned as following table.
- Simulation Business as Usual (BAU) and Intervention:** Data simulation against passenger in

Table 1. Number of Passanger, Vessel Trip, Health Cases and Health Post within Simulation Business as Usual (BAU) year 2012-2029.

Year	Passenger in Port Terminal (People)	Vessel Trip	Number of Health Posts (Unit)		Health Cases (People)	
			BAU	Intervention	BAU	Intervention
2012	1,453,465	100	5	467	467	
2013	1,496,662	109	5	489	489	
2014	1,541,143	114	5	512	512	
2015	1,586,946	116	5	537	537	
2016	1,634,110	118	6	562	562	
2017	1,682,675	118	6	588	588	
2018	1,732,684	119	6	615	615	
2019	1,784,180	119	6	643	620	
2020	1,837,206	119	6	672	625	
2021	1,891,807	119	6	702	630	
2022	1,948,032	119	6	734	636	
2023	2,005,927	119	7	767	641	
2024	2,065,544	119	7	801	646	
2025	2,126,931	119	7	836	651	
2026	2,190,144	119	7	873	656	
2027	2,255,253	119	7	911	662	
2028	2,391,261	119	7	951	667	
2029	2,391,278	119	8	992	673	

Source: Data extracted using powersim studio 8, 2018

Structural Intervention: The validity results are verified by using the AME (Absolute Mean Error) method. After calculating the AME value for passenger growth, number of vessel trips, health cases and number of health posts were 3.68%, 8.58%, 11.57%, and 3.70% respectively. These values are still below the error tolerance threshold for the controllable variable, which is 30%, so it can be stated that the dynamic model of ecoseaport for ferry port terminal crossing interisland sustainability, through the HSSE concept approach, in Merak, Banten Province is declared valid.

To enable controlling health case from passenger during peak time period, some strategies need further implemented to decrease the number, whilst terminal area, wharf and loading time are never significantly

changes time by time. Business as usual simulations are carried out to predict behavior trends of models that are construct at a certain time. The simulation period is set for 17 years from 2012-2029 by considering the implementation of 2 (two) periods of Indonesia presidential election starting in 2019, which seaport function must to be taken into consideration to accelerate maritime industry development and inland road infrastructure across Java and Sumatra island as most of population density in Indonesia⁵. Based on the simulation results, it can be seen that passenger growth, number of vessel trips, health cases and the number of health posts to be provided will continue to increase until 2029 by following to the exponential growth pattern. However, the number of vessel trips has been maximized in 2018 (Figure 1).

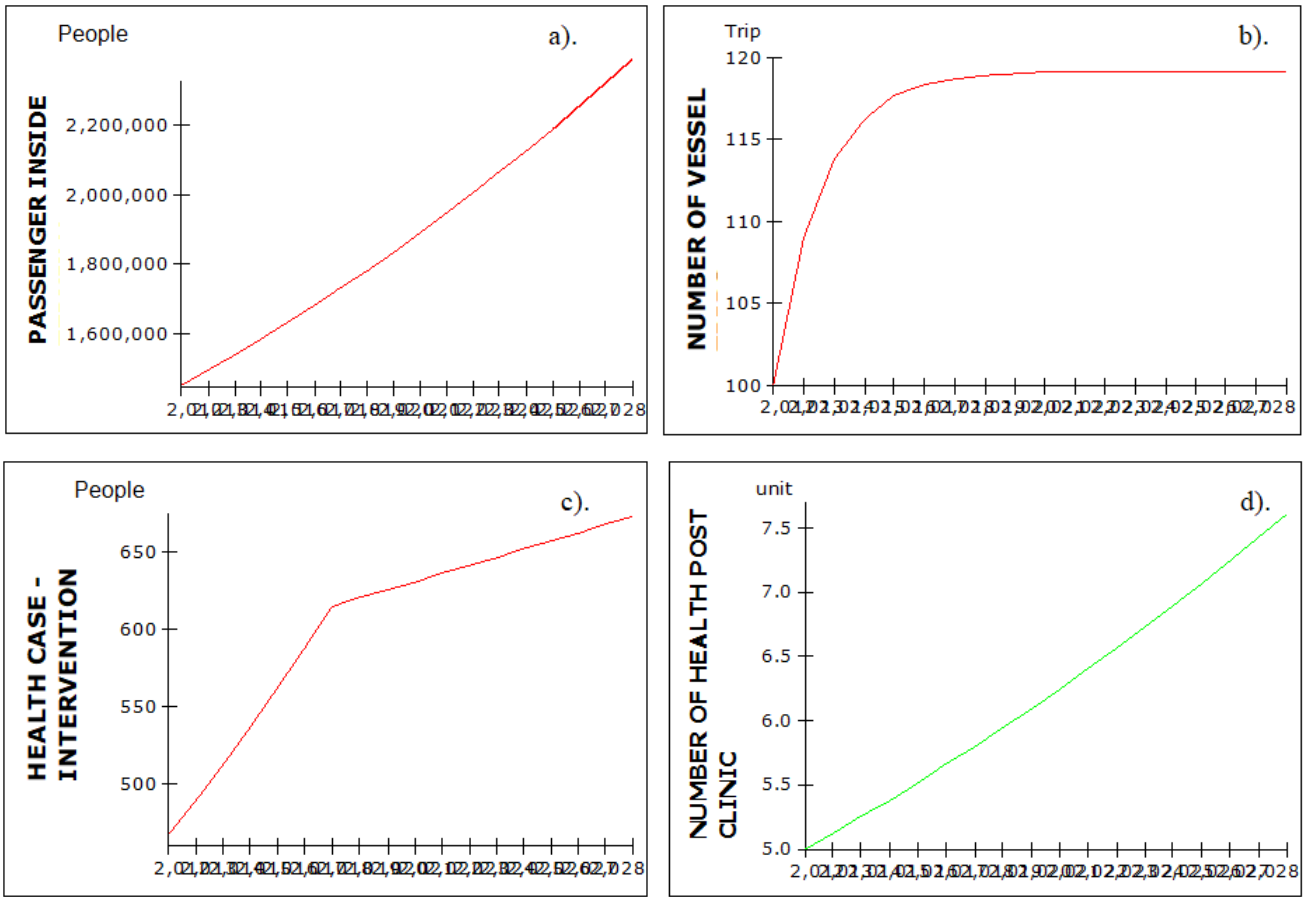


Figure 1: Business as usual simulation, (a) passenger growth, (b) number of vessel trips, (c) health cases - intervention, (d) number of posts health at Merak Port-Indonesia, 2012-2029.

The results of the structural interventions conducted showed that the reduction in the number of health cases in 2029 will 673 cases with the need for 8 health posts.

This decrease is equivalent to 32.2% of the total health cases over business as usual conditions (Table 1).

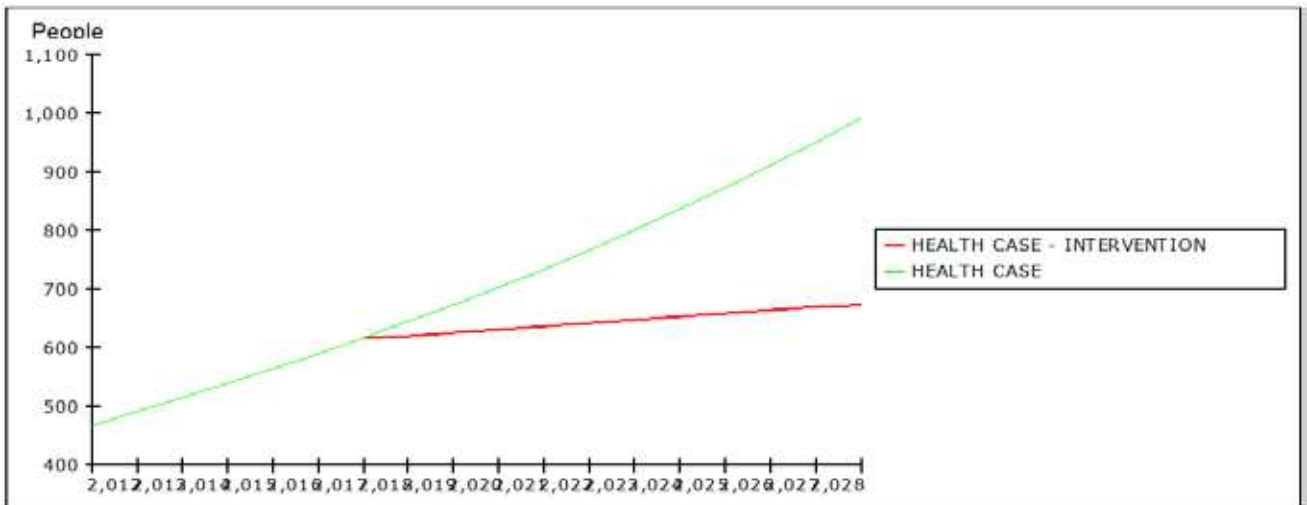


Figure 2: The ecoseaport ferry port terminal inter island model sustainability simulation, at Merak port by approaching HSSE concept 2012-2029, start in 2018 with a scenario of structural intervention in the number of health cases.

Refer to deep into detail on above figure analysis, most of respondent have a disparity opinion in regard HSSE aspect. The trend of health cases seems to continue to increase, in line with the condition of passengers entering the terminal, so the outcome of the intervention results must certainly be managed to the minimum level. Therefore, in the future, other structural and functional interventions that involve leverage variables are needed to be executed. It is assumed that the leverage variables of the health aspect in the dynamic model of sustainable ecoseaport are affected by fatigue due to the queue, or all the way long toward the port. This is reinforced by the average number of cases that must be handled by medical personnel, the highest 3 (three) diseases are respiratory disorders, myalgia-fatigue, and digestive disorders. Therefore, control programs as an intervention step can begin with subjects related to the queue reduction program and promotion of health programs on above mentioned highly health cases may arise⁶.

Based on the simulation results of ecoseaport sustainable model at ferry port terminal, Merak, province Banten Indonesia through the HSSE concept, it can be mentioned that number of health cases pattern will continue to increase along with the increase in the number of passengers each year, with the number of wharf space and vessel capacities tend to remain constant. Structural interventions will have performed to decrease by 25% from 4.1%/year to 3.1% per year against a program to reduce the number of health figures will reduce the number of health cases equivalent to 32.2% compared to business as usual conditions. However, the reduction is certainly not in the ideal condition if reflected and associated with the assumptions that being applied to construct this model.

Health cases predicted will potential continue for the future along with the interpersonal mobility of people, materials and goods, and current construction of infrastructure networks massively worked between the islands of Java and Sumatra or vice versa. This may encourage the behavior of passengers entering the sea port Merak and the number of patients visiting health posts based solely on assumptions concerning behavior, not on the extension of economic factors and the efficiency value of traveling between Java and Sumatra or vice versa, could be another driven factor in the increase in health cases at the Merak ferry port. Therefore, other intervention scenarios must still be tested and trial by involving any other leverage variables⁷. Another structural intervention that can be done is to add

economic sub models with profits variable as stock such ticket sales and port operational costs respectively as inflow and outflow structure. These interventions need to be supported by functional interventions that can reduce the port operating costs and vessel without diminished a HSSE aspect as a sustainable dimension driving element in the Merak ferry port, Banten. The manifestation of the structural intervention must then be designed in an integrated policy for environmental protection and economic growth of the port area and mapping important issues in port operations and establishing key elements, aligned with the concept of the European Union Co-founder (2012). The intervention program can be done to reduce the risk of health cases such as preparing tents for motorists before entering the port, tents for dock services, stretcher equipment to anticipate fainting passengers, portable toilets to minimize the movement of passengers already inside the port, which directly implicating the passenger density rate and the risk of the occurrence of health cases.

Conclusion

1. Based on the simulation results of ecoseaport sustainable model at ferry port terminal, Merak, province Banten Indonesia through the HSSE concept, it can be mentioned that number of health cases pattern will continue to increase along with the increase in the number of passengers each year, with the number of wharf space and vessel capacities tend to remain constant. Structural interventions will have performed to decrease by 25% from 4.1%/year to 3.1% per year against a program to reduce the number of health figures will reduce the number of health cases equivalent to 32.2% against business as usual conditions.
2. Health cases predicted will potential continue for the future along with the interpersonal mobility of people, materials and goods, and current construction of infrastructure networks massively worked between the islands of Java and Sumatra or vice versa. This may encourage the behavior of passengers entering the sea port Merak and the number of patients visiting health posts based solely on assumptions concerning behavior. Therefore, other intervention scenarios must still be trialed by involving any other leverage variables. Another structural intervention that can be done is to add economic sub models with profits variable as stock such ticket sales and port operational costs

respectively as inflow and outflow structure. These interventions need to be supported by functional interventions as well that can reduce the port operating costs without diminished a HSSE aspect as a sustainable dimension driving element in ferry port terminal. The manifestation of the structural intervention must then be designed in an integrated policy for environmental protection and economic growth of the port area and mapping important issues as aligned with the concept of the European Union Co-founder (2012). The intervention program can be done to reduce the risk of health cases such as preparing tents for motorists before entering the port, tents for dock services, stretcher equipment to anticipate fainting passengers, portable toilets to minimize the movement of passengers inside the port, which directly implicating to the density rate and risk occurrence on health cases.

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Ethical Clearance: Research ethics approval was obtained from ferry port terminal, Merak, Banten Province, Indonesia and school of environment, University of Indonesia.

References

1. Laporan Arus Balik dan Mudik Lebaran. Jakarta. Antara. 2016.

2. Pavlic. B, Cepak. F, Sucis. B, Peckaj. M, and Kandus. B. Sustainable Port Infrastructure, Practical Implementation of The Green Port Concept. *Journal. Thermal Science*. 2014; Vol. 18, No. 3, pp. 935-948.
3. Darbra. R. M, Ronza. A, Stojanovic T.A, Wooldridge C, Casal . J. A procedure for identifying significant environmental aspects in sea ports. *Marine Pollution Bulletin*. 2015; 50(8):866-74
4. Darbra. R.M, Pittamb. N, Roystona K.A, Darbra J.P, Journeea. H. Survey on environmental monitoring requirements of European ports. Amsterdam, The Netherlands. *Journal of Environmental Management* 90. 2009; 1396-1403.
5. Directorate General of Land Transportation. MOC/ JICA Report, 1978 – 2012. Jakarta. 2013.
6. Giulia. A & Raimonds. A. How to Turn an Innovative Concept Into a Success? An Application to Seaport Related Innovation. *Journal: Research in Transportation Economics*. 2013; 42. 97-107.
7. Hou. L, and Geerlings. H. Dynamics in Sustainable Port and Hinterland Operations: A Conceptual Framework and Simulation of Sustainability Measures and Their Effectiveness, Based on An Application to The Port of Shanghai. *Journal of Cleaner Production* 135. 2016; 449-456.
8. Yudhistira. M.H, and Sofiyandi. Y. Seaport Status, Port Access, and Regional Economic Development in Indonesia. *Journal: Marit Econ Logist*. 2018; 20:549-568.

CM Wire Endodontic Files Cyclic Fatigue after Irrigant's Immersion

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Abstract

Aim: Cyclic fatigue and scanning electron microscope analysis of a new preheated machined CM wire endodontic files after immersion for 5 and 10 minutes in irrigants.

Materials and Method: Twenty four size 20 Mpro files were used in this study divided into four groups according to irrigant of 6 files each; saline, chitosan 0.3%, chitosan 0.5% and ethylene diamine tetra acetic acid (EDTA) 17%. Files were immersed in irrigant for 5 or 10 minutes. Cyclic fatigue tests were performed using a static cyclic fatigue testing device. Parameters reported were time to fracture, number of cycles to failure and mean length of unfractured segments. The fractured segments were scanned using a scanning electron microscope to determine the crack initiation site and number of crack origins.

Results: A statistically significant difference existed in mean time to fracture between the different irrigants. At 5 mins immersion time for time of fracture and number of cycles to failure with Chitosan 0.3 group showing the highest mean. At 10 mins immersion time, there was no statistically significant difference but existed only in mean time to fracture between the two immersion times within Chitosan 0.3 and EDTA groups. There was no statistically significant difference in mean length of fractured segments between all groups at 5 mins immersion time but only existed. At 10 mins immersion time within EDTA group. Scanning electron microscope photomicrographs showed that 100% of samples of group 2 chitosan 0.3 showed one site of crack origin.

Conclusion: Chitosan 0.3% had the least destructive effect on the files.

Keywords: Cyclic fatigue, CM wires, Chitosan, SEM.

Introduction

Nickel-titanium instruments are trusted in endodontics over stainless steel.⁽¹⁾ Mpro file (Foshan stardent equipment co, gungdon, China) is a controlled memory file machined from a CM wire previously subjected to athermomechanical processing procedure

that shows outstanding clinical fatigue resistance⁽²⁾ and can retain the shape of the canal even when out of it.⁽³⁾ Cyclic fatigue fracture occurs when the file rotates around a curved root canal with repeated extension and compression cycles in the region of maximum bending stress.^(4,5) Gambarini⁽⁶⁾, Praisarnti et al.⁽⁷⁾ and Zender⁽⁸⁾ recognized factors affecting the fatigue resistance of NiTi rotary files as material properties, cross-sectional design, metal surface treatments, metallurgical characterization and root canal irrigants.

Chemomechanical preparation reduce bacterial populations located in root canal.⁽⁹⁾ Choice of irrigant depends on its effectiveness as lubricants, smear layer removal and efficacy on virulent bacteria present in the

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canal.⁽¹⁰⁾ The most common chelating irrigant solution is ethylenediamine-tetraacetic acid (EDTA) is used for the final irrigation of the root canals. Chitosan is a cationic biopolymer obtained from chitin of crustacean exoskeletons,⁽¹¹⁾ which was proposed to be used due to biocompatibility, no toxicity, bioactivity, biodegradability, selective permeability, antimicrobial activity, adsorption capacity and chelation ability⁽¹²⁾ Ametrano et al. and Kuhn et al.,^(13,14) stated that NaOCl and 17% EDTA solutions increased Protaper files surface roughness indicating deterioration that act as stress concentration areas and cause microcracks that may file's cyclic fatigue resistance.

This study focuses on the effect of root canal irrigation on the cyclic fatigue and study of the fractured surface of CM wires NiTi instruments after immersion in four irrigants for either 5 or 10 minutes. The irrigants used are saline, chitosan 0.3%, chitosan 0.5% and EDTA 17%.

Method

Twenty four size 20 MPro files (Foshan stardent equipment co, limited gungdon, China) were used in this study, divided into four groups of 6 files each according to irrigant: Group I saline, Group II chitosan 0.3%, Group III chitosan 0.5% and Group IV EDTA 17% . Each group was further divided according to immersion periods :5 and 10 minutes.

Before testing, each file was observed for defects with stereo microscope (Leica MZ 12.5, Heerbrugg, Germany) under $\times 10$ magnification. The chitosan irrigants were prepared using powder (Sigma-Aldrich Chemical Co., Germany) dissolved in 1% acetic acid at room temperature. The concentration of the final solutions were 0.3 and 0.5 mg/mL. All files were cleaned after immersion in ultrasonic cleaner to remove traces of irrigants.

Fatigue tests were performed using a static cyclic fatigue testing device, composed of two parts First section consisted of the stainless steel block part, which has an artificial canal with an inner diameter of 1.5 mm, a 60° angle of curvature, a curvature radius of 3 mm and has a Plexiglass preventive cover. The latter section included an Instron universal testing machine (Massachusetts, USA) machine with a hand piece holder part that positioned the hand piece in a precise relationship to the stainless steel block when testing file inside the artificial canal. The two main parts of the

apparatus were attached to a steel base. The file to be tested was inserted in the artificial canal to Working length of 16 mm. The motor was set at a Continuous rotational speed 450 rpm and Torque of 2 newton and all files were rotated until fracture occurred .

Parameters recorded were time to fracture, number of cycles to failure and mean length of unfractured segments using a digital micro caliper.

The detached fragment was examined under scanning electron microscope at various magnifications (400x to 1000x) (Quanta 250 FEG, with accelerating voltage 30 K.V., Magnification 14x up to 1000000. FEI company, Netherlands) to identify the crack initiation site and number of crack origins per group.

Results

The cyclic fatigue study statistical analysis was performed using IBM SPSS Statistics Version 2.0 for Windows. Data was presented as mean and standard deviation (SD). The significance level was set at $P \leq 0.05$. Kolmogorov-Smirnov and Shapiro-Wilk tests were used to assess data normality.

Because of the small sample size, a non-parametric test was used. Kruskal-Wallis test followed by Mann-Whitney U test was performed to compare between the different irrigants at each immersion time. Mann-Whitney U test was conducted to compare between the two immersion times within each irrigant group.

Time to fracture and Number of cycles to failure (NCF): At 5 mins immersion time, there was a statistically significant difference between the different irrigants. Chitosan 0.3 group showed the significantly highest mean value while the control group showed the lowest. At 10 mins immersion time, there was no statistically significant difference between Chitosan 0.3, Chitosan 0.5 and EDTA groups. The saline and EDTA groups had significantly lowest mean value. Within the saline and Chitosan 0.5% groups, there was no significant difference at the two immersion times but it existed within Chitosan 0.3% and EDTA groups.

Un Fractured segment length: At 5 mins immersion time, there was no statistically significant difference in mean length of unfractured segments between saline, Chitosan 0.3% and Chitosan 0.5% groups. At 10 mins immersion time, there was no statistically significant difference in mean length of unfractured segments

between the saline and Chitosan 0.3% groups. Chitosan 0.5% and EDTA groups had no statistically significant difference in mean fracture length. Within the saline, Chitosan 0.3% and Chitosan 0.5% groups, there was no significant difference in mean length of the unfractured segments between the two immersion times but it existed within EDTA group.

The scanning electron microscope study: The photomicrographs of magnifications 400x to 1000x were viewed blindly by two viewers and the number of crack origins per group were recorded. From the overall view, the crack initiation site were identified by noting the

chevron pattern, also called “herringbone marks”⁽¹⁵⁾ on the fracture surface. The fractographic appearance of a fatigued metallic material always progresses from the crack origin to a zone of fatigue striations and, finally, a region of dimple rupture⁽¹⁶⁾.

Results of crack origin sites showed 3 sites per sample in 100% of Group I (saline). One site in 100% of samples of Group II (Chitosan 0.3%) and 2 sites in 100% of samples of Groups III (Chitosan 0.5%) and IV (EDTA)

The number of crack origins did not get affected by the immersion times applied.

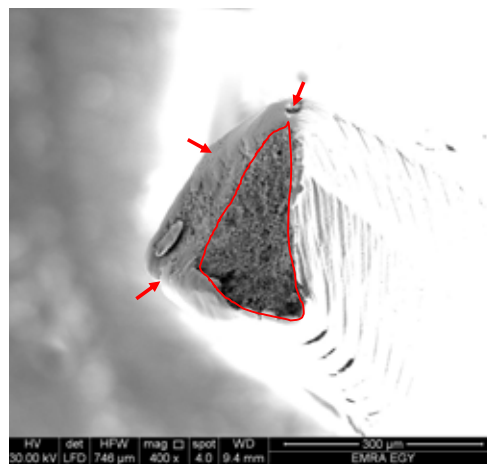


Figure 1: Photomicrograph of a sample of group I saline after 5 minutes immersion period showing the fracture surface of MPro file with region of fatigue crack propagation and dimple area outlined (redline) with three crack origins (arrows)

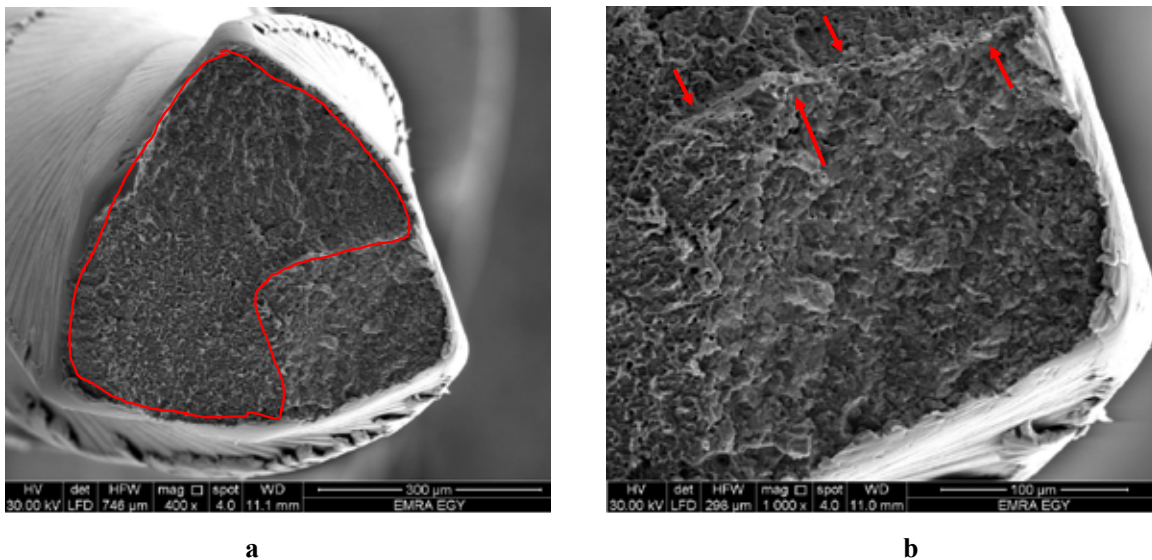


Figure 2: Photomicrograph of a sample of group II Chitosan 0.3% after 10 minutes immersion period with different magnifications showing (a) the fracture surface of MPro file with region of fatigue crack propagation and dimple area outlined (redline) (b) the magnified crack origin site (arrows)

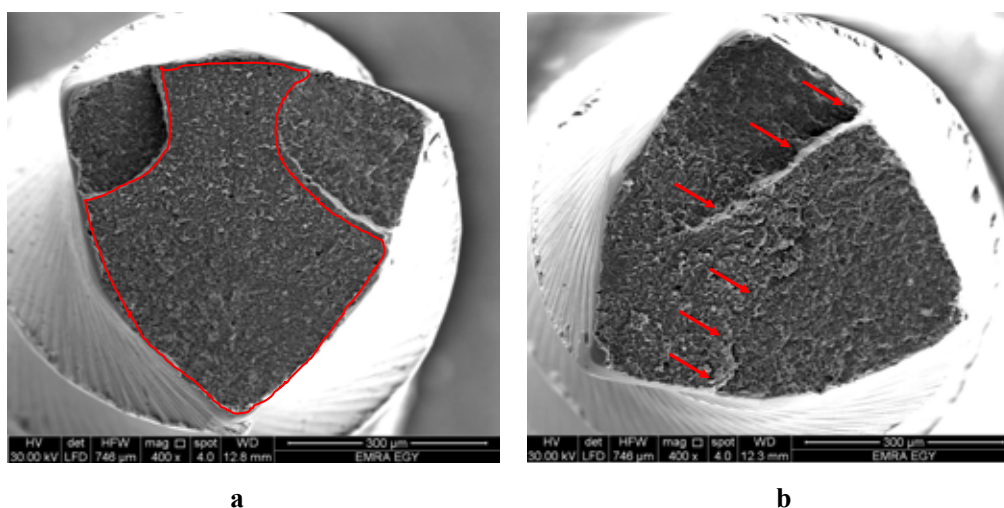


Figure 3: Photomicrographs of (a) sample of group III chitosan 0.5 % after 5 minutes immersion and (b) sample of group IV EDTA 17% after 10 minutes immersion period showing the fracture surface of MPro file with region of fatigue crack propagation and dimple area outlined (redline) with two crack origin sites (arrows)

Discussion

The removal of pulpal tissue, microorganisms, and their products is important for successful root canal treatment^(17,18). In studies examining the cyclic fatigue resistance of NiTi files, it is difficult to eliminate all factors that can affect study results.⁽¹⁹⁾ Although using extracted human teeth in cyclic fatigue studies represents clinical conditions, it is not possible to standardize the anatomical variations of teeth;⁽²⁰⁾ Thus in the present study, standard stainless steel artificial canals were employed to minimize various factors that can influence the results.

Capar et al⁽²¹⁾ reported that HyFlex CM file had high resistance to cyclic fatigue. Authors attributed that to the thermomechanical processes applied during its production and emphasized that other CM files could show same property. Both Hyflex and the Mpro file share same thermomechanical processes applied during production. The NiTi instruments were immersed in saline, Chitosan 0.3%, Chitosan 0.5% or EDTA 17% at 37°C for 5 or 10 min.

Factors influencing the fatigue resistance include file design, cross-sectional geometry and diameters of core, tip size, taper⁽²²⁾ radii, degree of curvature, rotation speed, torque, and movement kinematics.^(23, 24) In the present study, we used one type of file and same size in standardized artificial canals (60° angle of curvature

and a curvature radius of 3 mm) and same rotation speed (450 rpm), rotation type (continuous) were set to leave only two variables the type of irrigant and the time of immersion of the file in it.

Our results of the time to fracture and number of cycles to failure in the cyclic fatigue part of the study showed that chitosan 0.3% recorded the highest mean 12.93 ± 4.21 minutes and 5821.5 ± 1895.35 cycles to fracture while the saline recorded the lowest mean 2.82 ± 0.10 and 1230.33 ± 161.69 cycles to fracture. EDTA and chitosan 0.3 % had a significantly different value from 5 to 10 minutes, they had a more corrosive action by time elapsed to become closer to the mean recorded by chitosan 0.5 %. These results came higher than those recorded by Bhattand Rajkumar⁽²⁵⁾ and shen et al.,⁽²⁶⁾ where hyflex CM and typhoon files. The difference in the results may be due to different methodology where they used the EDTA gel during the test not as an immersion irrigant before testing. Our results were also higher than the results of Dagna et al.,⁽²⁷⁾ where they used dynamic cyclic fatigue testing after immersion of Mwire files in EDTA for 1 min or 5 mins. Increased fracture resistance of the file can be due to the crack propagation mechanism which presented as a large number of highly branched cracks that propagates very slowly in contrary to superelastic NiTi form where only a few fatigue cracks nucleates and propagates at faster speed.

The results of the unfractured segment length showed files breakage at apical 5 mm in all groups. At 10 minutes files broke more coronally at the 10 mm range with no significant difference among groups. Our results came close to those by pedullaet al.,⁽²⁸⁾. The EDTA group the 10 min group was significantly different than the 5 min group but still in the middle part of the file at the 10 mm range.

In the scanning electron microscope study, the photomicrographs were viewed blindly by two viewers and the number of crack origins per group were recorded. Results showed 100% of Group I (saline) showed 3 sites of crack origins per sample. 100% of samples of Group II (Chitosan 0.3%) showed one site of crack origin, 100% of samples of Groups III (Chitosan 0.5%) and IV (EDTA) showed two sites of crack origin. According to del Carpio- Perochena et al 2015⁽¹¹⁾ chitosan had same chelating effect as EDTA and had the potential to be used as an alternative to EDTA in root canal, this may explain the similar effects they had on the file when chitosan was used in a higher percent 0.5%, another similarity of action may be due to the preparation of chitosan solution by its dissolution in acetic acid.

Conclusion

Chitosan 0.3 % did not decrease cyclic fatigue and caused low number of crack origins of the preheated machined CM wire Mpro endodontic files when used for 5 or 10 minutes.

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Conflict of Interest: We the authors have no conflict of interest with any researchers and companies

We funded this research independently and we both contributed to the practical part of the study and the theoretical part

Ethical Clearance: This study is an invitro study that did not need an ethical committee approval cause no animal or human trial were involved and no human teeth or serums were tested.

References

1. Yahata Y, Yoneyama T, Hayashi Y, et al. Effect of heat treatment on transformation temperatures and bending properties of nickel titanium endodontic instruments. *Int Endod J* 2009;42:621-6.
2. Ninan E, Berzins DW. Torsion and bending properties of shape memory and superelastic nickel-titanium rotary instruments. *J Endod* 2013; 39: 101-104.
3. Singh H and Kapoor P Hyflex CM and EDM Files: Revolutionizing the Art and Science of Endodontics. *J Dent Health Oral Disord Ther* 2016, 5(7): 00182.
4. Cai JJ, Tang XN & Ge JY. Effect of irrigation on surface roughness and fatigue resistance of controlled memory wire nickel-titanium instruments. *Int Endod Journal* 2017; 50: 718–724.
5. Gambarini G, Gergi R, Naaman A, Osta N, Al Sudani D (2012) Cyclic fatigue analysis of twisted file rotary NiTi instruments used in reciprocating motion. *International Endodontic Journal* 45, 802-6.
6. Gambarini G, Grande NM, Plotino G et al. (2008) Fatigue resistance of engine-driven rotary nickel-titanium instruments produced by new manufacturing method. *Journal of Endodontics* 34, 1003–5.
7. Praisarnti C, Chang JW, Cheung GS (2010) Electropolishing enhances the resistance of nickel-titanium rotary files to corrosion-fatigue failure in hypochlorite. *Journal of Endodontics* 36, 1354–7.
8. Zehnder M. Root canal irrigants. *Journal of Endodontics* 2006; 32:389–98.
9. Brito PR, Machado de Oliveria JC, Alves FR, De-Deus G, Lopes HP et al. Comparison of the effectiveness of three irrigation techniques in reducing intracanal *Enterococcus faecalis* populations: an in vitro study. *J Endod.* 2009; 35:1422–7.
10. Wali IE, Eid GEM, Omar WA and ElRafie S. The Antimicrobial Efficacy of Ozonated Water, Chlorhexidine and Sodium Hypochlorite against Single Species Biofilms of *Enterococcus faecalis* and *Candida albicans*. *Egyptian Journal of Medical Microbiology.* 2008; 17:419-427.
11. del Carpio- Perochena A, Bramante C M, Duarte MAH, de Moura MR, Aouada FA, Anil Kishen A. Chelating and antibacterial properties of chitosan nanoparticles on dentin .*rde.2015.40.3.195*
12. Gusiyska A, Dyulgerova E, Vassileva R, Gyulbenkiyan E. The Effectiveness of a Chitosan-Citrate Solution to Remove the Smear Layer in Root Canal Treatment- An in-vitro study.

- International Journal of Science and Research (IJSR). 2016;5;169-1174.
13. Ametrano G, D'Anto V, Di Caprio MP, Simeone M, Rengo S, Spagnuolo G (2011) Effects of sodium hypochlorite and ethylenediaminetetraacetic acid on rotary nickel-titanium instruments evaluated using atomic force microscopy. *International Endodontic Journal* 44, 203–9.
 14. Kuhn G, Tavernier B, Jordan L (2001) Influence of structure on nickel-titanium endodontic instruments failure. *Journal of Endodontics* 27, 516–20
 15. Brooks CR, Choudhury A. Failure analysis of engineering materials. New York: McGraw-Hill; 2002.
 16. Hull D. Fractography: observing, measuring and interpreting fracture surface topography. Cambridge, UK: Cambridge University Press; 1999.
 17. Basmadjian-Charles C, Farge P, Bourgeois D, Lebrun T. Factors influencing the long-term results of end-odontic treatment: a review of the literature. *Int Dent J* 2002;52:81–6.
 18. Siqueira JF, Rôças IN. Clinical implications and microbiology of bacterial persistence after treatment procedures. *J Endod* 2008;34:1291–301.
 19. Pereira ES, Gomes RO, Leroy AM, Singh R, Peters OA, Bahia MG, et al. Mechanical behavior of M-Wire and conventional NiTi wire used to manufacture rotary endodontic instruments. *Dent Mater* 2013;29:318–24.
 20. Berendt C, Yang J. Endodontic instruments with improved fatigue resistance. In: *International Conference on Shape Memory and Superelastic Technologies*; 2006: ASM International Pacific Grove, CA; 2006.
 21. Capar ID, Ertas H, Arslan H. Comparison of cyclic fatigue resistance of novel nickel-titanium rotary instruments. *Aust Endod J* 2015;41:24–8.
 22. Zhang E-W, Cheung GS, Zheng Y-F. Influence of cross-sectional design and dimension on mechanical behavior of nickel-titanium instruments under torsion and bending: A numerical analysis. *J Endod* 2010;36:1394-98.
 23. Martin B, Zelada G, Varela P, Bahillo J, Magán F, Ahn S, et al. Factors influencing the fracture of nickel-titanium rotary instruments. *Int Endod J* 2003;36:262-66.
 24. Pérez-Higueras JJ, Arias A, de la Macorra JC. Cyclic fatigue resistance of K3, K3XF, and twisted file nickel-titanium files under continuous rotation or reciprocating motion. *J Endod* 2013;39:1585-88.
 25. Bhatt A and Rajkumar B. A comparative evaluation of cyclic fatigue resistance for different endodontic NiTi rotary files: An in-vitro study. *Journal of Oral Biology and Craniofacial Research* 9 (2019) 119–121.
 26. Shen Y, Qian W, Abtin H, Gao Y and Haapasalo M. Effect of Environment on Fatigue Failure of Controlled Memory Wire Nickel-Titanium Rotary Instruments. *JOE* 2012;38:376-80.
 27. Dagna A, Poggio C, Beltrami R, Chiesa M and Bianchi S. Cyclic Fatigue Resistance of Three Niti Single-File Systems after Immersion in EDTA. *Dentistry* 2013, 4:1
 28. Pedulla E, Lo Savio F, Boninelli S, Plotino G, Nicola M, Grande, La Rosa G, and Rapisarda E. Torsional and Cyclic Fatigue Resistance of a New Nickel-Titanium Instrument Manufactured by Electrical Discharge Machining. *J Endod* 2016;24:156-159.

Effect of Educational Protocol on Improving Nurses' Knowledge and Practice Regarding Skin Traction

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Abstract

The highest prevalence of traumatic fractures that need to use of orthopedic intervention such as skin traction has increased. This study aimed to the effect of educational protocol on improving nurses' knowledge and practice regarding skin traction. A quasi-experimental research design was used on convenience sample composed of 26 nurses working at orthopedic unit at Minia University and Minia General Hospitals. A Structured interviewing questionnaire about skin traction nurses' knowledge questionnaire and nursing skin traction observational checklist were used. A significant improvement in nurses' knowledge and practice about nursing care and principles of skin traction in post test. Implementation of the educational protocol. Increased nurses education and training for skin traction and periodic evaluation measures for these nurses should be constructed.

Keywords: Educational protocol, Nurses, Skintraction.

Introduction

Traction is the application of a pulling force to a part of the body to correct direction and magnitude for immobilize fractured body part and obtain its therapeutic effects through an extended period, include skin or skeletal traction. Skin traction may cause pressure exerted on the skin which results in skin damage and a risk of ischemia⁽¹⁾.

Orthopedic nursing specialty mainly focuses on musculoskeletal disorders, and complications⁽²⁾. An orthopedic nursing role is providing high quality nursing care to traction patients, through providing standardized patient care that is evidenced based practice, as performs musculoskeletal assessment, assists with traction, and administers prescribed pain medication. An orthopedic nurse support and train the patient for mobility, educates

the patient correct technique about how to protect their joint and bone health, and develop nursing care plan to minimize complications^(3,4).

Nurses should have a high level of nursing knowledge and standardized care for effective practice by education which is the most important aspect of orthopedic nurse role. An orthopedic nurse is an excellent educator that gives patients detailed, simple and comprehensive information. Who are well versed in educating patients on the risks and complications of orthopedic treatment and surgery^(5,6).

Nurses are also responsible for family members education who have may be involved in patients' care as concerns about pain management, and discharge service coordination⁽⁷⁾.

Nursing is deliberate as caring for a patient in a set of health related situations. This caring also involves teaching about health and the prevention of illness; nurses play a key role in promoting higher standards of health^(8,9). The nurse should be updated her knowledge and practice in the current field.

The educational nursing protocol contains basic

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guidelines for nursing knowledge and practices which would improve the quality of nursing care for skin traction patients⁽¹⁰⁾.

Significant of the Study: Fractures are common with younger patients resulting from high-energy physical traumas such as motor vehicle accidents and usually occur in the absence of any underlying disease⁽¹¹⁾.

Traction is commonly used for treating hip or femur fractures with regard to this fact and taking into account the vital role of orthopedic nurses in the care of patient with traction. So special orthopedic nursing training protocol was used and presented to these nurses in order to increase nurses' knowledge and also improve their practice to overcome these possible complications and increase the efficiency nursing care.

Methodology

Aim: The current study aims to investigate effect of educational protocol on improving nurses' knowledge and practice regarding skin traction.

Hypothesis: There are positive effect of educational protocol on improving nurses' knowledge and practice regarding skin traction.

Method :

A quasi-experimental research design was utilized to meet the aim of this study. A convenience study sample who were available nurses present during time of data collection, who were working at orthopedic unit with total number (26), in both Minia University and General Hospitals. Tools, A Structured interview questionnaire which was developed by the researcher it contains: Socio-demographic characteristics of nurses and their knowledge about skin traction⁽¹²⁾. An observational checklist was adopted from Royal College of Nursing, (2017)⁽¹³⁾ and modified by researchers. The total scores ranged from 0 to 37 score percentage. The nurses' practice and knowledge were satisfactory level if the score is 60% or more and unsatisfactory if less than 60%.

A pilot study on (10%) from nurses, was conducted to test clarity & completeness of the study tool According to the results of pilot, the needed modification, omissions and/or additions were done.

Validity and Reliability: The tools were submitted to a panel of five experts in (Medical & Surgical-Nursing Administration) at Minia and Assuit University to confirm content validity. Reliability of the tools were done and calculated statistically by Cronbach's alpha test = (0.87).

Procedure: The researcher's prepared educational booklet after assessment of nurse's knowledge to identify the weak point, and then give educational protocol skin traction care as using soft wear presentation- based on the review of relevant literature and books about nursing care of a patient with skin traction. The fieldwork was carried out through a period of 6 months starting from March to August 2018. The researchers first introduced themselves to nurses and give them a complete background about the study, then the pre-test format was distributed in order to collect the required data. The content of the protocol was designed based on the actual educational needs assessment of the studied nurses. Consequently, the educational protocol was done through six sessions. The whole was implemented during morning shifts. The period was estimated for each session ranged from 30 to 45 minutes. The first two sessions began by explaining the theoretical information about definition of skin traction, causes, precipitated factors and modalities of management the next four sessions were concerned to the practical part about principles of traction and nursing care of traction. Finally, a summary of what has been taught during the previous session also the objectives of the new session were always done before beginning any session.

Teaching method of the theoretical part was introduced using discussion, demonstration and re-demonstration. Each nurse was given a copy from hand-outs powered by photos, an open conversation was made between researchers and nurse to ensure that he understands, answer any query and verify information and practice. The effect of the learning protocol on the nurses' condition was reached by assessing the nurse's scores immediately and after two month educational protocol (follow up).

The statistically analysis was done using SPSS-22 statistical software package. The content of each tool was analyzed and statistical significance was used at P. value <0.05

Results

Table (1): Distribution of personal data characteristics for studied nurses n = 26

Items	No	%
Age/Years:		
< 20	2	7.6
20 < 30	16	61.6
30 < 40	8	30.8
$\bar{x} \pm SD$	29.0 \pm 9.32	
Sex		
Male	7	27
Female	19	73
Qualification of Nurses:		
Bachelor	10	38.4
Diploma of Technical Nursing	9	34.6
Diploma of Nursing School	7	27.0
Years of Experience:		
< 5	8	30.8
5 < 10	14	53.9
10 < 15	4	15.3
$\bar{x} \pm SD$	8.70 \pm 0.59	
Previous training courses about skin traction:		
Yes	4	15.3%
No	22	84.7%
Hospitals:		
Minia University Hospital	14	53.8
Minia General Hospital	12	46.2

Table (1) indicated that 61.6% of the studied nurses of Nursing School and (53%) of them had 5 < 10 years their age were ranging from 20 < 30 years old and 73% of experiences, female, also 27% of them were graduated from Diploma

Table (2): The total scores of the studied nurses' knowledge related to skin traction pre/post and follow up protocol. n = 26

Nurses' Knowledge	Pre (N/%)	Post (N/%)	Follow (N/%)	X ²	P. value
Definition and complication				14.45	0.02*
Satisfactory	4(15.3)	24(92.3)	21(80.8)		
Unsatisfactory	22(84.7)	2(7.7)	5(19.2)		
Principles & intervention				17.86	0.04*
Satisfactory	2(7.7)	23(88.4)	22(84.7)		
Unsatisfactory	24(92.3)	3(11.6)	4(15.3)		
Nursing care				15.35	0.05*
Satisfactory	8(30.8)	24(92.3)	23(88.4)		
Unsatisfactory	18(69.2)	2(7.7)	3(11.6)		
Total nurses' knowledge				21.97	0.001*
Satisfactory	9(34.7)	23(88.4)	22(84.7)		
Unsatisfactory	17(65.3)	3(11.6)	4(15.3)		

Table (2), demonstrates that an unsatisfactory implementation of the protocol While there was an knowledge about skin traction and complication, improvement in the level of knowledge immediately principles and nursing care of skin traction before after implementation of the protocol at $p = .001^*$

Table (3): The total scores of the studied nurses’ practices related to skin traction pre/post and follow up program. n = 26

Items	Nurses practices pre/post and follow up program						F. test	P. value
	Pre		Post		Follow up			
	Satisfactory	Unsatisfactory	Satisfactory	Unsatisfactory	Satisfactory	Unsatisfactory		
	N (%)							
Principles about traction	7(27.0)	19(73.0)	24(92.3)	2(7.7)	23(88.4)	3(11.6)	17.62	.003*
prevent of the cardiovascular and respiratory system problem	4(15.3)	22(84.7)	22(84.7)	4(15.3)	21(80.8)	5(19.2)	17.78	.002*
Prevention of neurovascular and musculoskeletal system problem	4(15.3)	22(84.7)	24(92.3)	2(7.7)	23(88.4)	3(11.6)	14.45	0.003*
Prevention urinary tract problem	4(15.3)	22(84.7)	23(88.4)	3(11.6)	21(80.8)	5(19.2)	15.34	0.005*
Skin care	2(7.7)	24(92.3)	22(84.7)	4(15.3)	21(80.8)	5(19.2)	19.76	0.003*
Avoid constipation	5(19.2)	21(80.8)	22(84.7)	4(15.3)	21(80.8)	5(19.2)	16.56	0.004*
Total of nurses’ practices about traction.	5(19.2)	21(80.8)	25(96.1)	1(3.9)	23(88.4)	3(11.6)	55.34	0.001*

Table (3) illustrates that 80%of nurses’ practice were unsatisfactory before application of protocol. While there was improvement in level of practice post and follow up implementation of the protocol, with high significant statistical difference in total nurses’ practice about skin traction at $p = 0.001^*$.

Table(4): The relation between the studied nurses’ knowledge pre/post and follow up protocol about skin traction and their characteristics, n = 26

Items	Pre		Post		Follow up		X ² P. value
	Satisfactory	Unsatisfactory	Satisfactory	Unsatisfactory	Satisfactory	Unsatisfactory	
	N(%)		N(%)		N(%)		
Age/Years:							
< 20	0(00)	2(7.7)	2(7.7)	0(00)	2(7.7)	0(00)	33.9 0.02*
20 < 30	4(15.3)	12(46.2)	14(53.8)	2(7.7)	11(42.4)	5(19.2)	
30 < 40	2(7.7)	6(23.1)	7(27)	1(3.8)	5(19.2)	3(11.5)	
Qualification of nurses:							
Bachelor	2(7.7)	8(30.8)	9(34.6)	1(3.8)	7(27)	3(11.5)	22.6 0.04*
Diploma of Technical Nursing.	3(11.5)	6(23.1)	8(30.8)	1(3.8)	7(27)	2(7.7)	
Diploma of Nursing School	2(7.7)	5(19.2)	7(27)	0(00)	6(23.0)	1(3.8)	
Years of experience:							
< 5	2(7.7)	6(23.0)	8(30.8)	0(00)	7(27)	1(3.8)	32.7 0.01*
5 < 10	3(11.5)	11(42.4)	12(46.2)	2(7.7)	12(46.2)	2(7.7)	
10 < 15	2(7.7)	2(7.7)	4(15.3)	0(00)	3(11.5)	1(3.8)	

Table (4) shows a significant statistical difference between nurses’ knowledge and demographic characteristic with the highest knowledge in post-test

and follow up was among 20 < 30 years, bachelor and experience from 5:10 years.

Table (5): The relation between the studied nurses’ practices pre/post and follow up protocol bout skin traction and their characteristics n= 26

Items	Pre		Post		Follow up		X ² P-value
	Satisfactory	Unsatisfactory	Satisfactory	Unsatisfactory	Satisfactory	Unsatisfactory	
	N(%)						
Age in Years:							
< 20	1(3.8)	1(3.8)	2(7.7)	0(00)	2(7.7)	0(00)	34.6 0.02*
20 < 30	5(19.2)	11(42.5)	15(57.7)	1(3.8)	13(50.1)	3(11.5)	
30 < 40	3(11.5)	5(19.2)	7(27)	1(3.8)	6(23.0)	2(7.7)	
Qualification of Nurses:							
Bachelor	3(11.5)	7(27)	9(34.7)	1(3.8)	8(30.7)	2(7.7)	25.7 0.04*
Diploma of Technical Nursing	2(7.7)	7(27)	8(30.7)	1(3.8)	7(27)	2(7.7)	
Diploma of Nursing School	1(3.8)	6(23.0)	7(27)	0(00)	5(19.2)	2(7.7)	
Years of Experience:							
< 5	1(3.8)	7(27)	8(30.7)	0(00)	6(23.0)	2(7.7)	33.8 0.01*
5 < 10	4(15.3)	10(38.6)	13(50.2)	1(3.8)	12(46.3)	2(7.7)	
10 < 15	1(3.8)	3(11.5)	4(15.3)	0(00)	3(11.5)	1(3.8)	

Table (5) shows a significant statistical difference between nurses’ practice and demographic characteristic. It was observed that the highest practice in post-test and follow up was among 20 < 30 years, bachelor and experience from 5:10 years.

Table (6): The correlation between the total scores of the nurses’ knowledge and practices in the studied hospitals n= 26

Knowledge	Practices	
	r	P. value
Minia University Hospital	0.92	0.001*
Minia General Hospital	0.90	0.001*

*= Significant

Table (6) demonstrates strong positive correlation r (0.92 – 0.90) between nurses’ knowledge and practice in both hospitals respectively.

Discussion

This research indicates that unsatisfactory knowledge about skin traction and their complication, principles of traction and nursing care, and observed the

highest percent of nurses didn’t attain any training, before the implementation of the educational protocol. While there was an improvement in the level of knowledge post implementation of the protocol which noticed that the majority of the nurses have a satisfactory level of knowledge in follow up. There was high significant statistical difference in total nurses’ knowledge about skin traction. These study findings were consistent with the study findings of⁽¹⁴⁾ who reported that more than two thirds of nurses had a sufficient knowledge regarding care of patients with external fixation

Also there is an agreement between this study results and the results of study that is done by⁽⁵⁾ showed that only 12% of the respondents had knowledge on complication of skin traction. The current research study is contradictory with⁽⁸⁾ who demonstrated that distributing the respondents who participated in this study, one-third had high level of awareness, majority had moderate level of awareness and 6.4% had low level of awareness.

The present study showed that the majority of nurses were unsatisfactory practice pre application of protocol. While there was an improvement in the level of practice post and follow up post implementation of the protocol,

which agreement with⁽¹⁵⁾ reported that most of the studied nurses had an unsatisfactory total practice support to the research results, the practice of respondents, less than half had high level of practice. Additionally⁽¹¹⁾ mentioned that nurses should increase their knowledge and performance in the field of management of patients in orthopedic departments, which disagree with⁽¹⁶⁾ reported that majority of nurses had poor practice scores related to nursing care plan after application of traction.

The present study that the relation between the studied sample practice pre/post and follow up protocol about skin traction and their characteristics; there was a significant statistical difference between nurses' practice and demographic characteristic. It was observed that the highest practice in post-test and follow up was among 20 < 30 years, bachelor, and experience from 5:10 years. In contrast⁽⁸⁾ reported in their studies that found association between level of awareness and age and education, also between level of practice and age, education, and occupation.

In the current study revealed that the positive correlation between the total scores of the nurses' knowledge and practices in the studied hospitals, evidence these findings were in congruence with⁽⁷⁾ which illustrate that there is a highly statistically significant positive correlation between total nurses' knowledge scores and total practice scores.

Conclusion & Recommendations: Lack in nurses' knowledge and practice regarding skin traction care before application of the educational protocol, while improvement was observed after application of an educational protocol. Training- based on education services for nurses may motivate their knowledge regarding nursing management of the orthopedic patients.

Source of Funding: Self-funding

Conflict of Interest: Nil

Ethical Clearance: An official permission was obtained from the ethical committee in faculty and the directors of the two hospitals after explaining the nature of the work and aim was explored for every interviewed nurses. An ethical right to agree or refuse participation in the study. They informed that their information will kept confidential and used only for the purpose of the study and there was no harm for their participation.

References

1. Tosun B, Aslan O, Tunay S. Preoperative position splint versus skin traction in patients with hip fracture: An experimental study. *International journal of orthopaedic and trauma nursing*. 2018; 28:8-15.
2. Obalum Dc, Sb. I. Current Place of Traction in Orthopaedic and Trauma Practice: A Review. *Ortho & Rheum Open Access J* 2019;13(5):555874.
3. Mohsin A, Atiyah H. Nurses knowledge Toward Cast Complications in Orthopedic Ward at Al-Najaf AL-Ashraf Hospitals. 2016.
4. Mersal FA, Mersal NA, Hussein HA. Effect of Educational Guidelines for Prevention of Immobilization Complications on Caregivers' Performance and Patients' Functional Condition. *American Journal of Nursing Research*. 2017;5(2):32-41.
5. Kambli S. Fractured Patient's Knowledge Regarding Care and Treatment. *International Journal of Science and Research (IJSR)*. 2014;3(7):1178-81.
6. WHO. Transforming and scaling up health professionals' education and training:. 2014, Published by World Health Organization. (Available): https://apps.who.int/iris/bitstream/10665/93635/1/9789241506502_eng.pdf.
7. Wahba MM, Qalawa SA, El-Ata ABA, Gouda RAK. Nurses' Performance for Orthopedic Patients with Traction or Internal Fixation. *Port Said Scientific Journal of Nursing*. 2017;4(2):193-218.
8. Panta S, Ban RK, Pandey B, Dhital A. Awareness and Practice of Caregivers Regarding Prevention of Complications in Traction Patient. *European Journal of Pharmaceutical and Medical Research*, *ejpmr*. 2019;6(1): 439-44.
9. Halse KM, Fonn M, Christiansen B. Health education and the pedagogical role of the nurse: Nursing students learning in the clinical setting. *Journal of Nursing Education and Practice*. 2014;4(3):30-7.
10. Centeno J. Method of Teaching and Learning of the Elderly: Care in Rehabilitation. *Canadian Journal of Nursing Informatics*. 2011;6(1).
11. Adib Hajbaghery M, Moradi T. Quality of care for patients with traction in shahid beheshti hospital in 2012. *Arch Trauma Res*. 2013;2(2):85-90.

12. Lewis SL, Dirksen SR, Heitkemper MM, Bucher L. *Medical-Surgical Nursing: Assessment and Management of Clinical Problems*,. 9, editor: Elsevier; 2014.
13. Royal, College, of, Nursing. *Traction: principles and application*. 2015; .
14. Elhakeem S. Standards of Nursing Care for Patients Undergoing External Fixation in Trauma Unit At Assiut University Hospital. *Assiut Scientific Nursing Journal*. 2014;2:128-35.
15. Poudyal S, Neupane M, Lopchan M. Knowledge on prevention of complications related to immobility among caregivers of orthopedic patients at selected hospitals of Chitwan district. *Journal of Chitwan Medical College*. 2015;3(4).
16. El-Dakhakhny A. Impact of an educational program on nurses' performance toward children in Thomas traction. *International journal of orthopaedic and trauma nursing*. 2010;14:206–19.

Sonographic Measurement of Renal Parenchymal Thickness in Healthy Adults

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Abstract

Background: Renal parenchymal thickness (RPT) was found to be a vital parameter that can offer prognostic information on end-stage kidneys diseases. The aim of the current study was to establish normal RPT value in our population; and to reveal its relationship with age, height, and weight.

Method: It was a cross-sectional analytic study conducted in the department of radiology/Azaditeaching hospital at Kirkuk city, where the sonographic assessment of RPT was performed from January 2016 to May 2018 for 253 adults with different complaints; Individuals with history of medical disorders/drugs known to affect the kidney, malignancy, pregnancy, those who had renal variant/pathology during ultrasound examination and abnormal laboratory tests were excluded from the study. Differences of RPT between two sides and gender were assessed with student's t-test, and its correlation with age, height, and weight were assessed with the Pearson's correlation coefficient (r).

Results: In males, the mean value (SD) of right RPT was 18.2(3.2) mm, and left RPT was 18.9(3) mm. In females, it was 16.4(2.4)mm in the right kidney and 16.9 (2.4) mm in left kidney. There was no statistical difference between RPT of the right and left kidneys ($p = 0.0001$). The RPT was significantly thicker in males (18.6 mm versus 16.7 mm) ($P = 0.0001$). There was significant moderate and strong negative correlation with age in right and left kidney respectively. There was a positive correlation with a person's height and weight which was significant ($P = 0.00001$).

Conclusion: Our population parenchymal thickness values are different from others, it is 18.6 mm male and 16.7 mm in female, parenchyma is considered thin if it was less than 13 mm in males and 10 mm in females, its decreased with age, taller and more obese persons have thicker parenchyma on both sides.

Keywords: Adults, healthy, measurement, Renal Parenchymal thickness (RPT), Sonographic.

Introduction

Renal parameters measurement by ultrasound is vital when evaluating patients with probable renal disease;^[1]

however, it requires prior information of actual normal renal measurement values in each specific population. Cortical thickness is differing according to ethnic group according to height and weight or even in twins.^[2,3,4] Chronic systemic diseases such as hypertension and diabetes also affect the kidneys parameters including the parenchymal thickness. ^[5]Renal ultrasound is inexpensive, simple and can be done at the bedside to provide the clinician with kidneys important anatomical details with low inter-observer variability. ^[6] Renal length and cortical thickness have been studied widely in animals and their parameters are well documented^[7,8]. In humans, on the other hand, there have been only a few

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studies considered to measure these parameters in adults who do not have a renal disease.^[9]

Since RPT measurement can offer prognostic information on end-stage kidneys diseases.^[10] This study was done to develop our population unique RPT in adults devoid of renal diseases, and to define its relationship with age, height, and weight.

Materials and Method

The permission was obtained from the Azadi Teaching Hospital Committee and informed consent was obtained from each individual before data collection was begun.

Study Group: This study was a cross-sectional study conducted in the department of Radiology in Azadi Teaching Hospital/Kirkuk/Iraq within a period from January 2016 to May 2018, for 253 adult patients how referred to perform abdominal ultrasound examination for different causes. The exclusion criteria were patients with known renal disease, conditions that were known to affect the kidney, such as diabetes and hypertension, those with prolonged use of toxic drugs,

malignancy, and pregnancy. Those who had congenital renal variants, and renal pathology during ultrasound examination were excluded from the study too. Other criteria for exclusion was those with abnormal laboratory tests, including blood urea nitrogen >20 mg/dL, serum creatinine >1.2 mg/dL; the presence of protein casts, or more than five white and red blood cells in the general urine examination. The laboratory tests were done at the same hospital. Age in years, weight in kilograms, and height in centimeters for each patient were recorded.

Ultrasound examination: was done using 3.5 MHZ convex transducer (Fukoda Denshimachine; Tokyo, Japan) in lateral position during suspended respiration, longitudinal image in midsagittal scan for kidneys was displayed and its outline, poles and central sinus echocomplex was seen. Dorsal RPT was measured at the middle third of the kidney. RPT was measured as the distance between renal cortex–perinephric fat interface and renalsinus–Parenchymal interface (Fig 1). The patients required no prior preparation. The examination was done by the same radiologist with 14 years of experience in abdominal ultrasound examinations.

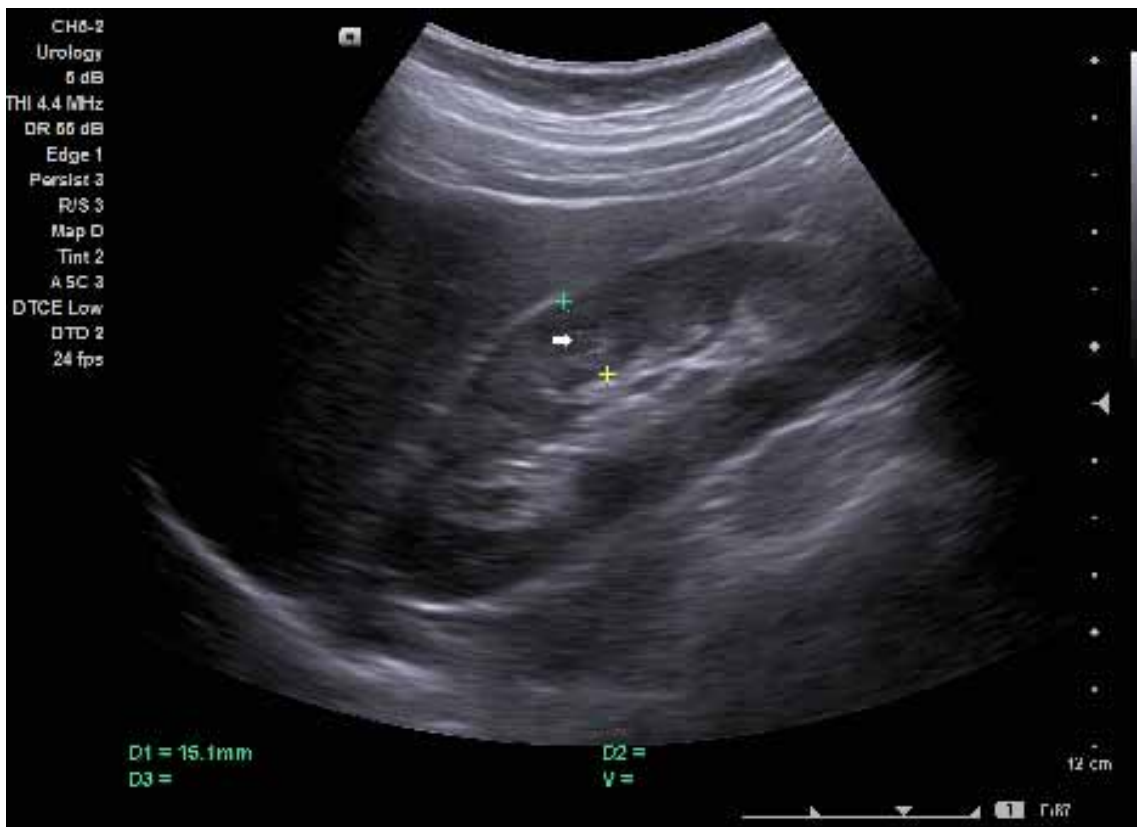


Fig 1. Ultrasound scan in sagittal section of right kidney for 25 years old female with epigastric pain. Renal parenchymal thickness (arrow) equals 15.1 mm.

Statistical Analysis: Differences of continuous variables between 2 independent groups were assessed with student's t-test. The Relationship of RPT with age, height, and weight were assessed with Pearson's correlation coefficient (r). Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) 18.0 software package (Version 18).

Results

The range, Mean and standard deviation values of the study sample characteristics and their RPT were seen in table 1.

Table 1: Descriptive data of study sample and their renal parenchymal thickness.

Parameters	Mean (SD)		t value	P value	
	Female (N=125)	Male (N=128)			
Age (Year)	40.9(15.9)	41.3(14.8)	0.4662	0.6415	
Height (cm)	163.1(3.1)	172.6(3.6)	22.4692	0.0001	
Weight (kg)	73.3(14.8)	87.2(12.4)	8.1049	0.0001	
RPT ^b (mm)	Right	16.4(2.1)	18.2(3.2)	5.2764	0.0001
	Left	16.9(2.4)	18.9(3)	5.8470	0.0001

^a Number, ^b renal parenchymal thickness.

The total number of subjects included was 253, there were 128 male (50.6%) and 125 (49.4%) females. In males, the mean (SD) values of, age was 41.3(14.8) years, height was 172.6(3.6) cm, weight was 87.3(12.4) Kg, and right RPT was 18.2(3.2) mm while left RPT was 18.9(3 mm). In females, the mean value of, age was 40.9(15.9) years, height was 163.1(3.1) cm, weight was 73.3(14.8) Kg, and right RPT was 16.4(2.4) mm, while left RPT was 16.9(2.4 mm). A statistical significant difference was not founded between RPT of right and left

kidneys in both genders ($P= 0.080$ in female, $P= 0.072$ in the male), but the renal parenchyma was significantly thicker in males (18.6mm) than females (16.7 mm) ($P= 0.0001$).

There was a negative correlation between RPT and age (Table 2). The correlation was moderate, significant ($r = -0.66, P = 0.00001$) in the right kidney, while it was strong and significant ($r = -0.82, P = 0.00001$) in the left kidney.

Table 2: Renal parenchymal thickness according to age.

Age (Year)	RPT ^a (mm)		Total N ^b	Percentage
	Right Kidney	Left Kidney		
18-27	17	18.1	52	20.55
28-37	18.3	18.9	68	26.78
38-47	17.4	18.5	50	19.76
48-57	17.7	18.4	34	13.43
58-67	16.3	16	40	15.81
68-77	16	14.1	9	3.55

^a Renal parenchymal thickness, ^b Number.

Right and left renal parenchyma was thicker in taller persons (table 3). On both sides there was significant ($P = 0.00001$) strong positive correlation between RPT and

person's height ($r = 0.92$ in the right kidney and $r = 0.88$ in the left).

Table 3: Renal parenchymal thickness according to height.

Height (cm)	RPT ^a (mm)		Total N ^b	Percentage
	Right Kidney	Left Kidney		
155-159	15.3	16.3	10	3.95
160-164	16.8	17.1	74	29.24
165-169	16	17.2	66	26.08
170-174	18.6	19.4	64	25.29
175-179	18.5	18.1	32	12.64
180-184	19.3	20	7	2.76

^a Renal parenchymal thickness, ^b Number.

There was a positive correlation between the RPT and person's weight (table 4). In the right kidney, this correlation was strong significant ($r=0.88$, $P=0.00001$), while in the Lt kidney it was weak significant ($r=0.38$, $P=0.00001$).

Table 4: Renal parenchymal thickness according to weight.

Weight (Kg)	RPT ^a (mm)		Total N ^b	Percentage
	Right Kidney	Left Kidney		
50-59	16	17.4	15	5.93
60-69	16.8	17.3	21	8.30
70-79	16.7	16.3	24	9.49
80-89	16.9	17.9	34	13.44
90-99	19.2	20.4	25	9.88
100-110	18.7	17.5	8	3.16

^a Renal parenchymal thickness, ^b Number.

Discussion

The mean value was 18.6 for males and 16.7 in females; these results were more than other studies^[1,8,11-13] and less than an African study,^[4] but it was comparable to Iranian, Pakistanian and Austrian studies^[15-17] these different values in different races probably were due to both genetic and environmental factors.

In the current study we founded that the difference of RPT between each kidney was not significant statistically like an Indian study.^[8] Other studies found that left kidney had significantly thicker parenchyma than the right kidney;^[4,11-14] the common and easiest way for comparison between right kidney examined from front (hepatic window) with left kidney examined from the flank (spleen window) might be the cause of thicker parenchyma of the left kidney as the front renal parenchyma is anatomically thin where the hilus is present.^[19] Males had significantly thicker parenchyma than the females, mostly due to their taller and bulkier

bodies; this was the same as other studies.^[11,12,18]

We founded a negative correlation between RPT and the age, previous studies result were generally agreed with this^[4,8,14] this change was attributed to changes in the renal vasculature, and genetic factors,^[20,21] other mechanisms including, interstitial fibrosis, glomerulosclerosis might also contribute.^[16] There was a positive correlation between RPT and people's height and weight, which was similar to other studies,^[8,12,14] as bigger patients will have a larger blood volume requiring larger kidneys for filtration.^[22]

Conclusion

Our population parenchymal thickness values are different from others, it is 18.6 mm male and 16.7 mm in female, parenchyma is considered thin if it was less than 13 mm in males and 10 mm in females, its decreased with age, taller and more obese persons have thicker parenchyma on both sides.

Conflict of Interest: None.

Source of Funding: None.

Ethical approval: The permission was obtained from the Azadi Teaching Hospital Committee and informed consent was obtained from each individual before data collection was begun. Personal data was not explored.

References

1. El-Reshaid W, and Abdul-Fattah H. Sonographic assessment of renal size in healthy adults. *Med Princ Pract.* 2014; 23:432–436.
2. Carrasco OJ, Castellanos RF, Kimura E, Hernandez DR, and Felix HJP. Renal length by ultrasound in Mexican adults. *Nefrologia.* 2009; 29: 30-34.
3. Otiw A, Mehta K, Ali U, and Nadkarni M. Sonographic measurement of renal size in normal Indian children. *Indian Pediatr* 2012; 49: 533-536.
4. Tarnoki, DL, Tarnoki, AD, Littvay L, Bata P, Berczi V, Garami Z, et al. Genetic and environmental variance of renal parenchymal thickness: a twin study. *Croatian medical journal.* 554–550: (6)54; 2013.
5. Noble VE, and Brown DF. Renal ultrasound. *Emerg Med Clin North Am.* 2004; 22: 641.659.
6. Debruyne K, Paepe D, Daminet S, Combes A, Duchateau L, Peremans K, et al. Renal dimensions at ultrasonography in healthy Ragdoll cats with normal kidney morphology: correlation with age, gender and body weight. *J Feline Med Surg.* 2013; 15: 1046.1051.
7. Draper AC, Bowen IM, Hallowell GD. Reference ranges and reliability of transabdominal ultrasonographic renal dimensions in thoroughbred horses. *Vet Radiol Ultrasound.* 2012; 53:336.341.
8. Siens M, Ignee A, Dietrich CF. Sonography today: reference values in abdominal ultrasound: aorta, inferior vena cava, kidneys. *Z Gastroenterol.* 2012; 50: 293.315.
9. Okoye IJ, Agwu KK, Eze CU. Relationship between sonographic renal length and renal parenchymal thickness in normal adult southeast Nigerians. *West Afr J Med.* 2006; 25(3): 231 –234.
10. Kadioglu A. Renal measurements, including length, parenchymal thickness, and medullary pyramid thickness, in healthy children: what are the normative ultrasound values? *American Journal of Roentgenology.* 2010; 194(2): 509-15.
11. Raza MI, Hameed A, Khan MI. Ultrasonic Assessment of Renal Size and its Correlation with Body Mass Index in Adults without Known Renal Disease. *J Ayub Med Coll Abbottabad.* 2011; 23 (3): 64-68.
12. AB AH, Mansour AA, Gar-el-nabi MEM, and Saeed EA. Ultrasonographic Renal Length and Parenchymal Thickness in Normal Sudanese Population. *International Journal of Science and Research.* 2016; 5 (1): 623-625.
13. O'Neill WC: *Atlas of Renal Ultrasound.* Philadelphia, Saunders, 2001, p 17–49.
14. Eze C, Okoye J, and Agwu K. Normative ultrasound values of renal parenchymal thickness among adults in Enugu, South-East Nigeria. *Afr Health Sci.* 2014; 14(3):689–697.
15. Jabbari M, Mollazade R, Esna Ashari F, and Alizadeh Z. Normal Renal Dimensions in Iranian Adults Measured by Ultrasound. *ASJ.* 2016; 13 (1):25-32.
16. Saeed Z, Mirza W, Sayani R, Sheikh A, Yazdani I, and Ather Hussain S. Sonographic measurement of renal dimensions in adults and its correlates. *International Journal of Collaborative Research on Internal Medicine & Public Health.* 2012; 4:1626-1641.
17. Glodny B, Unterholzner V, Taferner B, Hofmann KJ, Rehder P, Strasak A, et al. Normal kidney size and its influencing factors- a 64-slice MDCT study of 1.040 asymptomatic patients. *BMC Urology.* 2009; 9(1):19.
18. Ruchi Jain, Jyoti Chopra, Punita Manik, and Varun Arora. Sonographic Evaluation of Renal Dimensions and their Correlation with Gender, Weight, and Height in Normal Young Adults of Uttar Pradesh Region. *Indian Journal of Clinical Anatomy and Physiology,* April-June 2016; 3(2); 149-154.
19. Jermendy G, Littvay L, Steinbach R, Jermendy A, Tarnoki A, Tarnoki D, et al. Heritability of the risk factors characteristic for the metabolic syndrome: a twin study. *Orv Hetil.* 2011; 152:1265–71.
20. Franklin SS, Lopez VA, Wong ND, Mitchell GF, Larson MG, Vasan RS, et al. Single versus pressure components and risk for cardiovascular disease:

- the Framingham Heart Study. *Circulation*. 2009; 119(2):243–50.
21. Jermendy G, Horvath T, Littvay L, Steinbach R, Jermendy AL, Tarnoki AD, et al. Effect of genetic and environmental influences on cardiometabolic risk factors: a twin study. *Cardiovasc Diabetol*. 2011; 10: 96.
22. Harmse W. S. Normal variance in renal size in relation to body habitus. *South African Journal of Radiology*. 2011; 15(4): 123-126.

Relationship between Parasitic Infections in Protozoa and Female Secondary Infertility

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Abstract

Parasitic diseases in protozoa are endemic in many countries around the world, especially in developing countries, and infertility is a major burden. Such infections may be infertile through damage to the female reproductive system. There are some parasitic primary animals such as *Trichomonas vaginalis* which may cause genital tract abnormalities, cervical tumors and tubal and non-anomalous pelvic infections in women. *Toxoplasma gondii* causes endometriosis, dysplasia of reproductive tract and synthetic disorders such as intrauterine adhesions. Some epidemiological studies are indicate that infections with protozoa in women who suffer secondary infertility are higher than those of healthy controls. Some drugs used to treat giardiasis cause infertility in male rats by inhibiting of spermate in the epididymis, which reduces it's viscosity.

Keywords: Infections, Protozoan parasites, Secondary infertility.

Introduction

There are many parasites that have a role in women's miscarriage in different ways. 35% of women with an infertility suffered ovarian dysfunction and post-inflammatory changes in the ovarian duct and surrounding Pretorian membrane caused by infectious diseases¹. Granulomatous salpingitis caused by parasitic infection is a rare cause of tubal obstruction². Infection can cause significant damage to the human reproductive system and animals, including chronic cervical and endometriosis, dysplasia of the reproductive tract, decrease of sperm movement and deformation, synthetic disorders such as adhesions within Uterus and urged the immune mediators that interfere with the gametes or fetal tissue¹. It has been shown that the reasons related to

infection play an important role in the rate of infertility in developed countries³.

Protozoa are unicellular microorganisms and are a major health problem worldwide because of their increased prevalence and incidence. The clinical symptoms are closely associated with the pathological effects and their location in the host, whether in the blood, tissues or intestines. Among the parasitic protozoa that cause secondary infertility in women is the *Trichomonas vaginalis*, a flagellated that spreads all over the world and live in the urogenital system of humans. In females, in the urethra, and in the epididymis and prostate gland in males⁴. It is transmitted mainly by sexual intercourse, which is considered to be a sexually transmitted parasites. It may be transmitted through western sanitary seats or through the use or exchange of towels or wet clothing with this parasite secretions. In some studies, tubal infertility was repeated twice in women who reported a history of trichomoniasis compared with non-patient women⁵⁻⁶. El-Shazly and his group found that *T. vaginalis* is present in 14.58% of the women who are sterile compared to the control group⁷.

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Toxoplasma gondii is a intercellular protozoan that

effect 20-80% of the world's population in different regions⁸⁻⁹. There are some studies that have indicated the relationship between toxoplasmosis and infertility in females, and that the incidence of non-symptomatic latent toxoplasmosis has latent on the early development of fetus. Some studies have found that the incidence of congenital disease in women with infertility is higher than that of healthy women¹⁰⁻¹¹.

Some studies on laboratory animals have shown that infection with *T. gondii* can cause infertility in experimental animals. Chronic toxoplasmosis in rats female can cause endometriosis, impaired ovaries, weak follicles, atrophy in the ovaries and uterus, decrease in reproductive performance, adrenal glands inflation, vascular inflammation, cessation of menstrual dysplasia and failure to reproduce in experimental mice¹²⁻¹³⁻¹⁴.

Giardia lamblia is a protozoan flagellate that reproduce in in the small intestine, forming colonies that cause giardiasis. The parasite is attached to the small intestine by the adhesion ventral disc. The trophozoite can absorb its nutrients from the small intestinal cavity. *Giardia* can infect the human, It is also one of the most common parasites that can infect other mammals such as cats, dogs, beavers, cows, deer and sheep also infect birds¹⁵. Giardiasis spread when eating food or drinking water contaminated with the dormant stage of the parasite (cyst) or through arrive of a part of the faces of the mouth through non-healthy practices of some people. Cyst of the parasite can survive for weeks or months in cold water and may therefore be found in contaminated wells, water systems, stagnant water systems, falling running water from the mountains can also be found in urban water tanks as well as in treated wastewater, and the teasing phase is resistant to traditional method of sterilizing water with chlorine or ozone¹⁶. Symptoms of giardiasis include diarrhea, malaise, steatorrhea, abdominal cramps, bloating, lack of desire to eat, weight loss, flatulence and nausea¹⁷.

Secondary infertility is defined as a condition affecting women and men despite the occurrence of intercourse regularly and without using any means of contraception for at least 6 months and despite the occurrence of pregnancy¹⁸⁻¹⁹.

Materials and Method

The study was approved by the Iraqi health ministry, a prospective study was conducted based on the hospital during the period from February to July

2019, where the adoption of a woman suffering from secondary infertility, who visited the hospital for women and obstetric education in Karbala (a city located 110 Km south-west of Baghdad), collected venous blood distributed in gel tube, as well as samples were obtained from the vagina.

Serological detection of toxoplasmosis: The serum was separated from the blood collected by centrifugation (3000 rpm for 10 minutes), and then kept in sterilized Eppendorf tube at -20C° until they were used for serological assays. Serums were tested for IgG and Ig Manti-toxoplasmosis by the enzyme-testing kit (ELISA). In both types of tests, the manufacturer's instructions were followed.

Detection of Trichomonosis: A pap smear was obtained by a specialist gynecologist. Two swabs were approved. The swab was clamped in 1-2 cm in the endocervical canal by 2-3 rotations. The swabs were collected based on the manufacturer's instructions.

Swabs were immersed in a sterile tube containing 1 mL of normal saline solution, the samples examined for 10 minutes at least, positive samples containing one or more of *T. vaginalis* described by their jerky movement and morphology, swabs labeled of the patient's name and date of collection. The wet swab was examined in wet mount preparation²⁰⁻²¹⁻²².

Results and Discussion

Among 212 women examined, 162 (26.5%) were positive for toxoplasmosis and it was 30.3 % in the both of age groups of present study. Toxoplasmosis is a worldwide parasitic disease, affecting most population groups, Statistics based on the measurement of antibody parasites in serum individuals indicate that the incidence of infection in the world ranges from less than 10% to about 90%²³, Substantial differences between the different strains of *T.gondii* are important factors, Differences in the severity of virulence were observed between the parasite's strains, Some of them are virulence and non-virulence²⁴. A few medical studies have been conducted on the relationship between toxoplasmosis and female infertility. Kaňková & Flager has been reported that latent toxoplasmosis has adverse effects on the early development of fetuses in mothers²⁵. A number of recently published studies have shown that chronic toxoplasmosis infection in infertile women is more significant than healthy women¹⁰⁻¹¹. Zhou *et al.*, is reported that the prevalence of chronic

toxoplasmosis in infertile couples has reached 34.83% and was significantly (12.11%) higher than fertile couples²⁷. Toxoplasmosis has undesirable effects on the reproductive capacity of both males and females²⁸. An unexpectedly high correlation was observed between *T.gondii* and secondary infertility (66.7%) more than primary infertility (33.3%)²⁸, *T.gondii* cause damage deformities of genital tract, tubal inflammation and effects on semen quality²⁶⁻²⁹.

It was found that the incidence of infection with trichomoniasis 44.4% in infertile women, Previous studies have shown that *T.vaginalis* infection has high rates of recurrence due to its high resistance to metronidazole³⁰, this makes these microorganisms a serious infection of the reproductive system. Trichomoniasis is not routinely screened in patients with symptoms and the infection can last from 3-12 months in the reproductive system. Elderly patients with asymptomatic trichomoniasis are classified as carriers of long-term disease without any symptoms³¹⁻³²⁻³³. Patients with *T.vaginalis* have no symptoms of 70-100% of males versus women 35-85% . Recently, *T.vaginalis* have been isolated from the fallopian tubes and peritoneal fluid, suggesting that moving *T.vaginalis* may be able to invade the genital tract stream³⁴⁻³⁵. There have been many studies that have found that *T.vaginalis* cause damage to the genitourinary

system and various types of cells and tissues such as connective and muscular tissues due to the excessive cytotoxic effect suggesting a high risk of reproductive failure³⁶⁻³⁷. *T.vaginalis* is associated with cells, leading to shrinkage of the cell membrane, cell hemorrhage and apoptosis, These changes in cell structure can appear under a microscope, characterized by intensive chromatin and form dense vacuoles in the cytoplasm³⁶.

Trichomoniasis in women is associated with inflammation of the vagina, endometritis and can lead to inflammatory responses in the mucous genital tract, which increases the risk of pelvic inflammatory disease³⁸⁻³⁹. Vaginal trichomoniasis is associated with up to 30% acute salpingitis and 16% postpartum endometriosis cases during pregnancy as well as 30% premature births and 30% low birth weight infants⁴⁰. Trichomoniasis paves the way for many parasitic bacteria for inflammatory processes and thus increases the risk of reproductive failure and increases the risk of infection with 1.5-3 times of HIV⁴¹⁻³¹⁻⁴².

The incidence of infection with *Giardia lamblia* 29 % in women with secondary infertility. It was found that some drugs used to treat giardiasis cause infertility in male rats by inhibiting of spermate in the epididymis, which reduces it's viscosity⁴³.

Table (1): The infection in female secondary infertility and female controls.

Group	Number of Causes	Number of positive causes (%)			p-value
		G.lambliia	T.vaginalis	T.gondii	
Female Secondary infertility	162	47 (29)	72(44.4)	43(27)	0.000
Female controls	50	17 (34)	17 (34)	16 (32)	
Total	212	64(30.1)	89(42)	59 (28)	

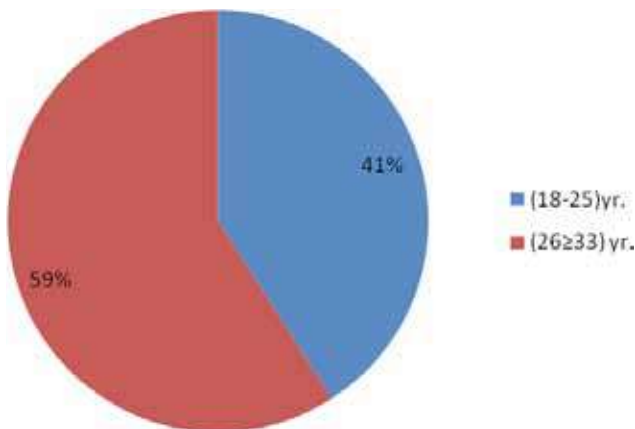


Fig. (1): The percentage of secondary infertile women according to their ages.

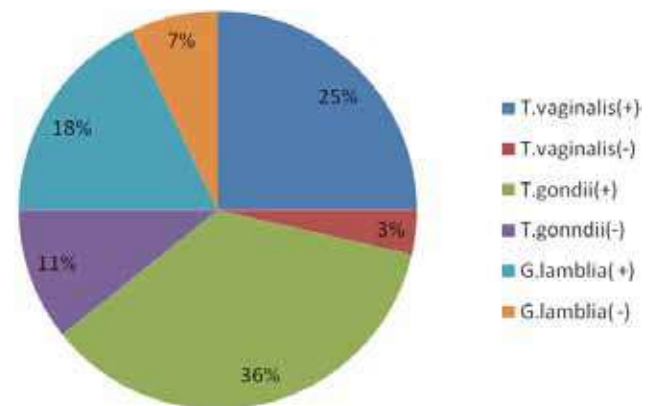


Fig. (2): The percentage of secondary infertile women according to their causes.

Table (2) :Correlation between the parameter under study of secondary infertile women.

Parameters N= 162	Parameters N= 162	r	p-value
Female Secondary infertility	Age	0.015	0.190
	Abortion	0.000	0.426*
Age	Abortion	0.043	-0.160*
Abortion	Female Secondary infertility	0.000	0.357**

*Correlation is significant at the 0.05 level., **Correlation is significant at the 0.01 level.

Table (3): The infection in female secondary infertility with protozoa according to their ages.

Age (Year)	Total number of examined causes	Direct test				ELISA test	
		Number of positive causes		Prevalence of infection (%)	Number of positive causes T. gondii (IgG, IgM)	Prevalence of infection (%)	
		T. vaginalis	G.lambliia				
18-25	56	16	23	28.5	41.0	17	30.3
26 ≥ 33	10	22	62	21.0	58.4	22	21.0
Total	162	38	85	23.4	52.4	39	24.0

Conclusions

The results of this study suggest that parasitic infection in protozoa may be an important cause of infertility according to the widespread spread of the parasites. Therefore, further studies are recommended to better understand the relationship between this infection and infertility as well as screening both the couple when treating infertility as these parasites are sexually transmitted diseases.

Ethical Clearance: This study was approved by institutional Ethics Committee from institute veterinary medicine committee, college of veterinary medicine, University of Kerbala.

Source of Funding: Self

Conflict of Interest: Nil

References

- Pellati, D., Mylonakis, I., Bertoloni, G., Fiore, C., Andrisani, A., Ambrosini, G., & Armanini, D. Genital tract infections and infertility. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 2008, 140.1: 3-11.
- Steinkeler, J. A., Woodfield, C. A., Lazarus, E., & Hillstrom, M. M. Female infertility: a systematic approach to radiologic imaging and diagnosis. *Radiographics*, 2009, 29.5: 1353-1370.
- Ombelet, W. Global access to infertility care in developing countries: a case of human rights, equity and social justice. *Facts, views & vision in ObGyn*, 2011, 3.4: 257.
- Hezarjaribi, H. Z., Fakhar, M., Shokri, A., Teshnizi, S. H., Sadough, A., & Taghavi, M. Trichomonas vaginalis infection among Iranian general population of women: a systematic review and meta-analysis. *Parasitology research*, 2015, 114.4: 1291-1300.
- Grodstein, Francine; GOLDMAN, Marlene B.; CRAMER, Daniel W. Relation of tubal infertility to history of sexually transmitted diseases. *American journal of epidemiology*, 1993, 137.5: 577-584.
- Sherman, Karen Joyce; DALING, JANET R.; WEISS, NOEL S. Sexually transmitted diseases and tubal infertility. *Sexually transmitted diseases*, 1987, 14.1: 12-16.
- El-Shazly, A. M., et al. A study on Trichomoniasis vaginalis and female infertility. *Journal of the Egyptian Society of Parasitology*, 2001, 31.2: 545-553.
- Meerburg, G.; Kijlstra, A. Changing climate—changing pathogens: Toxoplasma gondii in North-Western Europe. *Parasitology research*, 2009, 105.1: 17-24
- Skariah, S; Mcintyre, M. K.; Mordue, D. G. Toxoplasma gondii: determinants of tachyzoite to bradyzoite conversion. *Parasitology research*, 2010, 107.2: 253-260.
- Li S., Cui, L., Zhao, J., Dai, P., Zong, S., Zuo, W & Liu, Q. Seroprevalence of Toxoplasma gondii

- infection in female sterility patients in China. *Journal of Parasitology*, 2011, 97.3: 529-531.
11. El-Tantawy, N.; Taman, A.; Shalaby, H. Toxoplasmosis and female infertility: is there a correlation. *American Journal of Epidemiology and Infectious Disease*, 2014, 2.1: 29-32.
 12. Stahl, W., Kaneda, Y., & Noguchi, T. Reproductive failure in mice chronically infected with *Toxoplasma gondii*. *Parasitology research*, 1994, 80.1: 22-28.
 13. Stahl, W., Kaneda, Y., Tanabe, M., & Kumar, S. A. Uterine atrophy in chronic murine toxoplasmosis due to ovarian dysfunction. *Parasitology research*, 1995, 81.2: 109-113.
 14. Stahl, W., Dias, J. A., Turek, G., & Kaneda, Y. Etiology of ovarian dysfunction in chronic murine toxoplasmosis. *Parasitology research*, 1995, 81.2: 114-120.
 15. Vesey, C. J., & Peterson, W. L. the management of Giardiasis. *Alimentary pharmacology & therapeutics*, 1999, 13.7: 843-850.
 16. Laishram, S., Kang, G., & Ajjampur, S. S. R. Giardiasis: a review on assemblage distribution and epidemiology in India. *Indian Journal of Gastroenterology*, 2012, 31.1: 3-12.
 17. Hawrelak, J. Giardiasis: pathophysiology and management. *Alternative medicine review*, 2003, 8.2.
 18. Chandra, A., Copen, C. E., & Stephen, E. H. Infertility and impaired fecundity in the United States, 1982-2010: data from the National Survey of Family Growth. 2013.
 19. Benksim, A., Elkhoudri, N., Addi, R. A., Baali, A., & Cherkaoui, M. Difference between primary and secondary infertility in Morocco: frequencies and associated factors. *International journal of fertility & sterility*, 2018, 12.2: 142.
 20. Kingston, M. A., Bansal, D., & Carlin, E. M 'Shelf life' of *Trichomonas vaginalis*. *International journal of STD & AIDS*, 2003, 14.1.
 21. Patil, M. J., Nagamoti, J. M., & Metgud, S. C. Diagnosis of *Trichomonas vaginalis* from vaginal specimens by wet mount microscopy, in pouch TV culture system, and PCR. *Journal of global infectious diseases*, 2012, 4.1: 22.
 22. Hobbs, M. M., & Seña, A. C. Modern diagnosis of *Trichomonas vaginalis* infection. *Sex Transm Infect*, 2013, 89.6: 434-438.
 23. Torgerson, P. R., & Mastroiacovo, P. The global burden of congenital toxoplasmosis: a systematic review. *Bulletin of the World Health Organization*, 2013, 91: 501-508.
 24. Dubremetz, J. F., & Lebrun, M. Virulence factors of *Toxoplasma gondii*. *Microbes and infection*, 2012, 14.15: 1403-1410.
 25. Kaňková, Š., & Flegr, J. Longer pregnancy and slower fetal development in women with latent "asymptomatic" toxoplasmosis. *BMC Infectious Diseases*, 2007, 7.1: 114.
 26. Zhou, Y. H., Lu, Y. J., Wang, R. B., Song, L. M., Shi, F., Gao, Q. F., ... & Wang, P. Survey of infection of *Toxoplasma gondii* in infertile couples in Suzhou countryside. *Zhonghua nan ke xue= National Journal of Andrology*, 2002, 8.5: 350-352.
 27. Montoya, J. G.; Liesenfeld, O. Toxoplasmosis. *The lancet*, 2004, 363.9425: 1965-1976.
 28. Malik, A., Rizvi, M., Khan, F., Khan, N., Rabbani, T., & Khan, H. M. *Toxoplasma gondii* in women with bad obstetric history and infertility: a five-year study. *Asian Pacific Journal of Tropical Disease*, 2014, 4: S236-S239.
 29. Aral, G. A., Elhan, H. A., & Akarsu, C. Retrospective evaluation of *Toxoplasma gondii* seropositivity in fertile and infertile women. *Mikrobiyoloji bulteni*, 2011, 45.1: 174-180.
 30. Snipes, L. J., Gamard, P. M., Narcisi, E. M., Beard, C. B., Lehmann, T., & Secor, W. E. Molecular epidemiology of metronidazole resistance in a population of *Trichomonas vaginalis* clinical isolates. *Journal of clinical microbiology*, 2000, 38.8: 3004-3009.
 31. Ena, A. C., Miller, W. C., Hobbs, M. M., Schwebke, J. R., Leone, P. A., Swygard, H., ... & Cohen, M. S. *Trichomonas vaginalis* infection in male sexual partners: implications for diagnosis, treatment, and prevention. *Clinical infectious diseases*, 2007, 13-22.
 32. Utton, M., Sternberg, M., Koumans, E. H., McQuillan, G., Berman, S., & Markowitz, L. The prevalence of *Trichomonas vaginalis* infection among reproductive-age women in the United States, 2001-2004. *Clinical infectious diseases*, 2007, 45.10: 1319-1326.
 33. Johnston, V. J., & Mabey, D. C. Global epidemiology and control of *Trichomonas vaginalis*. *Current opinion in infectious diseases*, 2008, 21.1: 56-64.

34. Crucitti, T., Jespers, V., Mulenga, C., Khondowe, S., Vandepitte, J., & Buvé, A. Non-sexual transmission of *Trichomonas vaginalis* in adolescent girls attending school in Ndola, Zambia. *PloS one*, 2011, 6.1: e16310.
35. Ryan, C. M., Miguel, N. D., & Johnson, P. J. *Trichomonas vaginalis*: current understanding of host-parasite interactions. *Essays in biochemistry*, 2011, 51: 161-175.
36. Pindak, F. F., De Pindak, M. M., & Gardner, W. A. Contact-independent cytotoxicity of *Trichomonas vaginalis*. *Sexually Transmitted Infections*, 1993, 69.1: 35-40.
37. McClelland, R. S., Sangaré, L., Hassan, W. M., Lavreys, L., Mandaliya, K., Kiarie, J., ... & Baeten, J. M. Infection with *Trichomonas vaginalis* increases the risk of HIV-1 acquisition. *The Journal of infectious diseases*, 2007, 195.5: 698-702.
38. Pereira-Neves, A., & Benchimol, M. Phagocytosis by *Trichomonas vaginalis*: new insights. *Biology of the Cell*, 2007, 99.2: 87-101.
39. Chapin, K., & Andrea, S. *Trichomonas vaginalis*, a transcription-mediated amplification assay for detection of *Trichomonas vaginalis* in urogenital specimens. *Expert review of molecular diagnostics*, 2011, 11.7: 679-688.
40. Mielczarek, E., & Blaszkowska, J. *Trichomonas vaginalis*: pathogenicity and potential role in human reproductive failure. *Infection*, 2016, 44.4: 447-458.
41. Habib, F. S., Metwally, D. M., & Habib, K. S. Cryopreservation of *Trichomonas vaginalis*: a trial of using four different cryoprotectants. *Journal of the Egyptian Society of Parasitology*, 2004, 34.3: 931-940.
- 42- ucena, E., Moreno-Ortiz, H., Coral, L., Lombana, O., Moran, A., & Esteban-Pérez, C. I. Unexplained infertility caused by a latent but serious intruder: *Trichomonas vaginalis*. *JFIV Reprod Med Genet*, 2015, 3: 139.
43. Hizarciolu, Y. S., Zeynep, A. Y., & Ozyazici, M. Bioavailability file: ornidazole. *Fabad J Pharm Sci*, 2004, 29: 133-144

The Link between Demographic Profiles with Depression among Elderly Women in Private Care Institution

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Abstract

Depression among elderly women living in nursing home based on demographic profile become a phenomenon in many developed countries. In most research, depression has been identified as a negative feeling that can lead to death. Depression among elderly women occur when they are 60 years and above once their children grow up and married. Then, there retired from occupations and their spouse died and make they live alone. Thus, this study aimed to identify the factors of demographic profiles have an impact on depression among elderly women. This research was conducted at a private institution in Terengganu, Malaysia with 78 elderly women as respondents quantitatively. The questionnaires from Patient Health Questionnaire 9 (PHQ-9) were adopted to analyse the risk of elderly having depression and feeling lonely in nursing home. The result showed the factors of demographic profile have an impact on depression among elderly women in private institution its strength and significant. As a conclusion, the study on depression among elderly women in nursing home is important to raise awareness about this alarming issue in the society especially among elderly women.

Keywords: *Depression, demographic profiles, elderly women, private care institution.*

Introduction

Depression are prevalent among elderly women in the institution ¹. In a cross-sectional study by Barg et al. (2006), it was revealed that in persons 65 years and older, the perceived adequacy of emotional and tangible support was clearly associated with depressive symptoms three years later ². According to Adams et al. (2004), the elderly women living in retirement, nursing homes and institution, away from previous homes and neighborhoods and separated from extended families, will continue to increase ³. There are living in facilities

for the elderly women will have to modify to a changed living situation, and this modification can lead to fatal psychosocial problems of depression in the absence of positive social networks⁴. The elderly women and depression related when they are 60 years old and above when their children grow up and married ⁵. Then, there are retired and their spouse died and make they live alone⁶⁷.

Material and Method

Population and Sampling: The population of the study was the 78 elderly women in welfare institution in Terengganu, Malaysia during the years 2017.

Instruments: An individual information frame, the PHQ-9 were utilized as the information gathering devices in the exploration.

PHQ-9: This poll screening the dejection among elderly. The PHQ-9 is a self-regulated adaptation of the PRIME-MD demonstrative instrument for basic mental clutters. The PHQ-9 is the misery module,

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which scores every one of the 9 DSM-IV criteria as 0=not by any means, 1=several days, 2=more than a large portion of the days and 3=nearly consistently. The PHQ-9 was finished by 6,000 patients in eight essential consideration facilities and 7 obstetrics-gynecology centers. Moreover, standard legitimacy was evaluated against an autonomous organized emotional well-being proficient (MHP) meet in an example of 580 patient's especially elderly women.

Findings:

Respondent Backgrounds: Table 1 shows the marital status of the respondents who participated in this survey. Among the elderly women in PKWTNS, only 2.6 percent were single, (n=2). Similarly, only 3.8 percent were married, (n=3). The majority of the elderly women were widows at 93.6 percent (n=73). The age distribution of the respondents, the percentage of those who were, 60-64 and 70-74 years old was the same at 30.8 percent, with 24 respondents for each age group. Next, 19.2 percent (n=15) were of 65-69 years old while 17.9 percent (n=14) were between 75-80 years old. The smallest age group was the 80 and above, with only 1.3 percent (n=1). Meanwhile, the level of education of the elderly women participating in this research was low. The majority at 53.8 percent (n=42) only finished lower secondary education (SRP), while 18 percent (n=14) had no education experience whatsoever. Only 28.2 percent (n=22) received basic education (SPM). The working history of respondents in this research were majority of the respondents were self-employed (60.2 percent, n=47). Those who were not working comprised of 26.9 percent (n=21). Out of all of the respondents, only 10.3 percent (n=8) were public workers while 2.6 percent (n=2) were working in the non-government sector. Many of the elderly women interviewed came from small families. Table 1 shows that the majority of the respondents at 46.2 percent (n=36) had only 1-4 children. The next largest group was with 5-9 children that comprised of 37.2 percent (n=29) of the respondents. Only 12.8 percent (n=10) had 10-14 children in their families, 1.2 percent (n=1) had 15-19 children and 2.6 percent (n=2) had no children. Besides, the person(s) whom the respondents spent most their time before coming to PKWTNS are almost half of the respondents (47.5 percent, n=37), lived alone prior to coming to institution. The remaining 52.5 percent were living with someone else, of which 3.8 percent (n=3) was with a husband or spouse while 48.7 percent (n=38) either lived with children, relatives, or others. Below

the table shows the reasons to live in PKWTNS. The majority of them want a better life in the institution (21.8 percent) because they lack caretakers (19.2 percent), or because they have a family conflict (14.1 percent). A few respondents mentioned that they live in PKWTNS because they do not want to disturb their children (11.5 percent), or have been abandoned by children (10.3 percent) and lack of energy in doing household chores (6.4 percent). Other reasons for choosing to live in an institution are due to loneliness (10.3 percent) and being poor (6.4 percent). Table 1 shows the level of depression among elderly women in PKWTNS. Using the PHQ-9 instrument, only 7.7 percent (n=6) of the respondents were classified as normal (0-4) with no depression. About 12.8 percent (n=10) of the respondents were classified as having minimal depression (5-9) while 55.1 percent (n=43) were classified as having mild severity of depression (10-14). Meanwhile, 24.4 percent (n=19) of respondents were classified as having moderate severity of depression (15-19). None of the respondents in PKWTNS were classified as having high levels of depression (more than 20).

Table 1: Respondent Backgrounds

Respondent's Background	Frequency (n=78)	Percentage (%)
Marital Status		
Single	2	2.6
Married	3	3.8
Widowed	73	93.6
Age		
60-64	24	30.8
65-69	15	19.2
70-74	24	30.8
75-80	14	17.9
More than 80	1	1.3
Level of Education		
SRP	42	53.8
SPM	22	28.2
No Education	14	18.0
Working History		
Not Working	21	26.9
Self-employed	47	60.2
Public Worker	8	10.3
Non-government	2	2.6
Number of Children		
1-4	36	46.2
5-9	29	37.2
10-14	10	12.8

Respondent's Background	Frequency (n=78)	Percentage (%)
15-19	1	1.2
No Children	2	2.6
The Majority of Elderly Women Spent with		
Self	37	47.5
Husband/Spouse	3	3.8
Children	20	25.6
Relatives	17	21.8
Others	1	1.3
Reason for Choosing to live in institution		
Do not Want to Disturb Their Children	9	11.5
Abandoned by Children	8	10.3
Family Conflict	11	14.1
Lack of Caretakers	15	19.2
Lack of Energy in doing Household Chores	5	6.4
Want a better life in the Institution	17	21.8
Poor	5	6.4
Feeling Lonely in their home	8	10.3
The Level of Depression		
0-4	6	7.7
5-9	10	12.8
10-14	43	55.1
15-19	19	24.4
More than 20	0	0

The findings of regression analysis show the impacts of independent variables that are factors of demographic profile on respondents' depression. Based on the correlation analysis, only four factors showed insignificant value, network and communication and trust. Only factors with significant correlation value can be measured by the effects of regression analysis.

Table 2: Model Summary

Institution	Model	R	R Square
Private Institution	1	0.754	0.716

The r square value in the Model Summary in table 2 shows the amount of variance in the dependent variable that can be explained by the independent variables. In the research, the independent variables together account for 71.6 per cent of the variance in the depression scores. The r value (0.754) indicates the multiple correlation coefficient between all the entered independent variables and the dependent variable.

Table 3: Regression

Model	B	Std. Error	Beta	T	Sig.
Frequency of visitors	2.038	0.065	0.402	31.460	0.00
Period of stay	0.157	0.035	0.381	4.495	0.00
Level of health	-0.115	0.045	-0.269	-2.543	0.03

The coefficient for period of stay was 0.157. Hence, for every unit increase in frequency of visitors score, researcher expect a 0.157 point increase in the depression score keeping the scores for variables period of stay and level of health fixed. The result obtained was statistically significant ($p=0.00 < 0.05$). This is statistically significant ($p=0.03 < 0.05$). The coefficient for frequency of visitors was 2.038. Hence, for every unit increase in frequency of visitors score, researcher expect a 0.065 point increase in the depression score keeping the scores for variables period of stay and level of health was fixed. This result is statistically significant ($p=0.00 < 0.05$). Symbol of t and Sig. was a constant is significantly different from zero at the 0.05 alpha level as in $p=0.00 < 0.05$. Therefore, based on Table 3, a multiple regression was run to predict depression from frequency of visitors, period of stay and level of health. These variables statistically significant predicted depression, $F = 25.143$, $p < 0.05$, $R^2 = 0.716$. All three variables added statistically significantly to the prediction, $p < 0.05$. In this section, the researcher will discuss further on the relationship between depression and factors of demographic profiles among elderly women in private care institution. Meanwhile, the distribution of frequency of visitors was found that there was a significant relationship between frequency of visitors and depression among elderly women in institution. However, in this section, focus will be given on the residents who were never visited by their children, neighbors, friends, and relatives. It is human nature the lack of attention from loved ones could lead to mental illness, especially depression⁸⁹¹⁰. Hence, residents who did not have any visitors were detected as having depression. Elderly women who stayed longer in homecare tend to have depression¹¹¹². In the present research, it was found that most of the residents are staying more than 12 months. Hence, this might be another factor in most of the institution residents having depression. This statement is also supported by other researches which indicated that the elderly who are staying at nursing homes tend to have depression, regardless of having proper activities because for them, staying with children is more important than staying

in the nursing home^{13,14,15}. Table 3 shows that the prevalence of depression was higher in elderly women who were staying in institutions for longer more than 12 months a (37 people) as compared to those staying for less than 6 months (18 people). The rationale behind the increased prevalence of depression with increasing duration of stay could be due to the feeling of loneliness from the outside world especially in an institution^{16,17,18}. Thus, there are significant positive relationships between duration of stay with depression and loneliness among elderly women. The relationship between levels of health with depression is a well-known issue and has been reported by numerous other researches. The literature suggests that depression may increase the risk of the subsequent level of health among elderly women. According^{19,20,21}, many elderly women have diabetes and other chronic medical conditions that are associated with an increased risk of depression. The presence of a chronic medical illness may in fact decrease the chances of recognition and therefore treatment of depression in the setting. The more severe condition of the illness, the higher the risk of depression²². A meta-analysis of interventions among elderly women with diabetes and depression showed that both psychotherapies and antidepressants were efficacious in treating depression among the elderly women with diabetes. In the study, the relationship between financial support and depression among elderly women in institution was investigated. According to^{23,24} most elderly women are economically disadvantaged. In those cases, the economic crisis especially unemployment acts as a precipitant among elderly women. It is therefore especially important to screen for depression among them during these periods of economic hardship. In other researches by²⁵ depression among elderly women was found to be related to financial difficulties and poverty where lack of financial support was cited as the most prevalence factors for the occurrence of depression.

Conclusion

As a conclusion, the study on the link between demographic profiles with depression among elderly women in private care institution is important to raise awareness about this alarming issue in the society especially among elderly women. Hence, the findings of this research will give a better understanding regarding function of the nursing home in reducing depressions and loneliness among them.

Ethical Clearance: Taken from School of Social

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Reference

- Holwerda TJ, Van Tilburg TG, Deeg DJH, Schutter N, Dekker J, Stek ML, et al. Impact of loneliness and depression on mortality: Results from the longitudinal ageing study Amsterdam. *Br J Psychiatry*. 2016;
- Hao G, Bishwajit G, Tang S, Nie C, Ji L, Huang R. Social participation and perceived depression among elderly population in South Africa. *Clin Interv Aging*. 2017;
- Iannello P, Biassoni F, Bertola L, Antonietti A, Caserta VA, Panella L. The role of autobiographical story-telling during rehabilitation among hip-fracture geriatric patients. *Eur J Psychol*. 2018;
- Lampert MA, Rosso ALP. Depression in elderly women resident in a long-stay nursing home. *Dement Neuropsychol*. 2015;
- Stephoe A, Shankar A, Demakakos P, Wardle J. Social isolation, loneliness, and all-cause mortality in older men and women. *Proc Natl Acad Sci U S A*. 2013;110(15):5797–801.
- Manrique-Espinoza B, Salinas-Rodríguez A, Rosas-Carrasco O, Gutiérrez-Robledo LM, Avila-Funes JA. Sarcopenia Is Associated With Physical and Mental Components of Health-Related Quality of Life in Older Adults. *J Am Med Dir Assoc*. 2017;
- Nurun Saadah S, Lukman ZM, Syafiq MS, Zulaikha MZ, Bukhari WMY, Kamal MY. The Study of Depression and Loneliness among Elderly Women. 2018;II(X):110–3.
- Wei M, Russell DW, Zakalik RA. Adult attachment, social self-efficacy, self-disclosure, loneliness, and subsequent depression for freshman college students: A longitudinal study. *J Couns Psychol*. 2005;
- Singh A, Misra N. Loneliness, depression and sociability in old age. *Ind Psychiatry J*. 2009;18(1):51.
- Matthews T, Danese A, Wertz J, Odgers CL, Ambler A, Moffitt TE, et al. Social isolation, loneliness and depression in young adulthood:

- a behavioural genetic analysis. *Soc Psychiatry Psychiatr Epidemiol.* 2016;51(3):339–48.
11. Russell DW. UCLA Loneliness Scale Version 3 (description of Measure). *J Pers Soc Psychol.* 1996;
 12. S. IR, S. S. Impact of Widowhood and Disability Among Elderly. In 2018.
 13. Steventon A, Roberts A. Estimating length of stay in publicly-funded residential and nursing care homes: A retrospective analysis using linked administrative data sets. *BMC Health Serv Res.* 2012;
 14. B Sangma R, Konjengbam S, Laishram J, Elangbam V. Depression and its associated risk factors among elderly in an urban area: A cross-sectional study. *J Med Soc.* 2018;
 15. Liu HY, Yang CT, Tseng MY, Chen CY, Wu CC, Cheng HS, et al. Trajectories in postoperative recovery of elderly hip-fracture patients at risk for depression: A follow-up study. *Rehabil Psychol.* 2018;
 16. Oliveira PB de, Tavares DM dos S. Health conditions of elderly residents in Long-stay Institution second basic human needs. *Rev Bras Enferm.* 2014;
 17. Atif M, Saleem Q, Babar Z-U-D, Scahill S. Association between the Vicious Cycle of Diabetes-Associated Complications and Glycemic Control among the Elderly: A Systematic Review. *Medicina (B Aires).* 2018;
 18. Aarts JWF, Deckx L, Van Abbema DL, Tjan-Heijnen VCG, Van Den Akker M, Buntinx F. The relation between depression, coping and health locus of control: Differences between older and younger patients, with and without cancer. *Psychooncology.* 2015;
 19. Mata DA, Ramos MA, Bansal N, Khan R, Guille C, Di Angelantonio E, et al. Prevalence of depression and depressive symptoms among resident physicians: a systematic review and meta-analysis. *JAMA - J Am Med Assoc.* 2015;
 20. Adamson BC, Yang Y, Motl RW. Association between compliance with physical activity guidelines, sedentary behavior and depressive symptoms. *Prev Med (Baltim).* 2016;
 21. Liu Y, Li T, Guo L, Zhang R, Feng X, Liu K. The mediating role of sleep quality on the relationship between perceived stress and depression among the elderly in urban communities: a cross-sectional study. *Public Health.* 2017;
 22. Tapia-Muñoz T, Mascayano F, Toso-Salman J. Collaborative care models to address late-life depression: Lessons for low-and-middle-income countries. *Front Psychiatry.* 2015;
 23. Martínez-Alcalá CI, Pliego-Pastrana P, Rosales-Lagarde A, Lopez-Noguerola J, Molina-Trinidad EM. Information and Communication Technologies in the Care of the Elderly: Systematic Review of Applications Aimed at Patients With Dementia and Caregivers. *JMIR Rehabil Assist Technol.* 2016;
 24. Zin T, Myint T, Naing DK, Htay K, Wynn AA, SabaiAung T, et al. A study on health-related quality of life and comorbidity among elderly population in rural Sabah, Malaysia. *South East Asia J Public Heal.* 2016;
 25. Berman G, Muttuvelu D, Berman D, Larsen JI, Licht RW, Ledolter J, et al. Decreased retinal sensitivity in depressive disorder: a controlled study. *Acta Psychiatr Scand.* 2018.

Laparoscopic Sleeve Gastrectomy Versus Laparoscopicmini-Gastric Bypass in Management of Morbid Obesity and its Comorbidities

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Abstract

Background: Laparoscopicmini-gastric bypass (MGBP) is gaining popularity among the bariatric procedures today and laparoscopic sleeve gastrectomy (SG) as a single-stage procedure for the treatment of morbid obesity is becoming increasingly popular.

Patients and Method: Between October 2014 and July 2018, 100 obese patients were randomized, operated upon, and followed up for 24 months in Al Minia University Hospital. A total of 50 patients underwent SG, and 50 patients underwent MGBP. The mean BMI of all patients was $47.8 \pm 5.5 \text{ kg/m}^2$, their mean age was 30 ± 8.3 years and 80% of them were female. Patients were followed up at 1, 3, 6, 9, 12, 15, 18, 21 and 24 months.

Results: Age, sex, BMI, and comorbidities were equal. The mean operative time for SG was 86.9 ± 51.6 min and that for MGBP was 108.4 ± 41.8 min; the percentage of 1-year excess weight loss was similar ($76.2 \pm 4.49\%$ for SG and $80.3 \pm 8.3\%$ for MGBP). The comorbidities were significantly improved after both procedures, except for type 2 diabetes mellitus, which showed a higher resolution rate after MGBP.

Conclusion: Laparoscopic SG regarding excess weight loss is comparable to laparoscopic MGBP in short-term follow-up (2 year) with less metabolic effect. Further long-term studies are needed.

Keywords: Comorbidities, diabetes mellitus, mini-gastric bypass.

Introduction

Obesity is a major health burden worldwide, and although it was considered a disease of the western world, it seems to have expanded to the developing world.^[1] Significant obstructive sleep apnea (OSA) is present in 40% of obese persons and venous thromboembolism in 12%^[2]. More than 70% of patients

with sleep apnea present with obesity^[3]. Conservative measures, Conservative measures physical exercise, have proven inadequate^[4]. Depending on the type of operation, gastrointestinal surgery is also very effective in the resolution of diabetes^[5]. Traditionally, the primary mechanisms through which bariatric surgery achieves its outcomes are believed to be the mechanical restriction of food intake, reduction in the absorption of ingested foods, or a combination of both^[6]. Furthermore, little is known regarding the effect of the various surgical procedures on glycemic control and T2DM remission^[7]. SG was first described in 1999 as part of the biliopancreatic diversion duodenal switch procedure. Subsequently, LSG has been performed as a stand alone procedure^[8]. Although these procedures have proven to be good therapeutic options for some patients such as gastric leaks, which pose a

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particularly difficult challenge when they occur near the angle of His, potentially generating severe clinical conditions that require reoperation, and may even cause death^[9]. Mini-gastric bypass (MGBP), first reported by Rutledge, was proposed as a simple and effective treatment of morbid obesity. MGBP is a modification of the Mason’s loop gastric bypass, with weight loss results similar to laparoscopic Roux-en-Y gastric bypass (LRYGB)^[10], which was the most favored bariatric procedure in America.^[11] However, controversies about the relative safety of this procedure remain, mainly the incidence of marginal ulcer and reflux esophagitis^[12].

Patients and Method

It was done from October 2015 to July 2018. All patients were evaluated pre operatively (full examination, obesity and its comorbidities). Patients were chosen and divided randomly into two groups in accordance to their admission to the study: the first group underwent LSG, whereas the second group underwent laparoscopic MGBP. All patients were evaluated regarding operative time, postoperative recovery, complications, resolution of comorbidities, and percent excess weight loss (% EWL). Results were recorded intraoperatively, early postoperatively, and at 1 month, 3 month, 6 month, 9 month, 12 month, 15 month, 18 month, 21 month, and 24 month intervals. Written informed consent was obtained from all the patients to be included in this study.

Statistical Analysis: Data were collected in tables and then analyzed with respect to χ^2 and *P* value. Data

were fed to the computer and analyzed using IBM SPSS software package version 20.0 (IBM Corp., Armonk, New York, USA). *P* values less than 0.05 were considered significant.

Results

MGB. Overall, three patients with T2DM had complete and three had partial resolution in SG, whereas nine patients had complete and two partial resolution in MGB; three patients had complete and two partial resolution regarding hypertension in SG and five complete and three partial resolution in MGB; dyslipidemia remission was seen in four patients and improved in two patients in SG and seven patients had remission and one improved in MGB. There was resolution of osteoarthritis, OSA, and polycysticovary in all patients in both groups. Bleeding was seen in three cases in SG, where two of them were managed conservatively and one needed exploration, and only one case in MGB, which was managed conservative. Wound infection was recorded in one case in SG and in two cases in MGB. Postoperative nausea and vomiting was seen in five cases in SG and in two cases in MGB; all were managed with antiemetics. Moreover, four cases had port site hernia in SG and two in MGB. Symptomatic cholelithiasis was obvious in both groups; in SG, eleven patients were managed conservative and three patients needed surgery, whereas in MGB, six patients were managed conservatively and one needed surgery.

Table 1: Comparison between the two groups according to operative time and postoperative recovery (days)

Operative time and postoperative recovery (days)	Sleeve gastrectomy (n=25)	Mini-gastric bypass (n=25)	t	P
Operative time (min)				
Minimum-maximum	39.0-95.0	55.0-93.0	1.479	0.146
Mean±SD	68.0±12.56	73.0±11.32		
Begin oral liquids (days)				
Minimum-maximum	0.5-2.6	0.5-2.5	1.111	0.272
Mean±SD	1.23±0.59	1.0±0.85		
Duration of analgesic (days)				
Minimum-maximum	3.0-10.0	3.0-9.0	0.602	0.550
Mean±SD	5.67±2.53	5.27±2.15		
Hospital stay (days)				
Minimum-maximum	2.0-6.0	3.0-7.0	3.777*	<0.001*
Mean±SD	2.27±0.46	3.0±0.85		

Operative time and postoperative recovery (days)	Sleeve gastrectomy (n=25)	Mini-gastric bypass (n=25)	t	P
Return to daily activities (days)				
Minimum-maximum	4.0-12.0	5.0-9.0	3.500*	<0.001*
Mean±SD	4.07±1.44	5.87±2.13		
Return to work (days)				
Minimum-maximum	10.0-16.0	11.0-18.0	0.852	0.398
Mean±SD	11.53±1.68	13.07±8.88		

P, P value for comparing between the two groups. *P≤0.05, statistically significant.

Table 2: Comparison between the two groups according to percent excess weight loss

Percent Excess Weight Loss	Sleeve Gastrectomy (n=25)	Mini-gastric Bypass (n=25)	t	P
1 Month				
Minimum-maximum	23.9644.5	12.5-28.6	6.460*	<0.001*
Mean±SD	32.05±5.96	22.13±4.84		
3 Months				
Minimum-maximum	33.5-66.7	24.0-48.8	6.845*	<0.001*
Mean±SD	54.05±8.2	39.75±6.47		
6 Months				
Minimum-maximum	51.5-80.5	32.8-70.8	2.073	0.054
Mean±SD	67.6±6.45	63.32±8.06		
12 Months				
Minimum-maximum	66.7-87.0	45.6-87.8	2.070	0.054
Mean±SD	76.22±4.49	80.31±8.8		

P, P value for comparing between the two groups. *P≤0.05, statistically significant.

Discussion

A systematic analysis with pooled data from 19 prospective studies adjusted for age, study, physical activity, alcohol consumption, education, and marital status, over 160 000 deaths, showed that overall for men and women combined, for every five unit increase in BMI, a 31% increase in risk of death was observed^[13-14].

There is strong published evidence that bariatric surgery is the only effective means to sustain long-term weight loss, and this weight loss is also associated with the resolution of obesity-related comorbid conditions, which increase the risk of mortality associated with obesity^[15]. In our study, there were 19(38%) patients with T2DM8 in SG and 11 in MGB, 14(28%) patients with hypertension six in SG and eight in MGB, and 14 (28%) patients with dyslipidemia, with six in SG and eight in MGB.

Plamper *et al.*^[16] described in their study comparing SG with MGBP that both groups were comparable

for age, preoperative weight, and BMI as well as the distribution of the associated comorbidities.

In our study, there were 19(38%) patients with T2DM, eight in SG and 11 in MGB; 14 (28%) patients with hypertension, six in SG and eight in MGB; 14 (28%) patients with dyslipidemia, six in SG and eight in MGB; seven (28%) patients with OSA, three in SG and four in MGB; 13 (52%) patients with osteoarthritis, seven in SG and six in MGB; three (12%) patients with PCO, one in SG and two in MGB.

Weight loss is reported in many different ways. Sczepaniak *et al.* evaluated the weight loss has been reported as absolute weight loss, percentage of total weight loss, % EWL, percentage of excess BMI loss, and percentage of patients with successful weight loss^[17].

Boza *et al.*^[18] have reported excellent results of 1000 consecutive LSG procedures with a mean EWL of 84.5% at 3-year follow-up and with minimal weight regain after the first postoperative year. In our study, mean % EWL

was 32.05% at 1 month, 45.05% at 3 months, 67.6% at 6 months, and 76.22% at 12 months in SG and was 22.13% at 1 month, 39.75% at 3 months, 63.32% at 6 months, and 80.31% at 12 months in MGB.

Laparoscopic MGBP in morbidly obese patients with T2DM has been proved to be effective in prospective randomized controlled trials^[19], and in extensive reports in the literature^[20], Lee *et al.*^[21] have suggested that the efficacy of T2DM remission was similar regardless of BMI, and they recommend that more free use of gastric bypass should be considered in Asian patients with T2DM. We found three patients with T2DM had complete and three had partial resolution in SG whereas nine had complete and two had partial resolution in MGB; three patients had complete and two had partial resolution in hypertension in SG, whereas five had complete and three had partial resolution in MGB; dyslipidemia remission was seen in four patients and improvement in two patients in S Gandseven patients with remission and one with improvement in MGB; and resolution of osteoarthritis, OSA, and poly cystic ovary in all patients in both groups.

The primary risk factor for T2DM is obesity, and 90 % of all patients with type 2 diabetes are either over weight or obese^[22]. Gill *et al.*^[23] found that SG results in T2DM resolution ranging from 80% to 96% in morbidly obese subjects. Laparoscopic MGBP in morbidly obese patients with T2DM has been shown to be effective^[23]. Schauer *et al.*^[24] recently demonstrated the superiority of the RYGB over a SG for the morbidly obese patients with remission of T2DM at 3 years.

Obesity is associated with an increased risk of GERD, with up to 50% of morbidly obese patients suffering from this condition. Prachand and Alverdy also concluded that the incidence of GERD seems to be more frequent after LSG^[25]. There is no doubt that 0.5–1.0% of the patients develop malnutrition requiring surgical correction – reversal or shortening of biliopancreatic limb, or conversion to sleeve – after MGB^[26].

In the entire literature, there is only one reported case of Petersen's hernia after MGB^[27]. No internal hernia was recorded in our study, and only four cases developed symptomatic acid ref lux in SG and seven cases developed symptomatic (bile) reflux in MGB. It is believed that MGB results in less dumping and reactive hypoglycemia compared with RYGB. Carbajo *et al.*^[28] did not see any dumping syndrome in their study.

Conclusion

LSG regarding EWL is comparable to laparoscopic MGBP in short-term follow-up (1 year) with less metabolic effect. Further long-term studies are needed.

Ethics: This study was conducted at Minia university hospital and Minia Oncology Center.

Financial: Nil.

Conflicts of Interest: None

References

1. Tsigos C, Hainer V, Basdevant A, Finer N, Fried M, Mathus-Vliegen E, et al. Management of obesity in adults: European clinical practice guidelines. *Obes Facts* 2008;1:106–116.
2. Gruidah HSA, Eldsouky MS, Omran WM, Elhassan AEA. Risk factors for venous thromboembolism. *Menoufia Med J*. 2018; 31:169.
3. Toghaw P, Matone A, Lenbury Y, de Gaetano A. Bariatric surgery and T2DM improvement mechanisms: a mathematical model. *Theor Biol Med Model* 2012;9:16.
4. Blackburn GL, Walker WA. Science-based solutions to obesity: what are the roles of academia, government, industry, and health care? *Am J Clin Nutr* 2005;82:207s–210ss.
5. Rubino F, Kaplan LM, Schauer PR, Cummings DE. The Diabetes Surgery Summit consensus conference: recommendations for the evaluation and use of gastrointestinal surgery to treat type 2 diabetes mellitus. *Ann Surg* 2010; 251:399–405.
6. DeMaria EJ. Bariatric surgery for morbid obesity. *N Engl J Med*. 2007;356:2176–2183.
7. Lee WJ, Chong K, Ser KH, Lee YC, Chen SC, Chen JC, et al. Gastric bypass vs sleeve gastrectomy for type 2 diabetes mellitus: a randomized controlled trial. *Arch Surg* 2011;146:143–148.
8. Deitel M, Crosby RD, Gagner M. The first international consensus summit for sleeve gastrectomy (SG), New York City, October 25–27, 2007. *Obes Surg* 2008;18:487–496.
9. Nocca D, Frering V, Gallix B, des Hons CD, Noël P, Foulonge MP, et al. Migration of adjustable gastric banding from a cohort study of 4236 patients. *Surg Endosc* 2005;19:947–950.
10. Rutledge R. The mini-gastric bypass: experience

- with the first 1,274 cases. *Obes Surg* 2001;11:276–280.
11. Carbajo M, Castro MJ, Kleinfinger S, Gómez-Arenas S, Ortiz-Solórzano J, Wellman R, et al. Effects of a balanced energy and high protein formula diet (Vegestartcomplet®) vs. low-calorie regular diet in morbid obese patients prior to bariatric surgery (laparoscopic single anastomosis gastric bypass): a prospective, double-blind randomized study. *Nutr Hosp* 2010; 25:939–948.
 12. Fox SR, MacDonald KG, Greenville N, Mason EE, Iowa City I, Boyd E, et al. Mini-gastric bypass controversy. *Obes Surg* 2001; 11:773–777.
 13. Santry HP, Gillen DL, Lauderdale DS. Trends in bariatric surgical procedures. *JAMA* 2005;294:1909–1917.
 14. Berrington de Gonzalez A, Hartge P, Cerhan JR, Flint AJ, Hannan L, MacInnis RJ, et al. Body-mass index and mortality among 1.46 million white adults. *N Engl J Med*. 2010;363(23):2211–2219.
 15. Carlsson LM, Peltonen M, Ahlin S, Anveden Å, Bouchard C, Carlsson B, et al. Bariatric surgery and prevention of type 2 diabetes in Swedish obese subjects. *N Engl J Med* 2012;367:695–704.
 16. Plamper A, Lingohr P, Nadal J, Rheinwalt KP. Comparison of mini-gastric bypass with sleeve gastrectomy in a mainly super-obese patient group: first results. *Surg Endosc* 2017;31:1156–1162.
 17. Sczepaniak JP, Owens ML, Shukla H, Perlegos J, Garner W. Comparability of weight loss reporting after gastric bypass and sleeve gastrectomy using BOLD data 2008–2011. *Obes Surg* 2015;25:788–795.
 18. Boza C, Salinas J, Salgado N, Pérez G, Raddatz A, Funke R, et al. Laparoscopic sleeve gastrectomy as a stand-alone procedure for morbid obesity: report of 1,000 cases and 3-year follow-up. *Obes Surg* 2012; 22:866–871.
 19. Lee WJ, Ser KH, Lee YC, Tsou JJ, Chen SC, Chen JC. Laparoscopic Roux-en-Y vs. mini-gastric bypass for the treatment of morbid obesity: a 10-year experience. *Obes Surg* 2012;22:1827–1834.
 20. Wang W, Wei PL, Lee YC, Huang MT, Chiu CC, Lee WJ. Short-term results of laparoscopic mini-gastric bypass. *Obes Surg* 2005; 15:648–654.
 21. Lee WJ, Wang W, Lee YC, Huang MT, Ser KH, Chen JC. Effect of laparoscopic mini-gastric bypass for type 2 diabetes mellitus: comparison of BMI > 35 and < 35 kg/m². *J Gastrointest Surg* 2008; 12:945–952.
 22. Mokdad AH, Bowman BA, Ford ES, Vinicor F, Marks JS, Koplan JP. The continuing epidemics of obesity and diabetes in the United States. *JAMA* 2001; 286:1195–1200.
 23. Gill RS, Karmali S, Sharma AM. Treating type 2 diabetes mellitus with sleeve gastrectomy in obese patients. *Obesity* 2011; 19:701–702.
 24. Schauer PR, Bhatt DL, Kirwan JP, Wolski K, Brethauer SA, Navaneethan SD, et al. Bariatric surgery versus intensive medical therapy for diabetes 3-year outcomes. *N Engl J Med*. 2014; 370:2002–2013.
 25. Prachand VN, Alverdy JC. Gastroesophageal reflux disease and severe obesity: fundoplication or bariatric surgery? *World J Gastroenterol* 2010; 16:3757.
 26. Noun R, Skaff J, Riachi E, Daher R, Antoun NA, Nasr M. One thousand consecutive mini-gastric bypass: short- and long-term outcome. *Obes Surg* 2012; 22:697–703.
 27. Genser L, Carandina S, Soprani A. Petersen's internal hernia complicating a laparoscopic omega loop gastric bypass. *Surg Obes Relat Dis* 2015; 11:e33–e34.
 28. Carbajo M, García-Caballero M, Toledano M, Osorio D, García-Lanza C, Carmona JA. One-anastomosis gastric bypass by laparoscopy: results of the first 209 patients. *Obes Surg* 2005; 15:398–404.

A Real-Time Polymerase Chain Reaction assay for the Simultaneous Detection of Sexually Transmitted Pathogens in Women

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Abstract

Genital tract infection is a major source of morbidity in sexually active individuals. Reported rates of STD underestimate the exact problem of infection because the majority of STDs are asymptomatic and therefore go undetected especially in our community. The aim of this study was to investigate for the prevalence STD pathogens in females. 184 urogenital swabs collected from outpatient females then analyzed by Real-Time PCR for eight different pathogens (*Neisseria gonorrhoeae*, *Chlamydia trachomatis*, Herpes simplex virus, *Trichomonas vaginalis*, Hepatitis viruses B & C, *Mycoplasma genitalium* and Human papillomavirus). 90.21% of samples resulted positive for one of the targets named above. PCR is a beneficial diagnostic technique for STDs since it has a highly specific and sensitive. the most prevalence pathogen was Human papilloma virus 40.96%.

Keywords: STD; *Neisseria*; *Chlamydia*; *Herpes*; *Mycoplasma*; *Trichomonas*; *Hepatitis*; *Papillomavirus*.

Introduction

The term of Sexual transmitted diseases STDs define of an infection caused by more than 30 varied bacteria, viruses and parasites which are transmitted through sexual intercourse¹ and are a main cause of chronic and acute infection and their consequences like ectopic pregnancy, malignancy, infertility and death of neonates worldwide, not only in developing, but also in developed countries^{2,3}. Reported of STD rates underestimate the exact problem of infection because the majority of STDs are asymptomatic and undetected especially in our community⁴. Whereas many of these infections are preventable and curable but the morbidity and mortality related with STD remain high. The incidence STD pathogens is increasing for the first time in a decade even increasing in resistance to antibiotic is fast evolving too^{5,6}. WHO estimates that STDs are one of the five groups of diseases for which adults in the world most commonly search for medical assistance, contain a series of diseases of various infectious agents, in which sexual transmission remains a main epidemiologic role, from time to time the infectious agents can spread

in a diverse routes, from mother to her baby, by blood transfusion or tissue transfer^{7,8}. The problem with STDs are asymptomatic infections and about 70% of females with chlamydia infections and gonococcal experience no symptoms at all and so STDs can be passed on unaware way⁶. This type of infectious diseases caused by virus agents like bacteria, viruses, protozoa or arthropods that are mostly acquired by sexual contact⁹. All of above increasing the necessity for more sensitive, rapid and diagnostic examinations to decrease the prevalence of it. Whereas the complications of STDs can be serious, but on other side, several of these consequences are preventable if suitable, efficient, sensitive, specific and ease of handling appropriate and rapid screening is done to those are strongly suspected. The main purposes of diagnostic tests for STDs are helping in typical cases diagnosis, atypical cases, asymptomatic infections and likewise various infections¹⁰. However, not all sexual contacts with these microorganisms cause infections, then not all infections developing to be long-term problems, which propose that main factors for instance microbiota of vagina, host immunity status, pathogen appropriateness and load may modulate the natural

history of these infections¹¹. The current diagnostic tests for STDs are fraught with some challenges, with delay in results, absence of specificity and sensitivity. Though, Molecular diagnosis method is a new technique contributed to more fast diagnosis and effective treatment⁵. These method are suitable for organisms that are unculturable or difficult to culture since molecular diagnostic method offer elevated sensitivity, specificity and rapidity¹⁰. Based on the above, this study was done to determine the prevalence of STD pathogens in females by molecular diagnosis method.

Material and Method

Patients: We conducted a cross-section study among all patients who had go to the STD clinics. The study took place from April/2016 to December/2018. The information was collected via a questionnaire filled with the help of a physician during an interview. The patient was questioned for precise signs and symptoms at the time of inclusion. Since a patient subject to contact tracing has a higher risk of being positive for a specific STI. A total of 184 urogenital swabs was collected from 184 outpatient females with suspected genital infections or presenting with vaginal discharge to our study clinics. Urogenital swabs were sorted into 2 ml of sterile PBS, then were vortexed to use in DNA extraction step as shown by Liang and co-workers¹².

DNA extraction: was carried out via “AccuPrep Genomic DNA Extraction Kit”/BIONEER/South Korea. While for viral Extraction we used “Viral Nucleic Acid Extraction II” from Geneaid/Taiwan.

PCR Kits:

- Real-time PCR kit of Chlamydia and Neisseria gonorrhoeae from Liferiver/China.
- Singleplex PCR kit from Sacace Biotechnologies/ Italy used for HSV detection.
- “AccuPower® HPV 16 and 18/Korea” is a diagnostic kit aimed at detection of HPV.
- “RealAccurate® TVMGres” Kit used to detect *T.vaginalis* and *M.genitalium*.

Every single test was done in keeping with the manufacture’s instruction provided with each kit and all amplified products were subjected to electrophoresis via 1.5-2% of agarose gel.

Results

184 urogenital swabs were received and processed in the study period collected from females suffered for different reproductive problems, 166 samples were positive for one of eight types of organisms causing STD detected in this study. Table 1 summarizes the socio-demographic features of the participants. The mean was 37.7 year and Median of female was 32.40 year. The age range was 18 to 50 years, with near to 25% of the participants being younger than 29, and more than 75% was younger than 39. Overall, 48.91% attended secondary school. All females were classified with vaginal discharge or warts or abdominal pain but no woman was classified as vaginal discharge alone. Females which attending to reproductive clinic services because of infertility problems was 10.32% and 5.43% suffered spontaneous abortions.

Table 1: Sociodemographic analyses of sexual transmitted diseases

Variable	(n =184)	%
Female	184	
Baghdad/Iraq	184	
Age Groups (Years)		
≤<19	26	14.13
20–29	22	11.95
30 – 39	117	63.58
40-49	13	7.06
⇒>50	6	3.26
Married	155	84.23
Single	29	15.76
Symptoms	134	72.82
Infertility	29	15.76
Infected partner	21	11.41
Education: Yes	162	88.04
No	22	11.9
Educational Level		
None	22	11.95
Primary school	46	25.0
Secondary school	90	48.91
Higher education	26	14.13

Our PCR-based assay was established for the detection of eight major STIs in addition to a novel internal control DNA sequence for each one. Positive samples had been identified by PCR and showed one band at a specific DNA fragment of all STD pathogens in the first round of reaction when examined by gel electrophoresis as showing in Figure 1 & 2.

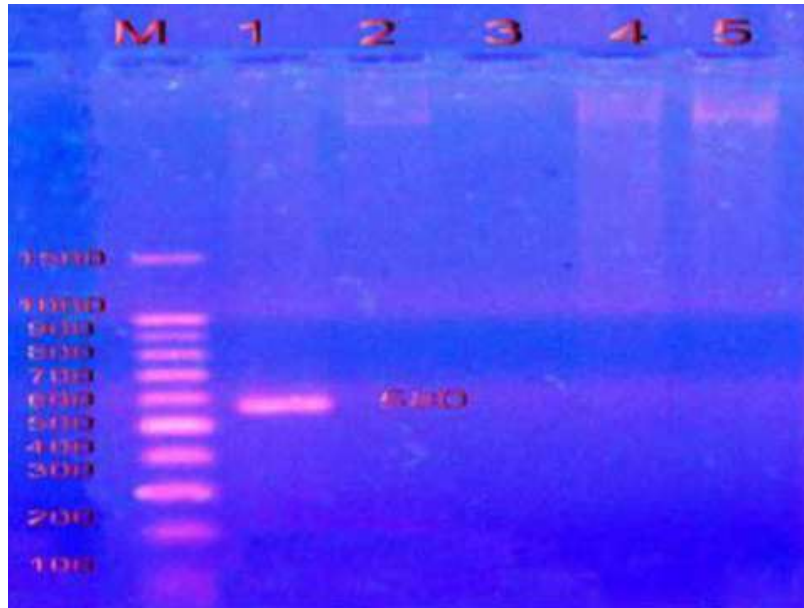


Figure 1: Electrophoresis of PCR product, lane-1 positive for HSV.

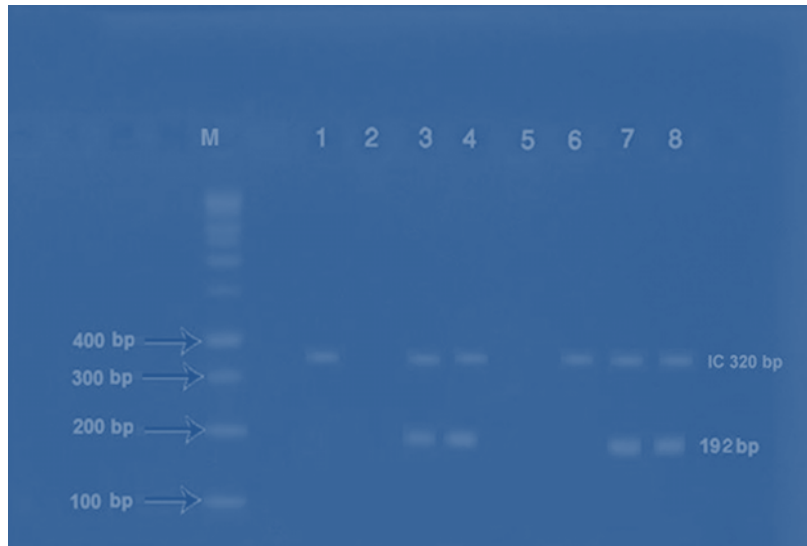


Figure 2: PCR product on 2% agarose gel, using Ethidium bromide.3, 4 and 7 positive samples. Lanes 5,6 negative samples

Table 2: Prevalence of STDs pathogens

Organism	Positive	%
Neisseria gonorrhoeae	39	23.49
Chlamydia trachomatis	10	6.02
Herpes simplex virus1	10	6.02
Trichomonas vaginalis	21	12.65
hepatitis B virus (HBV)	2	1.20
hepatitis B virus (HCV)	4	2.40
Mycoplasma genitalium	12	7.22
Papillomavirus	68	40.96
Total	166	100%

As shown in Table 2; Of the 184 urogenital swabs collected from suspected females with STD, 68 swabs were positive for HPV and it was the most frequent agent with 40.96% once considered in isolation and no cases of infection by Human Immunodeficiency Virus was diagnosed.

Discussion

STDs are often asymptomatic, difficult and very expensive to diagnose. This is mainly correct in countries with restricted health facilities of diagnosis and treatment. Then there is a social stigma attached to

people with STIs which lead them to looking for care from other alternative providers. Therefore, people embarrassed of looking for consultation from physicians in early stage of their infection. Identifying the genetic material of a pathogen doesn't necessitate the pathogen should be alive contrasting culture. It also doesn't need the infection to have occurred a long enough time ago for people to have developed a detectable specific antibody. which means that PCR can detect some diseases earlier than other tests, Even better. STDs can be detected without needs to be concerned about keeping samples alive or testing at exactly the right time. Our results clearly showed that women between 19 to 39 years old are mainly affected by STI which is also consistent with a study performed in China which found that 20-39 years the most prevalence age of STD¹². HPV infection is associated with the rising in prevalence of HPV-related cancer, nonetheless, at present there are no clinical precise guidelines differentiating in treatment between cancers which HPV positive or negative¹³. However, PCR test validation data showed that this technique is appropriate for the detection of HPV-DNA in specimens with a very high sensitivity and specificity. In our study, HPV was detected in 40.96% of positive patients for STD with the highest prevalence than all other detected pathogens in women. Amorim and co-workers detected high intensities of this virus among women tested in Brazilian study on woman with cervical lesions¹⁴. For practical purposes, diagnosis of *M.genitalium* is limited to PCR, as culture is extremely slow taken months, insensitive and challenging¹⁵. In our study, *M.genitalium* 7.1% has a higher incidence than *C.trachomatis* 6.02% in sample collected from females. Studies of *C.trachomatis* and *M.genitalium* in changed subpopulations have been obtainable over the years, and these demonstrate that the incidence and rate of these STIs change significantly in diverse situations, and this result similar to Sweden study done in 2018 showing that the incidence of *M.genitalium* was higher than *C.trachomatis* in study population 9.6-7.1%¹⁶. The majority of bacterial vaginosis serve as a common causative agent of "vaginal discharge syndrome" that has been described in other studies like^{17,18,19}. Using PCR for detection of STIs was most common assay for diagnosis of *N.gonorrhoeae* which consider as a significant health problem, especially with many evidences of increasing of resistance to antibiotics²⁰. Our research showed the positive rate of *N.gonorrhoeae* was 23.49%, which was close enough to previous reports with rate 24.0%¹⁷, but much higher than others 0.7%, 0.8% and 0.16 Sequentially^{18,20,21}.

In this study, 6.02% of positive patients for Human herpes virus, which close to result of a study done by Grech in 2017 found that 5.3% of females have HSV²¹. Nonetheless, in other Iraqi study done in 2018 shown that just 2 of 200 samples collected from females attending the Gynecology outpatient which lesser than our results²². In Turkey, Dinc reported a frequency of HSV in women was 2.2%²³. Chlamydial infections are one of the major contagious diseases in sexually active individuals which cause bacterial STI like urethritis and mucopurulent cervicitis in women²⁰. In our study *C.trachomatis* percentage is 6.02% which very near to the result of a study done by van Lierethat 6.8% of urogenital swabs detected by molecular assay was positive for *C.trachomatis*²⁴. While a study done in Italy exposed that just 23 of 1272 specimens collected from female patients were positive for *C.trachomatis*²⁰. In an Iranian study done on women with abortion found that 15.32% of samples diagnosed with *C.trachomatis* which could be an evidence of role of this organism in abortion²⁵. In our study, the prevalence of *T.vaginalis* was 12.65%. This finding was comparable with other study from Iraq, in which the prevalence of *T.vaginalis* was 14.5% besides 19.0% in Zimbabwe and 11% in Egypt^{26,17,27}. However, this result was lesser than the incidence of *T.vaginalis* in pregnant women posttreatment 40% reported by Lazenby and Thompson in 2019²⁸. In a study conducted in UK in 2014 suggest that 10–50% of women associated with asymptomatic infection with *T.vaginalis*²⁹. HBV can cause infections by sexual transmission but can also causing infections via many other routes. As atypical STD, infection of HBV is well documented and could present in all natures of populations³⁰. Though, hepatitis C virus not documented as STD. The present study has informed a low prevalence of HBV and HCV among screening women, which was 1.2% and 2.4% respectively, these results were very close to study done by Godha and co-worker in 2019 found that prevalence HBV was 1.09% and HCV 0.61%³¹. In other study done by Niama and co-worker found that prevalence of HBV and HCV were 4.2%, 0.7% respectively³².

As a final point, this study could limit in small size of the samples and its retrospective design³³. On the other hand, a lot of other studies suggest that is co-infection between two or more STI pathogens in the same specimen, However, such as this association wasn't confirmed in our study. Our data suggest the presence of eight analyzed pathogens that found samples

collected from sexually active women and detection of STD pathogens by real time PCR presented to be a very sensitive and specific technique for diagnosis STD pathogens in females' urogenital swabs.

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Conflict of Interest: Nil

References

1. Samkange-Zeeb, F. Assessing knowledge and awareness of sexually transmitted infections among school-going adolescents. MSC thesis. University of Bremen.2013.
2. Samkange-Zeeb, F. N., Spallek, L. & Zeeb, H.Awareness and knowledge of sexually transmitted diseases (STDs) among school-going adolescents in Europe: a systematic review of published literature. BMC Public Health.2013.11:727.
3. Fenton, K.A.and Lowndes, C.M.Recent trends in the epidemiology of sexually transmitted infections in the European Union. Sex Transm Infect.2004.80.
4. de Castro Rocha, D.F.N., da Cunha Rosa, L.R., deAlmeida Silva, C., deOliveira, B.R., Martins, T.L.S.; Martins, R.M.B., deMatos, M.A., Carneiro, M.A., dos Santos, S.J.P., de Oliveira e Silva, A.C., de Souza, M.M., Cook, R.L.Caetano, K. A.A. and Teles, S.A.Epidemiology of HIV, syphilis, and hepatitis B and C among manual cane cutters in low-income regions of Brazil. BMC Infectious Diseases.2018.18:546.
5. Yarbrough, M.L. & Burnham, C.D. The ABCs of STIs:An Update on Sexually Transmitted Infections. Clinical Chemistry.2016.62:6.
6. Shannon, C.L.and Klausner, J.D.The Growing Epidemic of Sexually Transmitted Infections in Adolescents: A Neglected Population.Curr Opin Pediatr.2018.V:30(1), p:137–143.
7. Díez, M and Díaz, A.Sexually transmitted infections:Epidemiology and control. Rev Esp Sanid Penit.2011.V13: 58-66
8. Wagenlehner, F.M.E., Brockmeyer, N.H., Discher, T., Friese, K. & Wichelhaus, T.A. The Presentation, Diagnosis, and Treatment of Sexually Transmitted Infections. Deutsches Ärzteblatt International. 2016.113: 11–22.
9. Drago, F; Ciccicarese, G.; Zangrillo, F; Gasparini, G; Cogorno, L; Riva, S; Javor, S; Cozzani, E; Broccolo, F; Esposito, S. & Parodi, A.A Survey of Current Knowledge on Sexually Transmitted Diseases and Sexual Behaviour in Italian Adolescents. Int.J.Environ.Res.Public Health.2016.13, 422.
10. Muralidhar, S.Molecular method in the laboratory diagnosis of sexually transmitted infections. Indian J Sex Transm Dis AIDS.2015.36(1).
11. Tamarelle, J.; Thiébaud, A.C.M.; de Barbeyrac, B.; Bébéar, C.; Ravel, J. & Delarocque-Astagneau, E.The vaginal microbiota and its association with Human Papillomavirus, Chlamydia trachomatis, Neisseria gonorrhoea and Mycoplasma genitalium infections: a systematic review and meta-analysis. Clinical Microbiology and Infection.2018.4:19.
12. Liang, Y.Y.; Zhai, H.Y.; Li, Z.J., Jin, X., Chen, Y., Chen, S.P. Prevalence of Ureaplasma urealyticum, Chlamydia trachomatis, Neisseria gonorrhoeae and herpes simplex virus in Beijing, China. Epidemiology and Infection.2019.147, e59
13. Harlé, A; Guillet, J.; Thomas, J.; Sastre-Garau, X.R.M.; Ramacci, C; Gilson, P; Dubois, C; Dolivet, G.; Leroux, A; Salleron, J. & Merlin, JL. Evaluation and validation of HPV real-time PCR assay for the detection of HPV DNA in oral cytobrush and FFPE samples. Scientific Reports.2018.8:11313.
14. Amorim, AIT; Marques, LM; Campos, G.B.; Lobão, T.N.; de Souza Lino, V.; Cintra, R.C.; Andreoli, M.A.; Villa, L.L.; Boccardo, E.; Braga Junior, A.C.R.; Mendoza López, R.V.; dos Santos, D.B.; de Souza, G.M.; Romano, C.C. and Timenetsky, J.Co-infection of sexually transmitted pathogens and Human Papillomavirus in cervical samples of women of Brazil.BMC Infectious Diseases:2017.17:769.
15. Unemo, M.; Ballard, R.; Ison, C.; Lewis, D.; Ndowa, F. & Peeling, R. Laboratory diagnosis of sexually transmitted infections, including human immunodeficiency virus.World Health Organization.2013.
16. Nolskog, P.; Backhaus, E.; Nasic, S. & Enroth, H. STI with Mycoplasma genitalium—more common than Chlamydia trachomatis in patients attending youth clinics in Sweden. European Journal of Clinical Microbiology & Infectious Diseases.2018.
17. Chirenje, Z.M.; Dhibi, N.; Handsfield, H., H;

- Gonese, E.; Tippett, B; Gwanzur, L.; Latif, AS.; Maseko, DV; Kularatne, R; Tshimanga, M; Kilmarx, PH.; Machiha, A; Mugurungi, O.; Rietmeijer, C.A. The Etiology of Vaginal Discharge Syndrome in Zimbabwe: Results from the Zimbabwe STI Etiology Study. *Sexually Transmitted Diseases*: 2018. V45:6, p422–428.
18. Mlisana K, Naicker N. & Werner L. Symptomatic vaginal discharge is a poor predictor of sexually transmitted infections and genital tract inflammation in high-risk women in South Africa. *J Infect Dis*. 2012.206:6–14.
 19. Khan, S.A., Amir, F. & Altaf, S. Evaluation of common organisms causing vaginal discharge. *J Ayub Med Coll Abbottabad*. 2009.21:90–93.
 20. Del Prete, R.; Ronga, L.; Lestingi, M.; Addati, G; Angelotti, UF; Di Carlo, D. & Miragliotta, G. Simultaneous detection and identification of STI pathogens by multiplex Real-Time PCR in genital tract specimens in a selected area of Apulia, a region of Southern Italy. *J.Infection*.2017.
 21. Grech, P.; Marchant, R. and Samuel, M. Sexual health of women aged 40 and over attending an inner city integrated sexual health clinic. *International Journal of STD & AIDS*. 2016. V.28(4); P:404–407.
 22. Ali, M.K.; Hathal, HD.; and Almoayed, HA. Prevalence and Diagnosis of Genital Herpes by Immunological and Molecular Study. *Iraqi JMS*; 2018. V:16(1).
 23. Dinc, B; Bozdayi, G; Biri, A; Kalkanci, A; Dogan, B.; Bozkurt, N & Rota, S. Molecular detection of cytomegalovirus, herpes simplex virus2, human papillomavirus 16-18 in Turkish pregnant. *Braz J Infect Dis*; 2010.14(6):p:569-574.
 24. van Lier, G.A.F.S.; Hoebe, C.J.P.A.; Dirks, J.A.M.C.; Wolffs, P.F.G. & Dukers-Muijers, N.H.T.M. Spontaneous clearance of urogenital, anorectal and oropharyngeal Chlamydia trachomatis and Neisseria gonorrhoeae in women, MSM and heterosexual men visiting the STI clinic: a prospective cohort study. *Sex Transm Infect*.2019.
 25. Zahirnia, Z.; Mansouri, S.; Saffari, F. & Mansouri, G. Frequency of Chlamydia trachomatis, Mycoplasma genitalium, and Ureaplasma urealyticum Isolated From Vaginal Samples of Women in Kerman, Iran. *Arch Clin Infect Dis*; 2018. 13(6):65334
 26. Geremew, R.A.; Agizie, B.M.; Bashaw, AA; Seid, ME and Yeshanew, A G. Prevalence of Selected Sexually Transmitted Infection (STI) and Associated Factors among Symptomatic Patients Attending Gondar Town Hospitals and Health Centers. *Ethiop J Health Sci*; 2017.27(6):589.
 27. Hussein, A.H.; Saleh, M.H.; Nagaty, I.M; Ghieth, K.A. and El-Azab, N.A. Prevalence, Clinical Criteria and Sociodemographic Predictors of Trichomonas vaginalis Infection in Suspected Egyptian Women, Using Direct Diagnostic Techniques. *Iran J Parasitol*: 2015. V:10(3), p. 432-440.
 28. Lazenby, G.B. & Thompson, L. Unexpected High Rates of Persistent Trichomonas vaginalis Infection in a Retrospective Cohort of Treated Pregnant Women. *Sexually Transmitted Diseases*. 2019. V:46(1).
 29. Sherrard, J.; Ison, C.; Moody, J.; Wainwright, E.; Wilson, J. & Sullivan, A. United Kingdom National Guideline on the Management of Trichomonas vaginalis 2014. *International Journal of STD & AIDS*, 2014.V:25(8) 541–549.
 30. Inoue, T. & Tanaka, Y. Hepatitis B virus and its sexually transmitted infection – an update. *Microbial Cell*; 2016.V:3(9), p:420-437.
 31. Godha, V.R; Prasad, J.V.D.S.; Kuman, V.; Pinjala, P; Ananthula, VK and Dudhipala, SR. Seroprevalence of HSV, HBSAg & HCV in STD clinic attendees of a tertiary care state headquarters hospital. *Journal of Evolution of Medical and Dental Sciences*.2019.V:6(63), p.4609.
 32. Niama, F.R; Bongolo, N.C.L.; Mayengue, P.I.; Mboussou, F.F.; Bayonne, E.S.K.; Nzingoula, F.M.K.; Dossou-Yovo, L.R.; Louzolo, I.; Etoke-Beka, M.K.; Lanzy, A.; Yameogo, I.; Louvouezo, D.; Kobawila, S.C.; Puruhence, M. & Parra, H.J.A study on HIV, Syphilis, and Hepatitis B and C virus infections among female sex workers in the Republic of Congo. *The official journal of the Belgian Public Health Association*, 2017.75:21.
 33. Taher, Noor M. Pathogenic Bacteria Isolated from Personal CellPhones of Health Care Staff in Iraqi Hospitals. *Journal of Pure & Applied Microbiology*. 2019.13(2).

The Impact of Social Media on Undergraduate Medical Students in the University of Kerbala, Iraq

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Abstract

Background: Social networks refer to web-based and mobile applications available on various platforms that allow users to exchange information, ideas, feelings, files, update their status and interact with other user-generated contents over internet. Social networks are becoming increasingly popular among university students.

Objectives: Explore the impact of social media on undergraduate medical students in the University of Kerbala and to determine the factors affecting the attitude and practice of medical students to the social media networks.

Method: A cross sectional study, was conducted among medical students, of both gender, from first to sixth stage in University of Kerbala/Iraq. The total sample collected was 774 students, 40 students were excluded, and accordingly, the sample was 734 students. The data were collected using a valid self-administered questionnaire that was modified to be suitable for Iraqi society. Student T test and Analysis of variance test were used to identify factors correlated with the impact of social media and p-value at the level of less than 0.05 is considered as significant value.

Results: About 98.2% of the medical students were used social media daily, they were used more than 4 sites to access, Majority of them used Telegram 93.7% and YouTube 89.6%. spent about 6 hours/day, more than 10 time/day, they were used social media during free time, more active at night, also the students had got a benefit from the site of college. There was a high significant difference between positive impact and stage, time spent. While there was no significant correlation with duration of sleep at night.

Conclusions: Overall, the impact of social media on undergraduate medical students in the University of Kerbala was positive. There was no significant correlation between gender, time spent on social media, duration of sleep at night and students' performance.

Keywords: Social media, medical students, Telegram.

Introduction

Social media (SM) is a form of electronic communication intended to create online communities, it

is one of the factors that can affect our life style⁽¹⁻²⁾. Fifty years ago, no one knew a term of "Social Media". But now, everyone knows about it⁽³⁾. In the beginning, the Facebook was created as social networking for college students. YouTube was launched in 2005, Twitter was launched in 2006, it was known as social networking and microblogging site⁽⁴⁻⁶⁾. Worldwide, the number of internet users was 3.9 billion up from 3.65 billion in the previous years and 2.31 billion persons are SM users, delivering 31% global penetration⁽⁷⁻⁸⁾. Facebook is the most popular and top-visited SMS⁽⁹⁾. Telegram has

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recently reached 200 million monthly active users⁽¹⁰⁾. In Iraq the types of SM are Facebook, YouTube, Twitter, WhatsApp, Instagram, Telegram, Viber, Google, Games, Blogs, LinkedIn, VK Kontakte and Q Zone⁽¹¹⁾. Internet users in Iraq reached about 19,000,000 users in 2018 and a survey by Arab Advisors Group of Iraqis above 18 years old reported that 77.9% of the responders are using one or more social network^(12, 13). One of the most crucial areas in which SM has made an impact is the world of education⁽¹⁴⁾. Whether SM sites is favorable or unfavorable, every day, many students are spending countless hours immersed in SM⁽¹⁵⁻¹⁶⁾.

Data on the influence of SM on Iraqi students are limited. The aim of this study was to assess the impact of SM at the College of Medicine, University of Karbala, Iraq.

Subject and Method

A cross sectional study, was done in University of Kerbala among students of both genders, First through sixth stage in college of medicine. From the period of February 15, 2019 till 1st of May 2019, data collection was carried out two days a week. The collected total sample was 774 students, 40 students were excluded (because they did not answer the questionnaire completely), accordingly, the sample was 734 students. A specially designed questionnaire has been prepared; it was quoted from other studies which were modified, validated and evaluated by specialists. The data collection was done through a self-administered questionnaire from participant's students. It was designed to include 3 parts. The first part of questionnaire includes questions (Q) about sociodemographic status of participant student that consists of 8 questions which include (Gender, age, stage, marital status, father and mother educational attainment, place of residence and household income). The second part consist of 17 questions that include information about how the student uses the social media. The third part of questionnaire was including a statements about the positive and negative impact of social media on medical students. The positive influence

statements were about 9 items and the negative influence statements were 9 items also. Questionnaire had been tested by a pilot study included 50 students of collage of medicine for all stages, to assess the clarity of questions, the feasibility of the questionnaire and to overcome any difficulties or related issues that may arise during data collection and to estimate the time needed to complete the questionnaire. Based on a pilot study minor changes were done on questionnaire. Pilot sample was excluded from the study sample.

Statistical Analysis: The data was entered and analyzed using the statistical package for social science program (SPSS version 25). Quantitative data are presented as means, standard deviation while qualitative data are presented as frequency, percentage. Student-T test and F test were used to find the association between categorical variable and continuous variable. To examine correlations, parametric (Pearson's) simple correlation coefficients (r) was used. The mean differences were considered to be statistically significant when the P-value was found to be less than 0.05.

Scoring system of social media impact: Each correct answer was given 1 while incorrect answer and don't know answers were given zero. The impact of SM on participant's students was positive and negative impact for each impact was 9 questions. The analysis on average response on a 4-point scale. The total score of SM impact were 36 score. For a maximum score of 36 points (100%), and the total impact score was calculated as:

$$\frac{\text{Subject impact score}}{\text{Maximum impact score (36)}} \times 100\%$$

Results

The total number of participants was 734 students from college of medicine, with a response rate of (85.6%) in this study 98.2% of medical students were used social media daily, most students were entering more than 10 time/day, more active at night and the students had got a benefit from the site of college as shown in table 1.

Table 1: The relationship between positive impact mean score and pattern of SM usage:

		N	Mean	SD	P value
How often do you log to SNSs	Everyday	720	70.42	14.03	0.002*
	Alternate day	7	69.84	8.09	
	Once a week	4	50.00	21.15	
	2-3 times weekly	2	44.44	15.71	
How many times do you enter SNSs a day	Not every day	21	62.96	18.29	0.007*
	Once a day	29	69.83	14.24	
	2-5 times a day	230	69.47	13.25	
	6-10 times a day	159	68.68	12.93	
	More than 10 times	294	72.24	14.86	
At what time are you most active on SM	At the morning	16	65.28	14.20	0.566*
	At the noon	48	70.54	13.69	
	At the afternoon	117	70.49	15.06	
	At the night	552	70.30	14.00	
Benefit from site of medical college	No	264	68.15	14.81	< 0.001*
	Sometime	271	69.75	12.84	
	Yes	198	73.68	14.38	

*F test significant P value ≤ 0.05

All students (100%) were using SM sites, the average time spent by students on SM was (4.64±2.56) hours/day, whereas the duration of sleep was (6.10±1.47) hours at night as shown in table2.

Table 2: The time spent by students on social media sites per a day and the duration of sleep at night

	N	Min	Max	Mean	SD
How many hours do you spend on social media per day?	734	1	12	4.64	2.56
How many hours do you sleep at night?	734	1	9	6.10	1.47

Most students (represent 32%) were using more than 4 sites to access social networking sites as shown in figure 1.

Correlation between negative impact mean score and duration of sleep at night: There is a negative correlation with a high significant difference (Pearson (r) =- 0.153, p> 0.001) between positive impact mean score and age\years for participant’s students. There is a direct relationship (positive correlation) with statistically significant difference between positive Mean score and time spent on SM in hours\day, (r=0.103), (p=0.003). There is a positive correlation with no statistically

difference between positive impact mean score and duration of sleep at night (r=0.041) (p=0.242).

There is no significant correlation, (r= 0.014, p=0.704) between negative impact mean score and age\years for participant’s students. There is a positive correlation) with a high significant correlation between negative mean score and time spent on SM in hours/day, (r=0.153), (p>0.001). There is negative correlation, with

statistically significant correlation ($r=-0.083$) ($p=0.024$) between negative impact mean score and duration of sleep at night.

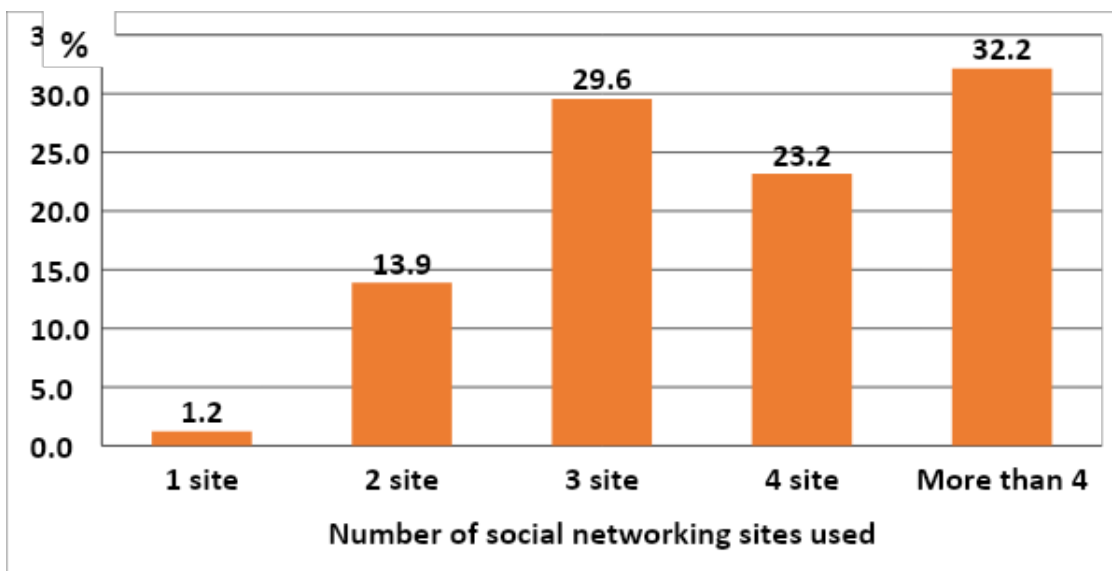


Figure 1: Number of social networking sites used by students.

Telegram was the first social media sites used by students followed by Instagram, then YouTube and Facebook come in 4th place as shown in figure 2.

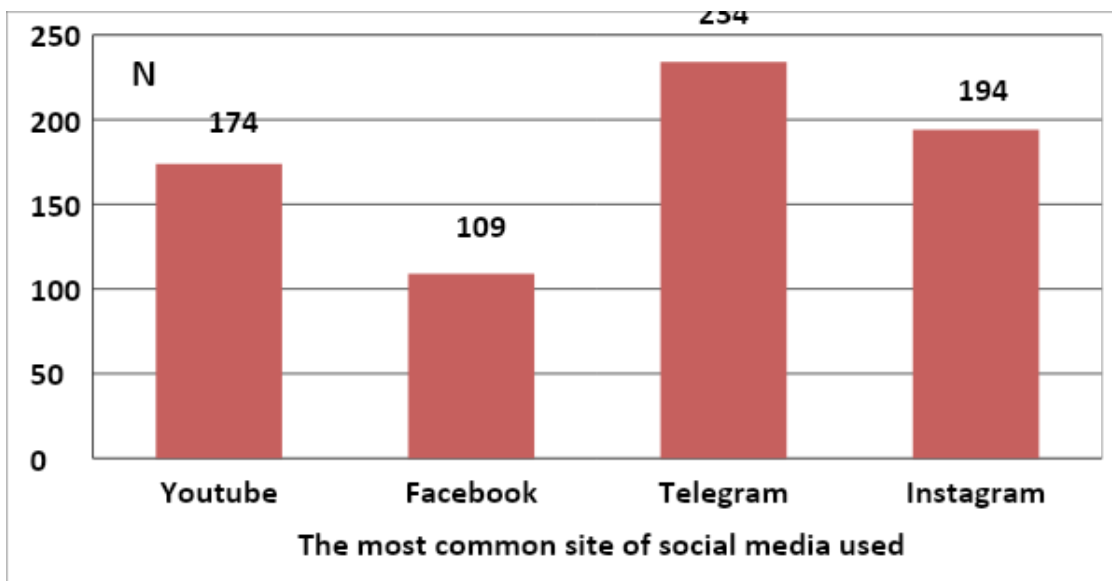


Figure 2: The most common site of social media used by participants.

Discussion

Social networking sites has emerged not only as an effective means of communication during free time patterns rather it has been described as efficacious means of professional communication and professional learning as well as knowledge-management⁽¹⁷⁾. Regarding to patterns of SM usage. Majority of participants were

using SMS daily (98.2%), which was similar to study done in India (2017)(18). also the majority of students were access SMS during free time (97.4%), and they were more active at night (75. 3%).which was similar to a study done in Iran (2016)⁽¹⁾. Most of students in this study were using more than 4 sites to access SMS while the students in Baghdad (2018), Babylon (2017)

University and Sultanate Oman were use 2 sites⁽¹⁹⁻²¹⁾. About 42% of students were entering SM more than 10 times/day which was similar to a study done in Saudi Arabia (2018)⁽⁸⁾. The mean time spent by students on social networks was (4.64±2.56) hours per day which highlight that medical students have been spending significant time on these social networks. Our results are consistent with a study performed on the students of University of Baghdad (2018) and University of Babylon (2017)^(19,20). Which demonstrated that a significant proportion of students spent more than three hours per day on social networks. While our results are different from a study conducted among medical students in Saudi Arabia (2018), Oman (2013), Ghana (2018), India (2017)^(8,18,21,22). Which reported that most students spent 2 hours per a day and another study reported 60 minutes per a day usage in Italian university (2016) (23). About the duration of sleep at night predominant percentage of students had duration of sleep at night about 6 hours, this result was similar to a study done by Abbas et al in Hilla/Iraq. It is worth mentioning that 7 hours of sleep a day is the minimum number of hours of sleep need for young people between the ages of 18 to 25 years, according to National Sleep Foundation⁽²⁴⁾. The Telegram was the most popular site, this result was different from results in Baghdad (2018), Babylon (2017) university in Iraq, Oman (2013), India (2018), Malaysia (2018), Ghana (2018), in which Facebook was the most popular^(19-22, 25, 26). While in Saudi Arabia (2018) the most common site was WhatsApp⁽⁸⁾, this different might be due to the students in current study preferred to use the Telegram because it is more speed and more security very easy to use, fast in uploading and downloading files, and easy to connect with members. The predominant number of students had got a benefit from the site of medical college on social websites. This result was similar to study done in Babylon University in Iraq (2015)⁽²⁷⁾. The current study showed that the correlation between positive impact mean score and age/years for participant's students was indirect relationship (negative correlation). there was direct relationship (positive correlation) between positive mean score and time spent on SM in hours/day, this might be due to that the students who use these SMSs more time tend to appreciate their advantages more than the others, and they were find more benefit from SM to improve their educational level. Which was similar to study done in University of Baghdad (2018)⁽¹⁹⁾: there was direct relationship (positive correlation) but no statistically significant correlation between positive impact mean

score and duration of sleep at night, while the correlation between negative impact mean score and age/years for participant's students there was no statistically significant correlation, there was direct relationship (positive correlation) between negative mean score and time spent on SM in hours/day, In current study, there was indirect relationship (negative correlation) with statistically significant correlation between negative impact mean score and duration of sleep at night which was similar to the study done in University of Babylon (2015)⁽²⁷⁾.

Conclusions

Overall, the impact of social media on undergraduate medical students in the University of Kerbala was positive. There was no significant correlation between genders, time spent on social media, duration of sleep at night and students' performance.

Conflict of Interest: nil

Source of Funding: Self-source of funding.

Ethical Clearance: Study protocol was taken from ethical committee in collage of medicine/Kerbala University.

Reference

1. Shiva HF, Fahimeh J, Ghani M. The relationship between the using of virtual social networking and academic performance on students. *International Journal of Humanities and Cultural Studies (IJHCS)* ISSN 2356-5926. 2016:2426-33.
2. Avcı K, Çelikden SG, Eren S, Aydenizöz D. Assessment of medical students' attitudes on social media use in medicine: a cross-sectional study. *BMC medical education*. 2015;15(1):18.
3. Leonardi PM, Huysman M, Steinfield C. Enterprise social media: Definition, history, and prospects for the study of social technologies in organizations. *Journal of Computer-Mediated Communication*. 2013;19(1):1-19.
4. Hurt NE, Moss GS, Bradley CL, Larson LR, Lovelace M, Prevost LB, et al. The "Facebook" Effect: College Students' Perceptions of Online Discussions in the Age of Social Networking. *International Journal for the Scholarship of Teaching and Learning*. 2012;6(2):n2.
5. Terantino JM. YouTube for foreign languages: You have to see this video. *Language Learning and*

- Technology. 2011;15(1):10.
6. Knight CG, Kaye LK. 'To tweet or not to tweet?' A comparison of academics' and students' usage of Twitter in academic contexts. *Innovations in education and teaching international*. 2016;53(2):145-55.
 7. Statista. Number of internet users Worldwide from 2005 to 2018 The Statistics Portal. 2018([https://www.statista.com/statistics/273018/number of internet-users-Worldwide](https://www.statista.com/statistics/273018/number-of-internet-users-Worldwide)).
 8. AlFaris E, Irfan F, Ponnampereuma G, Jamal A, Van der Vleuten C, Al Maflehi N, et al. The pattern of social media use and its association with academic performance among medical students. *Medical teacher*. 2018:1-6.
 9. Kircaburun K, Alhabash S, Tosuntaş ŞB, Griffiths MD. Uses and gratifications of problematic social media use among university students: A simultaneous examination of the Big Five of personality traits, social media platforms, and social media use motives. *International Journal of Mental Health and Addiction*. 2018:1-23.
 10. Faramarzi S, Tabrizi HH, Chalak A. TELEGRAM: AN INSTANT MESSAGING APPLICATION TO ASSIST DISTANCE LANGUAGE LEARNING. *Teaching English with Technology*. 2019;19(1):132-47.
 11. Wali AA. The Social Media (Concept, Type, Uses, Positives). 2017(<https://www.researchgate.net/publication/322128709>).
 12. Internet world status, Iraq Internet Usage and Telecommunications. 2018(<https://www.internetworldstats.com>).
 13. Report AG. Majority of internet users in Iraq have Facebook account. *Arabian Gazette Reporter*. 2013(<http://WWW.arabiangazette.com>).
 14. Deka P. A study on impact of social media on educational efforts in Guwahati City, Assam. *International Journal of Advanced Research in Education Technology*. 2015;2(3):90-4.
 15. Griffiths MD. Facebook addiction: concerns, criticism, and recommendations—a response to Andreassen and colleagues. *Psychological reports*. 2012;110(2):518-20.
 16. Hale L, Li X, Hartstein LE, LeBourgeois MK. Media Use and Sleep in Teenagers: What Do We Know? *Current Sleep Medicine Reports*. 2019;5(3):128-34.
 17. Masood A, Awais S, Kamran F, Rafique R, Mazahir S. Perceived Efficacy of Social Networking Sites as A Tool of Learning for Medical Students. *Ann Pak Inst Med Sci*. 2017:88.
 18. Madaiah M, Seshaiyengar CT, Suresh P, Munipapanna S, Sonnappa SD. Study to assess the effects of social networking sites on medical college students. *International Journal Of Community Medicine And Public Health*. 2017;3(5):1204-8.
 19. Mohammed ADAT. Patterns and motives of the use of Iraqi university students to social networks. *Mustansiriyah Journal of Arts (MuJA)*. 2018(68):1: 40-1: .
 20. Aahmar AT. The influence of social networks on the grades of medical students at University of Babylon, Iraq. *Journal of Medical & Allied Sciences*. 2017;7(2):108.
 21. Mehmood S, Taswir T. The effects of social networking sites on the academic performance of students in college of applied sciences, Nizwa, Oman. *International Journal of Arts and Commerce*. 2013;2(1):111-25.
 22. Kolan BJ, Dzandza PE. Effect of Social Media on Academic Performance of Students in Ghanaian Universities: A Case Study of University of Ghana, Legon. 2018.
 23. Persico D, Chiorri C, Ferraris M, Pozzi F. Effects of social networking on learning: the opinions of Italian university students. *Social networking and education: Springer*; 2016. p. 145-63.
 24. Foundation NS. National Sleep Foundation recommends new sleep times. 2015(<https://sleepfoundation.org/press-release/national-sleep-foundation-recommends-new-sleep-times>).
 25. Al-Rahmi WM, Alias N, Othman MS, Marin VI, Tur G. A model of factors affecting learning performance through the use of social media in Malaysian higher education. *Computers & Education*. 2018;121:59-72.
 26. Sinha D, Jaiswal SV. Use of social networking sites (SNS), social integration and social support in Indian medical students: a cross sectional investigation. *International Journal of Research in Medical Sciences*. 2018;6(6):2027-31.
 27. Abbas AH, Hammoud SS, Abed SK. The effects of social media on the undergraduate medical students. *Kerbala Jorunal of Medicine*. 2015;8(1):2161-6.

Analysis on Relationship between Bacillus and Enterobacter Bacteria in Air with Hospital Acquired Infections Potential in Intensive Care Unit of Dr. Wahidin Sudirohusodo Hospital

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Abstract

Introduction: Poor hospital building environment quality is due to presence of potential sources of airborne microbial and may lead to HAIs (Hospital Acquired Infections). The research aimed to find out the relationship between the Bacillus sp. and Enterobacter sp. in the air with HAIs incident potential.

Material and Method: This research was conducted in Dr. Wahidin Sudirohusodo hospital. This was an analytic observational research with the cross-sectional study design. Samples taken were human samples based on the criteria of the research as many as 61 patients, and the environmental samples were as many as 8 ICU rooms. The data were analyzed using the Chi-square test.

Findings and Discussion: The research result indicates that the air quality related to the microbial pollution in the air in intensive care unit room does not qualify. The result of the microorganism culture and identification is found the HAIs causing bacteria namely Bacillus sp. and Enterobacter sp. Based on the statistic test, the value of $p=0.014$ (95% confidence intervals) is obtained, so there is the relationship between Bacillus sp. with HAIs incident potential. The Enterobacter sp. bacterium indicates the value of $p=0.437$ (95% confidence intervals), so there is not have the relationship between the Enterobacter sp. bacterium with HAIs incident potential.

Conclusion: Bacillus in the air has the potential to cause HAIs in the ICU. Aspects of hygiene and sanitation appeared to be important factor in maintaining low microbial load in the air and further research is needed related to fungi and viruses in the air because of the potential source of HAIs.

Keywords: *Bacillus, Enterobacter, HAIs, ICU.*

Introduction

Transmission of airborne microbial infections can occur in ICU (intensive care unit)¹. Microbial exposure that exceeds the threshold value required in hospital ICU

rooms is one of the main causes of HAIs, acute toxic effects, and can even lead to disability to death, especially for people who have immune system disorders². HAIs are variables that have a strong association with length of hospital stay among patients admitted to the ICU³.

The source and spread of microbial related to HAIs are found in visitor clothing, human activities, the presence of medical staff, other sources such as air dust, soil, and water that can be distributed through air conditioning in room⁴, hand hygiene and environmental hygiene and medical equipment⁵. HAIs affect patient

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safety, estimates of deaths associated with HAIs in hospitals were 98.987 where for pneumonia cases were 35.967, blood flow infections were 30.655, urinary tract infections were 13.088, surgical site infections were 8.205, and for infections elsewhere there were 11.062^{6,7}. Levels range of HAIs from 2.7%-3.8%⁸. Microbial associated with HAIs are Staphylococcus sp., Micrococcus sp., Pseudomonas sp., Proteus sp., Escherichia coli, Enterobacter sp., Bacillus sp., Cladosporium sp., Aspergillus sp., And viruses^{8,9}.

Bacillus species belonging to aerobic gram-positive bacilli and reported to cause HAIs. Spread of Bacillus related to HAIs among hospitalized patients in the hospital environment can increase morbidity and mortality in patients with immune system disorders. Environmental reservoir identified for Bacillus sp. including contaminated air and ventilation filtration equipment in the ICU¹⁰.

Enterobacter is a gram negative pathogenic bacterium that can pose a serious triple threat for patients admitted to hospitals throughout the world¹¹. Infections caused by spectrum-producing β -lactamase Enterobacter increase cases of death in treated patients mainly related to HAIs¹². Significant risk factors, identified by multivariate analysis, were the use of antibiotics, the duration of long-term care, patients aged ≥ 65 years, and having a male sex¹³. Extended-spectrum beta-lactamase (ESBL) describes HAIs in ICU care, caused by Enterobacter sp.¹⁴.

The research aimed to find out the relationship between the Bacillus sp. and Enterobacter sp. bacterium in the air with HAIs incident potential. This research is expected to be used as a guide in improving aspects of sanitation and hygiene Hospital so that patient safety factors can be improved.

Material and Method

The type of this research was observational analytic with cross-sectional study design. The process of culture and identification of bacterial types using a tool namely "Microbiological Air Sampler" (MAS) 100 NT and KIA medium (Krigler Iron Agar) which is useful as a differential medium for distinguishing types of microbial. The research sample consisted of human samples and environmental samples. The samples in this research are ICU 1, ICU 2, PICU (Pediatric Intensive Care Unit), NICU (Neonatal Intensive Care Unit), RPK (ICU for Lontara 1), HCU (ICU for Neurosurgery), CVCU (ICU

for Cardiac Vascular Care Unit), ICU for Burns. Human samples in this research were all patients treated in the ICU who were at risk of infection, namely being treated for at least 3x24 hours and the results of the patient's medical record analysis with the help of a doctor/nurse. The results of the examination data are then processed using a Chi-square test.

Findings and Discussion

The results of the culture and identification of the types of air bacteria in the ICU showed that overall Bacillus sp. (87.5%) and Enterobacter sp. (50%). The potential for HAIs caused by Bacillus sp. greater than Enterobacter sp. However, the presence of Bacillus sp. and Enterobacter sp. in the air, the level of vulnerability of patients is higher in infections, especially immuno compromised patients. Table 1 shows that ICU 1, ICU 2, and RPK had the greatest influence on the potential occurrence of HAIs where based on culture results and identification of types of bacteria in the air, Bacillus sp. and Enterobacter sp.

Table 1: Results of culture and identification of Bacillus sp. and Enterobacter sp. in the air intensive care unit Dr. Wahidin Sudirohusodo hospital

Type of Room	Identification of Airborne Bacteria
HCU	Enterobacter sp.
ICU 1	Enterobacter sp., Bacillus sp.
ICU 2	Bacillus sp., Enterobacter sp.
PICU	Bacillus sp.
NICU	Bacillus sp.
CVCU	Bacillus sp.
RPK	Bacillus sp., Enterobacter sp.
ICU for Burns	Bacillus sp.

Chi-square test results for Bacillus sp. shows p value = 0.014 (95% confidence intervals) while for Enterobacter sp. shows p = 0.437 (95% confidence intervals). The statistical test results concluded that Bacillus sp. in the air of the ICU room it is associated with the potential for HAIs and Enterobacter sp. in the air the ICU room has no relation to the potential for HAIs.

Research related to microbial in the air conducted by Palawe in the Central Surgery Installation operating room found Bacillus sp.¹⁵. Another research by Jaffal found Bacillus sp. and Enterobacter sp. in the pediatric intensive care unit, male medical, and female surgical¹⁶.

Bacillus sp. is the dominant microbial found in the ICU room as much as 33.3%¹⁷. The concentration of bacteria is positively correlated with the number of people in the room¹⁸. Patients who were admitted to the ICU for few time were 1,241 (9.7%) and 819 (6.4%) were admitted to the ICU. The results showed that 800 patients (6.3%) were identified as having 1 or more HAIs¹⁹. SSI (surgical site infection) included HAIs which were first identified (n = 882; 38%). The average percentage of HAIs due to SSI in each hospital is 43%²⁰.

Conclusions

The results of culture and identification of microorganisms in the ICU found bacteria related to HAIs, namely, Bacillus Sp. and Enterobacter Sp. The results of the research statistically concluded that Bacillus sp. related to HAIs. Improvement of hygiene, sanitation and disinfection aspects is needed to control total microbes in the air.

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Source of Funding: Self or other source

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References

1. Septiari BB. Infeksi Nosokomial. 1st ed. Septiari BB, editor. Yogyakarta: Nuha Medika; 2012. 160 p.
2. Yoo K, Lee TK, Choi EJ, Yang J, Shukla SK, Hwang S il, et al. Molecular approaches for the detection and monitoring of microbial communities in bioaerosols: A review [Internet]. Vol. 51, Journal of Environmental Sciences. Elsevier B.V.; 2017. p. 234–47. Available from: <http://dx.doi.org/10.1016/j.jes.2016.07.002>
3. Olaechea PM, Ulibarrena MA, Lerma FÁ, Insausti J, Palomar M, Angel M, et al. Factor Related to Hospital Stay among Patients with Nosocomial Infection Acquired in The Intensive Care Unit. Infect Control Hosp Epidemiol [Internet]. 2003;24(3):2017–213. Available from: <https://www.cambridge.org/core/journals/infection-control-and-hospital-epidemiology/article/factors-related-to-hospital-stay-among-patients-with-nosocomial-infection-acquired-in-the-intensive-care-unit/0554AC19574ECCEBAD678A73590F8E44>
4. Verde SC, Almeida SM, Matos J, Guerreiro D, Meneses M, Faria T, et al. Microbiological assessment of indoor air quality at different hospital sites. Res Microbiol [Internet]. 2015;166(7):557–63. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/25869221>
5. Dancer SJ. Controlling Hospital-Acquired Infection: Focus on the role of the environment and new technologies for decontamination. Clin Microbiol Rev [Internet]. 2014;27(4):665–90. Available from: <https://cmr.asm.org/content/27/4/665>
6. Klevens RM, Edwards JR, Richards CL, Horan TC, Gaynes RP, Pollock DA, et al. Estimating health care-associated infections and deaths in U.S. hospitals, 2002. Public Health Rep [Internet]. 2007;122(2):160–6. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/17357358>
7. Peleg AY, Hooper DC. Hospital-acquired infections due to gram-negative bacteria. N Engl J Med [Internet]. 2010;362:1804–13. Available from: <https://www.nejm.org/doi/full/10.1056/Nejmra0904124>
8. Awosika SA, Olajubu FA, Amusa NA. Microbiological assessment of indoor air of a teaching hospital in Nigeria. Asian Pac J Trop Biomed [Internet]. 2012;2(6):465–8. Available from: [http://dx.doi.org/10.1016/S2221-1691\(12\)60077-X](http://dx.doi.org/10.1016/S2221-1691(12)60077-X)
9. Abdel-Hady H, Hawas S, El-Daker M, El-Kady R. Extended-spectrum β -lactamase producing Klebsiella pneumoniae in neonatal intensive care unit. J Perinatol [Internet]. 2008;28:685–90. Available from: <https://www.nature.com/articles/jp200873>
10. Bottone EJ. Bacillus cereus, a volatile human pathogen. Clin Microbiol Rev [Internet]. 2010;23(2):382–98. Available from: <https://cmr.asm.org/content/23/2/382>

11. Conlan S, Thomas PJ, Deming C, Park M, Lau AF, Dekker JP, et al. Single-molecule sequencing to track plasmid diversity of hospital-associated carbapenemase-producing Enterobacteriaceae. *Sci Transl Med* [Internet]. 2014;6(254):254ra126-254ra126. Available from: <https://stm.sciencemag.org/content/6/254/254ra126.short>
12. Tumbarello M, Trecarichi EM, Bassetti M, De Rosa FG, Spanu T, Di Meco E, et al. Identifying Patients Harboring Extended-Spectrum- β -Lactamase-Producing Enterobacteriaceae on Hospital Admission: Derivation and Validation of a Scoring System. *Antimicrob Agents Chemother* [Internet]. 2011;55(7):3485–90. Available from: <https://aac.asm.org/content/55/7/3485.short>
13. Ben-Ami R, Rodríguez-Baño J, Arslan H, Pitout JDD, Quentin C, Calbo ES, et al. A Multinational Survey of Risk Factors for Infection with Extended-Spectrum β -Lactamase-Producing Enterobacteriaceae in Nonhospitalized Patients. *Clin Infect Dis* [Internet]. 2009;49(5):682–90. Available from: <https://academic.oup.com/cid/article/49/5/682/307483>
14. Muro S, Garza-Gonzalez E, Camacho-Ortiz A, Gonzalez GM, Llaca-Daz JM, Bosques F, et al. Risk factors associated with extended-spectrum β -lactamase-producing enterobacteriaceae nosocomial bloodstream infections in a tertiary care hospital: A clinical and molecular analysis. *Chemotherapy* [Internet]. 2012;58(3):217–24. Available from: <https://www.karger.com/Article/Abstract/339483>
15. Palawe B V., Kountul C, Waworuntu O. Identifikasi Bakteri Aerob Di Udara Ruang Operasi Instalasi Bedah Sentral (IBS) RSUP. Prof. DR.R.D. Kandou Manado. *J E-Biomedik* [Internet]. 2015;3(3). Available from: <https://ejournal.unsrat.ac.id/index.php/ebiomedik/article/view/10563>
16. Jaffal AA, Nsanze H, Bener A, Ameen AS, Banat IM, El Mogheth AA. Hospital airborne microbial pollution in a desert country. *Environ Int* [Internet]. 1997;23(2):167–72. Available from: <https://www.sciencedirect.com/science/article/pii/S0160412097000032>
17. Sulistya CE, Waworuntu O, Porotu'o J. Pola Bakteri yang Berpotensi Menjadi Sumber Penularan Infeksi Nosokomial di IRINA C Ruang Intermediate Care (IMC) BLU RSUP Prof.Dr.R.D.Kandou Manado. *EBIOMEDIK* [Internet]. 2015;3(1). Available from: <https://ejournal.unsrat.ac.id/index.php/ebiomedik/article/view/6636>
18. Wan GH, Chung FF, Tang CS. Long-term surveillance of air quality in medical center operating rooms. *Am J Infect Control* [Internet]. 2011;39(4):302–8. Available from: <http://dx.doi.org/10.1016/j.ajic.2010.07.006>
19. Geffers C, Sohr D, Gastmeier P. Mortality Attributable to Hospital-Acquired Infections Among Surgical Patients. *Infect Control Hosp Epidemiol*. 2008;29(12):1167–70.
20. Lewis SS, Moehring RW, Chen LF, Sexton DJ, Anderson DJ. Assessing the Relative Burden of Hospital Acquired Infections in a Network of Community Hospitals. *Infect Control Hosp Epidemiol* [Internet]. 2013;34(11):1229–30. Available from: <https://www.cambridge.org/core/journals/infection-control-and-hospital-epidemiology/article/assessing-the-relative-burden-of-hospital-acquired-infections-in-a-network-of-community-hospitals/2EE28C2E70DD9AF589413B07CF43F614>.

Salmonella Pollution in Swimming Pool Water in Makassar: before and After Cleaning Assessment

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Abstract

Introduction: The swimming pool as one of the public places frequented by people for recreation and physical exercise must have water quality that is protected from Salmonella bacteria that can endanger public health. This study aims to determine the quality of salmonella bacteria and pH (Power of Hydrogen) in Andi Mattalatta Stadium swimming pool water and Hasanuddin University pool water before cleaning and after cleaning.

Material and Method: This research was conducted in the Andi Mattalatta Stadium swimming pool and Hasanuddin University pool water. This was descriptive observational research with a cross-sectional study design supported by laboratory examinations. Sampling each pool water two times ie sampling in the morning (after cleaning) and sampling in the afternoon (before cleaning). Pool water samples were examined in the integrated laboratory of the Faculty of Public Health, Hasanuddin University, using Bismuth Sulfite Agar.

Findings and Discussion: The results showed that the water quality of swimming pool Andi Mattalatta stadium after cleaning was found Salmonella Sp. 8 colony/100 ml with pH: 6.0 and before cleaning was found Salmonella Sp. 30 colony/100 ml with pH: 5.0. The water quality of swimming pool Hasanuddin University after cleaning was found Salmonella Sp. 14 colony/100 ml with pH: 7.0 and before cleaning was found Salmonella Sp. 38 colony/100 ml with pH: 7.0. Water quality of swimming pool Andi Mattalatta stadium and Hasanuddin University pool already has been polluted by Salmonella Sp. and pH quality of swimming pool Andi Mattalatta stadium doesn't qualify.

Conclusion: It is recommended to the pool manager to improve the pool water disinfection system to reduce the total salmonella colonies that endanger visitors.

Keywords: *After cleaning, Before cleaning, pH, Salmonella, Swimming pool.*

Introduction

The swimming pool is the most visited place for recreation or physical exercise. The average visit is 13-

24 times/year with an average swimming duration of 67-81 minutes. Men ingest an average of 27-34 ml per swimming event, women 18-23 ml, and children 31-51 ml¹. Therefore, health risks arising from poor swimming pool water such as bacteriological risk².

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Outbreaks of water-related swimming pools result from exposure to pathogenic bacteria or chemical agents in treated recreational water sites (eg, pools and hot tubs or spas) or untreated recreational water sites (eg, lakes and oceans). In 2009-2010, public health officials

from 28 states of Puerto Rico electronically reported 81 outbreaks of recreational water-related diseases to the CDC’s Waterborne Disease and Outbreak Surveillance System (WBDOS) through National Outbreak Reporting. 1,326 outbreak-related cases were reported to result in at least 62 (5%) inpatient cases³.

Poor bacteriological quality in swimming pool water can pose health risks for swimmers such as gastroenteritis, intestinal inflammation, due to bacterial, viruses, or parasitic infections⁴. The existence of Salmonella sp. in swimming pool water can cause paratyphoid fever⁵ because it is a pathogenic bacterium⁶.

The CDC (Centers for Disease Control and Prevention) reports that diseases caused by Salmonella are categorized as outbreaks of waterborne diseases and among them cause death by 7% of 6,939⁷. Most people infected with Salmonella experience diarrhea, fever, and stomach cramps between 12 and 72 hours after infection. Salmonella infections can spread from the intestine to the bloodstream, and spread to other parts of the body. In this case, Salmonella can cause death where children under 5 have the highest risk of infection⁸.

Visitor behavior and poor swimming pool sanitation are very supportive factors for Salmonella disease transmission. Most diseases often occur due to unclean visitor behavior. For example, most visitors who deliberately urinate in the pool, spit in the pool, do not use clean swimwear and throw garbage around the pool. The poor sanitation is often associated with disinfection systems that are not considered by the pool manager⁹.

In addition, related to chemical parameters such as acidity (pH) of a swimming pool must be maintained so that the quality of swimming pool water quality is guaranteed and prevent pathogenic bacteria such

as Salmonella sp. to be able to grow and develop. Salmonella sp. is anaerobic facultative bacteria and usually can live well in temperatures between 7- 48° and pH between 4-8¹⁰.

This research was conducted to obtain an overview of water quality before cleaning and after cleaning in the Andi Mattalatta stadium swimming pool and Hasanuddin University swimming pool according to Salmonella Sp and pH parameters.

Material and Method

This research was conducted in the swimming pool of Andi Mattalatta stadium and the swimming pool of Hasanuddin University. This research was an observational study with a descriptive approach supported by laboratory examinations. The laboratory examination process is related to the process of identifying Salmonella bacteria in pool water using the media "Bismuth Sulfite Agar". The sample in this research is the water contained in the swimming pool of Hasanuddin University and the swimming pool of Andi Mattalatta stadium.

The type of sampling used in this research is grab sampling. The frequency of sampling in each swimming pool as much as 2 (two) times, namely sampling in the morning (after cleaning) and sampling in the afternoon (before cleaning).

Findings and Discussion

The swimming pool water of Andi Mattalatta stadium and Hasanuddin University in table 1 and figure 1 shows a significant difference between the total colony of the Salmonella in pool water after cleaning and before cleaning.

Table 1. Examination results of Swimming pool water

Location	Total colony Salmonella Sp./100 ml		Standard of EPA (440/5-86-001) Salmonella Sp./100 ml
	After cleaning (Colony)	Before cleaning (Colony)	
Andi Mattalatta Stadium	8	30	0/100 ml
Hasanuddin University	14	38	0/100 ml

Swimming pool water of stadium Andi Mattalatta after cleaning has Salmonella Sp. as many as 8 colonies/100 ml of water samples and before cleaning has Salmonella Sp. as many as 30 colonies/100 ml water samples. Swimming pool water of Hasanuddin

University after cleaning has Salmonella Sp. as many as 14 colonies/100 ml of water samples and before cleaning has Salmonella Sp. as many as 38 colonies/100 ml water samples.



Figure 1: Salmonella examination results with Bismuth Sulfit Agar

The results of the pH measurement of the swimming pool water of Andi Mattalatta stadium and the swimming pool water of Hasanuddin University in table 2 show the difference in the pH of the swimming pool water after cleaning and before cleaning. Swimming pool water

of Andi Mattalatta stadium after cleaning has a pH of 6.0 and before cleaning has a pH of 5.0. Whereas the swimming pool water of Hasanuddin University after cleaning has a pH of 7.0 and before cleaning has a pH of 7.0.

Table 2. Results of Measurement pH of Swimming Pool Water Stadium Andi Mattalatta and Hasanuddin University

Location	pH Measurement		pH standard (Permenkes No. 416/Menkes/Per/IX/1990)
	After Cleaning	Before Cleaning	
Stadion Andi Mattalatta	6.0	5.0	6.5 – 8.5
Universitas Hasanuddin	7.0	7.0	6.5 – 8.5

The total bacterial colony of Salmonella sp. found in the swimming pool water of Andi Mattalatta stadium and Hasanuddin University after cleaning and before cleaning do not meet health requirements as determined by the Environmental Protection Agency (EPA 440/5-86-001) Water Quality Requirements for Recreational Activities and Bathing, i.e. 0/100 ml of the water sample. This is caused by the number of visitors doing swimming activities that directly affect the presence of pathogenic microbes and the growth of Salmonella sp. where after cleaning the amount of Salmonella sp. still lacking in the swimming pool water because there is no visitor activity. However, before cleaning the amount of Salmonella sp. experiencing an increase in swimming pool water because has been filled by many visitors who do activities. In addition, the quality of the water source used does not meet bacteriological requirements, the behavior of some visitors who do not comply with the

rules imposed by the pool manager which is required to wear a bathing suit before swimming, poor swimming pool sanitation, and disinfection systems that are not given enough attention the management and does not rule out the possibility of Chlor levels given is not proportional to the quantity of pool water and the number visitors. Based on the results of Salmonella Sp. in water is strongly influenced by several factors including pH. Salmonella sp. is known to grow well with a pH between 4-8¹⁰.

Conclusions

The poor quality of swimming pool water is caused by the water management system and visitor behavior that is not considered by the management. It is expected that the pool managers improve the water disinfection system to prevent pathogenic salmonella bacteria.

Conflict of Interest: There is no conflict of interest to be declared.

Source of Funding: Self or other source

The source of funding for this research came from private funds

Ethical Clearance: This research was approved by the manager of the Swimming pool of Hasanuddin University and Andi Mattalatta Stadium.

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References

1. Schets FM, Schijven JF, de Roda Husman AM. Exposure assessment for swimmers in bathing waters and swimming pools. *Water Res* [Internet]. 2011;45(7):2392–400. Available from: <http://dx.doi.org/10.1016/j.watres.2011.01.025>
2. Liguori G, Capelli G, Carraro E, Di Rosa E, Fabiani L, Leoni E, et al. A new checklist for swimming pools evaluation: A pilot study. *Microchem J* [Internet]. 2014;112:181–5. Available from: <http://dx.doi.org/10.1016/j.microc.2013.09.018>
3. Hlavsa MC, Roberts VA, Kahler AM, Hilborn ED, Wade TJ, Backer LC, et al. Recreational Water–Associated Disease Outbreaks — United States, 2009–2010 [Internet]. Vol. 63, CDC-Morbidity and Mortality Weekly Report (MMWR). Washington, DC; 2014. Available from: <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6301a2.htm>
4. Arvanitidou M, Kanellou K, Vagiona DG. Diversity of *Salmonella* spp. and fungi in northern Greek rivers and their correlation to fecal pollution indicators. *Environ Res* [Internet]. 2005;99(2):278–84. Available from: <https://www.sciencedirect.com/science/article/pii/S0013935105000046>
5. WHO - World Health Organization. Guidelines for safe recreational water environments [Internet]. Vol. 1, WHO Library Catalogue-in-Publication Data. Geneva, Switzerland; 2003. p. 253. Available from: <https://apps.who.int/iris/bitstream/handle/10665/42591/9241545801.pdf;jsessionid=1241B130CD0B5E205C987A01249E1121?sequence=1>
6. Geldreich EE. Applying Bacteriological Parameters To Recreational Water Quality. *J Am Water Works Assoc* [Internet]. 1970;62(2):113–20. Available from: <https://awwa.onlinelibrary.wiley.com/doi/pdf/10.1002/j.1551-8833.1970.tb03870.x#accessDenialLayout>
7. CDC. Current Waterborne Disease Burden Data & Gaps [Internet]. United States; 2017. Available from: <https://www.cdc.gov/healthywater/burden/current-data.html>
8. CDC. Salmonella [Internet]. United States; 2019. Available from: <https://www.cdc.gov/salmonella/general/index.html>
9. Casanovas-Massana A, Blanch AR. Characterization of microbial populations associated with natural swimming pools. *Int J Hyg Environ Health* [Internet]. 2013;216(2):132–7. Available from: <http://dx.doi.org/10.1016/j.ijheh.2012.04.002>
10. Melnick J, Adelberg's. *Medical Microbiology* [Internet]. 27th ed. Carroll KC, Butel JS, Morse SA, Mietzner T, editors. Mc Graw Hill Education: LANGE; 2016. 864 p. Available from: <https://b-ok.cc/book/2609596/85662b>

The Measurement of Urinary Ammonium as an Indicator for Smoking Effect on Acid Base Balance

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Abstract

Respiratory acidosis occurs when the gas exchange between oxygen and carbon dioxide in the lungs is not sufficient. Chronic obstructive pulmonary disease (COPD) which is a general group of diseases, including smoking, that causes respiratory acidosis. The study included 50 smokers and 20 healthy individuals as a control, all of the smokers are: non diabetic, non obese, normal heart and kidneys and no administration of analgesics. The excretion of ammonium in urine and its measurement is a good parameter to quantify acid excretion of kidneys, the excretion of acid is increased when the acidity of blood is increased due to respiratory problems which is the compensation mechanism between lungs and kidneys. The study results showed an increase in urinary ammonium concentration ($48.18 \pm 1.15 \mu\text{M}$) for smokers compared with control group. The high levels of urinary ammonium ions for smokers means that gas exchange is affected by smoking which leads to an increase in CO_2 causing an increase in hydrogen ion concentration $[\text{H}^+]$ which is respiratory acidosis. In this case the kidneys compensate the lungs by excretion more hydrogen ions in combination with ammonia derived from glutamic acid as ammonium ions to restore normal pH. Therefore we can use the concentration of urinary ammonium as an indicator for respiratory acidosis induced by smoking.

Keywords: Respiratory acidosis. Urinary ammonium. Smoking.

Introduction

Respiratory acidosis occurs when the lungs are unable to excrete adequate amounts of carbon dioxide (CO_2). An increase in CO_2 lowers the pH of blood making it acidic (less than 7.35)^[1]. The body has a compensation mechanism that restores normal pH. The lungs inhale oxygen and exhale carbon dioxide, sometimes lungs are unable to remove sufficient amounts of carbon dioxide because decreased respiratory rate due to main conditions like: asthma, pneumonia, sleep apnea and COPD^[2]. Smoking may cause chronic obstructive pulmonary diseases which affect the function of lungs to exchange gases, leading to an increase of carbon dioxide level then an increase in hydrogen ion concentration causing blood acidosis^[3]. In case of respiratory acidosis the kidneys will compensate the elevation in hydrogen ion concentration via the formation of excess

bicarbonate and via the excretion of hydrogen ions with urine, the hydrogen ions can be excreted with urine by two main pathways, the first predominant pathway is the combination of hydrogen ions with ammonia derived from glutamate to excrete ammonium ions (NH_4^+) with urine, the second pathway is the combination of hydrogen ions with sodium hydrogen phosphate to excrete sodium dihydrogen phosphate^[4]. Therefore those with respiratory acidosis have an increase in the concentration of urinary ammonium concentration^[5]. The normal value of urinary ammonium for adults is 6-47 μM and 22-26 mEq/L for serum (CO_2)^[6]. Smoke inhalation to the lungs has a harmful effect because an incomplete burning of organic material produces carbon monoxide which impairs the blood to transport oxygen^[7].

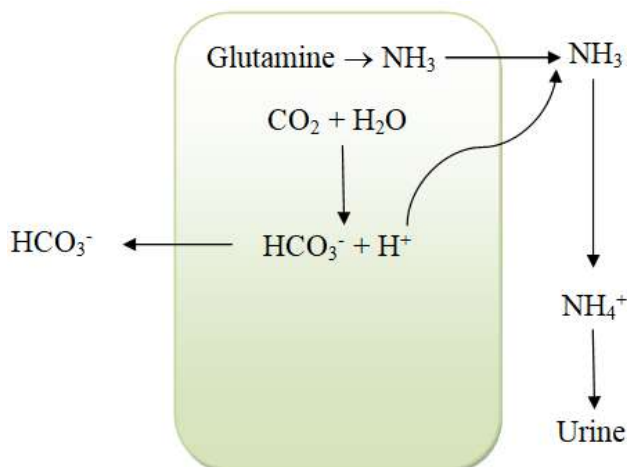
Blood Kidney Tubular Cell:

Figure 1: The excretion of hydrogen ions as ammonium by kidneys

Materials and Method

Urinary ammonium concentration was determined for 50 smokers and for 20 healthy individuals by using colorimetric enzymatic method. All the reagents and chemicals were used of a high purity.

Estimation of urinary ammonium: The principle of this test depends upon the reaction of ammonia with α -ketoglutaric acid and NADPH in the presence of L-glutamate dehydrogenase to produce L-glutamate and NADP⁺. The decrease in absorbance at 340 nm because the the oxidation of NADPH is directly proportional to the concentration of ammonia in the sample. The components of ammonia assay kit are NADPH, α -ketoglutaric acid, ammonia standard solution and buffers. Urine samples should be diluted 1/10 times with distilled water^[8,9,10].

Procedure:

1. Pipette in marked cuvette 1 ml of ammonia assay reagent and add 100 μ l of urine sample. This is the test cuvette.
2. Pipette in another marked cuvette 1 ml of ammonia assay reagent and add 100 μ l of water. This is the reagent blank cuvette.
3. Pipette in another marked cuvette 1 ml of ammonia assay reagent and add 0.05 ml of ammonia standard solution. This is the standard cuvette.
4. Incubate all cuvettes at 35 °C for 5 minutes and read the absorbance for each cuvette at 340 nm.

5. For each cuvette add 10 μ l of L-glutamate dehydrogenase solution and incubate again at 35 °C for 5 minutes.
6. Read the absorbance for each cuvette at 340 nm, and repeat the absorbance after 1 and 2 minutes.
7. Calculate the concentration of ammonia from the equation:

$$\text{Ammonia} = \frac{\Delta(\Delta A_{340}) \times \text{TV} \times \text{MW ammonia} \times \epsilon}{D \times \text{SV} \times 1000}$$

$$(\Delta A_{340}) = A_{\text{Initial}} - A_{\text{Final}}$$

$$\Delta(\Delta A_{340})_{\text{Test}} = (\Delta A_{\text{Test}}) - (\Delta A_{\text{Blank}})$$

$$\Delta(\Delta A_{340})_{\text{Standard}} = (\Delta A_{\text{Standard}}) - (\Delta A_{\text{Blank}})$$

TV = Total assay volume in ml.

ϵ = Millimolar extinction coefficient for NADPH.

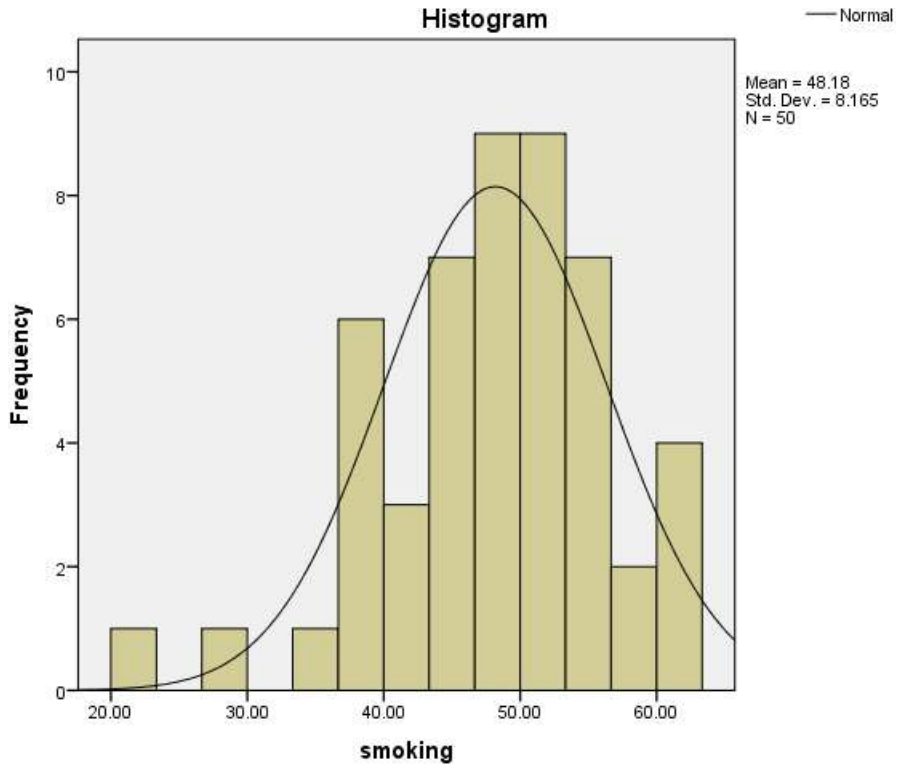
D = light path 1 cm.

SV = Sample volume in ml.

Results and Discussion

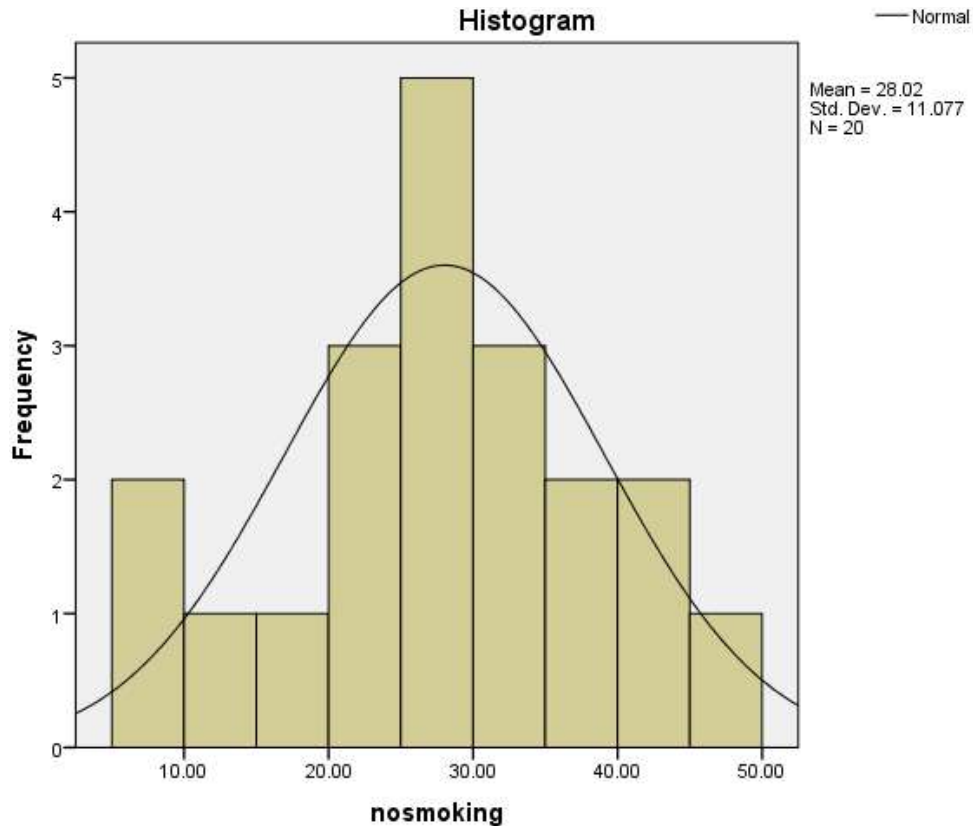
The results of the study showed a significant increase in the concentration of urinary ammonium (48.18 \pm 1.15 μ M) for smokers compared with control group as shown in histogram 1 and 2. An increase in the concentration of urinary ammonium concentration is an indicator for respiratory acidosis occurrence because smoking may cause chronic obstructive pulmonary diseases which affect the function of lungs to exchange gases, leading to an increase of carbon dioxide level then an increase in hydrogen ion concentration causing blood acidosis.

Concentration of urinary ammonium μM



Histogram 1: Levels of ammonium concentration for smokers.

Concentration of urinary ammonium μM



Histogram 2: Levels of ammonium concentration for non-smokers.

In case of respiratory acidosis the kidneys will compensate the elevation in hydrogen ion concentration via the formation of excess bicarbonate and via the excretion of hydrogen ions with urine, the hydrogen ions can be excreted with urine by two main pathways, the first predominant pathway is the combination of hydrogen ions with ammonia derived from glutamate to excrete ammonium ions (NH_4^+) with urine. Smoke inhalation to the lungs has a harmful effect because an incomplete burning of organic material produces carbon monoxide which impairs the blood to transport oxygen. Therefore the urinary ammonium concentration is considered an indicator to determine the effect extent of smoking on acid base balance. The mechanism of compensation between kidneys and lungs is highly efficient but can be overwhelmed swiftly; therefore any increase in the concentration of hydrogen ions will convert the medium to acidic. From the results showed in histogram 1 and 2, any smoker has an elevation of urinary ammonium must get rid of smoking or to decrease the smoking ratio because, despite pH still within normal range, the concentration and carbonate and the pressure of CO_2 are abnormal, any further increase in the hydrogen ions concentration causes blood acidosis which has a potential effects on health except the other effects of smoking.

Conclusions: the results of the study showed a significant increase in the concentration of urinary ammonium for smokers compared with non smokers; this increase indicates that the smoking affects the balance of acid-base toward acid causing respiratory acidosis. The kidneys compensate this change in pH by excretion of hydrogen ions in many ways. One predominant way is the excretion of hydrogen ions as ammonium; therefore urinary ammonium concentration could be used as an indicator for smoking effect on acid base balance.

Conflict of Interest: Nil.

Source of Funding: Self funding.

Ethical Clearance:

References

1. Contreras M, Masterson C, Laffey JG. Permissive hypercapnia: what to remember. *Curr Opin Anaesthesiol*. 2015 Feb;28(1):26-37.
2. Cove M, Federspiel W. Venovenous extracorporeal CO_2 removal for the treatment of severe respiratory acidosis. *Crit Care*. 2015 Apr 17;19:176.
3. Respiratory acidosis.[Internet]. (n.d.). Retrieved April 05, 2017, from <https://medlineplus.gov/ency/article/000092>.
4. Gallo de Moraes A, Surani S. Effects of diabetic ketoacidosis in the respiratory system. *World J Diabetes*. 2019 Jan 15;10(1):16-22.
5. Sirker A, Rhodes A, Gounds R, Bennet E. Acid-base physiology: the 'traditional' and the 'modern' approach. *Anaesthesia* 2002; 57: 348-56
6. Morganroth M. An analytic approach to diagnosing acid-base disorders. *J. Crit. Illness* (1990); 5(2):138-150.
7. Talhout R, Schulz T, Florek E, van Benthem J, Wester P, Opperhuizen A. Hazardous compounds in tobacco smoke. *Int J Environ Res Public Health*. (2011); 8 (2): 613–28.
8. Bergmeyer H. Beutler H. *Method of Enzymatic Analysis*. 3rd Edition, Vol. VIII (Bergmeyer, H. U., ed.), Academic Press (New York, NY: 1985), pp 454-461.
9. Cheuk, W. Finne G. Enzymatic Determination of Urea and Ammonia in Refrigerated Seafood Products. *J. Agric. Food Chem.* (1984); 32, 14-18.
10. Mondzac, A. et al. An Enzymatic Determination of Ammonia in Biological Fluids. *J. Lab. Clin. Med.* (1965); 66, 526-531.

Ozone Exposure Intake in the Ambient and the Impairment of Pulmonary Function to among Street Sweeper Workers in Jagakarsa District, South Jakarta, Indonesia

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Abstract

This study aimed to analyze the association between ozone (O₃) exposure and the impairment pulmonary function of the highway sweeper workers

This research applied a cross-sectional study design. The respondents of this study were 78 respondents and total samples of pulmonary function measurement were 30 people who have been working for more than 5 years which derived from 6 Villages in Jagakarsa. The measurement of O₃ using an ultraviolet ray absorption method. The respondent data collection and impairment pulmonary functions were conducted through questionnaire distribution, body height and weight, also spirometry measurement. The data analysis was conducted with univariate, bivariate and multivariate analysis.

The average of measurement within 3 days of O₃ concentration was 193.96 ug/m³. The respondents intake average value is 0.000296 mg/kg/day; respondents age of ≤ 43 years old are 42 people (53.8%); mostly wearing mask when working, there are 68 people (87.2%); respondents who have smoking habit are higher which are 51 respondents (65.4%); most of the respondents who are not doing physical activity are 42 people (53.8%). From 30 respondents, 17 respondents (56.7%) have impaired pulmonary function. The bivariate analysis result shows that smoking habits (p=0.011) and physical activities (p=0.049) have a relation to the impaired pulmonary function. According to the multivariable analysis, the smoking habit has the most influence on the impaired pulmonary function with the Odds Ratio OR =7.779 (95%CI= 1.099-55.054).

The study result shows that there is no significant relationship intake of ozone exposure in the ambient and impaired pulmonary function. There are other factors that may reduce pulmonary function which are ages, smoking habits, and physical activity.

Keywords: Ozone Concentration, Intake, Pulmonary Function, and Street Sweeper Workers.

Introduction

Air pollution becomes the source that contributes to producing polluted substances in the atmosphere

which can raise a destructive effect on humans and the environment¹. Air pollution specified in *indoor* or *outdoor* pollution by vapor and solid materials which changes the natural characteristic. Air pollution can occur from natural, anthropogenic and biogenic sources^{2,3}. O₃ is the secondary air pollutant that is formed by a chemical reaction between *volatile organic compounds* (VOCs), nitrogen dioxide (NO₂), and carbon monoxide (CO) by heating and sun radiation^{3,4,5}. The main sources of ozone are vapor from exhaust and power plants, even natural sources such as trees can also contribute. Ozone in the forming process needs sun radiation which raises

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the heat at noon at 12.00 pm due to UV ray intensity is higher⁶.

In the north part of the earth, O₃ concentration raises until 10 µg/m³ during 20-30 years lately. The annual average of O₃ concentration in the future in the south of Great Britain raises around 6 µg/m³.⁷ According to the National Standard of Ambient Air Quality (NAAQS) in the United States, O₃ average concentration in 8 hours is 0.070 ppm⁸. Annual average of O₃ concentration in ambient air in Jagakarsa Sub-district, South Jakarta is more than annual quality standards which are from 2016-2018 continuously 70,42 µg/m³; 74,69 µg/m³; 82,65 µg/m³ respectively⁹.

O₃ is pollutants which considered strong oxidizer, so it can cause a negative impact on human¹⁰. Short-term radiation by O₃ can cause some health problems related to breathing, including pleurisy, pulmonary function reduction, and breathing symptoms such as cough, wheezing, chest pain, chest heat up, and shortness of breath¹¹. The long-term effects of ozone are giving inflammation response, lung damage, and changes in structure and tissue of lung in the early of living¹².

It is globally estimated that 4,2 million early death are related to air pollution. The diseases caused by ambient air in the earth are reaching 43% of all death which is caused by chronic obstructive pulmonary (PPOK)². In Indonesia, The result of Riskesdas (2013) shows that the total case of PPOK occurs at the age of ≥ 30 years consist of 508.330 cases¹³. Respiratory disorders related to the reduction of pulmonary function. There are factors that can influence pulmonary function such as age, smoking, indoor air pollution, outdoor air pollution, allergens, diet, and nutrition, wearing a mask, physical activity^{14,15}. The research result of Kim (2011), said that ozone radiation to adults in the age of 19-35 years for 6,6 hours significantly can cause FEV₁ reduction¹⁶. In addition, the research conducted by Oktavianti (2014), said that there is a relation between ambient air ozone content to the respiratory disorders with the OR value of 3,0¹⁷.

According to the data, a street sweeper is in the group with risk for high O₃ concentration exposure. Therefore, it needs to be conducted a study about the influence of ambient air O₃ exposure intake to the impairment pulmonary function of street sweeper in Jagakarsa Sub-district, South Jakarta. This study aims to analyze the relation between O₃ concentration in ambient air and

the pulmonary function of a street sweeper in Jagakarsa Sub-district, South Jakarta.

Materials and Method

Participants: This research applied a *cross-sectional* study design. Population on this study all street sweeper workers in Jagakarsa, South Jakarta. The sampling in this research used *total sampling* with a total of 78 people and measuring pulmonary function were 30 people which were taken in 6 Villages in Jagakarsa with the inclusion criteria of a street sweeper with a working period of (> 5 years).

Data Collection: The type of data in this research was primary and secondary data. Primary data consisted of pulmonary function measurement (spirometry), bodyweight measurement (scale), respondent data consist of age, personal protective equipment (PPE) usage, smoking habits, and physical activity (questionnaire). Respondent data measurement was conducted by the researcher and was helped by 2 enumerators. Secondary data in this research was ambient air O₃ concentration data and environment meteorology condition (temperature, air pressure humidity, wind speed, and direction). Ambient air O₃ concentration measurement used Horiba APOA A370 with the method of ultraviolet ray absorption.

Measurement and Statistical analysis: O₃ data concentration were going to be calculated in exposure intake to the respondents with the formula as follows^{18,19}:

$$\text{Intake} = \frac{C \times IR \times EF \times ED \times CF}{BW \times AT} = \text{mg/kg} - \text{day}$$

C = concentration (mg/kg-soil; mg/L-water; -ug/m³-air)

IR = intake rate (mg soil/day; L-water/day; m³/day)

EF = exposure frequency (days/yr)

ED = exposure duration (yrs)

CF = soil conversion factor (10⁻⁶ kg/mg)

BW = body weight (kg)

AT = averaging time (days)

Pulmonary function in measure using spirometry with the results seen is on the values FVC and FEV₁. Indication of normal pulmonary function when the value of FEV₁/FVC ≥ 75% and impaired pulmonary function

when $FEV_1/FVC < 75^{20}$. The data analysis was conducted by using computer software SPSS 22.0 (R) for windows. The data analysis result was conducted with univariate, bivariate and multivariate analysis.

Results

The study result shows that O₃ concentration measurement in air quality monitoring station in

Jagakarsa Sub-district is obtained the average of measurement result for 3 days of O₃ concentration which is 193.96 ug/m³. According to the data, then it is calculated O₃ concentration intake of each respondent based on body weight and period of time. The average respondent intake is 0.000296 mg/kg/day with the minimum value of 0.0001mg/kg/day and maximum value of 0.0021 mg/kg/day. (Table 1).

Table 1. Descriptive Statistic for Respondent Intake

Variable	Mean	SD	Minimum-maximum	95%CI
Respondent Intake	0.000296	0.000252	0.0001-0.0021	0.000239-0.000353

Table 2. The Demographic Characteristic of The Street Sweeper Workers

Variable	N(78)	%
Age		
- ≤ 43 years	42	53.8
- > 43 years	36	46.2
PPE usage		
- used masks	68	87.2
- Not used mask	10	12.8
Smoking habits		
- Not smoking	27	34.6
- Smoking	51	65.4
Physical activity		
- Physical activity	36	46.2
- No physical activity	42	53.8
Variable	N(30)	%
Pulmonary function		
- Normal	13	43.3
- Impaired pulmonary function	17	56.7

According to the study result on 78 respondents, it is obtained the result that respondents who are at the age of ≤ 43 years are 42 people (53.8%). The total respondents who used masks when working is 68 people (87.2%). Respondents who have smoking habits are 51 respondents (65.4%). Most respondents with no physical activity are 42 people (53.8%). Next, the result of pulmonary function measurement, from 30 respondents have obtained 17 respondents (56.7%) who have an impaired pulmonary function. (Table 2).

Table 3. The bivariate result shows that impaired pulmonary function is related to the smoking habits (p=0.011) and physical activity (p=0.049) variables. Next, impaired pulmonary function has no relation with age (p=0.247), PPE usage (p=0.672), and ozone concentration intake (p=0.503).

Table 3. Correlation of Variables with Pulmonary Function

Variable	Pulmonary Function				P-Value
	Normal		Impaired Pulmonary Function		
	N	%	N	%	
Age					
- ≤ 43 years	4	28.6	10	71.4	0.247
- > 43 years	9	56.3	7	43.8	
PPE usage					
- Wear mask	11	45.8	13	54.2	0.672
- Not wear mask	2	33.3	4	66.7	

Variable	Pulmonary Function				P-Value
	Normal		Impaired Pulmonary Function		
	N	%	N	%	
Smoking habits					
- Not smoking	10	71.4	4	28.6	0.011
- Smoking	3	18.8	13	81.3	
Physical activity					
- Physical activity	6	75.0	2	25.0	0.049
- No physical activity	7	31.8	15	68.2	
Respondent intake	13	43.3	17	56.7	0.503

Table 4. The final results of multivariable logistic regression are age, smoking habits, and physical activity variables. The analysis result shows that the smoking variable is related to impaired pulmonary function (p = 0.040). The highest variable influence for impaired pulmonary function is a smoking habit with OR = 7.779.

Table 4. Logistic Regression Model of Pulmonary Function

	B	S.E.	Wald	Df	Sig.	Exp(B)	95%CI
Age	-1.683	1.251	1.809	1	0.179	0.186	0.16-2.159
Smoking habits	2.051	0.998	4.222	1	0.040	7.779	1.099-55.054
Physical activity	2.771	1.430	3.755	1	0.053	15.978	0.969-263.472

Discussion

Air ambient O₃ concentration measurement result for 3 days is 193.96 ug/m³. This result is still below the quality standard set in Indonesia especially in DKI Jakarta which is 200 ug/m³²¹. The measurement result of the average O₃ concentration daily exposure intake is 0.000296 mg/kg BW/day. The previous research said O₃ concentration between 20-80 ppb with the intake average is > 10⁻⁶ L/minute²². According to the research result, ambient air O₃ concentration on respondent exposure intake has no relation to the impaired pulmonary function. According to the research conducted in Belgium, there was no significant relation between O₃ concentration and pulmonary function. This matter can be influenced by other factors such as age and respondent smoking status²³. In this research, ozone exposure intake is not related to the impaired pulmonary functions, the however impaired pulmonary function can be caused by the other observed variable such as age, PPE usage, smoking activity, and physical activity.

In addition to the research result, it is obtained that age has no relation with the impaired pulmonary function on the respondents (p=0.247). This matter is aligned with the previous study that there is no relation between

age and impaired pulmonary function case (p=0.180)²⁴. In this study, respondent distribution is referring to the age of ≤43 years. Fargo (2016) stated that older age-related to pulmonary function reduction²⁵. Breathing muscle strength reduces along with the increasing of age which is related to the reducing ability of lung tissue in grasping the air when breathing²⁶.

The use of PPE is not related to impaired pulmonary function (p=0.672). In this study, most of the respondents wear a disposable mask made of clothes and can be washed after usage. This study is aligned to the previous research which stated that there is no significant relation between PPE usage and impaired pulmonary function of a mask which is mostly worn by the respondents, it is a mask made of white clothes of shirts²⁷. Cloth mask might be able for particle penetration for almost 97% compared to the medical mask²⁸.

Smoking habits are related to impaired pulmonary function (p=0.011). This research result is obtained the respondent average period of smoking which is 16 years with the total of cigarette consumption in the average of 10 cigarettes a day. The previous research stated that there is a significant relation to the smoking with FEV1 rate with a total of 10 cigarettes a day for 10

years²⁹. Another research explained that the FEV1 rate is significantly related to smoking activity. However, smoking habits are significantly not related to FEV1 on the smoker who rarely smokes once or stop smoking for one year³⁰.

Physical activity is related to impaired pulmonary function (p=0.049). Physical activity (sport) is mostly done by the respondents in this research are futsal and jogging. Physical activities which are done by using large muscle group (such as walking, power walk, jogging, cycling, swimming, ball sports, and etc) for some minutes can give a person to grasp enough oxygen³¹. Another research found that physical disturbed the FVC and FEV1. Physical activity can increase breathing muscle performance so it can increase FVC and FEV1³².

Conclusion

The study result shows that there is no significant relationship between ambient air O₃ exposure intake to the impaired pulmonary function. There are some other factors that can reduce the pulmonary function which are age, smoking habits, and physical activity.

Conflict of Interest: Considered no conflict of interest.

Ethical Clearance: This research has been approved by the Ethics Committee of the Faculty of Public Health, Universitas Indonesia.

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References

- Vallero, D. Fundamental of Air Pollution. 4th edition. California, USA: Academic Press; 2007. P. 3-6
- WHO[Internet]. Ambient air pollution: Pollutants. [cited 2019 Apr 24]. Available from: <https://www.who.int/airpollution/ambient/pollutants/en/>
- Villanyi V, Turk B, Batic F, et al. Chapter 7: Ozone Pollution and its Bioindication. European Union: InteachOpen; 2010. P 155-156
- WHO[Internet]. Outdoor Air Pollution. [cited 2019 Apr 28]. Available from: https://www.who.int/ceh/capacity/Outdoor_air_pollution.pdf
- EPA[Internet]. Ozone Air Quality Standards: EPA's 2015 Revision. [cited 2019 Jul 24]. Available from: <https://www.lankford.senate.gov/imo/media/doc/Ozone%20Air%20Quality%20Standards%20EPAs%202015%20Revision.pdf>
- Cahyono, W.E. Ozone Research in Jakarta. Proceedings of the National Seminar on Research, Education, and Application of Mathematics and Natural Sciences, Faculty of Mathematics and Natural Sciences, Yogyakarta State University; 2009: 567-571
- Department for Environment, Food and Rural Affairs, Scottish Executive, Welsh Assembly Government, & Department of the Environment in Northern Ireland. Fifth Report Air Quality Expert Group Ozone in The United Kingdom. London: Air Quality Expert Group; 2009
- US EPA[Internet]. NAAQS Table. [cited 2019 Mei 13]. Available from: <https://www.epa.gov/criteria-air-pollutants/naaqs-table>
- Jakarta Environmental Agency. Yearly Mean Year (YMMV) of DKI3 stands for 2016 to 2018. Jakarta: Jakarta Provincial Environment Agency; 2019
- Ministry of Environment of the Republic of Indonesia. Indonesian Environmental Statistics 2010. Jakarta: Ministry of Environment of the Republic of Indonesia; 2010
- EPA[Internet]. Criteria Air Pollutants. [cited 2019 Apr 28]. Available from: https://www.epa.gov/sites/production/files/2015-10/documents/ace3_criteria_air_pollutants.pdf
- WHO. Health Risks of Ozone From Long-Range Transboundary Air Pollution. Europe: WHO Regional Office for Europe; 2008
- Ministry of Health of the Republic of Indonesia. Basic Health Research 2013. Jakarta: Health Research and Development Agency Ministry of Health Republic of Indonesia; 2013
- WHO[Internet]. Risk Factors for Chronic Respiratory Disease [cited 2019 Oct 26]. Available from: <https://www.who.int/gard/publications/Risk%20factors.pdf>
- CDC[Internet]. NIOSH Alert: Preventing Lung Disease in Workers Who Use or Make Flavoring. [cited 2019 Oct 26]. Available from: <https://www.cdc.gov/niosh/docs/2004-110/pdfs/2004-110.pdf>
- Kim CS, Alexis NE, Rappold AG, et al. Lung Function and Inflammatory Responses in Healthy Young Adults Exposed to 0,06 ppm Ozone for

- 6,6 Hours. *American Journal of Respiratory and Critical Care Medicine* 2011;183(9): 1215-21
17. Oktavianti T. Risk Factors for the Occurrence of Ambien Air Ozone (O3) Respiratory Disorders in Jagakarsa District in 2014. Thesis. Depok: University of Indonesia; 2014
 18. ATSDR[Internet]. Environmental Health Resources Self Learning Module. [cited 2019 Oct 26]. Available from: <https://www.atsdr.cdc.gov/sites/brownfields/pdfs/toxicology-508.pdf>
 19. EnHealth[Internet]. Environmental Health Risk Assessment. [cited 2019 Oct 26]. Available from: [https://www1.health.gov.au/internet/main/publishing.nsf/Content/A12B57E41EC9F326CA257BF0001F9E7D/\\$File/Environmental-health-Risk-Assessment.pdf](https://www1.health.gov.au/internet/main/publishing.nsf/Content/A12B57E41EC9F326CA257BF0001F9E7D/$File/Environmental-health-Risk-Assessment.pdf)
 20. Ministry of Manpower and Transmigration Republic of Indonesia [Internet]. Diagnosis and assessment guidelines for occupational accidents and illnesses. [cited 2019 Dec 04]. Available from: https://toolsfortransformation.net/wp-content/uploads/2017/05/Permenakertrans-no.25-tahun-2008_Pedoman-diagnosis-dan-penilaian-cacat_E.pdf
 21. Jakarta Governor Decree [Internet]. Determination of Ambient Air Quality Standards and Noise Level Quality Standards in DKI Jakarta Province [cited 2019 Oct 26]. Available from: <http://sipsn.menlhk.go.id/sites/default/files/produk-hukum/Kepgub%20551-2001%20BM%20Ambien%20dan%20Kebisingan.pdf>
 22. Yongmei Lu, Berni Fang, T. Examining Personal Air Pollution Exposure, Intake, and Health Danger Zone Using Time Geography and 3D Geovisualization. *ISPRS International Journal of Geo-Information* 2015;4: 32-46;doi:10.339/ijgi4010032
 23. Panis LI, Provost EB, Cox B, et al. Short-term Air Pollution Exposure Decreases Lung Function: A Repeated Measures Study in Health Adults. *Environmental Health Journal* 2017; 16(60): 1-7. doi: 10.1186/s12940-017-0271-z
 24. Amaliyah RA, Setiani O, Dangiran HL. Factors related to the occurrence of pulmonary dysfunction in traffic police at the Semarang Police Traffic Police Unit. *Journal of Public Health* 2018;6(6): 305-14
 25. Vaz Fragoso CA, McAvay G, Van Ness PH, et al. Aging-Related Consideration When Evaluating the Forced Expiratory Volume in 1 Second (FEV1) over Time. *Journal of Gerontology: Medical Sciences* 2016; 71(7): 929-34
 26. Sharma G, Goodwin J. Effect of Aging on Respiratory System Physiology and Immunology. *Clinical Intervention of Aging* 2006; I(3):253-60
 27. Handari MC, Sugiharto, Pawenang ET. Characteristics of Workers with Lung Disorders Occurrence in Locomotive Dipo Workers. *Higeia Journal of Public Health Research and Development* 2018;2(1):45-56
 28. MacIntyre CR, Sealle H, Dung TC, et al. A Cluster Randomised Trial of Cloth Masks Compared with Medical Mask in Healthcare Workers. *BMJ Open* 2015;5:e006577.doi:10.1136/bmjopen-2014-006577:1-10
 29. Jaakkola MS, Jaakkola JJK, Becklake MR. Ventilatory Lung Function in Young Cigarette Smokers: A Study of Susceptibility. *Eur Respir J* 1991;4(6):643-50
 30. Jaakkola JJK, Hernberg S, Lajunen KT, et al. Smoking and Lung Function Among Adults with Newly Onset Asthma. *BMJ Open Respiratory Research* 2019;6:e000377. Doi:10.1136/bmjresp-2018-000377:1-10
 31. Loponen J, Ilmarinen P, Tuomisto LE, et al. Daily Physical Activity and Lung Function Decline in Adult-Onset Asthma: a 12-Year Follow-up Study. *European Clinical Respiratory Journal* 2018; 5(1): 1-9
 32. Azad A, Gharakhanlou R, Niknam A, et al. Effects of Aerobic Exercise on Lung Function in Overweight and Obese Students. *Tanaffos Journal of Respiratory Disease, Thoracic Surgery, Intensive Care and Tuberculosis* 2011;10(3):24-31

The Development of T-CBT Model to Improve the Competence of Midwives in Prevention Depression of Sexual Violence Victims

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Abstract

Background: Around 15 million adolescent girls aged 15-19 years old experience sexual violence. Based on data from 28 countries, 90 percent of girls in that country admitted the perpetrators of violence acts were people they knew. This literature review aimed to identify and explain empirical facts of research on sexual violence in children. It also detected the acts early and formulated the prevention of persistent depression. This study explained the influence of applying the T-CBT model on the increasing midwife competence in the service of depressed children due to sexual violence.

Material and Method: The literature sources were from online journal databases published by PubMed, Proquest, Google Scholar, and other sources like Indonesian Child Protection Commission Report, P2TP2A, Indonesian Midwives Association, and relevant theses and dissertations. The data were all documents published in the last 10 years from 2008-2019 collected manually and systematically.

Findings and Discussion: The T-CBT model was proven effective in preventing trauma and severe anxiety in victims of the child due to sexual violence. Empirical facts showed the impact of emotional reactivity and depressive symptoms such as ideas and attempted suicide, as well as emotional distress. The results of other studies also indicated a moderate relationship between psychopathology and objective characteristics of abuse, such as the number and types of violent incidents and the duration of abuse. The obstacles most often experienced by teenagers were having parents with a history of mental illness, intimidation, divorce, or separation from parents, physical, emotional, or sexual abuse, as well as child neglect and traumatic incidents.

Conclusion: The CBT model is a service strategy that strengthens behavioral skills-based interventions, information-based needs, family and parent involvement, and midwife services with a patient-therapist approach, and respects the needs of traumatized adolescents.

Keywords: *Child sexual violence, early detection of depression, T-CBT model.*

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Introduction

The cases of violence against women and adolescents are increasing and becoming a serious concern for the government to implement comprehensive, inclusive, and integrative protection. In the 2015-2019 RPJMN, the government has implemented an effort to protect women

and children from violence. The program has been carried out through prevention, service, and empowerment. The adolescents who are victims of sexual crimes generally experience rape, incest or other forms of sexual exploitation, which rarely get legal protection, physical or mental treatment and recovery (deserving legal protection and remedies)¹. Almost 100% of perpetrators use the mode of giving something to victims, seducing, sexually exploiting through peer calls and electronic transactions. Besides, some perpetrators use the mode by helping victims to do their schoolwork, or telling the fake story with mystical messages. Therefore, it needs an effort to stop more victims of sexual violence by creating a primary prevention model that includes increasing elementary school student's knowledge, actions, and attitudes².

15 million adolescent girls aged between 15 and 19 years old worldwide experience sexual violence. According to the data from 28 countries, 90% of girls admitted the perpetrators of the first incidents of sexual violence were people they knew. The data from six countries reveal that classmates and spouses are the people most often referred to as perpetrators of sexual violence against adolescent boys³. Globally, every 7 minutes a young woman dies due to violence in the United States (Latvia 33%, Lithuania 42%, Macedonia 18%, Moldova 43%)⁴. There are three types of sexual violence in the community, such as sexual abuse (911 cases), non-sexual abuse (708 cases), and rape (669 cases). Moreover, Eastern European countries recorded 247 cases of sexual violence⁵.

The United States is one of the countries with a high number of the sexual victim (SV). SV is defined by the Centers for Disease Control and Prevention as sexual acts committed against someone without consent - including forced sex (rape), attempts at forced sexual penetration, unwanted sexual contact, and contactless sexual experiences such as sexual harassment⁶. In Germany, the prevalence rate for sexual abuse is around 25 percent for girls and between 5 and 10 percent for boy⁷.

Promotive, preventive, curative, and rehabilitative actions to prevent sexual violence against children can be applied in an integrated manner; in the context of public health. Secondary prevention includes high-risk situations, for example, to stop continuing violence. Reactions to sexual crimes committed are tertiary domains, which the prevention aims to reduce the consequences of abuse and minimize secondary

consequences. In addition, therapies and actions to prevent recurrence of trauma to strengthen the psychological and physical health of those affected are needed⁸.

Considering a large number of acts of sexual violence against adolescents in DKI Jakarta, it requires an integrated handling strategy. One of the preventive actions for victims of sexual violence against children is to prevent further physical and mental disorders and to deal with psychiatric problems for victims in a primary, secondary, and tertiary manner or a combination of the three categories. The implementation of preventive measures can be through training of parents, teachers, communities, and health workers. Therefore, this literature review aimed to identify and explain empirical facts of research on sexual violence in adolescent girls, early detection, and prevention of severe depression. This study also explained the effect of applying the T-CBT model on the increasing midwife competence in giving the service of depressed adolescents as the victims of sexual violence.

Material and Method

Literature Resources: The sources of literature in the study were from an online journal database such as Pubmed, Proquest, Google Scholar, American Journal of Public Health, European Journal of Women's Studies, BioMed Central, Sage Journal, European Journal of Psych traumatology, and other E-book sources, report of the Indonesian Child Protection Commission, P2TP2A, Indonesian Midwives Association and relevant theses and dissertations. The literature studies were taken from the data of the last 10 years from 2008 to 2019.

Article Management Procedure: The researcher chose articles in several stages, starting from gathering information based on several sources related to the research topic, then incorporating it into Endnote software, summarizing the information in the matrix and integrating the some information, and analyzing as well as synthesizing the data from the articles obtained.

Findings and Discussion

Searching Results: The articles were looked for using relevant keywords (Figure 1) and it successfully identified 750 articles. After sketching the title, abstract, and the research method, it found 80 articles reviewed independently based on inclusion and exclusion criteria; it resulted in 12 synthesized articles.

Data Analysis: The data analysis resulted in 12 articles. The grouping research applied quantitative, qualitative, and review method. The relevant respondents were nurses, doctors, psychologists, and counselors who served outpatient and inpatient practices in hospitals as

well as several health care providers. The themes were grouped and collected by longitudinal observation, intervention in the experimental group, clinical practice trials, in-depth interviews, and medical record reports.

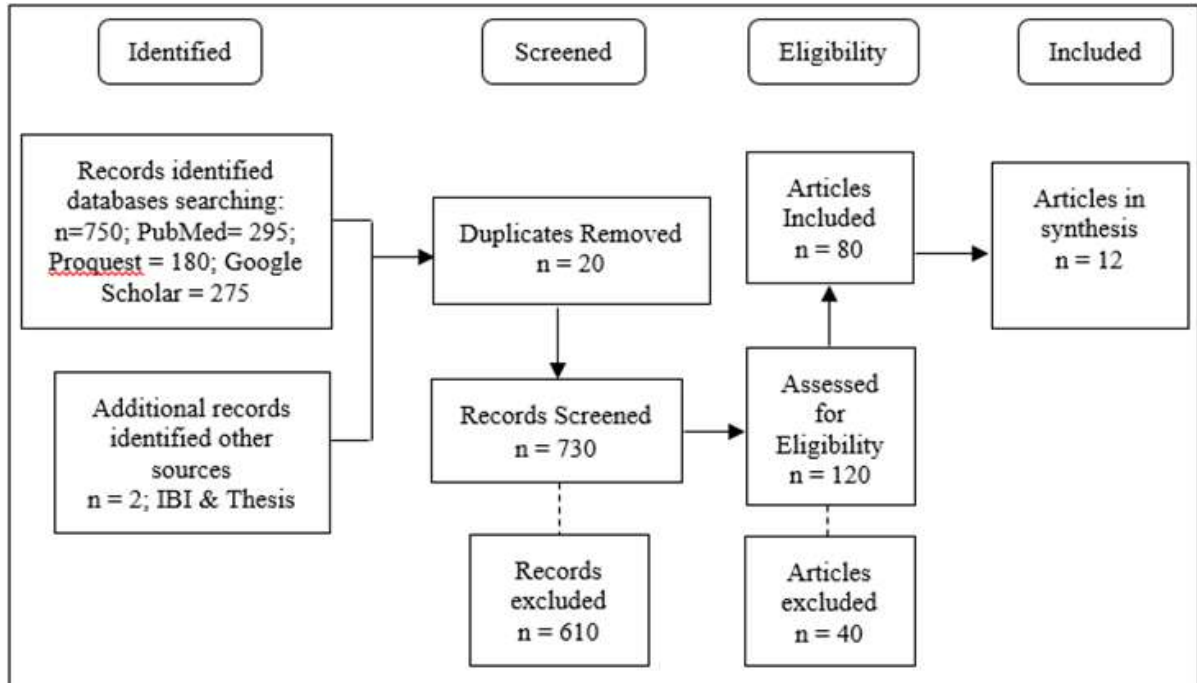


Figure 1: Search flow of article synthesis

The researcher assessed the results of the analysis through the problems arising because of sexual violence in adolescents and the effects of trauma and depression. These impacts generally affected adolescents themselves and their families. Moreover, the researcher also formulated appropriate treatment and prevention to overcome problems, determined dropouts treatment and prevent severe complications. We also evaluated the feasibility of training programs and interventions used to assess their responses and effects of trauma such as TIC, TF-CBT, and TCP-PTSD.

The experience of sexual abuse of adolescent girls, according to McLean has four theoretical conformities in recognizing problems and overcoming their impacts such as the adaptation and integration of CFT into psychotherapy approaches, caring effectiveness, new relationships, and positive affiliations with themselves and others. Hence, there are alternative and positive approaches to regulating emotions, reducing criticism and avoidance in responding to trauma symptoms⁹.

Changes in the positive and emotional control are in line with the study of Deblinger. He found the effects of shame as victims of sexual violence treated on the TF-CBT psychotherapy compared to CCT 6, which was conducted for 12 months. Some trauma and depression rates were higher during pre-treatment and positively associated with the treatment of PTSD symptoms¹⁰. Based on the study of Steil, outpatient treatment of TCD - PTSD could be applied safely to reduce PTSD symptoms as well as comorbid psychopathology in adolescent patients who experience sexual violence¹¹.

The studies on the theme of intervention programs and training in adolescent trauma management have been widely conducted (Rapee; Agustin; Palfrey and Niimura). The results of the study revealed that the 1-day program consisting of 3.5-hour lectures and 1-hour group discussions influenced the feasibility of the Professional intervention program in the mental health field. The development of a good attitude towards TIC was the main result, as assessed by the Attitude Related Trauma-

Informed Care scale. The workshop was considered relevant and useful to help the doctor's practice that would increase participants' trust, awareness, and attitude^{12,13}. At the end of treatment, there was no significant difference between the groups that needed more attention because they were being threatened by the disease or the group that was responding to treatment. Both groups showed a decrease in diagnostic severity, symptoms of social anxiety, depressive symptoms, and disruption of daily life after treatment¹⁴. Most cases increased at 6 months of advanced treatment. The forms of child abuse consist of physical, verbal, and relational abuse. Experts considered Cognitive-behavioral counseling activities with strict training techniques to deal with abuse and there was a significant impact of cognitive-behavioral counseling activities in minimizing the number of cases of child abuse¹⁵.

Reay in his study reported the role and support of families, especially mothers, who were more active in reporting their family difficulties than fathers. The most common difficulties experienced by adolescents were having parents with mental illness (66%), intimidated (63%) and divorced parents (43%). 69% of total CAMHS clients had traumatic potential (physical, emotional or sexual abuse, child neglect or traumatic events). Furthermore, children/adolescents with a history of trauma tend to have parents with a history of trauma¹⁶.

Harper presented that the difficulty of managing the feelings after getting inpatient treatment created new problems when they could not discuss their problems honestly with their community-based therapists. The participants emphasized the need to get trauma-based care obtained from doctors¹⁷. Based on the survey results on preliminary data presented by Hanson and Lang it required cross-system professional staff and their role to get feedback on problem definitions and conceptual issues related to TIC. Specifically, they can provide empirical representations, explain the significant gaps between research and TIC practice, and then compare them with important implications for obtaining better services in the future¹⁸.

Bounds stated that the program was assessed in 3 & 6 months. The study yielded significantly lower mean values for emotional distress (-0.67, -0.91) self-injury (-0.30, -0.55), suicidal ideation (45.45, -0.57), attempted suicide (-0.58, -0.61), and trauma symptoms (-11.8, -16.2, all $p < 0.001$) for 12 months. In the growth curve model, the nurse visit independently decreased with details of emotional distress (38.038), self-injury

(-2.020), suicidal ideation (25.025), and effort (32.032). The empowerment group was predicted to experience symptoms of trauma (-0.525) and subsequently was the rest, except for suicide attempts¹⁹. DeCou and Lynch, succeeded in uncovering the indirect effect of univariate groups of trauma on suicidal ideation through emotional reactivity in adolescents who survived sexual harassment when they were child ($\beta = 0.10$, ACI 95 %: 0.04-0.17), as well as the group's direct effects from depressive symptoms ($\beta = 0.88$, $p < 0.001$). Two other domains of resilience, namely a sense of mastery and a sense of connection did not mediate the relationship between trauma-related stress and the idea of suicide²⁰. These findings indicated the importance of emotional reactivity associated with the idea of suicide, as well as the relationship between depressive symptoms and suicide ideas in the clinical population. Moreover, this study also suggested the potential use of skills-based interventions and the need for information and trauma-based policies.

Conclusions

Suitable for midwife competency enhancement were TF-CBT and CCT-centered therapy and modified with training as conducted by Niimura, J., et al and Palfrey, N. et al, namely trauma informed care. thoroughly if reviewed from the time of its evaluation research conducted by Bounds, D.T, et al Canada Child Abuse & Neglect is better because the twelfth month is evaluated even though the possibility of dropout is greater.

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References

1. Agustin M, Saripah I, Gustiana AD. The Effectivity of Cognitive-Behavior Counselling With Assertive Technique To Address Child Abuse. *J Ilm Pendidik dan Tenaga Kependidikan Pendidik non Form* [Internet]. 2016;11(2):121-9. Available from: <https://doi.org/10.21009/JIV.1102.6>

2. Basile KC, DeGue S, Jones K, Freire K, Dills J, Smith SG, et al. Stop SV: A Technical Package to Prevent Sexual Violence [Internet]. Atlanta, Georgia; 2016. Available from: <https://www.cdc.gov/violenceprevention/pdf/SV-Prevention-Technical-Package.pdf>
3. Beck JS. Cognitive behavior therapy: Basics and beyond [Internet]. 2nd ed. New York: The Guilford Press; 2011. 391 p. Available from: https://www.academia.edu/16995757/Cognitive_Behavior_Therapy_Second_Edition_Basics_and_Beyond_Beck
4. Chinawa JM, Aronu A., Chukwu B., Obu H. Prevalence and pattern of child abuse and associated factors in four secondary institutions in Enugu, Southeast Nigeria. *Eur J Pediatr* [Internet]. 2014;173(4):451–6. Available from: <https://link.springer.com/article/10.1007/s00431-013-2191-4>
5. Cohen JA, Mannarino AP, Murray LK, Igelman R. Psychosocial Interventions for Maltreated and Violence Exposed Children. *J Soc Issues* [Internet]. 2006;62(4):737–66. Available from: <https://spssi.onlinelibrary.wiley.com/doi/abs/10.1111/j.1540-4560.2006.00485.x>
6. Cohen JA, Staron V, Mannarino AP, Perel JM. A Pilot Randomized Controlled Trial of Combined Trauma-Focused CBT and Sertraline for Childhood PTSD Symptoms. *J Am Acad Child Adolesc Psychiatry* [Internet]. 2007;46(7):811–9. Available from: <https://www.sciencedirect.com/science/article/abs/pii/S0890856709621699>
7. Osborne MC, Jackson M, Chege E, Baker E, Whitaker D, Brown SS. Technology-Based Innovations in Child Maltreatment Prevention Programs: Examples from SafeCare. *Soc Sci* [Internet]. 2014;3(3):427–40. Available from: <https://www.mdpi.com/2076-0760/3/3/427>
8. Cohen JA, Deblinger E, Mannarino AP, Steer RA. A Multisite, Randomized Controlled Trial for Children With Sexual Abuse-Related PTSD Symptoms. *J Am Acad Child Adolesc Psychiatry* [Internet]. 2004;43(4):393–402. Available from: <https://doi.org/10.1097/00004583-200404000-00005>
9. DeGue S, Valle LA, Holt MK, Massetti GM, Matjasko JL, Tharp AT. A systematic review of primary prevention strategies for sexual violence perpetration. *Aggress Violent Behav* [Internet]. 2014;19(4):346–62. Available from: <https://www.sciencedirect.com/science/article/pii/S1359178914000536>
10. Dickson S, Willis GM. Primary Prevention of Sexual Violence in Aotearoa New Zealand: A Survey of Prevention Activities. *Sex Abuse* [Internet]. 2017;29(2). Available from: <https://journals.sagepub.com/doi/abs/10.1177/1079063215583852>
11. Murray S, Powell A. “What’s the Problem?”: Australian Public Policy Constructions of Domestic and Family Violence. *Violence Against Women* [Internet]. 2009;15(5). Available from: <https://doi.org/10.1177/1077801209331408>
12. Eddyono SW, Sofian A, Akbari AR. Menguji Euforia Kebiri Catatan Kritis atas Rencana Kebijakan Kebiri (Chemical Castration) Bagi Pelaku Kejahatan Seksual Anak di Indonesia [Internet]. Anggara, Kamilah AG, editors. Jakarta: Institute for Criminal Justice Reform; 2016. 43 p. Available from: <http://mappifhui.org/wp-content/uploads/2016/03/Menguji-Euforia-Kebiri.pdf>
13. Ejikeme C, Threats KP, Bayo M, Toddle KL, O’Connor J. Assessing a comprehensive approach to prevent sexual violence on campus: Implications for program improvement. *J Georg Public Heal Assoc* [Internet]. 2017;6(4). Available from: <https://www.gapha.org/wp-content/uploads/2017/08/6.404-jGPHA-Spring-2017-pg-411-419.pdf>
14. Gershoff ET. More Harm Than Good: A Summary of Scientific Research on the Intended and Unintended Effects of Corporal Punishment on Children. *Law Contemp Probl* [Internet]. 2010;73(2):31–56. Available from: <https://scholarship.law.duke.edu/lcp/vol73/iss2/3/>
15. Handayani T. Perlindungan Dan Penegakan Hukum Terhadap Kasus Kekerasan Seksual Pada Anak. *J Huk Mimb Justitia* [Internet]. 2016;2(2):826–39. Available from: <https://jurnal.unsur.ac.id/jmj/article/view/33/25>
16. Harvey A, Moreno CG, Butchart A. Primary prevention of intimate-partner violence and sexual violence: Background paper for WHO expert meeting May 2–3, 2007 [Internet]. Geneva, Switzerland: WHO; 2007. p. 38. Available from: https://www.who.int/violence_injury_prevention/publications/violence/IPV-SV.pdf
17. Herman-Giddens ME, Brown G, Verbiest S. Underascertainment of Child Abuse Mortality in the United States. *JAMA* [Internet]. 1999;282(5):463-7.

Available from: <https://jamanetwork.com/journals/jama/fullarticle/190980>

18. Herrenkohl. The definition of child maltreatment: from case study to construct. *Child Abuse Negl* [Internet]. 2005;29(4):413–24. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/15970317>
19. Hilton NZ, Harris GT, Rice ME, Krans TS, Lavigne SE. Antiviolence Education in High Schools: Implementation and Evaluation. *J Interpers Violence* [Internet]. 1998;13(6):726–42. Available from: <https://doi.org/10.1177/088626098013006004>
20. Holguin G, Hansen DJ. “Sexually Abused Child”: Potential Mechanisms of Adverse Influences of Such a Label. *Aggress Violent Behav* [Internet]. 2003;8(6):645–70. Available from: <https://www.ncjrs.gov/App/Publications/abstract.aspx?ID=203220>

Literature Trend Analysis for Hospital Acquired Infection

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Abstract

Hospital acquired infection is the cause of many issues for health facilities, society and patients. In this study the trend of studies in this field have been analysed systematically. For that the main source of data was Scopus database. Additionally, the gap of literature identified for future studies. This article will enhance the general knowledge on the area for hospital managers, researchers, as well as policy makers.

Keywords: Hospital acquired infection, Nosocomial infection, Literature trend, Literature gap.

Introduction

The prevention and the control of the Hospital Acquired Infection (also known as Nosocomial infections or NIs) is the primary responsibility of the community and the health facilities (HFs)⁽¹⁻⁵⁾. It is stated⁽⁶⁾, that the infection control strategies would vary based on their type, need and resources provided by the HFs. Khan, Baig⁽⁷⁾ stated that despite all the efforts made for preventing the NIs, more work needs to be carried out to control the infections. Though some improvement was observed, more work must be carried out. The monitoring of the NIs is an important step for controlling the infections and is also considered as a basic step for preventing the department-specific infections⁽¹⁾.

Material and Method

The current study can be classified as a literature analysis. The data for there search is from Scopus database. Analysis is using Scopus analysing tool and VOS viewer software. Additionally, a qualitative review of a few current study was performed to propose literature gaps.

Finding and Discussion

In this study, the researcher acknowledged 61,559 relevant articles by systemically searching on the Scopus Database with the key words “Nosocomial infection” or “Hospital acquired infection”. Articles from the period 1915–2020 were analysed. Figure 1 displays specific distribution of article publication over the targeted years particularly belongs in research area of NIs. As it is shown, most of researches in field of NIs published in 2014, three thousand one hundred articles, and after that the number is decreased to 2895 articles at the end of 2018 based on the information achieved from Scopus database on September 2019.

Also, the articles analysed based on the publisher country from 1915 to 2020. Referring to the result as shown in Figure 2; United States has the greatest number of published articles, 16648 articles, though many other contuse have contributed to the field. Figure 2 is showing the top ten contributors.

Result shows that how many percentages of articles are published in each subject area, Medicine has highest percentage, with 67.2% of total subject area. Immunology with 9.9% is in the second level and the third level belongs to Biochemistry with 5.8%.

Furthermore, the research articles were analysed based on Title, Keywords and Abstract by use of VOS viewer which is a software tool for constructing and visualizing bibliometric networks. In systematic literature review, this software recognized different keywords on

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the research area. Keywords of “Nosocomial infection” or “Hospital acquired infection”, in Scopus search engine, shows the connections among the keywords and clustered them. The studies that were found were

downloaded into Microsoft Excel in a CSV (comma separated value) format to be analysed. Table 1 is from the result of the VOS viewer analysing.

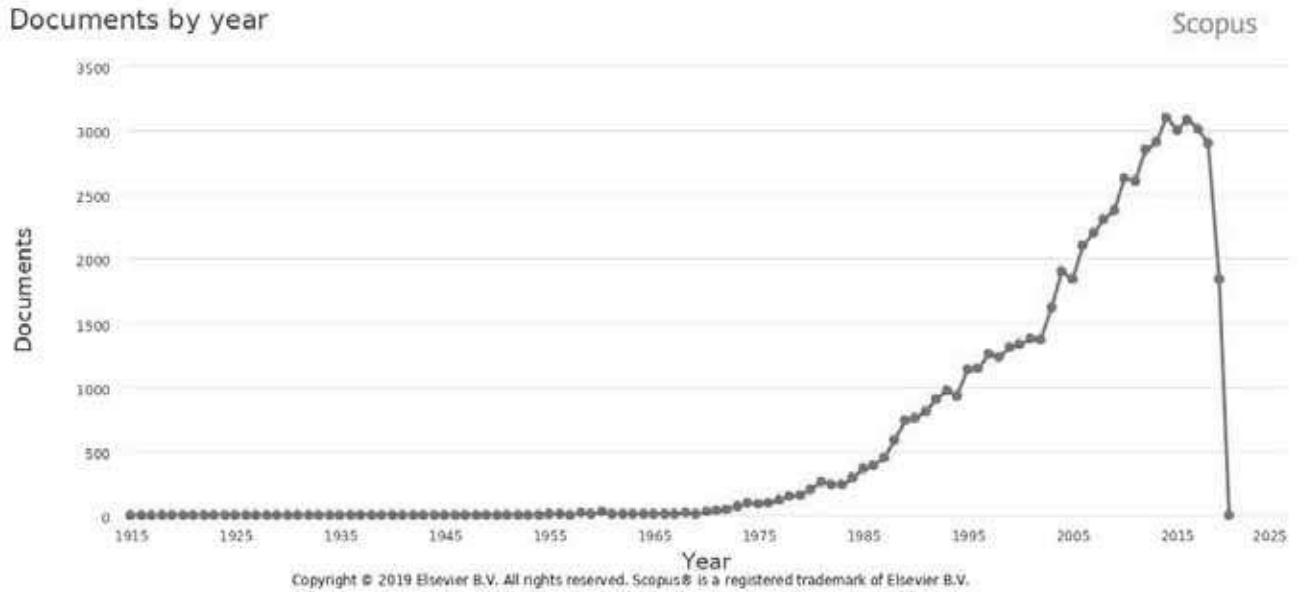


Figure 1: Range of published articles in field of NIs from 1915.

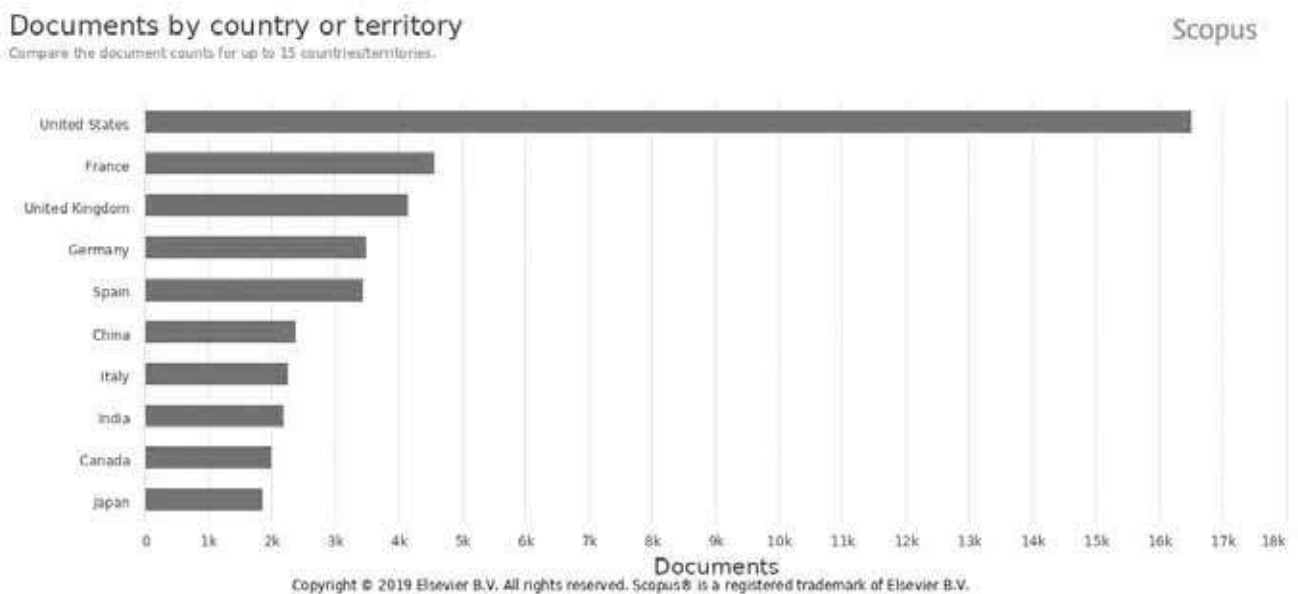


Figure 2: Country contribution to the NI research

The result is an evidence to prove multidisciplinary nature of NI studies. From the result, the keywords in each cluster in Table 1, have high connections. As it is

shows in the Table 1, most of the keywords are from to medicine field.

Table 1: The clusters of keywords with Highest Occurrence

No.	Cluster 1	Cluster 2	Cluster3	Cluster 4
1	Adult	Draft genome sequence	Acinetobacterbaumannii	Carbapenem resistant Acintobacterbaumannii
2	Case report	Emergence	Antimicrobial susceptibility	Meta analysis
3	Clostridium	Escherichia coli	Biofilm formation	Nosocomial infection
4	Clostridium difficile infection	HIV	Clinical isolate	Systematic review
5	Control	Investigation	Detection	
6	Diagnosis	Klebsiellapneumoniae	Development	
7	Effect	Molecular characterization	Distribution	
8	Evidence	Molecular epidemiology	Gene	
9	Implementation	Neonotalintencive care unit	Identification	
10	Incidence	Nosocomial outbreak	Resistance	
11	Management	Outbreak	Virulence factor	
12	Occurrence	Staphylococcus aureus		
13	Practice			
14	Prevention			
15	Sepsis			
16	Surgical site infection			
17	Tertiary care hospital			
18	Ventilator			

In continue, some recent –published researches in fields of NIs are discussed: Some medical researchers have tried to introduce new disinfectants and inhibitors in the area of NIs. Meanwhile, the other groups of researchers have worked on antibiotics in the area of NIs, Next group of researcher try to decline the rate of NIs through some administrative medical protocol, such as, prevention of occur and repeat infections by practicing good hygiene, especially cleaning of hands⁽⁸⁾, maintaining aseptic practices after inserting the urinary catheters and similar other urological procedures⁽⁹⁾.

Although above studies concentrated in a special group of pathogen microorganisms, there are many types of NIs with the different responsible group of NIs microorganisms. Therefore, the limitation of the reviewed researches just minimizes the risk of one type of NIs, meanwhile, the procedures of this study tried to decrease the total rate of NIs, for all types of them in each HF around the world.

Next to be studied, a group of the researchers in the area of management have worked on cost effective

protocol to decrease the financial load because of NIs. In addition, the other group of researchers have worked on the satisfactory of staff used an important indicator of organisational effectiveness in the healthcare.

Based on findings of a research in 2017, using risk management processes including elements of active surveillance and efficient monitoring can help to minimize the risk of NIs ⁽¹⁰⁾. In addition, researchers have introduced analytical network process as a tool to identify main reasons of NI and, therefore, the performance of doctors can be systematically calculated, which will greatly benefit the hospital management ⁽¹¹⁾.

Referring to the above discussed studies there are a few which tried to research on NIs by considering a factor of management, such as, cost, satisfaction, hygiene, quality of service, risk management and etcetera. The research gap in these researches in field of NIs through managerial viewpoint is they did not attention to the multi-criteria chief managerial criteria in their study. However, the present study has considered all the managerial criteria based on the viewpoints of managers

in each HFs and presented a general procedure in this area to minimize NIs risks.

Last but not least, Gazzarata, Monteverde, Bonetto and Savini⁽¹²⁾ have designed a surveillance system to monitor the prevalence of multi drug resistant organisms in both infected and colonized patients, to verify appropriateness of antibiotic prescription in hospitalized patients and to interact with other national and supra-national networks. Service Oriented Architecture approach, different healthcare service specification project standards, local, national and international terminology and clinical document architecture release two were adopted to design the overall architecture of this regional surveillance system. Then, Janowicz⁽¹³⁾ evaluate the relations between architectural actions and epidemiological safety in field of NIs, as well as presenting the need for an on-going assessment of architectural solutions by interdisciplinary teams of specialists.

However, some studies have presented guidelines to improve environmental factors and the HF architectural design and layout of HF, by set hand hygiene system in different parts of HF, in order to decline rate of NIs. But, the other group of researchers suggested to use an appropriate architecture hardware and software which helps in monitoring the hand hygiene for decreasing the spread of the NIs⁽¹⁴⁾. Although, the mentioned studies in field of architecture tried to solve the problem of NIs. But they didn't pay attention to department configuration and identify the risky department to remove from HF or selected low risky departments for adding. Most of them focus on interior design factors of HF, such as, air disinfection system and etcetera. Although, the present study tried to attention this missed factor, department configuration, during upgrading and rearchitecting of HF to minimize NIs risks.

Recently, many studies were published which stated that the HF environment (like the design and the layout) played an important role in the pathogen transmission within the HFs and any suitable change in the HF design could decrease the infection risk^(15,16). Some recent studies have explored the impact of the HF environment on the type of services provided and the quality of life⁽¹⁷⁾. Despite the fact that many researchers established the link between the architecture of the HF and human health, people are still reluctant to alter the structures of those HFs which affect human health, like cause NIs⁽¹⁸⁾. Studies on the evidence-based designs

have shown that the HF's physical environment along with its layout can affect human health, decrease the treatment duration, reduce the dosage of the medicines and also relieve the stress which is experienced by the patients, their family and the nursing staff⁽¹⁷⁾. However, Shikder and Price⁽¹⁹⁾ described, the different factors which must be considered while designing an effective healthcare system. A supportive HF environment with a good-quality layout and circulation creates an inviting, engaging, hygienic, calm and productive environment for the patients, their families and the staff⁽¹⁹⁾.

Hussain and Babalghith⁽²⁰⁾ noted, HFs were places where people sought medical treatment, while the HF staff provided a constant support. Hence, creating a calm environment in the HFs, with proper physical aspects was very important⁽²⁰⁾. However, Elf, Fröst⁽¹⁷⁾ stated, a good implementation of the novel techniques and HF models helped in improving the patient health as the patient-related services were associated with the HF environment (or HF architecture). Decisions regarding the healthcare design and architecture are seen to be very important as these designs affect the people and the work processes for a long time and need a financial commitment from the whole community⁽¹⁷⁾. Many studies recognised the fact that a well-planned HF architecture was beneficial in improving the patient health for many years⁽¹⁸⁾. In addition, studies⁽²⁾ stated that a poor HF building could lead to many problems and risks for patients, such as, NI risks and dissatisfied patients. Additionally, a poor HF architecture could prove to be very costly and lead to a lack of confidence in the HF's healthcare system⁽¹⁷⁾. Also, Dettenkofer, Seegers⁽²¹⁾ mentioned, the infection controlling measures are also supported by a good HF architecture (for example, they provide enough space for treating and taking proper care of the patients). However, there are many variations in the HF layout designs around the world, and control of infections by applying specific engineering designs, is still a topic of debate⁽²¹⁾. The scientific research is focused on determining the manner in which an improved design can reduce the risks in the HFs⁽¹⁸⁾. Hence, the HF design is considered to be an important factor affecting the modern healthcare system and the HFs must be constructed after integrating proper architectural designs, which would further help the patients⁽¹⁷⁾. Although, Nowadays, a lot of attention is given to the environment in the HFs and its relationship with patient health, which has led to the development of effective designs⁽¹⁷⁾, not enough studies are available to discuss department configuration in HFs.

Conclusion

This study tried to enhance understanding on the importance of the hospital acquired infection for the readers. Existing literature of the field have been analysed with the aim of Scopus database. Lack of knowledge and gaps for future studies have been alarm. Although limitation of the gap analysis was in the small size of reviewed literature, though future researchers may enhance this study with more comprehensive systematic literature review. Scholars and policymakers may use the findings of this study to design their research.

Conflict of Interest: None

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Ethical Clearance: Not applicable.

References

- Berket W, Hemalatha K, Getenet B, Wondwossen T. Update on bacterial nosocomial infections. *European review for medical and pharmacological sciences* 2012;16:1039-44.
- Parsia Y, Tamyaz PF. ROLE OF HEALTHCARE-FACILITIES LAYOUT DESIGN, HEALING ARCHITECTURE, ON QUALITY OF SERVICES. *International Journal of Civil Engineering and Technology (IJCIET)* 2018;6(7):80-92.
- Parsia Y, Puteri FMT, Sorooshian S. Microbial Troubles Of Hospitalization. *International Journal of Pharmacy & Technology* 2017;9(1):28447-50.
- Parsia Y, Puteri FMT. A Solution for Nosocomial Infection in Healthcare Facilities. *Indian Journal of Public Health Research & Development* 2019;10(2).
- Parsia Y, Puteri FMT, Sorooshian S. A Framework for Hospital Characterization. *Research Journal of Medical Sciences*. 2017;11(1):46-8.
- Ducel G, Fabry J, Nicolle L. *Prevention of hospital-acquired infections: a practical guide*. 2 ed: World Health Organization; 2002.
- Khan HA, Baig FK, Mehboob R. Nosocomial infections: Epidemiology, prevention, control and surveillance. *Asian Pacific Journal of Tropical Biomedicine*. 2017;7(5):478-82.
- Agarwal M, Larson EL. Risk of drug resistance in repeat gram-negative infections among patients with multiple hospitalizations. *Journal of critical care*. 2018;43:260-4.
- Nautiyal A, Satheesh NV, Madhav RKS, Ojha A, Ojha M, and, Bhargava S. Review on nosocomial infections. *Caribbean Journal of Science and Technology*. 2015;3:781-8.
- Sitek M, Witczak I, Kiedik D. Risk management of hospital infections as a supporting tool for the improvement of hospital quality-some European examples. *Wiadomosci lekarskie (Warsaw, Poland: 1960)*. 2017;70(1):105-11.
- Ning X. The application of analytic network process in hospital management *International journal of the analytic hierarchy process* 2014:1-3.
- Gazzarata R, Monteverde ME, Bonetto M, Savini V. A SOA based solution for MDRO surveillance and improved antibiotic prescription in the Abruzzo region. *Studies in health technology and informatics* 2019;261 49-54.
- Janowicz. Interdisciplinary Design Teams in Poland - Architecture as a Tool for Preventing Hospital Acquired Infections. *International Conference on Human Systems Engineering and Design: Future Trends and Applications*. 2019;879: 826-31.
- service-oriented architecture for preventing nosocomial infections [Internet]. *International Institute of Informatics and Systemics*. 2010.
- Zimring C, Jacob JT, Denham ME, Kamerow DB, Hall KK, Cowan DZ, et al. The role of facility design in preventing the transmission of healthcare-associated infections: Background and conceptual framework. *HERD: Health Environments Research & Design Journal*. 2013;7(1_suppl):18-30.
- Zimring C, Denham ME, Jacob JT, Cowan DZ, Do E, Hall K, et al. Evidence-based design of healthcare facilities: opportunities for research and practice in infection prevention. *Infection control and hospital epidemiology*. 2013;34(5):514-6.
- Elf M, Fröst P, Lindahl G, Wijk H. Shared decision making in designing new healthcare environments—time to begin improving quality. *BMC health services research*. 2015;15(1):114.
- Kembel SW, Jones E, Kline J, Northcutt D, Stenson J, Womack AM, et al. Architectural design influences the diversity and structure of the built environment microbiome. *The ISME journal*. 2012;6(8):1469.
- Shikder SH, Price AD. Design and decision making to improve healthcare infrastructure: School of

Civil and Building Engineering, Loughborough University (© Loughborough University); 2011.

20. Hussain M, Babalghith AO. Quality of hospital design in healthcare industry: history, benefits and future prospect. *Impact: Int J Res Appl Nat Soc Sci.* 2014;2(5):61-8.
21. Dettenkofer M, Seegers S, Antes G, Motschall E, Schumacher M, Daschner F. Does the architecture of hospital facilities influence nosocomial infection rates? A systematic review. *Infection Control & Hospital Epidemiology.* 2004;25(1):21-5.

Effect of Smoking on Disease Activity and Functional Impairment in a Sample of Iraqi Patients with Ankylosing Spondylitis

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Abstract

Background: The etiology of AS is unknown, but a combination of genetic and non- genetic risk factors works in concert to produce clinical disease. Smoking has a negative impact on disease activity and functional ability in AS with more severe radiographic damage. The aim of this study is to assess the effect of smoking on AS disease indices (activity, and functional impairment).

Patients and Method: A cross sectional study was conducted on 150 AS patients. Information concerning smoking, demographic characteristics & clinical criteria data were gathered consisted of age, gender, BMI, duration of disease, Ankylosing Spondylitis Disease Activity Score (ASDAS-ESR), Bath ankylosing spondylitis disease activity index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI). All cases were investigated for HLA-B27 and ESR.

Results: A total of 150 patients with AS were involved in this research. The non-smokers constituted 52% of cases. Ex-smokers formed 14.7% of patients. Low grade smokers (<15 pack-year) formed 18% of patients and high grade smoker (15+ pack-year) formed 15.3% of patients. There is a positive relation and statistically significant moderately strong to strong positive linear correlation between AS disease activity, functional impairment. The mean ASDAS, BASDAI and BASFI was the lowest in non-smokers and elevate with increment in the number of cigarette smoking.

Conclusion: AS smoker cases had elevated disease activity & functional impairment.

Keyword: *Smoking in Ankylosing Spondylitis, Smoking & AS Disease Activity, physical function in Iraqi Patients.*

Introduction

Ankylosing Spondylitis (AS) is a chronic, systemic, inflammatory, rheumatic disorder.¹ AS prevalence varies with human leukocyte antigen (HLA)-B27 gene in a given population, 1-2% of all people who are HLA-B27 positive develop AS.² It occurs in 0.1-1% of the general

population varying according to both geography and ethnical group.³ HLA-B27 prevalence among AS patients in the Arab world is generally lower than the worldwide.⁴ Eighty four percent of Iraqi patients with AS are HLA-B27 positive.⁵ It commonly starts in the second or third decade of life, with a male to female ratio (3:1).^(6,7) Incident AS was associated with current smoking, especially in those at a higher AS risk.⁸ AS etiology is unknown, but a combination of genetic and non- genetic risk factors works to produce clinical disease.⁹ AS is known to be highly heritable, as >90% of the risk of developing the disease has been shown to be genetically determined strongly associated with HLA-B27.^(10,11) Smoking has a negative impact on disease activity and

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functional ability in AS with more severe radiographic damage.^(12, 13) Smoking should be discouraged in those at a higher AS risk, e.g., with a family history or carrying HLA-B27.⁸ The aim of this study is to assess the effect of smoking on AS disease indices.

Methodology

A cross-sectional study was conducted at Rheumatology Unit of Baghdad Teaching Hospital from August-2014 to May-2015. A total of 150 Iraqi patients were fulfilling the modified New York criteria for AS (50 current smokers, 21 former smokers, 79 non-smokers) were enrolled in the study.¹⁴ A signed consent from each of the participants was obtained. An ethical approval and official permission were obtained from Baghdad College of Medicine to conduct the study. Data were collected which included the following: sociodemographic data, clinical data, disease duration according to the onset of symptoms, ASDAS, BASDAI, and BASFI. Patients were investigated for HLA-B27 and ESR using the Westergreen method (normal values < 20-30 mm/h according to sex and age).

Evaluation of disease activity:

1. Ankylosing Spondylitis Disease Activity Score (ASDAS-ESR): includes ESR-levels (mm/h) in addition to patient assessment of peripheral joint pain/swelling, total back pain, duration of morning and patient global assessment of disease activity (0 to 10).¹⁵ The scores were categorized according to published cut-offs with low ASDAS defined as < 1.3, moderate ASDAS < 2.1, high ASDAS 2.1- 3.5 and very high ASDAS > 3.5.^(16,17)
2. Bath Ankylosing Spondylitis Disease Activity Index (BASDAI): consists of 6 questions about the 5 major symptoms (fatigue, pain in the spine and hips, pain or swelling of the peripheral joints, enthesitis, severity and duration of morning stiffness). The questions are answered on a 10-cm VAS. Higher BASDAI scores indicate higher disease activity.¹⁸

Evaluation of physical function:

Bath Ankylosing Spondylitis Functional Index (BASFI): A functional index which can accurately assess a patient's functional impairment due to the disease, as well as improvements following therapy consists of eight questions relating to specific functions on activity level and two questions reflecting the person's ability to cope with everyday life. The mean score of 10 items

gave the final BASFI score ranging from 0 (easy) to 10 (impossible).¹⁹

Results:

The majority of study subjects were males (92.7%), with a male to female ratio of 12.6:1. HLA-B27 was positive in 41.1% of cases. The non-smokers constituted 52% of cases. Former (Ex) smokers constituted 14.7% of cases. The currently smokers were classified into low grade smokers (<15 pack-year) constituting 18% of cases and high grade smoker (15+ pack-year) constituting 15.3% of cases as shown in table 1.

The mean BASDAI, ASDAS, and BASFI was lowest among non-smokers and increase in magnitude with increasing amount of smoking to reach its highest mean among those with current high grade smoker (15+ pack -year). The observed positive trend indicating a worse disease status with increase in smoking habit was statistically significant, as shown in table 2.

Table 3 shows that there is no statistically significant relation between status of HLA-B27 phenotype and the mean of the 3 indices of AS activity, and function.

Table 1: Demographic and clinical characteristics of study sample

		N	%
1.	Gender		
	Female	11	7.3
	Male	139	92.7
	Total	150	100.0
2.	HLA-B27		
	Negative	83	58.9
	Positive	58	41.1
	Total	141	100.0
3.	Smoking status		
	Non-smoker	78	52.0
	Former smoker	22	14.7
	Current low grade smoker (<15 pack-year)	27	18.0
	Current high grade smoker (15+ pack-year)	23	15.3
	Total	150	100.0

N, number; HLA, human leukocyte antigen.

Table 2: The mean of selected indices of AS disease by smoking habit

	Smoking Status				P ANOVA trend
	Non-smoker (n=78)	Former smoker (n=22)	Current low grade smoker (<15 pack-year) (n=27)	Current high grade smoker (15+ pack-year) (n=23)	
BASDAI					<0.001
Range	(0.1 to 5)	(2.6 to 9)	(3.8 to 8.8)	(3.4 to 8)	
Mean	2.6	4.6	5.2	5.6	
SD	1.2	1.3	1.3	1.1	
SE	0.13	0.28	0.24	0.23	
ASDAS					<0.001
Range	(0.1 to 4)	(1 to 7.2)	(0.82 to 4.66)	(1.9 to 4.53)	
Mean	1.2	2.4	2.6	3	
SD	0.6	1.4	0.9	0.7	
SE	0.07	0.31	0.18	0.14	
BASFI					<0.001
Range	(0 to 6)	(0.8 to 7.9)	(4 to 8)	(2.7 to 8)	
Mean	3.2	5	5.9	6.2	
SD	1.5	1.6	1.1	1.4	
SE	0.18	0.34	0.22	0.29	

P<0.001 is significant.

AS, ankylosing spondylitis; n, number; ANOVA, analysis of variance; BASDAI, Bath ankylosing spondylitis disease activity index; ASDAS, ankylosing spondylitis disease activity score; BASFI, Bath ankylosing spondylitis functional index; SD, standard deviation, SE; standard error.

HLA, human leukocyte antigen; n, number; BASDAI, Bath ankylosing spondylitis disease activity index; ASDAS, ankylosing spondylitis disease activity score; BASFI, Bath ankylosing spondylitis functional index; NS; not significant; SD, standard deviation, SE; standard error.

Table 3: The difference mean of selected indices of AS disease between those with a positive HLA-B27 and those negative for it

	HLA-B27		P (t-test)
	Negative (n=83)	Positive (n=58)	
BASDAI			0.24[NS]
Range	(0.1 to 9)	(0.2 to 7)	
Mean	4	3.6	
SD	1.9	1.4	
SE	0.2	0.19	
ASDAS			0.86[NS]
Range	(0.2 to 4.8)	(0.3 to 7.2)	
Mean	1.9	1.9	
SD	1.1	1.2	
SE	0.12	0.16	
BASFI			0.13[NS]
Range	(0 to 8)	(0.4 to 8)	
Mean	4.6	4.1	
SD	2	1.8	
SE	0.22	0.24	

As shown in table 4, only smoking habit had a statistically significant association with mean of BASDAI score after adjusting for HLA-B27 status, age, gender, BMI and duration of the disease. Being a former smoker is expected to increase BASDAI score by a mean of 1.9 compared to non-smokers. Being a low grade smoker is expected to increase BASDAI score by a mean of 2.4 compared to non-smokers. Finally moving to the high grade smoking category is associated with the highest increase in disease activity (2.9 points) compared to non-smokers. The resulting regression model was statistically significant and able to explain 55% of observed changes in BASDAI.

Table 5 show that, smoking habit had a statistically significant association with mean of ASDAS after adjusting for HLA-B27 status, age, gender, BMI and duration of the disease. Being a former smoker is expected to increase ASDAS by a mean of 1.1 compared to non-smokers. Being a low grade smoker is expected to increase ASDAS by a mean of 1.5 compared to non-smokers. Finally moving to the high grade smoking

category is associated with the highest increase in disease activity (1.6 points) compared to non-smokers. Age was significantly associated with this index after adjusting (controlling) for the remaining variables. For each one year increase in age the disease activity is increased by 0.02. The resulting regression model was statistically significant and able to explain 47% of observed changes in ASDAS score.

As shown in table 6, only smoking habit and age had a statistically significant association with mean of BASFI score after adjusting for HLA-B27 status, gender, BMI and duration of the disease. Being a former smoker is expected to increase BASFI score by a mean of 1.7 compared to non-smokers. Being a low grade smoker is expected to increase BASFI score by a mean of 2.5 compared to non-smokers. Finally moving to the high grade smoking category is associated with the highest increase in functional impairment (2.8 points) compared to non-smokers. Age was significantly associated with BASFI after adjusting (controlling) for the remaining variables. For each one year increase in age the functional impairment is increased by 0.04. The resulting regression model was statistically significant and able to explain 51% of observed changes in BASFI score.

Table 4: Multiple linear regression model with BASDAI score as the dependent (response) variable and selected variables, smoking habit as the explanatory (independent) variables.

	Partial Regression Coefficient	P
(Constant)	2.71	<0.001
BMI (Kg/m2)	0.003	0.9[NS]
Age (years)	0.02	0.32[NS]
Duration of the disease (years)	-0.001	0.94[NS]
Male gender compared to female	-0.76	0.06[NS]
Positive HLA-B27	-0.23	0.27[NS]
Former smoker compared to non-smoker	1.9	<0.001
Current low grade smoker (<15 pack-year) compared to non-smoker	2.4	<0.001
Current high grade smoker (15+ pack-year) compared to non-smoker	2.9	<0.001

R2=0.55; P (Model) <0.001 is significant

BASDAI, Bath ankylosing spondylitis disease activity index; BMI, body mass index, HLA, human leukocyte antigen, NS, not significant.

Table 5: Multiple linear regression model with ASDAS as the dependent (response) variable and smoking habit as the explanatory (independent) variables.

	Partial Regression Coefficient	P
(Constant)	0.31	0.59[NS]
BMI (Kg/m2)	0.02	0.37[NS]
Age (years)	0.02	0.043
Duration of the disease (years)	-0.03	0.04
Male gender compared to female	-0.06	0.83[NS]
Positive HLA-B27	0.04	0.77[NS]
Former smoker compared to non-smoker	1.1	<0.001
Current low grade smoker (<15 pack-year) compared to non-smoker	1.5	<0.001
Current high grade smoker (15+ pack-year) compared to non-smoker	1.6	<0.001

R2=0.47; P (Model) <0.001 is significant.

ASDAS, ankylosing spondylitis disease activity score; BMI, body mass index, HLA, human leukocyte antigen, NS, not significant.

Table 6: Multiple linear regression model with BASFI score as the dependent (response) variable and selected variables, smoking habit as the explanatory (independent) variables.

	Partial Regression Coefficient	P
(Constant)	2.82	0.003
BMI (Kg/m2)	-0.02	0.5[NS]
Age (years)	0.04	0.015
Duration of the disease (years)	0.002	0.93[NS]
Male gender compared to female	-0.51	0.27[NS]
Positive HLA-B27	-0.39	0.12[NS]
Former smoker compared to non-smoker	1.7	<0.001
Current low grade smoker (<15 pack-year) compared to non-smoker	2.5	<0.001
Current high grade smoker (15+ pack-year) compared to non-smoker	2.8	<0.001

R2=0.51; P (Model) <0.001 is significant.

BASFI, Bath ankylosing spondylitis functional index; BMI, body mass index, HLA, human leukocyte antigen, NS, not significant.

This study revealed that more elevated disease activity (ASDAS), the worse functional impairment (BASFI) in smokers and that there was statistically significant relation with that of nonsmokers. This result is agree Chung HY, et al research²⁰ and Kaan U²¹ which revealed that cigarette smoking was related with higher disease activity (ASDAS), worse functional status (BASFI). In addition; near to Chen C research's results²² which proved that it was significantly impaired among smokers as compared to nonsmokers. This study disagree with Bouaddi I study which showed that in univariate analysis smoking in Moroccan AS patients proved to be not associated with BASFI.²³ This may be explained by different sample size and using univariate analysis. Also research results evaluated the habit of smoking which involved; duration of smoking, and quantity of smoking (pack-years) with disease activity, functional ability in AS patients and showed that there was an association between the pack-years of smoking and disease activity indices which elevate the magnitude with increasing amount of smoking to reach its highest AS disease activity, functional impairment in those with current high grade smokers (15+ pack-year). The noticed positive trend indicating a bad and worse disease activity with increment in habit of smoking was statistically significant. This is in agreement with Fallahi S et al research results in Turkey²⁴. A multivariate analysis proved a significant relation between the pack-years of smoking and the BASDAI. This goes in accordance with results of Chen C²² who revealed that the higher smoking index in AS smokers causes the poor disease outcome including physical mobility. This research revealed significant moderately strong correlation between AS disease activity (ASDAS, BASDAI), and functional impairment (BASFI). This means that getting worse in one AS disease domain is anticipated to affect in a similar way in another disease domain. These results are in agreement with Kaan U's result.²¹

Conclusion

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Faculty of Dentistry, University of Babylon, Hillah city, Iraq and all experiments were carried out in accordance with approved guidelines.

References

1. Braun J, Sieper J. Ankylosing spondylitis. *Lancet* 2007; 369:1379-90.
2. Van der Linden S, van der Heijde D. Ankylosing spondylitis: Clinical features. *Rheum Dis Clin North Am.* Nov 1998; 24(4):663-76.
3. De Angelis R, Salaffi F, Grassi W. Prevalence of spondyloarthropathies in an Italian population sample: a regional community-based study. *Scand J Rheumatol.* 2007; 36(1):14-21.
4. Abdelrahman MH, Mahdy S, Khanjar IA, et al. Prevalence of HLA-B27 in patients with ankylosing spondylitis in Qatar. *Int J Rheumatol* 2012; 8(6):213-6.
5. Al-Rawi ZS, Al-Shakarchi HA, Hasan F, et al. Ankylosing spondylitis and its association with the histocompatibility antigen HLA-B27: an epidemiological and clinical study. *Rheumatol Rehabil* 1978; 17(2):72-5.
6. Braun J, Sieper J. Inception cohorts for spondyloarthropathies. *Z Rheumatol* 2000; 59:117-21.
7. Braun J, Sieper J. Ankylosing spondylitis. *Lancet* .2007; 369(9570): 1379-90.
8. Videm V, Cortes A, Thomas R, et al. Current smoking is associated with incident ankylosing spondylitis: the HUNT population-based Norwegian health study. *J Rheumatol* 2014; 41(10):2041-8.
9. Khan MA. Update on spondyloarthropathies. *Ann Intern Med.* 2002; 136(12):896-907.
10. Brown MA, Breakthroughs in genetic studies of ankylosing spondylitis. *Rheumatology* 2008; 47: 132-7.
11. Van der Linden SM, Valkenburg HA, De Jongh BM, et al. The risk of developing ankylosing spondylitis in HLA-B27 positive individuals: A comparison of relatives of spondylitis patients with the general population. *Arthritis Rheum* 1984; 27(3):241-9.
12. Reed MD, Dharmage S, Boers A, et al. Ankylosing spondylitis: an Australian experience. *Intern Med J* 2008; 38:321-7.
13. Ward MM, Hendrey MR, Malley JD, et al. Clinical and immunogenetic prognostic factors for radiographic severity in ankylosing spondylitis. *Arthritis Care Res* 2009; 61:859-66.

14. Van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis: a proposal for modification of the New York criteria. *Arthritis Rheum* 1984; 27: 361-68.
15. Van der Heijde D, Lie E, Kvien TK, et al. ASDAS, a highly discriminatory ASAS-endorsed disease activity score in patients with ankylosing spondylitis. *Ann Rheum Dis*. 2009; 68(12):1811-18.
16. Machado P, Landewe R, Lie E, et al. Ankylosing Spondylitis Disease Activity Score (ASDAS): defining cut-off values for disease activity states and improvement scores. *Ann Rheum* 2011; 70(1): 47-53.
17. Lukas C, Landewe R, Sieper J, et al. Development of an ASAS-endorsed disease activity score (ASDAS) in patients with ankylosing spondylitis. *Ann Rheum Dis*. 2009 Jan; 68(1):18-24.
18. Sieper J, Rudwaleit M, Baraliakos X, et al. The Assessment of Spondyloarthritis international Society (ASAS) handbook: a guide to assess spondyloarthritis. *Ann Reum Dis* 2009; 68(2):1-44.
19. Calin A, Garrett S, Whitelock H, et al. A new approach to defining functional ability in ankylosing spondylitis: the development of the Bath Ankylosing Spondylitis Functional Index. *J Rheumatol* 1994; 21:2281-85.
20. Chung HY, Machado P, Van der Heijde D, et al. Smokers in early axial spondyloarthritis have earlier disease onset, more disease activity, inflammation and damage, and poorer function and health-related quality of life. *Ann Rheum Dis* 2012; 71:809–16.
21. Kaan U, Ferda O. Evaluation of clinical activity and functional impairment in smokers with ankylosing spondylitis. *Rheumatol-Int* 2005; 25:357-60.
22. Chen C, Chen H, Lu C, et al. Association of cigarette smoking with Chinese ankylosing spondylitis patients in Taiwan: a poor disease outcome in systemic inflammation, functional ability and physical mobility. *Clin Rheumatol* 2013;32:659-63.
23. Bouaddi I, Rkain H, Hmamouchi I, et al. Relationship between smoking, clinical activity and functional impairment in ankylosing spondylitis patients. *Ann Rheum Dis* 2013; 71:703.
24. Fallahi S, Jamshidi AR, Gharibdoost F. The correlation between pack-years of smoking and disease activity, quality of life, spinal mobility, and sacroiliitis grading in patients with ankylosing spondylitis. *Turk J Rheumatol* 2013; 28(3):181-8.
25. Matthey DL, Dawson SR, Healey EL, et al. Relationship between smoking and patient-reported measures of disease outcome in ankylosing spondylitis. *J Rheumatol* 2011 Dec; 38(12):-2608-15.

Epidemiology of Fibromyalgia in Basra City

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Abstract

Fibromyalgia syndrome is one the prevalent disabling disorder which may skip diagnosis in outpatient's clinic. The most common symptoms in fibromyalgia may presented commonly with generalized pain, fatigue mooring stiffness, non-restorative sleep, problems of memory and concentration, as well as general symptom. Fibromyalgia syndrome in general population has mean global prevalence (2.7%), in comparison to (15-20%) rheumatology outpatient clinic (15-20%). This research aims at study epidemiology of fibromyalgia in Basra city. This is a cross sectional study carried out on patients attended Basra Rheumatology Clinic. They were clinically examined for fibromyalgia according to ACR criteria 2010. The study conducted in the period from January-March 2018. Study results revealed that the mean prevalence of fibromyalgia in Basra rheumatology clinic was 16.6% with male to female ratio 1:5. The mean score for widespread pain was (10±4.2), and symptom severity was (6±1.7) while the total score was 15. The more prevalent painful site was neck and shoulder. All patients had fatigue, waken unrefreshed and cognitive symptom, headache, and irritable bowel. Intolerance to high sound, bright light and to weather changes was notable in FMS patients.

Keywords: *Fibromyalgia, Prevalence, Fibromyalgia Basra.*

Introduction

Patients with Fibromyalgia (FM) are presented with chronic generalized tenderness & pain in addition to the fact that it is debilitating and frustrating disorder. FM prevalence rate is of 4.9% in the general population¹. In spite of unclear pathogenesis and treatment², FM has been related to the appearance of different types of physical trauma³, infectious diseases⁴, emotional and psychological trauma⁵ and genetic agents⁶. There is a significant overlap between FM and depression with many affected persons having both diagnoses⁷; and drugs therapy agents for the depression are usually carried out in the FM therapy⁸. American College of Rheumatology (ACR) founded the criteria for FM in 2010^(9,10). By this the common significant diagnostic characteristics were as follows; widespread pain (WPI), score and symptom

severity (SS) score including fatigue, un refreshed sleep and cognitive symptoms instead of 18 tender points as in ACR 1990 criteria. Thereafter in 2011 modified ACR criteria for FM was developed, that involve (the WPI and SS for the past week), somatic symptom include only; (headache, depression and lower abdominal pain) for previous 6 month.¹¹ According to 2010-ACR-criteria for FM diagnosis. FM prevalence in general population was (6.4% in America), (2.1% in Germany) and (0.6% in Thailand)¹². Globally, the mean prevalence is (2.7% in general population), 4.1% in women and 1.4% in men¹³. General outpatient clinic's prevalence was (1% in Kenyatta National Hospital), but the prevalence in rheumatology outpatient clinic was (13%)¹⁴. While an American study found (15.9%) of new rheumatology patients have FMS. In Iraq, there is no FM prevalence in general population nor its prevalence in rheumatology clinic, this study aims at finding the FM prevalence in rheumatology clinic.

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Methodology

This is a cross sectional study for the Patients attended the rheumatology clinic in Basra General Hospital, were examined for FM according to ACR

criteria-2010 for diagnosis of FM in which the patient who had WPI >7 and SS > 5 or WPI 3-6 and SS >9 with total score >12 will be included in the study as fibromyalgia. The study conducted in the period between January-March 2018, and included (1156) randomly selected patients of both sexes over constant working days and hours. An authorized permission were taken from Department of Medical Training & Research in Basra Health Directorate. Written consents were taken from the patients included in the study. Statistical analysis and data management: The Statistical Package for Social Sciences (SPSS, version 18) was used for data entry and analysis. Chi (χ^2) square test, and t- test was used to compare means and proportions of different factors among different groups of study sample. P value of ≤ 0.05 was regarded as statistically significant. Bar charts and tables used to present the data.

Results: Gender distribution of the study sample were as follows as shown in table 1: females represent (83.9%) in comparison to males were only (16%), with Male; Female ratio was (1:5.3) the mean age was 41.5 ± 11.34 year, and the females were older than males. Almost the majorly of the female were house wife.

Table 1: FMS patient’s demographic distribution

Variables	Male N (%)	Female N (%)
Gender No %	31 (16%)	162 (83.9%)
Mean age	41.5 ± 11.34	42.5 ± 11.18
Occupation		
Worker No (%)	26 (83%)	54 (33.3%)
Not work No (%)	5 (16.1%)	108 (66.7%) House wife

Table 2: Distribution of the study sample according to FM 2010 criteria

Scores	Mean	SD
Mean WPI Score	10.56	4.2 SD
Mean Symptom score	6.15	1.7 SD
Total score	16.03	1.7SD

The WPI local distribution for the FMS patient in our study include: shoulder 85% and neck 83%, lower back 73.5% while less prevalent in pain site chest, abdomen, jaw as shown in table (3).

Table 3: WPI local distribution

Pain Site	No %	Single	Bilateral
Neck	162 (84%)		
Shoulder	165 (85.5%)	18 (9.3%)	147 (76%)
Upper arm	103 (53.4%)	11 (5.7%)	92 (47.6%)
Lower arm	87 (45%)	23 (12%)	64 (33%)
Hip (buttock)	74 (38.3%)	44 (22.7%)	30 (15.5%)
Jaw	42 (21.7%)	18 (9.3%)	24 (12.4%)
Thigh	100 (51.8%)	30 (15.5%)	70 (36.2%)
Leg	124 (64.2%)	28 (14.5%)	96 (49.7%)
Upper back	115 (59.5%)		
Lower back	142 (73.5%)		
Chest	56 (29%)		
Abdomen	45 (23.3%)		

Table 4: FM patient’s distribution according to symptom severity

Symptoms Severity	%	SS. Mean Score	SD
Fatigue	94.9	2	
Waken Unsatisfied	97.1	2.16	
Cognitive	93.4	1.76	

severity. (Table 4). All the FMS patients had waken unsatisfied 97%, fatigue 94%, cognitive symptoms.

Concerning the associated major somatic general symptom study revealed that were as follows; all most all patients complain from headache 90%, and memory problems 72.5%, irritable bowel 68.9% also was reported complain the as well as depression 51% as shown in table 5.

The second item in 2010 criteria were the symptom

Table 5: Associated Somatic general symptom

Symptom	N (%)
Headache	174 (90%)
Memory	140 (72.5%)
Irritable bawl	133 (69%)
Depression	100 (51.8%)
Nervous	93 (48%)

Also the results revealed that there were associated somatic symptoms in FM patients as follows; high sound or bright light intolerance, abdominal discomfort and weather changes intolerance as shown in table 6.

Table 6: Other associated somatic symptoms in FM patients.

Symptoms	N (%)
High sound intolerance	132 (68%)
Bright light intolerance	128 (66%)
Abdominal pain	100 (51.8%)
Weather changes intolerance	66 (34.2%)
Dizziness	59 (30.6%)
Chest tightness	56 (29%)
Insomnia	55 (28.5%)
Numbness	50 (26%)
Short of breath	48 (24.8%)
Allergy	41 (21.2%)

Study results showed that FMS prevalence in rheumatology outpatient clinic was 16.6%, and is similar to prevalence reported USA (10-20%)¹⁵, and (15.7%), in rheumatology clinic in European countries^(4,16). In Iraq there were studies showed that prevalence of FM in specialized clinics was (58.9%) in Behest's disease, (24%) in irritable bowel disease and (18%) in ischemic heart disease.⁽¹⁷⁻²¹⁾ Females were prevalent in all previous researches. About 90% of FM patient are women⁸, male: female ratio 1:9²². The ratio of females: males was 4.8:1²³. In our study the male: female ratio was 1:5.3. The mean age of FM patients was 40-50 years, in comparison to results of other studies (48.5 years), (30-49Year)^(14, 15). All female were older than male, (49.2-year-old women and 39.3-year-old men)^(15,24). In this study the women were of age 42.5 years and men were of age 35.9 years.

According to ACR 2010 criteria, patients with FMS from Basra Rheumatology clinic show mean WPI (10.5±4.17) and for SS (6.15±1.7), which is just like an Egyptian FMS study WPI (11.96 ±3.7) and for SS

(7.3±2.4) (18, 24), and similar to what was reported by Wolfe F, Korean study; WPI (11.4±4.4) and the SS (8±2.6), WPI (10.6±0.4), SS (8.4±0.3) respectively^(18,25).

A Korean study found that sex ratio male: female (1:5.5), mean age 49 years²⁵. The pain distribution according to the WPI in this research was as follows; shoulders, neck and lower back were more frequent complain, as in Egyptian study; shoulders 95.8%, neck 87.5%, and lower back 83.3²⁴. All the FM patient share the high frequency of fatigue, unrefreshed sleep, cognitive symptoms and headache as reported in previous studies^(15-18, 26-27). In this study. FM patients show more intolerance to high sound, bright light and weather changes similar to what found by Julia that FM have increased sensitivities to stimuli in the environment.²⁸ A French study found that FM women have hypersensitivity to stress and stimuli (clod, moisture, heat, flavors)²⁹, the generalized increase in sensitivity may be explained by dysfunction of endogenous systems modulating afferent activity.³⁰ Or due to a generalized disturbance of perceptual thresholds in patient with fibromyalgia not restricted to the perception of pain.³¹

Conclusion

FM is a chronic disorder in which the affected person suffer from a generalized pain and disturbance of sleep, fatigue, cognitive symptom. FM is existed in Iraqi community and prevalent in the rheumatology outpatient clinics. There is an urgent need for more attention and early detection to prevent complications and future life disability. Although FM prevalence and symptom severity frequency may vary according to various factors like cultural, social, and economic characteristics, environmental factor, it require further researches to better understand the FM symptomatology in our community.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Faculty of Dentistry, University of Babylon, Hillah city, Iraq and all experiments were carried out in accordance with approved guidelines.

References

1. White KP, Speechley M, Harth M, et al. The London Fibromyalgia epidemiology study: the

- prevalence of fibromyalgia syndrome in London, Ontario. *J Rheumatol* 1999;26:1570–1576.
2. Clauw DJ, Crofford LJ: Chronic widespread pain and fibromyalgia: what we know and what we need to know. *Best Pract Res Clin Rheumatol* 2003; 17 (4):685–701.
 3. McLean SA, Williams DA, Clauw DJ. Fibromyalgia after motor vehicle collision: evidence and implications. *Traffic Inj Prev.* 2005;6(2):97–104.
 4. Adak B, Tekeoglu I, Ediz L, et al. Fibromyalgia frequency in hepatitis B carriers. *J Clin Rheumatol* 2005;11(3):157–159.
 5. Aaron LA, Bradley LA, Alarcon GS, et al. Perceived physical and emotional trauma as precipitating events in fibromyalgia. Associations with health care seeking and disability status but not pain severity. *Arthritis Rheum* 1997;40(3):453–460.
 6. Ablin JN, Cohen H, Buskila D. Mechanisms of disease: genetics of fibromyalgia. *Nat Clin Pract Rheumatol* 2006;2(12):671–678.
 7. Hassett AL, Cone JD, Patella SJ, et al. The role of catastrophizing in the pain and depression of women with fibromyalgia syndrome. *Arthritis Rheum* 2000;43(11): 2493–500.
 8. Rao SG, Bennett RM. Pharmacological therapies in fibromyalgia. *Best Pract Res Clin Rheumatol* 2003;17(4):611–627.
 9. Frederick Wolfe. New American College of Rheumatology Criteria for Fibromyalgia: A Twenty-Year Journey *Arthritis Care & Research* 2010;62 (5): 583-4.
 10. Wolfe F, Clauw DJ, Fitzcharles MA. Fibromyalgia Criteria and Severity Scales for Clinical and Epidemiological Studies: A Modification of the ACR Preliminary Diagnostic Criteria for Fibromyalgia. *Journal of Rheumatology* June 2011; 38 (6) :1113-22.
 11. Wolfe F, Clauw DJ, Fitzcharles MA. The American College of Rheumatology preliminary Diagnostic Criteria for Fibromyalgia and Measurement of Symptom Severity. *Arthritis Care & Research* 2010; 62 (5);23: 600-610.
 12. Lily Neumann, Dan Buskila, Epidemiology of Fibromyalgia. *Current Pain and Headache Reports* 2003; 17 (5): 362-8.
 13. Frederick Wolfe, Fibromyalgia: The clinical syndrome. *Rheum. Dis.clin Nortg. Am* 1989; 15:1-18.
 14. MS Dokwe, G Omondioyoo, EO Amayo. Prevalence of Fibromyalgia at the Medical out Patient Clinic, Kenyatta National Hospital. *East African Medical Journal* 2011; 88 (15).
 15. Wolfe F . fibromyalgia: Rheumatic diseases clinic of north America 01 . *Agu* 1990;16(3):681-98.
 16. Branco JC, Bannwarth B, Faide I. Prevalence of Fibromyalgia: a survey in Five European Countries. *Semin Arthritis Rheum* 2010 Jun;39(6):448-53
 17. Al-Izzi MK, Jabber AS. Fibromyalgia in Iraqi patient with Behcets disease. *J Med Lib.* 2004 Apr-Jun;52 (2): 86-90.
 18. Jassim NA, Gorial FI, Asker BA. Fibromyalgia syndrome in 104 Iraqi patient with inflamotary bowel disease. *The Iraqi postgraduate medical Journal* 2011;10 (3).
 19. Khudhir M, Al-bidri, Faiq I, Gorial, Ziad S, Al-Rawi. Prevalence of fibromyalgia in Iraqi patient with Ischemic Heart Disease. *J Fac Med. Baghdad* 2009; 51(2).
 20. Khudhir Zghayer Mayouf AL-Bidri. Prevalence of Fibromyalgia in Iraqi people with Joint Hypermobility syndrome . *Journal of Faculty of Medicine* 2008;7 (1): 18-21.
 21. Bartels EM, Dreyer L, Jacobsen S, Jespersen A. Fibromyalgia, Diagnosis and Prevalence. Are gender differences explainable ? *UgeskrLaeger* .2009; 30: 171.
 22. GarethTJones, Fabiola Atzeni, Marcus Beasley. The prevalence of fibromyalgia in the general population : A Comparison of the American College of Rheumatology 1990,2010 and modified 2010 Classification Criteria. *Arthritis & Rheumatology* 2014; 67(2): 568-75.
 23. White KP. The London Fibromyalgia Epidimiology Study. *The Journal of Rheumatology* 1999; 26(7): 1570-6.
 24. Omar GM, Kamel SR, Abdel-Magedied RA. Use of the SS Scale, FIQR, and FIQ VASs for assessment of symptom severity in Egyptian Fibromyalgia patients. *Journal of Egyptian Society for Rheumatology & Rehabilitation* 2014;41:28-3.
 25. So Mikim, Sang Heon Lee, Hae Rim Kim. Applying the ACR preliminary Diagnostic criteria in the diagnosis & assessment of fibromyalgia. *Korean J. pain* . 2012 Jul;25 (3):173-182

26. Peres MF. Fibromyalgia, fatigue, and headache disorders. *CurrNeurosci Rep.* 2003 Mar;3 (2): 97-103.
27. Marcus DA, Bernstein C, Rudy TE. Fibromyalgia and headache : an epidemiological study supporting migraine as part of the fibromyalgia syndrome. *Clin Rheumatol* 2005; 24 (6) :596- 601.
28. Julia L, Wilbarger, Dane B . Cook. Multisensory Hypersensitivity in women with Fibromyalgia : Implications for well being and Intervention. *Arch Phys Med Rehabil.* 2011 Apr; 92(4): 653- 6.
29. PDe Roa, P Paris, J L Poindessous, O Maillet. Subjective Experience and Sensitivities in Women with Fibromyalgia : Quantitative and Comparative Study. *Pain Research and Management* 2018;ID 8269564: 8
30. Kosek E, Ekholm J, Hansson P. Sensory dysfunction in fibromyalgia patient with implication for pathogenic mechanisms. *Pain* 1996;68(2-3):375-83.
31. Dohrenbusch R, Sodhi H, Lamprecht J, Genth E. Fibromyalgia as a disorder of perceptual organization ? An analysis of acoustic stimulus processing in patients with widespread pain. *Rheumatol.* 1997;56(6):34-41.

Pulmonary Function Test is More Restrictive in a smoker Patients with Ankylosing Spondylitis than in Non Smokers and is Associated with Impaired Spinal Mobility

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Abstract

Background: Ankylosing Spondylitis (AS) is a chronic, systemic, inflammatory, rheumatic disease affecting mainly the axial skeleton, with extra-skeletal manifestations, involving lung and an increased risk of cardiovascular morbidity. This research aims to assess the effect of smoking on pulmonary function test and spinal mobility.

Patients and Method: A cross sectional study was conducted on 150 AS patients. Information concerning smoking history, demographic and clinical data were collected. All patients were investigated for HLA-B27, complete blood count, chest x ray and pulmonary function test. AS metrology index (ASMI) measured depending five measurements.

Results: A total of 150 patients with AS were enrolled in this study (139 male and 11 female) with a mean age 36.7+/-8.2 years and mean duration of the disease 11.6+/-6.9 years. The mean FVC and FEV1 was highest among non-smokers and decrease increasing amount of smoking to reach its lowest mean among those with current high grade smoker but failed to reach the level of statistical significance. Smoking habit and age had a statistically significant association with mean of ASMI after adjusting for HLA-B27 status, gender, BMI and duration of the disease. Being a former smoker or low grade smoker is equally expected to increase ASMI by a mean of 0.85 compared to non-smokers.

Conclusion: Smoker AS patients had worse spinal mobility and restrictive PFT.

Keywords: *Smoking & Pulmonary Function Test in Ankylosing Spondylitis Iraq.*

Introduction

Ankylosing Spondylitis (AS) is a chronic, systemic, inflammatory, rheumatic disease affecting mainly axial skeleton with structural and functional impairments¹. It may also be associated with extra-skeletal manifestations, involving lung, eye, skin, bowel and an increased risk of cardiovascular morbidity.² Incidence of pulmonary involvement in AS is estimated to be 1%, emerging either as interstitial lung disease or as a consequence of chest wall abnormalities.⁽³⁻⁵⁾ AS is characterized by inflammation of the thoracic vertebrae and of costovertebral joints, causing gradual fusion and ossification of the joints, resulting in increased dorsal kyphosis, rigidity of the thorax and permanent chest wall

immobility with impairment of chest wall expansion with breathing.⁶ AS patient's pulmonary function show a restrictive pattern caused by stiffness with increased FEV1/FVC and reduced lung capacity.⁽⁷⁻⁹⁾ Both FEV1 and FVC were reduced related to impairment in spinal mobility and correlated with disease activity.^(10,11) The incidence of pulmonary involvement in AS is estimated to be 1%, emerging either as interstitial lung disease (fibrosis of the upper lobes of the lungs) or as a consequence of chest wall abnormalities.⁽³⁻⁵⁾ It is characterized by inflammation in the thoracic vertebrae and in the costovertebral joints, causing gradual fusion and ossification of the joints, resulting in increased dorsal kyphosis, rigidity of the thorax and permanent

chest wall immobility with impairment of chest wall expansion with breathing.⁶

AS patient’s pulmonary function tests show a restrictive pattern caused by stiffness with increased FEV1/FVC and reduced lung capacity.⁽⁷⁻⁹⁾ Both FEV1 and FVC were reduced related to impairment in spinal mobility and correlated with disease activity.^(10,11)

Smokers do not respond as well to treatment compared with non-smokers, which might be another reason for the higher disease activity and subsequent increased restriction in spinal mobility in AS smokers versus AS non-smokers.¹² Exposure to cigarette smoke results in the depression of phagocytic and antibacterial functions of alveolar macrophages, decrease in primary antibody response, also result T-cell attenuation by impairing the antigen receptor-mediated signaling and a decline in TNF production.⁽¹³⁻¹⁶⁾ The aim of this study is to assess the effect of smoking on PFT and spinal mobility among AS patients.

Patients and Method

This study done at Rheumatology unit in Baghdad Teaching Hospital from August 2014-May 2015. A randomly selected sample of 150 Iraqi AS patients who were fulfilling the modified New York criteria for AS (50 current smokers, 21 former smokers, 79 non-smokers) included in the study.¹⁷ A written consent taken from all patients. Approval and official permission were obtained from Baghdad College of Medicine to conduct the present study. Collection of the data done by taking a detailed medical history and clinical examination, laboratory investigations which include; sociodemographic information, and disease duration. Investigation data: patients were investigated for HLA-B27, complete blood count, chest x ray, pulmonary function test (PFT), evaluated by means of a spirometer included measurements of: FVC-Forced Vital Capacity⁸ FEV1 - Forced Expiratory Volume in one second⁸ FEV1/FVC% the absolute ratio: The patients were categorized as having a restrictive ventilator pattern (FVC ≤ 80%, FEV1/FVC ≥ 70%, decreased or normal FEV1).^(8, 9)

Evaluation of Spinal Mobility: Ankylosing spondylitis metrology index (ASMI): Calculating the ASMI score was based on 5 measurements. The score ranged between a minimum of zero and a maximum value of 2. The higher the score the worse is the functional aspect of spine: Occiput-wall distance (cm)-tertile, Chest expansion (cm)-tertile, Modified Schober

test (cm)- tertile, Lateral lumbar flexion (cm)-tertile, and Fingertip to floor distance (cm)-tertile.⁽¹⁸⁻²⁰⁾ All 5 scores obtained from the evaluation questionnaire are added, and the total is divided by 5 to obtain the ASMI value.

Results

The majority of study subjects were males (92.7%), with a male to female ratio of 12.6:1. HLA-B27 was positive in 41.1% of cases. The pulmonary function test was labeled as a “restrictive pattern” in 60% of cases. An obstructive pattern was observed in only 2% of cases. The non-smokers constituted 52% of cases. Former (Ex) smokers constituted 14.7% of cases. The currently smokers were classified into low grade smokers (<15 pack-year) constituting 18% of cases and high grade smoker (15+ pack-year) constituting 15.3% of cases as shown in table 1.

Table 1: Demographic and clinical characteristics of study sample

		N	%
1.	Gender		
	Female	11	7.3
	Male	139	92.7
	Total	150	100.0
2.	HLA-B27		
	Negative	83	58.9
	Positive	58	41.1
	Total	141	100.0
3.	PFT pattern		
	Normal	57	38.0
	Restrictive	90	60.0
	Obstructive	3	2.0
	Total	150	100.0
4.	Smoking status		
	Non-smoker	78	52.0
	Former smoker	22	14.7
	Current low grade smoker (<15 pack-year)	27	18.0
	Current high grade smoker (15+ pack-year)	23	15.3
	Total	150	100.0

N, number; HLA, human leukocyte antigen; PFT, pulmonary function test.

As shown in table 2, the mean ASMI, was lowest among non-smokers and increase in magnitude with increasing amount of smoking to reach its highest mean among those with current high grade smoker (15+

pack -year). The observed positive trend indicating a worse spinal mobility with increase in smoking habit was statistically significant. Although the mean FVC and FEV1 was obviously highest among non-smokers and decrease in magnitude with increasing amount of smoking to reach its lowest mean among those with current high grade smoker(15+pack-year), the differences observed failed to reach the level of statistical significance. The mean FEV1/FVC ratio showed no obvious or statistically significant difference between the 4 categories of smoking habit.

Table 3 demonstrate that the status of HLA-B27 phenotype had no important or statistically significant association with mean of the PFT and spinal mobility.

As shown in table 4, only smoking habit and age had a statistically significant association with mean of ASMI after adjusting for HLA-B27 status, gender, BMI and duration of the disease. Being a former smoker or low grade smoker is equally expected to increase ASMI by a mean of 0.85 compared to non-smokers. Moving to the high grade smoking category is associated with the highest increase in ASMI (1.14 points) compared to non-smokers. Age was significantly associated with this index after adjusting for the remaining variables. For each one year increase in age the metrology index is increased by 0.02. The remaining confounding variables, had no statistically significant effect on the mean ASMI. The resulting regression model was statistically significant and able to explain 68% of observed changes in the response variable.

Table 2: The mean of selected indices of AS disease by smoking habit.

	Smoking Status				P ANOVA trend
	Non-smoker (n=78)	Former smoker (n=22)	Current low grade smoker (<15 pack-year) (n=27)	Current high grade smoker (15+ pack-year) (n=23)	
ASMI					<0.001
Range	(0 to 1.4)	(0.2 to 2)	(0.4 to 2)	(1.4 to 2)	
Mean	0.6	1.5	1.5	1.9	
SD	0.4	0.5	0.4	0.2	
SE	0.04	0.1	0.08	0.04	
FVC					0.16[NS]
Range	(52.8 to 171)	(56.4 to 98)	(30.5 to 129)	(52.5 to 109.7)	
Mean	80.9	71	75.3	72.8	
SD	19.9	11.3	21.6	12.3	
SE	2.26	2.42	4.16	2.57	
FEV1					0.09[NS]
Range	(45.6 to 177.6)	(57.3 to 122.2)	(35.4 to 148)	(47.5 to 132.3)	
Mean	85.2	75.4	78.3	75.4	
SD	20.9	13.9	24.2	15.9	
SE	2.36	2.96	4.67	3.32	
FEV1/FVC					0.91[NS]
Range	(62.9 to 110)	(76.2 to 100)	(70.7 to 114.3)	(67.7 to 124.4)	
Mean	89.1	88.3	91.3	87.8	
SD	9.2	7.6	12	12.7	
SE	1.04	1.61	2.31	2.65	

P<0.001 is significant.

AS, ankylosing spondylitis; n, number; ANOVA, analysis of variance ASMI, ankylosing spondylitis metrology index; NS; not significant; SD, standard deviation, SE; standard error, FVC, forced vital capacity; FEV1; forced expiratory volume in first second.

Table 3: The difference mean of PFT and spinal mobility of AS disease between those with a positive HLA-B27 and those negative for it

	HLA-B27		P (t-test)
	Negative (n=83)	Positive (n=58)	
ASMI			0.52[NS]
Range	(0 to 2)	(0.2 to 2)	
Mean	1.1	1.1	
SD	0.6	0.6	
SE	0.07	0.08	
FVC			0.49[NS]
Range	(47.8 to 165.8)	(54 to 171)	
Mean	76.8	79	
SD	18	19.1	
SE	1.97	2.51	
FEV1			0.48[NS]
Range	(45.6 to 177.6)	(39 to 176.8)	
Mean	80.5	83	
SD	19.3	21.8	
SE	2.11	2.86	
FEV1/FVC			0.82[NS]
Range	(62.9 to 114)	(67.7 to 124.4)	
Mean	89.1	88.7	
SD	10	10.2	
SE	1.09	1.35	

HLA, human leukocyte antigen; n, number; ASMI, ankylosing spondylitis metrology index; NS; not significant; SD, standard deviation, SE; standard error, FVC, forced vital capacity; FEV1; forced expiratory volume in first second.

Table 4: Multiple linear regression model with AS metrology index as the dependent (response) variable and selected variables, in addition to smoking habit as the explanatory (independent) variables.

	Partial Regression Coefficient	P
(Constant)	0.14	0.58[NS]
BMI (Kg/m2)	-0.01	0.21[NS]
Age (years)	0.02	<0.001
Duration of the disease (years)	0.0001	0.98[NS]
Male gender compared to female	0.11	0.38[NS]
Positive HLA-B27	-0.04	0.5[NS]
Former smoker compared to non-smoker	0.85	<0.001
Current low grade smoker (<15 pack-year) compared to non-smoker	0.85	<0.001
Current high grade smoker (15+ pack-year) compared to non-smoker	1.14	<0.001

R2=0.68; P (Model) <0.001 is significant., BMI, body mass index; HLA, human leukocyte antigen; NS, not significant.

Discussion

The negative impact of smoking on AS disease parameters has been reported in various studies, and confirmed more robustly in our study. To the best of our knowledge this study was the first study in Iraq explained the association of cigarette smoking with PFT and spinal mobility in AS patients.

The results showed that AS patients had lowest spinal mobility (including modified Schober test, lateral lumbar flexion, chest expansion, occiput-wall distance and fingertip to floor distance) among smokers and statistically significant in comparison to nonsmokers. This finding is in close to the results of Chen C study at (2013)²¹ which reported that physical mobility parameters modified Schober test, lateral lumbar flexion, chest expansion, occiput to wall distance and fingertip to floor distance were significantly impaired among smokers as compared to nonsmokers.

Also data assessed the smoking habit included smoking duration, and smoking quantity (pack-years) with spinal mobility in patients with AS and revealed that there was a correlation between the pack-years of smoking and PFT and spinal mobility, with increasing smoking duration and quantity there is increased ASMI score and decreased in PFT levels

Among those with current high grade smokers (15+ pack-year). The observed positive trend indicating a worse disease status with increase in smoking habit was statistically significant. This is in accordance with the finding of Fallahi S, et al study in Turkey (2013)²². A multivariate analysis revealed a significant association between the pack-years of smoking and the ASMI. Also Chen C²¹ showed that higher smoking index in AS smokers are associated with poor disease outcome including physical mobility.

This study revealed that the forced vital capacity (FVC) was highest among non-smokers and decrease in magnitude with increasing amount of smoking to reach lowest capacity in high grade current smokers.

This is due to effect of smoking on disease activity also the disease itself due to involvement of costovertebral joint lead to decrease in chest expansion and vital capacity, and these can result in decrease of FVC (restrictive pulmonary pattern). This finding was match the result of Kaan U.²³ Forced expiratory volume in first second (FEV1) was lowest among smokers

due to the direct effect of smoking on FEV1 resulting in obstructive pattern. The observed negative trend in this study indicating a worse ventilator function with increase in smoking habit, however failed to reach the level of statistical significance. This finding is match the result of Berdal G.⁸ which showed that chest expansion and oxygen consumption were significantly poorer in the group of smokers and ex-smokers. The current study revealed that FEV1/FVC ratio showed no obvious or statistically significant difference between current smokers, former smokers and nonsmokers. As explained previously due to direct and indirect effect of smoking on FVC and FEV1 (decreased) among smokers result in no change in ratio.

Conclusion

Smoker AS patients had worse spinal mobility and restrictive PFT.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Babylon Health Directorate, Marjan Medical City, Rheumatology unit, Iraq and all experiments were carried out in accordance with approved guidelines.

References

1. Braun J, Sieper J. Ankylosing spondylitis. *Lancet* 2007; 369:1379-90.
2. Zarco P, Gonzalez CM, Rodriguez de la Serna A, et al. Extra-articular disease in patients with spondyloarthritis. Baseline characteristics of the spondyloarthritis cohort of the AQUILES Study. *ReumatolClin*. 2015; 11(2):83-89
3. Casserly IP, Fenlon HM, Breatnach E, et al. Lung findings on high resolution computed tomography in idiopathic ankylosing spondylitis: correlation with clinical findings, pulmonary function testing and plain radiography. *Br J Rheumatol* 1997; 36: 677-82.
4. Kanathur N, Lee-Chiong T. Pulmonary manifestations of ankylosing spondylitis. *Clin Chest Med* 2010; 31:547-54.
5. Dincer U, Cakar E, Kiralp MZ, et al. The pulmonary involvement in rheumatic diseases: pulmonary effects of ankylosing spondylitis and its impact on

- functionality and quality of life. *Tohoku J Exp Med* 2007; 212:423-30.
6. Donath J, Miller A. Restrictive chest wall disorders. *SeminRespirCrit Care Med* 2009; 30:275-92
 7. Momeni M, Taylor N, Tehrani M. Cardiopulmonary manifestations of ankylosing spondylitis. *International Journal of Rheumatology* 2011; 1:1-6.
 8. Berdal G, Halvorsen S, van der Heijde D, et al. Restrictive pulmonary function is more prevalent in patients with ankylosing spondylitis than in matched population controls and is associated with impaired spinal mobility: a comparative study. *Arthritis Res Ther* 2012; 14:1-10.
 9. Solak O, Fidan F, Dundar U, et al. The prevalence of obstructive sleep apnoea syndrome in ankylosing spondylitis patients. *Rheumatology (Oxford)* 2009; 48:433-35.
 10. Cho H, Kim T, Kim TH, et al. Spinal mobility, vertebral squaring, pulmonary function, pain, fatigue, and quality of life in patients with ankylosing spondylitis. *Ann Rehabil Med* 2013; 37(5):675-82.
 11. El Maghraoui A, Chaouir S, Abid A, et al. Lung findings on thoracic high-resolution computed tomography in patients with ankylosing spondylitis. Correlations with disease duration, clinical findings and pulmonary function testing. *ClinRheumatol* 2004; 23(2): 123–28.
 12. Saevarsdottir S, Wedren S, Seddighzadeh M, et al. Patients with early rheumatoid arthritis who smoke are less likely to respond to treatment with methotrexate and tumor necrosis factor inhibitors: observations from the Epidemiological investigation of rheumatoid arthritis and the Swedish rheumatology register cohorts. *Arthritis Rheum* 2011; 63:26-36.
 13. Ortega E, Barriga C, Rodriguez AB. Decline in the phagocytic function of alveolar macrophages from mice exposed to cigarette smoke. *Comp ImmunolMicrobiol Infect Dis* 1994; 17:77–84.
 14. Nguyen Van Binh P, Zhou D, Baudouin F, et al. Modulation of the primary and the secondary antibody response by tobacco smoke condensates. *Biomed Pharmacother* 2004; 58:527–30.
 15. De Jonge WJ, Ulloa L. The alpha 7 nicotinic acetylcholine receptor as a pharmacological target for inflammation. *Br J Pharmacol* 2007;151: 915-29.
 16. Higashimoto Y, Shimada Y, Fukuchi Y, et al. Inhibition of mouse alveolar macrophage production of tumor necrosis factor alpha by acute in vivo and in vitro exposure to tobacco smoke. *Respiration* 1992; 59: 77–80.
 17. Van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis: a proposal for modification of the New York criteria. *Arthritis Rheum* 1984; 27: 361-68.
 18. Davis JC, Gladman DD. Spinal mobility measures in spondyloarthritis: application of the OMERACT filter. *J Rheumatol.* 2007; 34(4):666-70.
 19. Shinjo SK, Gonçalves R, Kowalski S, et al. Brazilian-Portuguese version and applicability questionnaire of the mobility index for ankylosing spondylitis. *Clinics* 2007; 62(2):139-44.
 20. Magnusson SP, Simonsen EB, Aagaard P, et al. Determinants of musculoskeletal flexibility: viscoelastic properties, cross-sectional area, EMG and stretch tolerance. *Scand J Med Sci Sports.* 1997; 7:195-202.
 21. Chen C, Chen H, Lu C, et al. Association of cigarette smoking with Chinese ankylosing spondylitis patients in Taiwan: a poor disease outcome in systemic inflammation, functional ability and physical mobility. *ClinRheumatol* 2013; 32:659–63.
 22. Fallahi S, Jamshidi AR, Gharibdoost F. The correlation between pack-years of smoking and disease activity, quality of life, spinal mobility, and sacroiliitis grading in patients with ankylosing spondylitis. *Turk J Rheumatol* 2013; 28(3):181-8.
 23. Kaan U, Ferda O. Evaluation of clinical activity and functional impairment in smokers with ankylosing spondylitis. *RheumatolInt* 2005; 25:357-60.
 24. Matthey DL, Dawson SR, Healey EL, et al. Relationship between smoking and patient-reported measures of disease outcome in ankylosing spondylitis. Smoker AS patients had worse PFT and spinal mobility 2011; 38(12):2608-15.

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